Acta Medica Academica

Journal of Department of Medical Sciences
of Academy of Sciences and Arts of Bosnia and Herzegovina

ISSN 1840-1848 (Print) Volume 45 Number 1 May 2016 ISSN 1840-2879 (Online)

Online First www.ama.ba

Acta Medica Academica

Contents
2016 Vol. 45, No. 1

Acta Medica Academica

www.ama.ba

AIMS AND SCOPE

Acta Medica Academica is a biannual, peer-reviewed journal that publishes: (1) reports of original research, (2) original clinical observations accompanied by analysis and discussion, (3) analysis of philosophical, ethical, or social aspects of the health profession or biomedical sciences, (4) critical reviews, (5) statistical compilations, (6) descriptions of evaluation of methods or procedures, (7) case reports, and (8) images in clinical medicine. The fields covered include basic biomedical research, clinical and laboratory medicine, veterinary medicine, clinical research, epidemiology, phramacology, public health, oral health, and medical information.

EDITORIAL CONTACT INFORMATION

Address of the Editorial Board: *Acta Medica Academica*, Academy of Sciences and Arts of Bosnia and Herzegovina, Bistrik 7, 71000 Sarajevo, Bosnia and Herzegovina, Tel.: 00 387 33 560 718, Fax.: 00 387 33 560 703. Contact person: Nerma Tanović, E-mail: amabih@anubih.ba

SUBSCRIPTION

Acta Medica Academica is published semi-annually. The annual subscription fee is € 50 outside of Bosnia and Herzegovina.

PUBLISHER CONTACT INFORMATION

Academy of Sciences and Arts of Bosnia and Herzegovina, Sarajevo, Bosnia and Herzegovina. Contact person: Husref Tahirović, E-mail: husref.tahirovic@untz.ba

COVER PHOTO PICTURE

Adela Ber Vukić (1887-1966), "The landscape", 1951, oil on cardboard, 340x365 mm. Courtesy of the International gallery of portrait Tuzla.

INSTRUCTIONS TO AUTHORS

Instructions to authors in English language are published in each new issue. Home page of the Journal www.ama.ba offers free access to all articles and Instructions to authors.

EDITORIAL ASSISTANT

Nerma Tanović, Sarajevo, BA

TECHNICAL EDITOR

Husref Tahirović, Tuzla, BA

DTP

Narcis Pozderac, Sarajevo, BA

PRINT

Dobra knjiga, Sarajevo, BA. Printed on acid-free paper.

CIRCULATION

500 copies

THE JOURNAL IS INDEXED IN

Medline/PubMed; EBSCOhost; Index Copernicus; CAB Abstract/Global Health Databases; IndexScholar.com; DOAJ; CrossRef; InfoBase Index

Acta Medica Academica (ISSN 1840-1848) is an international peer-reviewed biannual journal which is printed as a continuation of the journal Works of the Academy of Sciences and Arts of Bosnia and Herzegovina, Department of Medical Sciences, founded in 1953. *Acta Medica Academica* Online (ISSN 1840-2879) offers free access to all articles at www.ama.ba.

Original article

Acta Medica Academica 2016;45(1):1-9
DOI: 10.5644/ama2006-124.150

Symmetry, asymmetry and hypoplasia of the intracranial internal carotid artery on magnetic resonance angiography

Svjetlana Mujagić[1*], Duško Kozić[2], Haris Huseinagić[1], Dževdet Smajlović[3]

[1]Department of Radiology and Nuclear Medicine of the University Clinical Center Tuzla, Bosnia and Herzegovina
[2]Oncology Institute of Vojvodina Diagnostic Imaging Center and University of Novi Sad, School of Medicine, Novi Sad, Serbia, [3]Department of Neurology of the University Clinical Center Tuzla, Bosnia and Herzegovina

*Corresponding author:
svjetlanamm@gmail.com
Tel.: + 387 35 303 585
Fax.: + 387 35 251 456

Received: 24 October 2015
Accepted: 21 March 2016

Key words: Symmetry ▪ Asymmetry ▪ Hypoplasia ▪ Internal carotid artery.

Objective. The aim of this study was to determine the prevalence of symmetry, asymmetry and hypoplasia of the intracranial internal carotid artery (ICA), and the possible presence of other variants of the ICA by magnetic resonance angiography (MRA). **Subjects and methods.** This prospective-retrospective study included 1000 subjects who underwent consecutively MRA of the cerebral arteries. 3D–time of flight angiograms were performed according to the standard protocol. We measured the diameter of the ICA and the diameter of the A1 segment of the anterior cerebral artery (ACA). The symmetry, asymmetry and hypoplasia of the ICA, as well hypoplasia of the A1 segment of the ACA were analysed using the vascular asymmetry coefficient. **Results.** The right and left ICA were symmetrical in 93.9% examinees, and asymmetrical in 6%, while ICA hypoplasia was found in only one patient (0.1%). Other variants of the ICA were not found. There was no significant difference in the prevalence of individual variations between male and female patients, and no significant frequency difference was found between anatomical variations in terms of the right and left ICA. In 38.3% patients with asymmetrical ICAs, aplasia or hypoplasia of the A1 segment of the ACA was found on the side of the ICA with a reduced diameter. **Conclusion.** Congenital hypoplasia of ICAs is a very rare abnormality, while asymmetry of ICAs is more common. After evaluating severe asymmetry of intracranial ICAs by MRA, MRA of the neck is recommended, especially in patients with a complete anterior part of the circle of Willis.

Introduction

Congenital anomalies of the internal carotid artery (ICA), in contrast to the anatomical variations of its terminal branches and vertebrobasilar arteries, are extremely rare (1). Carotid dysgenesis has been classified by Lie into three groups: agenesis, aplasia and hypoplasia. Agenesis is defined as complete failure of an organ to develop, aplasia as lack of development (but its precursor did exist at one time), and hypoplasia as incomplete development of the organ (2). The term "absence" is more common and encompasses the spectrum of these three developmental abnormalities. In that case, agenesis and aplasia signify total absence of the vessel. Hypoplasia is characterized by the narrowing of the ICA along its entire course, as a reflection of incomplete development (3). Agenesis of the ICA is very rare and occurs in less than 0.01% of the population (4-6). This variation is commonly seen unilaterally, while its bilateral occurrence is extremely

rare (5). Diagnosis of ICA agenesis or hypoplasia is made by visualizing its absence or the presence of a small bony carotid canal by CT of the skull base, which indicates the congenital nature of the pathology and that it was not acquired pathologically (7).

The right and left ICA, like other paired arteries, may be symmetrical or asymmetrical. Blood vessel diameter is the most frequent and accurate parameter analysed by different authors for the purpose of comparing hypoplasia, and symmetry and asymmetry of arteries. However, researchers often do not give a thorough explanation of how they calculated the symmetry, asymmetry and hypoplasia of the blood vessels. Also, when an artery is slightly larger than its contralateral artery, the question arises whether it should be classified as asymmetrical or symmetrical (8). Some authors' size discrepancies between ICA diameters are categorized as being equal (no appreciable size discrepancy), slightly asymmetric, or markedly asymmetric (9).

In 2007, Zurada and Gielecki (8) presented a new mathematical formula, known as the Vascular Asymmetry Coefficient (VAC), for calculating the symmetry, asymmetry and hypoplasia of blood vessels. The novel formula was derived for this purpose, to display the differences between the mean diameters of blood vessel segments, expressed as a percentage of the wider vessel with respect to the major diameter. The VAC may be applied to an analysis of all the paired intracerebral arteries, including ICAs (8). Very rare variants of the ICA include: duplication, ICA fenestration, aberrant ICA, and high or low branching of the carotid artery (from Th2 to C1 level) (10-12).

The aim of this study was to determine the prevalence of symmetry, asymmetry and hypoplasia of the intracranial ICA using VAC, and the possible presence of other variants of the ICA, by magnetic resonance angiography (MRA).

Subjects and methods

Subjects

In a prospective-retrospective study, performed in the period from July 2008 to May 2013 at the Department of Radiology and Nuclear Medicine of the University Clinical Centre, Tuzla, 1000 consecutive subjects were included (376 men and 624 women). We retrospectively analyzed 110 MRAs of the cerebral arteries which were performed in the period from July 2008 to Decembar 2008. Additionaly, 890 MRAs of the cerebral arteries were prospective collected and analyzed in the period from December 2008 to May 2013.

For both groups the same inclusion criteria were used: subjects older than 18 years, without cerebrovascular disease, vascular malformations or brain tumours in the immediate vicinity of the analyzed arteries on CT or MR imaging.

Methods

MRA was performed using one of two machines, with 1.5 Tesla power (Siemens, model Avanto, Germany or Philips, model Achieva, The Netherlands). The MRA protocol consisted of non-contrast three-dimensional time of flight (3D TOF) angiograms, with axial slice thickness at 0.9 mm, covering the area of the first cervical vertebra up to the upper contour of the corpus callosum. On the Siemens 1.5T machine, the following imaging parameters were set: 25 ms time of repetition (TR), 7ms time of echo (TE); 20° flip angle; 256×256 matrix size; 220 mm field of view (FOV). The imaging parameters on the Phillips machine were: TR 23 ms; TE 6.91 ms, flip angle 20°; matrix 328×208; FOV 180 mm. In the study, the axial 3D TOF angiograms, maximum intensity projection (MIP) images, and volume rendering of the 3D MR angiograms were analysed by the Voxar system.

All images were analysed by a single radiologist with five years' experience in MRI, and all unclear cases were further analysed by a neuro-radiologist with many years' experience. The inner diameter of the ICA was measured at the C4, C5 and C6 segments. Three measurements were carried out to obtain the average value.

The A1 segment of the anterior cerebral artery was measured in the middle part, and if the width of the artery was uneven longitudinally, measurement was done at the proximal, middle and distal segments of the vessel, and the diameter of the artery was taken to be the arithmetic average mean of those three measurements.

Symmetry, asymmetry and hypoplasia of the ICA, as well hypoplasia of the A1 segment of ACA and were analysed using VAC (8), by the formula:

$$VAC = \left(1 - \frac{dICAn}{dICAw}\right) \times 100\%$$

where *d*ICA*n* is the mean diameter of the narrower artery and *d*ICA*w* is the mean diameter of the wider artery. Where: VAC≤10% — the ICAs were classified as symmetrical; where *VAC*>10% and ≤40%, the ICAs were classified as asymmetrical; and where *VAC*>40% — the ICA was classified as hypoplastic, but only if CT of the skull base showed narrowing of the bone carotid canal.

Hypoplasia of the A1 segment of the anterior cerebral artery was defined by two criteria: VAC>40%, regardless of the diameter of the artery, or diameter artery <1 mm. If the definition of hypoplasia is based only on the first criterion, there is a possibility that bilateral hypoplasia of the arteries is not verified, if it exists. Namely, if the diameters of both arteries are less than 1 mm (e.g. 0.9 mm) the VAC coefficient would amount to 0, which would mean that the arteries are maximally symmetric and "normal", but in fact they both hypoplastic.

Statistical analysis

The collected data were stored in the Microsoft Access database while statistical analysis was performed using MedCalc statistical software. The standard methods of descriptive statistics were used for statistical data processing (mean, standard deviation). As the inner diameter differences of the ICAs between males and females were approximately normally distributed variables, they were tested with the parametric t-test for independent samples. Frequency differences in symmetrical and asymmetrical ICAs between men and women were evaluated by the chi-square test. Differences on the level of $p<0.05$ were considered statistically significant.

Results

The average inner diameter of the ICA was 4.24±0.44 mm. The average diameter of the ICA in males (4.4±0.45 mm) was significantly ($p<0.0001$) higher than in females (4.14±0.39 mm).

Table 1 shows the prevalence of the ICA variations and the relationship between the genders. The right and left ICAs in most cases were symmetrical (93.9%), while ICA hypoplasia was found in only one patient (0.1%), a 21 year-old man with long-term recurrent headaches but normal neurological examination. There was no significant difference in the prevalence of individual variations between male and female patients (Table 1). No significant frequency difference was found in anatomical variations (asymmetry and hypoplasia) between the right and left ICA ($\chi2=0.015$; $p>0.05$ and $\chi2= 0.00000025$; $p>0.05$). Figures 1, 2 and 5 show the anatomic variations of the ICA on the MR angiograms. In a patient with suspected hypoplastic left ICA (Figure 2, 5) CT scans of the skull base (Figure 3) showed that the left carotid canal was significantly narrower than the right (the average width of the right carotid canal was

Table 1 Prevalence of the symmetry, asymmetry and hypoplasia of the internal carotid arteries according to the gender

Variation of ICA		Subjects			p*
		Men n (%)	Women n (%)	Total n (%)	
Symmetry		356 (94.6)	583 (93.4)	939 (93.9)	0.92
Asymmetry	Smaller right	8 (2.1)	21 (3.4)	29 (2.9)	0.37
	Smaller left	11 (2.9)	20 (3.2)	31 (3.1)	0.96
	Total	19 (5)	41 (6.6)	60 (6)	0.43
Hypoplasia	Right	1 (0.3)	-	1 (0.1)	0.80
	Left	-	-	-	-
	Total	1 (0.3)	-	1(0.1)	0.8

ICA=Internal carotid artery; *χ2 test.

8 mm, and of the left 4.2 mm). Contrast-enhanced CT scans showed the much smaller diameter of the cervical segment of the left than the right ICA (Figure 4). In the same person, we verified the dominant left vertebral artery, the hypoplastic right posterior cerebral artery, and bilateral foetal-type posterior circulation (Figure 5).

In 23 patients (38.3%) with asymmetrical ICAs, aplasia or hypoplasia of the A1 segment of the anterior cerebral artery was found on the side of the ICA with a reduced diameter (Figure 6). In 6 (10%) we found aplasia, while in 28.3% hypoplasia of the A1 segment was found.

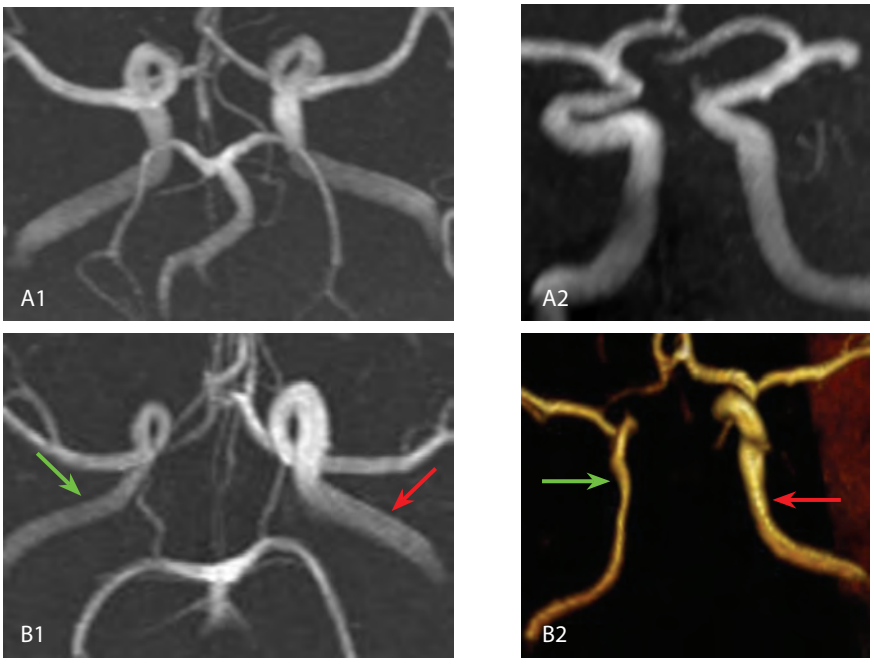


Figure 1 Symmetry and asymmetry of the ICAs on MIP and volume rendering images of the 3D TOF MR angiograms; A1-2 Symmetrical ICAs; B1-2 Asymmetrical ICAs-the diameter of the right ICA (green arrow) is smaller than the diameter of the left ICA (red arrow) ICA= internal carotid artery.

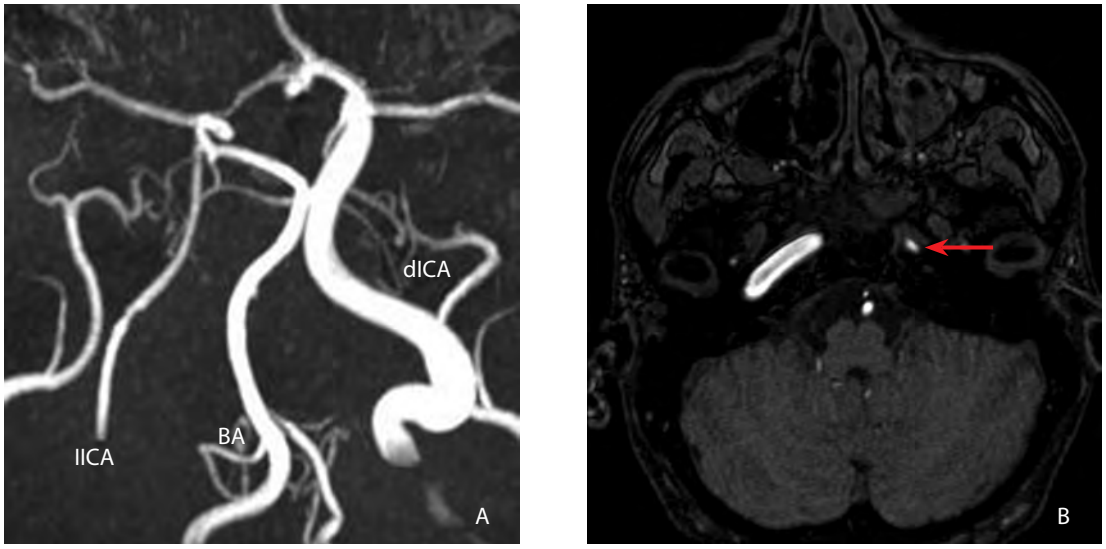


Figure 2 Hypoplasia of the left ICA on MIP image of the 3D TOF MR angiograms (A) and on the axial 3D TOF angiogram (B) - red arrow. dICA=right internal carotid artery; IICA=left internal carotid artery; BA=basilar artery.

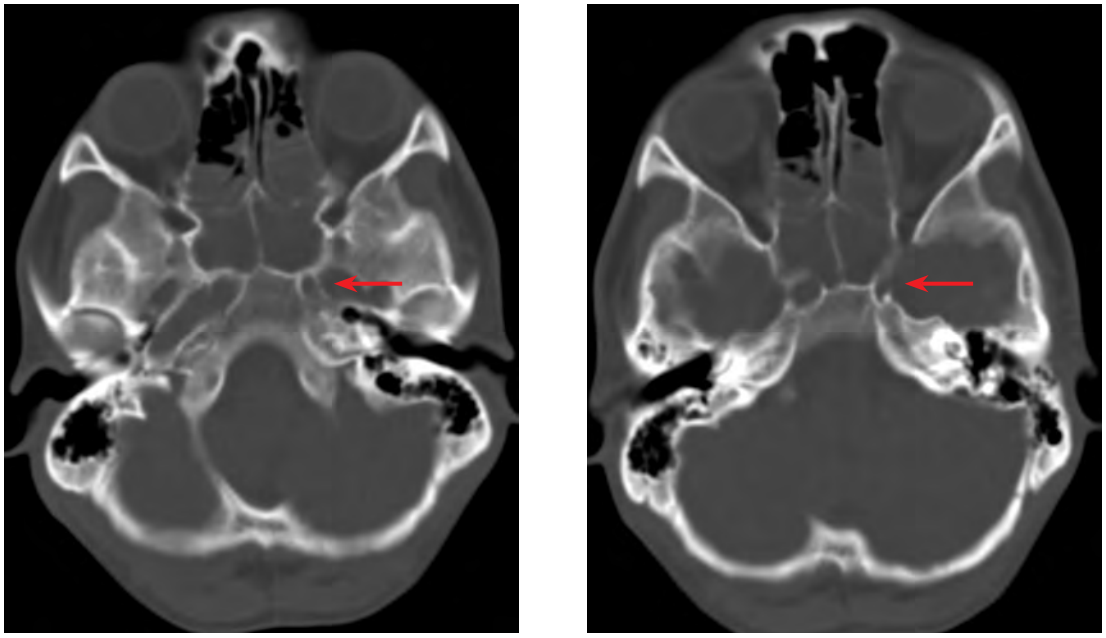


Figure 3 The bone window image from the axial CT scan of the skull base shows a hypoplastic left carotid canal (red arrows).

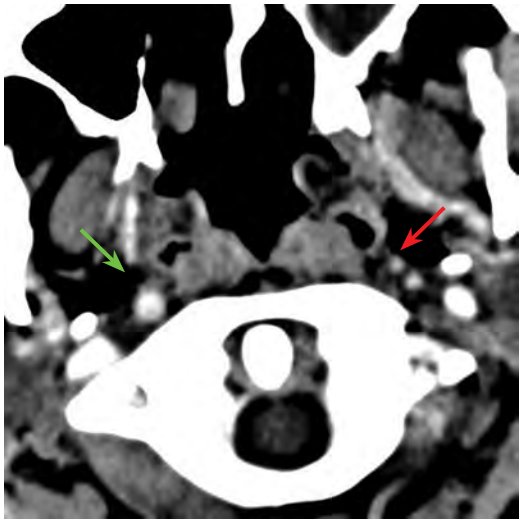


Figure 4 The axial contrast enhanced CT scan shows a hypoplastic cervical segment of the left internal carotid artery (red arrow) in relation to the diameter of the right ICA (green arrow).

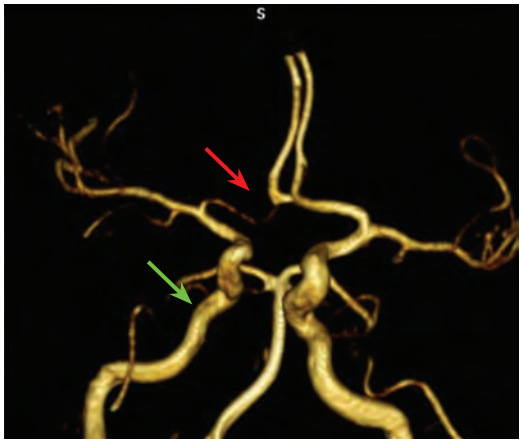


Figure 6 The volume rendering image of the 3D TOF MR angiograms shows asymmetrical internal carotid arteries with the smaller diameter of the right internal artery (green arrow) and the hypoplastic ipsilateral A1 segment of the anterior cerebral artery (red arrow).

Discussion

Developmental abnormalities of the ICA are rare and associated with a higher prevalence of intracranial aneurysms (13). The absence of the ICA occurs in less than 0.01% of the population (4, 13). In 2014, Ulger et al. (14)

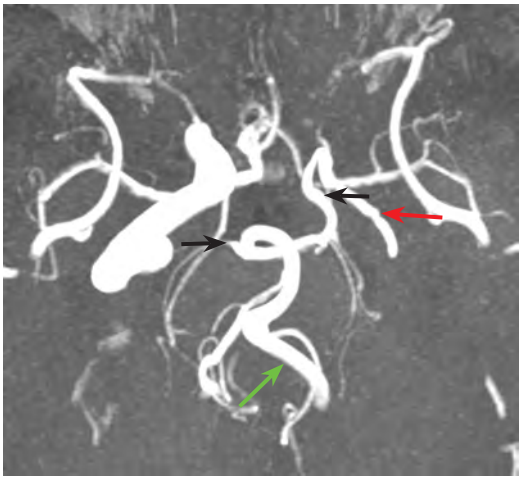


Figure 5 Hypoplastic left internal carotid artery (red arrow), dominant left vertebral artery (green arrow), bilateral foetal-type posterior cerebral circulation (black arrows) on the MIP image of the 3D time-of-flight MR angiograms.

stated that 35 cases of agenesis of the ICA had been reported in literature, while Oliveira et al. (15) found only 26 cases agenesis of the ICA in literature. In the study conducted by Taşar et al. (1) the prevalence of aplasia and hypoplasia of the ICA was 0.13%. These two congenital variations should not be confused with acquired causes of narrowing of the ICA, such as: aortic aneurysms, fibromuscular dysplasia, Moyoamoyoa disease, severe atherosclerosis or chronic dissection. Development of the carotid canal at the skull base occurs in the presence of the embryonic ICA in early gestation. So, demonstration of a small or absent carotid canal therefore indicates a congenital and not an acquired cause of ICA abnormality (16, 17). Absence of the ICA may be complete, or only a portion of the ICA may be missing. A tiny fibrous band may be the only remnant of the ICA in cases of aplasia, and angiography alone may be incapable of differentiating it from agenesis (2). Bilateral ICA agenesis is rare and can be incompatible with life, but more cases of bilateral ICA agenesis have been reported in children and adults (15-20). About 60 cases of ICA hypo-

plasia have been reported in the literature to date, of which 24 cases were bilateral (21). Hypoplasia of the ICA may also be unilateral or bilateral, but the bilateral variety is rarer. A hypoplastic ICA may continue distally as the ophthalmic artery (22). While in unilateral agenesis or hypoplasia of the ICA the predominant arterial supply is through the contralateral ICA (18), in bilateral agenesis the collateral supply is through the vertebrobasilar system (1), usually through the posterior communicating arteries. The arterial supply may also be through a primitive trigeminal artery or transcranial collaterals, from branches of the internal maxillary artery or inter-cavernous collaterals (1, 16, 23).

Many patients with aplasia or hypoplasia of the ICA may remain asymptomatic (2), but they may also present with transient ischemic attacks, infarct, seizures, aneurysmal subarachnoid haemorrhage, or parenchymal bleeds (4, 16, 24). There is a greater risk of cerebral aneurysm in the Circle of Willis, or vertebrobasilar system arteries, among patients with ICA agenesis. This is caused by the hemodynamic stress placed on vessels due to the increased flow through the collateral channels. In patients with ICA agenesis the prevalence of cerebral aneurysms is 24%-34%, while in the general population it is 2%-4% (1, 18).

Congenital ICA absence can be seen in association with other congenital abnormalities and syndromes, such as: mastoid hypoplasia, Horner syndrome, congenital hypopituitarism, anencephaly, transphenoidal encephalocele, basal telangiectasia, agenesis of the corpus callosum, olivopontocerebellar atrophy, arachnoid cyst, facial haemangioma, atlantoaxial dislocation and megadoliho-basilar anomalies (25-29).

Asymmetry of the ICA is usually the result of extracranial stenosis of one of the ICAs. The size asymmetry of the intracranial ICAs reveals the presence of an underlying high-grade cervical stenosis, with a high degree of confidence, especially in patients without an anatomical variant of the anterior part of the Circle of Willis. Naggar et al. (30) verified asymmetrical ICA in MR angiographic studies in 28 of 32 patients with a high degree of stenosis in the cervical segment of the ICA (≥70%). The reason for the size asymmetry of the intracranial ICAs may also be that the anterior part of the Circle of Willis is incomplete. There is an association of unilaterally absent or hypoplastic A1 segments of the anterior cerebral artery with an ipsilateral decrease in ICA calibre (9).

In this study, aplasia of the ICA was not found, while hypoplastic ICA was found in one (0.1%) patient (Figure 2, 5). CT of the skull base showed that the diameter of the carotid canal, ipsilateral to the anomaly, was almost half the diameter of the contralateral one (Figure 3), which confirmed the congenital cause of the narrowing of the ICA. Hypoplasia of ICA was not associated with abnormalities of the brain or cerebral aneurysms. In this study, most patients had symmetrical ICAs (93.6%), while in 6% of patients smaller or greater asymmetrical diameters of the ICAs were found. The mean inner diameter of the right ICA in 29 (2.9%) patients was smaller than the diameter of the left ICA, while a smaller diameter of the left ICA in comparison with the right ICA was found in 31 (3.1%) patients. In the majority of cases, patients with verified asymmetrical ICAs did not undergo computer or MRA of the neck, so we cannot say whether the determined asymmetry is the result of an acquired abnormality of the extracranial ICA segment. In 38.3% of patients with asymmetric ICAs, aplasia or hypoplasia of the A1 segment of the anterior cerebral artery was found, which may be the cause of the reduced diameter of the ipsilateral ICA, but the aim of this study was to determine the prevalence of ICA variations and not the possible causes of variations.

Conclusion

Congenital hypoplasia or aplasia of ICAs is a very rare abnormality, while asymmetry of ICAs is more common. A reduction in ICA diameter may be associated with an ipsilateral aplastic or hypoplastic A1segment of the anterior cerebral artery.

What is already known on this topic

Congenital anomalies of the ICA, in contrast to the anatomical variations of its terminal branches and vertebrobasilar arteries, are extremely rare. The right and left ICA, like other paired arteries, may be symmetrical or asymmetrical. Blood vessel diameter is the most frequent and accurate parameter analysed by different authors for the purpose of comparing hypoplasia, and symmetry and asymmetry of arteries.

What this study adds

Researchers often do not give a thorough explanation of how they calculated the symmetry, asymmetry and hypoplasia of the blood vessels. When an artery is slightly larger than its contralateral artery, the question arises whether it should be classified as asymmetrical or symmetrical. In the conducted study, which is one of the largest so far, the prevalence of symmetry, asymmetry and hypoplasia of the intracranial ICA were determined using VAC. This new mathematical formula that has been in use since 2007, for the first time is applied in the analysis of symmetry, asymmetry and hypoplasia of the ICA in this study.

Authors' contributions: Conception and design: SM; Acquisition, analysis and interpretation of data: SM; DK; Drafting the manuscript: SM, DK, HH, DžS; Revising it critically for important intellectual content: SM, DK; Approved final version of the manuscript: SM.

Conflict of interest: The authors declare that they have no conflict of interest.

References

1. Taşar M, Yetişer S, Taşar A, Uğurel S, Gonul E, Sağlam M. Congenital absence or hypoplasia of the carotid artery: radioclinical issues. Am J Otolaryngol. 2004;25(5):339-49.
2. Lie TA. Congenital Anomalies of the Carotid Arteries. Amsterdam: Excerpta Medica; 1968. p. 35-51.
3. Makowicz G, Poniatowska R, Lusawa M. Variants of cerebral arteries – anterior circulation. Pol J Radiol. 2013;78(3):42-7.
4. Chen CJ, Chen ST, Hsieh FY, Wang LJ, Wong YC. Hypoplasia of the internal carotid artery with intercavernous anastomosis. Neuroradiology. 1998;40:252-4.
5. Luk YS, Man EM, Sy A. Bilateral hypoplasia of the internal carotid arteries. Singapore Med J. 2010;51(9):163-5.
6. Nicoletti G, Sanguigni S, Bruno F, Tardi S, Malferrari G. Hypoplasia of the internal carotid artery: collateral circulation and ultrasonographic findings. A case report. J Ultrasound. 2009;12(1):41-4.
7. Pilleul F, Guibaud L, Badinand N, Rouviere O, Pracros JP. Bilateral internal carotid artery agenesis: value of CT angiography and correlation to embryogenesis. Eur Radiol. 2001;11:858-60.
8. Zurada A, Gielecki JS. A novel formula for the classification of blood vessels according to symmetry, asymmetry and hypoplasia. Folia Morphol (Warsz). 2007;66:339-45.
9. Kane AG, Dillon WP, Barkovich AJ, Norman D, Dowd CF, Kane TT. Reduced caliber of the internal carotid artery: a normal finding with ipsilateral absence or hypoplasia of the A1 segment. AJNR Am J Neuroradiol. 1996;17(7):1295-301.
10. Ng PP, Steinfort B, Stoodley MA. Internal carotid artery fenestration with dual aneurysms. J Neurosurg. 2006;104:979.
11. Roll JD, Urban MA, Larson TC, Gailloud P, Jacob P, Harnsberger HR. Bilateral aberrant internal carotid arteries with bilateral persistent stapedial arteries and bilateral duplicated internal carotid arteries. AJNR Am J Neuroradiol. 2003;24(4):762-5.
12. Sauvaget E, Paris J, Kici S, Kania R, Guichard JP, Chapot R, et al. Aberrant internal carotid artery in the temporal bone: imaging findings and management. Arch Otolaryngol Head Neck Surg. 2006;132(1):86-91.
13. Afifi AK, Godersky JC, Menezes A, Smoker WR, Bell WE, Jacoby CG. Cerebral hemiatrophy, hypoplasia of internal carotid artery, and intracranial aneurysm: a rare association occurring in an infant. Arch Neurol. 1987;44(2):232-5.
14. Ulger FE, Ulger A, Colak M. Absence of the right common carotid artery: Doppler ultrasonographic and MR angiographic findings. Vascular J. 2014;22(5):364-7.
15. Oliveira G , Soares N, Oliveira G , Vale BP. Bilateral internal carotid artery agenesis: a case report. J Vasc Bras. 2014;13(4):336-9.
16. Given CA, Huang-Hellinger F, Chepuri NB, Morris PP. Congenital absence of the internal carotid artery: case reports and review of the

collateral circulation. AJNR Am J Neuroradiol. 2001;22(10):1953-9.

17. Rumboldt Z, Castillo M, Solander S. Bilateral congenital absence of the internal carotid artery. Eur Radiol. 2003;13:130-2.
18. Cali RL, Berg R, Rama K. Bilateral internal carotid agenesis: a case study and review of the literature. Surgery. 1993;113(2):227-33.
19. Sunada I, Inoue T. Bilateral internal carotid artery agenesis. J Neurol Neurosurg Psychiatry. 1996;61:206-7.
20. Sreedhar M, Reddy K, Agrawal MK. Case report: Bilateral agenesis of internal carotid arteries associated with aneurysmally dilated plexus of vessels in the posterior fossa. Indian J Radiol Imaging. 2007;17(3):159-61.
21. Siddiqui AA, Sobani ZA. Bilateral hypoplasia of the internal carotid artery, presenting as a subarachnoid hemorrhage secondary to intracranial aneurysmal formation: a case report. J Med Case Rep. 2012;6:45.
22. Lath N, Taneja M. Bilateral congenital hypoplasia of the internal carotid arteries. J HK Coll Radiol. 2008;11:129-31.
23. Quint DJ, Boulos RS, Spera TD. Congenital absence of the cervical and petrous internal carotid artery with intercavernous anastomosis. AJNR Am J Neuroradiol. 1989;10:435-9.
24. Erdem Y, Yilmaz A, Ergun E, Kofiar U, Karatay M, Bayar MA. Bilateral internal carotid artery hypoplasia and multiple posterior circulation aneurysms. Importance of 3D CTA for the diagnosis. Turk Neurosurg. 2009;19(2):168-71.
25. Bernini FP, Cioffi FA, Muras I, Rinaldi F, Vaino R. Agenesis of the right internal carotid artery associated with an aneurysm of the anterior communicating artery. Case report. Acta Neurochir (Wien). 1980;54:257-63.
26. Pascual-Castroviejo I, Viano J, Pascual-Pascual SI, Martinez V. Facial hemangioma, agenesis of the internal carotid artery and dysplasia of the cerebral cortex: case report. Neuroradiology. 1995;37:692-5.
27. Neves WS, Kakudate MY, Centola CP, Garzon RG, Agua AP, Sanches R. Agenesis of the internal carotid artery: A case report. Radiol Bras. 2008;41:63-6.
28. Choh NA, Choh SA, Jehangir M. Right internal carotid artery agenesis. Indian J Pediatr. 2008;75:1269-71.
29. Mehrotra A, Chunnilal JS, Das KK, Srivastava A, Kumar R. Atlanto-axial dislocation associated with anomalous single vertebral artery and agenesis of unilateral internal carotid artery. Asian J Neurosurg. 2013;8(3):164.
30. Naggara O, Touzé E, Seiller N, Gobin-Metteil MP, Mas JL, Meder JF, Oppenheim C. Asymmetry of intracranial internal carotid artery on 3D TOF MR angiography: a sign of unilateral extracranial stenosis. Eur Radiol. 2008;18(5):1038-42.

Original article

Acta Medica Academica 2016;45(1):10-18
DOI: 10.5644/ama2006-124.151

Retrospective analysis of the role and performance of family medicine versus emergency medical services in the pre-hospital management of patients with AMI in Banja Luka

Biljana Lakić[*1], Maja Račić[2], Duško Vulić[3]

[1]Department for family medicine Primary Health Center Banja Luka
[2]University of East Sarajevo, Faculty of Medicine Foča, Bosnia and Herzegovina
[3]School of Medicine, University of Banja Luka, Bosnia and Herzegovina

*Corresponding author:
biljanakd@yahoo.com
Tel.: + 387 51 215 447
Fax.: + 387 58 210 420

Received: 26 August 2015
Accepted: 9 March 2016

Key words: Acute myocardial infarction ▪ Family medicine ▪ Emergency medical services.

Objective. The aim of this study was to investigate the differences in pre-hospital care of patients with acute myocardial infarction between emergency medical services and family medicine. **Patients and methods**. This retrospective descriptive study included patients treated for acute myocardial infarction at the University Clinical Centre of Banja Luka, in the period from 1st January to 31st December 2011. The patients were divided into two groups: patients who received a hospital referral from the family medicine service and those who received one from the emergency medical service. **Results**. The majority of patients (54.8%) received pre-hospital care from emergency medical services, while in 24.8% of cases the care was provided by family medicine physicians. The analysis showed that the time that passed from the onset of symptoms to the visit to the health institution of first medical contact was shorter in the emergency medical service ($p<0.001$). The average time from the onset of symptoms to arrival at the family practice was 24 hours, and to the emergency service 2 hours. The patients who established their first medical contact with the emergency service reported more severe symptoms than the ones who visited a family practice over the same period of time. **Conclusion**. The severity of symptoms affected the patients' decisions to seek help in a timely manner and to choose the facility of first medical contact. Interventions to decrease delay must focus on improving public awareness of acute myocardial infarction symptoms and increasing their knowledge of the benefits of early medical contact and treatment. Continuing education of family practitioners in this field is required.

Introduction

Acute myocardial infarction (AMI) is, according to the electrocardiographic changes, divided into two types, and, alongside unstable angina pectoris, represents one aspect of acute coronary syndrome (ACS), as defined in the special guidebooks (1, 2) used for rapid disease risk assessment and pertinent treatment. New findings confirm that AMI may be defined on the basis of different aspects based on clinical, electrocardiographic, biochemical and pathological characteristics, which are all presented in the new universal definition of AMI (3).

Every year over 17 million people in the world die from cardiovascular disease (CVD). AMI alone affects over 6 million people worldwide, while approximately 25% case result in mortality. It has been predicted

that by 2020, CVD will be responsible for the majority of lethal outcomes in both developed and developing countries (4-6). In the Republika Srpska (RS), according to data provided by the Republic's Statistics Agency, during the past two decades, from 1998 to 2010, mortality ranged between 47.5% and 54.5%. According to the Public Health Institute of the RS, in 1999 outpatient morbidity was 8.4%, 13% in hospitals, while the morbidity rate among the population aged 18-65 years amounted to 15.6% (7).

With the reform of health care, the family medicine model in the RS extended the scope of services delivered in the primary health setting by family practitioners and family medicine nurses to include health education, and disease prevention interventions, and expanded diagnostic and curative services, thus enabling the family medicine team to act as a gate keeper while providing more comprehensive and continuous health care services to its registered population. One family medicine team (consisting of one family practitioner and two nurses) provides primary care for 2000 inhabitants (8). The actual visit length for patients and physicians is approximately 10 minutes. Depending on the number of teams, the number of inhabitants, population density and the risk of injuries and acute illness, emergency care could be organized as: a "standby" service in the primary care centers, employing less than 5 family medicine teams (<10,000 inhabitants); a "duty" service in the towns with populations between 10,000 and 40,000 and as an "emergency service" in the health centers providing primary care for more than 75,000 inhabitants and able to employ 5 or more teams (a physician with specialization in emergency medicine or family medicine, two nurses and a driver) working in shifts (one team per 12,000 in towns of up to 80,000 inhabitants, and one team more for every further 20,000 inhabitants). It is estimated that the total population of the RS is 1,200,000. Care is provided by 54 primary care centers and 11 hospitals.

There are different approaches to the management of patients with suspected AMI around the world. Patients with chest pain are initially seen by their family practitioner (9). Due to the fear of possible consequences of AMI for heart function, primary health care providers tend to refer the majority of patients with symptoms of chest pain to a hospital, so national health systems in different countries are trying to make strategies for improving the diagnosis and treatment of patients with chest pain caused by AMI at the level of family medicine, especially in places where no emergency service is available (10-13).

The accuracy of family practitioners' diagnoses and pre-hospital treatment of AMI is not easily studied. It is necessary to find out not only how often AMI is diagnosed correctly but also how often this diagnosis is missed. Frequently, family practitioners base their diagnoses to an unjustifiable extent on the presence or absence of particular symptoms which are thought to be specific for AMI. On the other hand, the diagnostic accuracy of a family practitioner who does not have the support of diagnostic aids, such as laboratory biomarkers, would be expected to be less distinctive in comparison to the emergency medical service. The role of family practitioners should include responding quickly to patients with chest pain, giving adequate analgesia, aspirin, initiating treatment of complications and introducing antithrombolitic therapy (14).

In order to secure the resources for the greatest possible improvement in pre-hospital diagnoses and treatment of patients with myocardial infarction, in 2009 the Ministry of Health of the RS, published clinical guidelines for primary health care: "Acute myocardial infarction". The guidelines were distributed in printed and electronic form to all family practitioners registered in the

MoH base. However, no impact evaluation has been conducted since then and the degree of change in pre-hospital diagnoses and treatment delivered by family practitioners remains unknown (15).

The aim of this study was to investigate the differences in pre-hospital diagnoses and treatment for patients with acute myocardial infarction between the emergency medical services and family medicine. We hypothesized that emergency medical services provide more accurate diagnosis and treatment to patients before hospitalization in an acute coronary unit.

Patients and methods

A retrospective descriptive study included patients treated for acute myocardial infarction at the University Clinical Centre of Banja Luka, in the period from 1st January to 31st December, 2011. The first inclusion criterion was that the patients were resident in Banja Luka or Laktaši. The second was written consent obtained from patients for participation in the research.

The population of the town of Banja Luka is 240,000. Emergency services are provided by a separate unit which provides 24-hour emergency care and several teams working within one shift. The nearest hospital is a few kilometers away. The population of the town of Laktaši is 31,000. Emergency cases are handled by all family practitioners until 3 pm and from that time until 7 am the next day by a single team. The nearest hospital is 30 kilometers away. In respect to the location of these two towns, the parameters of the pre-hospital care provided were compared.

The patients who had positive laboratory markers for myocardial necrosis (e.g., troponin I), along with supportive evidence in the form of typical symptoms, suggestive electrocardiographic (ECG) changes, or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality, were diagnosed as having AMI at the University Clinical Centre of Banja Luka. The list of the patients with AMI was obtained from the administrative office of the University Clinical Centre of Banja Luka. The National Insurance Company provided a list and contact details of family practices who were involved in the pre-hospital care of patients.

The patients were divided into two groups: patients with AMI who received a hospital referral from their family medicine service (FMS) and those who received one from the emergency medical services (EMS). Data were extracted from the patient's medical history and discharge letters, as well as from

Table 1 The analyzed parameters

Parameters	
Location of pre-hospital care	FMS or EMS
Chest pain	Present or absent
Associated symptoms	Shortness of breath; Nausea and vomiting; Sweating; Other
The circumstances of the occurrence of symptoms	At home/rest/work /during physical activity
The time of the occurrence of symptoms	Morning/afternoon/evening/night
The time that passed from the occurrence of pain to the health center visit	Minutes/Hours
ECG changes	STEMI/NSTEMI
Referral diagnosis	AMI/angina pectoris/other
Pre-hospital treatment received	Oxygen; Analgesics; Nitroglycerin; Aspirin

FMS=Family medicine service; EMS=Eemergency medical service; ECG=electrocardiographic/gram; STEMI=ST-elevation myocardial infarction; NSTEMI= non-ST-elevation myocardial infarction.

their electronic and paper records, to analyze the parameters of pre-hospital care. All aspects of the medical records were included in the search for evidence of the quality of the pre-hospital care provided, such as free text. The entire paper record from the date of diagnosis was also included. The protocols at the Primary Care Centers were analyzed, and then telephone interviews were carried out by the researchers.

According to the national clinical guidelines for primary care, the diagnostic criteria for AMI are defined as: the presence of the typical chest pain, evolutionary changes in consecutive ECGs and evolutive changes in cardiac biomarkers. For each patient, the parameters of pre-hospital care were analyzed as shown in Table 1.

Ethics statement

The study was conducted in accordance with the 1975 World Medical Association Declaration of Helsinki and its amendments from 1983. The study was approved by the Committee of the Medical Faculty of the University of Banja Luka (18-3-27/2015).

Statistical analysis

The data were analyzed and are presented using descriptive statistics and the appropriate statistical methods ($\chi 2$ test, Mann-Whitney, Fisher test) and SPSS statistical software. A probability level or p value less than 0.05 ($p<0.05$) was considered statistically significant.

Results

During 2011, 516 patients were treated at the University Clinical Centre of Banja Luka for AMI. Of those, 173 were excluded from the study because they did not meet the inclusion criteria. The study included 343 patients with residence in Banja Luka or Laktaši.

The average age of the patients was 66±11 years and 63.8% were male. Out of 343 patients, 270 had recorded data on pre-hospital care. The majority of patients (54.8%) received care through emergency medical services, while in 24.8% of cases pre-hospital care was provided by a family medicine service (Table 2). In 83.5% of patients the pain and/or other symptoms started at home, with onset mainly while resting (59.5%).

As shown in Figure 1, 48% of patients reported that their symptoms first started during the morning hours. Chest pain was the most predominant symptom in both genders and all age groups. However, female patients older than 75 years of age reported pain less often as the most predominant symptom compared to the male patients of the same age ($p=0.014$) (Table 3).

No significant difference in the frequency of associated symptoms between the patients referred from FMS and EMS was found ($p>0.05$) (Figure 2).

The analysis showed that the time that passed from the onset of symptoms to the visit to the health institution of first medical contact was shorter in patients receiving pre-hospital care from an EMS ($p<0.001$). The average time from onset of symptoms until arrival at the FMS was 24 hours and at the EMS 2 hours. The patients who used the services of EMS reported more severe symptoms than those who visited their FMS over the same period of time ($p<0.001$). During

Table 2 Distribution of patients according to the first medical contact

First medical contact	n (%)
Family medicine	85 (24.8)
Emergency medical service	188 (54.8)
Other*	53 (15.4)
Unknown	17 (5.0)

*Direct hospitalization without pre-hospital care, being referred from a private medical institution, intra-hospital transfer, patients who suffered acute myocardial infarction in different cities, outside of their place of residence.

Table 3 The presence of pain as the predominant symptom according to age and gender

Age and gender groups		Chest pain		Total	p
		Present	Absent		
≤54	Female	11	0	11	0.565**
	Male	36	4	40	
	Total	47	4	51	
55-64	Female	17	2	19	1.000**
	Male	46	7	53	
	Total	63	9	72	
65-74	Female	28	2	30	1.000**
	Male	44	4	48	
	Total	72	6	78	
≥75	Female	27	9	36	0.014**
	Male	32	1	33	
	Total	59	10	69	
Total	Female	83	13	96	0.369*
	Male	158	16	174	
	Total	241	29	270	

*$\chi 2$ test with Yates correction; **Fisher test; p value <0.05 is considered significant.

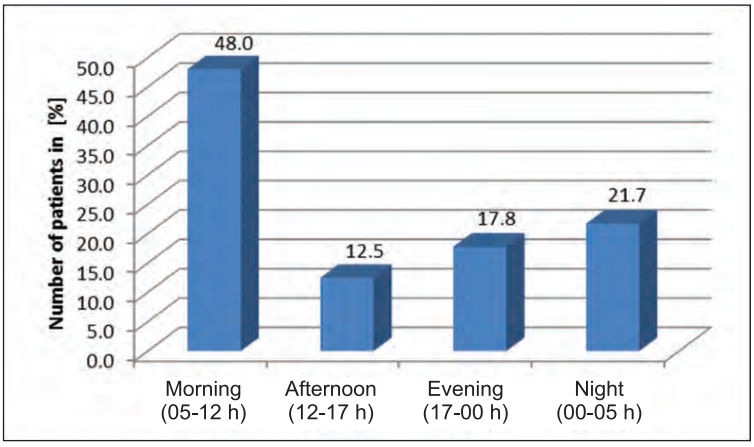


Figure 1 The onset of the AMI symptoms according to the time of the day.

the telephone interviews, the patients who received pre-hospital care in an EMS reported that they chose the EMS as the first point of care (89.3%) because it was easier to access it either by phone or by a personal visit. On the other hand, 92% of patients referred from the FMS preferred to have the first contact with their family practitioner.

AMI, as the referral diagnosis, was more often confirmed in patients referred from the EMS (52%) to the University Clinical Centre of Banja Luka than in the patients referred from a family medicine service (33%). This difference was statistically significant (p=0.013) as shown in Table 4.

However, the referral diagnoses in FMS were made on the basis of ECG findings and clinical presentation, because cardiac biomarkers were not available (85 patients). On the basis of ECG changes, STEMI (ST-

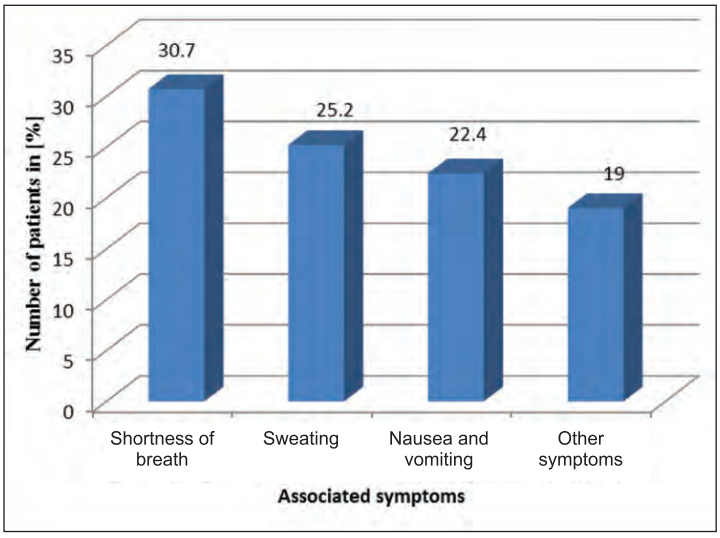


Figure 2 Associated symptoms in patients with acute myocardial infarction.

Table 4 Referral diagnoses according to the institution of first medical contact

Referral diagnosis	The first medical contact	
	FMS (%)	EMS (%)
Myocardial infarction	33	52
Angina pectoris	51	34
Other	16	14

FMS=Family medicine service; EMS=Emergency medical service; $\chi 2$ (2. 247) = 8.686, p=0.013.

segment elevation myocardial infarction) occurred more often than NSTEMI (non ST-segment elevation myocardial infarction) (54.8% vs. 44.7%), regardless of the institution where the first medical contact was made.

Pre-hospital antithrombotic therapy (aspirin) was employed equally in both institutions, without any statistical significance (p=0.057). From the analysis of the use of the remaining pre-hospital therapies (oxygen, nitroglycerin and analgesics), a statistically significant difference was found between empirical treatment in the FMS and the EMS (p=0.002; vs. p=0.006; vs. p=0.001). From the analysis of the pre-hospital treatment approach, it was shown that cardiopulmonary resuscitation (CPR) was performed in 7 (2%) patients with AMI, mainly in the EMS (1.7% vs. 0.3%), while anti-shock therapy (adrenalin) was used in 3 (0.9%) patients.

Discussion

In this study it has been shown that patients with AMI are twice as likely to seek the first medical contact in an emergency service than from their family practitioner. The results are in accordance with the results of different studies showing that a minority of patients with cardiogenic chest pain seek help from a family practitioner, while in the majority of cases help is sought in an EMS (16-18). Patients referred from the EMS reported more severe chest pain compared with FMS patients. This could possibly explain why the majority of patients established their first medical contact in an EMS, as well as the shorter delay in seeking medical help and the greater accuracy in the diagnosis. However, the time frame for seeking medical help might also be related to a lack of information, not only to the severity

of symptoms, concerning the significance of the pain, denial that the chest pain may actually signal a heart attack, misinterpretation of the chest pain, reluctance to call the family practitioners at an inconvenient time and lack of encouragement from family members for seeking medical help (19-22).

The definitive and referral diagnosis from the FMS coincided to a lesser degree with the diagnosis made in the EMS. A patient with myocardial infarction must be rated as one of the most serious emergency conditions family practitioners have to deal with. As the first doctors to see the patients, they are in very good position to make a proper diagnosis and apply the recommended therapy, which could save patients' lives, especially in rural areas where the nearest hospital is far away. The initial goal is to determine whether the patient needs to be referred for further testing to rule out an AMI (23). Differentiating ischemic from non-ischemic causes is often difficult, and patients with chest pain of ischemic etiology often appear to be well.

In FMS, the physicians only used an electrocardiogram to confirm the diagnosis. On the basis of the results of this study it may be said that in family practice acute myocardial infarction cannot be diagnosed with satisfactory accuracy on the basis of symptoms and electrocardiogram findings alone. Laboratory biomarkers could solve the diagnostic dilemma of the family physician, but they often lacking in primary care, although the majority of FMS in the RS were supplied with adequate laboratory apparatus by the Ministry of Health of the RS several years ago. Easier access to biomarkers could enable the physician to diagnose and treat AMI, or to exclude this condition if its presence is suspected, thereby reassuring both the physician and the patient (24-26). The problem of supplying the FMS in Banja Luka with the chemicals for determining biomarker needs to be addressed at the level of the national insurance company.

Besides being better equipped for diagnosing AMI, an EMS is oriented toward emergency care, rather than delivering and coordinating comprehensive care for patients. In Bosnia and Herzegovina, family physicians look after 1500-2000 registered patients. Their daily schedule is very busy and includes seeing approximately 50 or more patients a day. Public and health expectations, their paper workload as well as the constantly changing administrative regulations contribute to the perception of an increased level of pressure. This pressure often negatively affects the family physician's work-productivity, and thus potentially compromises not just the quality of care but also patient safety. Accordingly, family physicians with a higher proportion of patient visits and a higher numbers of patients are more likely to miss diagnoses of emergencies than EMS physicians. The false negative diagnoses of AMI made by the family practitioner represented a significant proportion of cases, which shows that the diagnostic accuracy of primary care practitioners should be improved, through continuing medical education and better equipment. It is also very important to improve education in the field of emergency medicine during undergraduate studies and residency in family medicine at all five medical schools in Bosnia and Herzegovina.

Some important differences between the management practices of family practitioners and EMS physicians emerged. Aspirin was commonly used in the FMS as well as in the EMS. However, EMS physicians were significantly more likely to use analgesics, oxygen and thrombolytic therapy. Family physicians, especially working in an urban environment, prefer to refer the patients to the hospital than to give thrombolytic therapy to the patients themselves. One British study conducted in primary health care

(27) showed that general practitioners more seldom decide to use thrombolytic therapy (1%), despite good knowledge and available guidelines, due to the fear of bleeding. Further research on the influences of family practitioners' management choices would be valuable and could help guide educational responses.

The present study showed discrepancies between the guideline recommendations and clinical practice, indicating the need for quality improvement of pre-hospital diagnostic and therapeutic approaches to AIM patients in the primary care centers in Banja Luka and Laktaši. The recent study from the United Kingdom showed that implementing a Quality Improvement Collaborative could be very successful in the context of pre-hospital urgent care through engagement of staff in the use of quality improvement methods and by providing individual feedback to frontline clinicians (28).

The study does, however, have some limitations. This was a retrospective study so it could only identify potential associations. Larger and more longitudinal data are needed to provide an assessment of quality indicators and outcomes of pre-hospital care.

Conclusion

Emergency medical services provide a more accurate diagnosis and treatment approach to patients with AMI before hospitalization in an acute coronary unit compared to family medicine services. Top priority in primary care should be given to patients with chest pain in whom acute myocardial infarction is suspected. The severity of symptoms affects the patient's decision to seek help in a timely manner and to choose the facility of first medical contact. Continuing education of family practitioners in the field of acute myocardial infarction is required. Physicians should consider applying a validated clinical decision rule to predict coronary heart disease as a cause of chest pain. Interventions to decrease delay must focus on improving public awareness of the symptoms of acute myocardial infarction and increasing their knowledge of early response and treatment benefits.

What is already known on this topic

In most patients with acute myocardial infarction, the dominant symptom is chest pain that occurs mainly in the morning. Patients with symptoms of acute myocardial infarction seek help predominantly from an emergency medical service.

What this study adds

The severity of symptoms affects the patient's decision to seek help in a timely manner and to choose the facility of first medical contact. This study has shown that patients with acute myocardial infarction are twice as likely to seek help from an emergency medical service than from a family medicine surgery. Emergency medical services provide more accurate diagnosis and treatment to patients with AMI. This study gives recommendations for improving the work of all health care services responsible for the pre-hospital care of patients with acute myocardial infarction.

Authors' contributions: Conception and design: BL; Acquisition, analysis and interpretation of data: BL and MR; Drafting the article: BL; Revising it critically for important intellectual content: BL, MR and DV; Approved final version of the manuscript: BL, MR, and DV.

Conflict of interest: The authors declare that they have no conflict of interest.

References

1. Van de Werf F, Bax J, Betriu A, Blomstrom-Lundqvist C, Crea F, Falk V, et al. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: the Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology. Eur Heart J. 2008;29(23):2909-45.
2. Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2011;32(23):2999-3054.

3. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. Third universal definition of myocardial infarction. Circulation. 2012;126(16):2020-35.
4. World Health Organization. The global burden of disease: 2004 update. Geneva: WHO; 2008.
5. Fuster V, Kelly BB. Promoting Cardiovascular Health in the Developing World: A Critical Challenge to Achieve Global Health. Institute of Medicine (US) Committee on Preventing the Global Epidemic of Cardiovascular Disease: Meeting the Challenges in Developing Countries. Washington (DC): National Academies Press (US); 2010.
6. Mathers CD, Boerma T, Ma Fat D. Global and regional causes of death. Br Med Bull. 2009;92(1):7-32.
7. Vulić D, Krneta M, Šobot M. Guidelines for secondary prevention of coronary heart disease [in Serbian]. Srce i krvni sudovi. 2011;30(4):241-5.
8. Račić M. Family Medicine in Republic of Srpska. Opšta medicina. 2015;21(3-4):75-80.
9. Haasenritter J, Biroga T, Keunecke C, Becker A, Donner-Banzhoff N, Dornieden K, et al. Causes of chest pain in primary care - a systematic review and meta-analysis. Croat Med J. 2015;56(5):422-30.
10. Willemsen RTA, Buntinx F, Winkens B, Glatz JF, Dinant GJ, The 'RAPIDA'-study team. The value of signs, symptoms and plasma heart-type fatty acid-binding protein (H-FABP) in evaluating patients presenting with symptoms possibly matching acute coronary syndrome: background and methods of a diagnostic study in primary care. BMC Fam Pract. 2014;15:203.
11. British Heart Foundation working group. Role of the general practitioner in managing patients with myocardial infarction: impact of thrombolytic treatment. BMJ. 1989;299:555-7.
12. Burman RA, Zakariassen E, Hunskaar S. Management of chest pain: a prospective study from Norwegian out-of-hours primary care. BMC Fam Pract. 2014;15:51.
13. Krčmar N, Pristaš I, Stevanović R, Tonković A. The Role of the County's Health Centre in the Management of Patients with Acute Coronary Syndrome [in Croatian]. Hrvatski časopis za javno zdravstvo. 2010. [cited 2012 Mar 20]. Available from: http://www.hcjz.hr/old/clanak.php.
14. Murphy AW, McCafferty D, Dowling J, Bury G. One-year prospective study of cases of suspected acute myocardial infarction managed by urban and rural general practitioners. Br J Gen Pract. 1996;46(403):73-6.
15. Krneta M, Kuprešak D, Šatara-Stoisavljević S, Tepić R, Vulić D. Acute myocardial infarction: guidelines for Primary Health Care [in Serbian]. Banja Luka: Ministry of Health and Social Welfare of the Republic of Srpska; 2009.
16. Klinkman MS, Stevens D, Gorenflo DW. Episodes of care for chest pain. J Fam Pract. 1994;38(4):345-52.
17. Svavarsdóttir AE, Jónasson MR, Gudmundsson GH, Fjeldsted K. Chest pain in family practice. Diagnosis and long-term outcome in a community setting. Can Fam Physician. 1996;42:1122-8.
18. Miljuš D, Katalina Miskovski N. Incidence and Mortality of Acute Coronary Syndrome in Serbia. Belgrade: Institute of Public Health of Serbia "Dr Milan Jovanović Batut"; 2011.
19. Taghaddosi M, Dianati M, Bidgoli JFG. Bahonaran J. Delay and its Related Factors in Seeking Treatment in Patients with Acute Myocardial Infarction. ARYA Atheroscler. 2010;6(1):35-41.
20. Yu PN. Prehospital care of acute myocardial infarction. Circulation. 1972;45(1):189-204.
21. Ghazawy ER, Seedhom AE, Mahfouz EM. Predictors of Delay in Seeking Health Care among Myocardial Infarction Patients, Minia District, Egypt. Adv Prev Med. 2015;2015:342361.
22. Mussi FC, Mendes AS, de Queiroz TL, Costa AL, Pereira A, Caramelli B. Pre-hospital delay in acute myocardial infarction: judgement of symptoms and resistance to pain. Revista da Associação Médica Brasileira. 2014;60(1):63-9.
23. Bruyninckx R, Aertgeerts B, Bruyninckx P, Buntinx F. Signs and symptoms in diagnosing acute myocardial infarction and acute coronary syndrome: a diagnostic meta-analysis. Br J Gen Pract. 2008;58(547):105-11.
24. Kontos MC, Diercks DB, Kirk JD. Emergency department and office-based evaluation of patients with chest pain. Mayo Clin Proc. 2010;85(3):284-99.
25. McConaghy JR, Rupal O. Outpatient diagnosis of acute chest pain in adults. Am Fam Physician. 2013;87(3):177-82.
26. Cooper A, Timmis A, Skinner J; Guideline Development Group. Assessment of recent onset chest pain or discomfort of suspected cardiac origin: summary of NICE guidance. BMJ. 2010;340:c1118.
27. Round A, Marshall AJ. Survey of general practitioners' prehospital management of suspected acute myocardial infarction. BMJ. 1994;309(6951):375-6.
28. Siriwardena AN, Shaw D, Essam N, Togher FJ, Davy Y, Spaight A, et al. The effect of a national quality improvement collaborative on prehospital care for acute myocardial infarction and stroke in England. Implement Sci. 2014;9:17.

Original article

Acta Medica Academica 2016;45(1):19-25
DOI: 10.5644/ama2006-124.152

The prevalence and severity of early childhood caries in preschool children in the Federation of Bosnia and Herzegovina

Lejla Šačić, Nina Marković*, Amra Arslanagić Muratbegović, Amila Zukanović, Sedin Kobašlija

Department of Preventive and Pediatric Dentistry, Faculty of Dentistry, University of Sarajevo

*Corresponding author:
ninamarkovic37@gmail.com
Tel.: +387 33 214 249, ext. 107
Fax.: +387 33 443 395

Received: 14 January 2016
Accepted: 10 May 2016

Key words: Early childhood caries ▪ Oral health ▪ Behavioral factors ▪ Epidemiology.

Objective. The aim of this study was to assess caries prevalence and severity in preschool children in the Federation of Bosnia and Herzegovina. In addition, the relationship between the frequency and clinical types of early childhood caries and behavioral factors, oral hygiene and eating habits were assessed. **Subjects and methods.** An oral health survey was performed in line with the World Health Organization methodology and criteria. The research consisted of clinical examinations of children to determine dentition status, oral hygiene and severity of caries distribution according to Wyne's classification. Information about behavioral factors was collected by means of a questionnaire administered to parents/guardians. **Results.** The sample consisted of a total of 165 preschool children aged 3-5 years. Mean dmft (decay, missing, filled teeth index for primary dentition) was 6.79. The percentage of caries-free children was 17.0%. The results showed a statistically significant correlation between oral hygiene and eating habits, and also the frequency and types of early childhood caries. **Conclusion.** The present study demonstrates high caries prevalence in preschool children in the Federation of Bosnia and Herzegovina. Community based preventive programs should be developed and urgently implemented, in order to achieve the WHO goals, improve oral and general health, thus improving the quality of life of these populations.

Introduction

Early childhood caries is defined as the presence of one or more decayed (non-cavitated or cavitated lesions), missing (due to caries) or filled tooth surfaces in any primary tooth in a preschool-aged child between birth and 71 months of age (1, 2). Caries is a rapid and progressive disease that eventually affects permanent dentition. Early childhood caries is the most common chronic disease in children. The teeth are infected immediately after their eruption (3). The Center for Disease Control and Prevention reports that nowadays dental caries is perhaps the most prevalent infectious disease, five times more common than asthma, and seven times more common than hay fever (4). Although the prevalence of caries has decreased worldwide, the problem persists in many parts of the world in certain segments of society, especially socially vulnerable groups. Common risk factors for this disease are poor nutrition and oral hygiene (5, 6). Some

of the factors that favor the development of early childhood caries are dietary habits, the quality and the frequency of meals, night meals and bottle feeding. Studies show that sugars (sucrose, glucose and fructose), as well as other fermentable carbohydrates, may be triggers for the development of early childhood caries (7, 8). Sweetened drinks, fruit juices and soft drinks, with the inadequate re-mineralizing activity of saliva (especially at night due to the reduced flow of saliva), can lead to enamel demineralization and caries lesions (5). Alongside nutrition, oral hygiene is another important etiological factor for early childhood caries. The lack of adequate oral hygiene allows for the prolonged oral presence of fermentable carbohydrates, which enhances the metabolism of cariogenic bacteria from the accumulated dental plaque. Early childhood caries affects the quality of life of affected children and their families, causes dental pain, tooth loss over time and problems eating, sleeping, speaking and socializing. The effects of early childhood caries are predictably severe. Major oral hygiene promotion activities must be focused on good dietary habits, oral hygiene improvement, fluoride program development, and the proper education of youth and future parents.

The aim of this study was to assess caries prevalence and severity in preschool children in the Federation of Bosnia and Herzegovina (FBH). In addition, the relationship between the frequency and clinical types of early childhood caries and behavioral factors, oral hygiene and eating habits was assessed.

Subjects and methods

Design and setting

This cross-sectional study of preschool children and their parents or guardians was conducted during 2014. The study consisted of an oral health survey of children, accompanied by a questionnaire for parents or guardians.

Participants

The total sample was 165 healthy preschool children, living in Sarajevo Canton, which is the largest administrative center and could be considered as representative of FBH. The basic criterion for selection was: preschool children who registered for the first time as patients at the Department of Preventive and Pediatric Dentistry of the Faculty of Dentistry, University of Sarajevo, and the Preschool Dental Office at the Public Health Center of the Sarajevo Canton. The target age was from 3 to 5 years old (mean age was 4.08 years, SD 0.799). Of the total sample, 48.5% were boys and 51.5% girls.

Measurements

The Oral Health Survey was performed in accordance with the WHO guidelines for assessment of dental status (9). Wyne's classification was used to determine the progression and severity of the disease.

There are three types of early childhood caries, according to Wyne's Classification (10): Type 1 (mild to moderate) – the existence of isolated carious lesions involving molars and/or incisors. Type 2 (moderate to severe) – labial-lingual carious lesions affecting maxillary incisors, with or without molar caries, depending on the age of the child and the stage of the disease. Mandibular incisors are unaffected. Type 3 (severe) - carious lesions affecting almost all the teeth including the mandibular incisors.

Possible behavioral factors that might lead to the presence and progression of early childhood caries were assessed by a survey questionnaire, administrated to parents/guardians, who accompanied their children to the dentist. The questionnaire contained

questions on demographics and also about general medical history, dietary intake, fluoride programs, oral hygiene habits and previous dental care. Parents were questioned about the total number of meals per day (used as an ordinal variable, ranked from higher to lowest frequency), the total number of night meals (used as an ordinal variable, ranked from higher to lowest frequency), the age of the child when the practice of oral hygiene began (used as ordinal variables with appropriate age ranks applied), whether fluoride toothpaste was used for daily brushing of teeth (used as ordinal variables with ranked answers from lower (e.g. almost never) , medium (1-2 times per week use) and higher (used daily after meals (3-5 times per day)), whether fluorides protect the teeth from development of caries (observed as an ordinal variable, from lowest to highest implication to oral health protection (as: don't know, disagree, agree, strongly agree), and whether the child was fed by bottle or breastfed (used as ordinary variables, ranked per month of infant feeding). The offered answers were ranked in order to assess the degree of behavioral influence on oral health from highest to lowest susceptibility to development of dental caries. Written consent was obtained from parents/guardians who agreed to participate. All data were kept anonymous and only patient gender and age were noted.

Ethics statement

The study protocol was reviewed and approved by the Local Ethics Committee of the Faculty of Dentistry, University of Sarajevo.

Statistical analysis

The results were presented by means of descriptive statistics (frequency distribution, percentage, mean ± SD, Median, Range, Minimum, Maximum and Percentiles). Statistic differences between studied groups were tested by the Kruskal Wallis test with the Sidak post- hoc test to note exact differences. The Spearman correlation was used to assess the relationship between dmft, Wyne types and oral hygiene and dietary habits. The level of significance was set at $p<0.05$. The statistical packages Microsoft Office Excel 2007 and IBM SPSS Statistics 21 were used for data analysis.

Results

In accordance with the WHO Oral Health Surveys prescribed methodology, the prevalence of dental caries was recorded and analyzed using the dmft index (9). The results of descriptive statistics show that 50% of subjects had dmft values in a range of 2 to 10.5, 25% of subjects had the lowest dmft values in a range of 0-2, and 25% of subjects had the highest values in a range of 10.5 to 20. The median was 7 and the mean dmft was 6.8 (SD 5.25). The percentage of children without caries was 17%. The percentage of caries free children decreased with age from 41.3% of children aged 3 to 13.6% at age 4 and only 1.7% at age 5. The percentage of untreated decay was highest among five year olds (98.3%). The caries experience, in study groups and in the total sample, presented as dmft index values and distribution of its components is given in Table 1.

The severity of caries distribution in preschool children using Wyne's classification is shown in Table 2.

Despite the high values of untreated caries in the examined population, most of the children scored as Wyne type 1. The Kruskal Wallis test was used to test differences in dmft values between age groups. A significant difference was observed (Chi-square=14.431, $p<0.001$). The Sidak post hoc test confirmed a significant difference between children aged 3 and 5 ($p<0.001$), whereas dmft was lower in children age 3

Table 1 Summary of decay experience in preschool children, presented in the total sample by age groups

Age grups (years)	dmft (mean±SD)	Decay teeth (mean±SD)	Missing teeth (mean±SD)	Filled teeth (mean±SD)
3 (n=46)	5.1±5.8	4.7±5.6	0.0±0.0	0.3±0.8
4 (n=59)	6.5±5.1	6.0±5.2	0.1±0.3	0.5±1.1
5 (n=60)	8.3±4.4	6.9±4.2	0.1±0.4	1.3±2.4
Total (n=165)	6.8±5.2	5.9±5.1	0.1±0.3	0.7±1.7

dmft= decay missing filled teeth for primary dentition.

Table 2 Severity of caries distribution in preschool children by Wyne's classification according to age groups

Age groups (years)	Caries free n (%)	Wyne Type 1 n (%)	Wyne Type 2 n (%)	Wyne Type 3 n (%)	Total n (%)
3 (n=46)	19 (41.3)	19 (41.3)	3 (6.5)	5 (10.9)	46 (100)
4 (n=59)	8 (13.6)	37 (62.7)	10 (16.9)	4 (6.8)	59 (100)
5 (n=60)	1 (1.7)	43 (71.7)	13 (21.7)	3 (5)	60 (100)
Total (n=165)	28 (17)	99 (60)	26 (15.8)	12 (7.3)	165 (100)

Caries free=percentages of examinees without caries; Wyne Class 1=mild to moderate progression of disease; Wyne Class 2=moderate to severe progression of disease; Wyne Class 3=severe progression of disease.

by 3.28 respectively. There were no statistically significant differences between children aged 3 and 4, and 4 and 5 ($p>0.05$). Differences between age groups and Wyne class scoring were also tested with the Kruskal Wallis test. A significant difference was observed between the tested variables (Chi-square=13.448, $p<0.001$). Differences were found by the Sidak post hoc test between age groups 3 and 5 ($p<0.01$). Post hoc testing did not confirm any significant difference between the other tested aged groups ($p>0.05$).

A total of 165 parents/guardians were surveyed, 90.9% of them indicated that caries may be prevented by good oral hygiene. Almost the same percentage of parents knew that fluoride can protect teeth from caries (67.3%) and were using fluoride toothpaste for brushing (68.5%). A high percentage of parents/guardians (95.2%) indicated the use of a toothbrush and toothpaste for brushing their children's teeth every day. Seventy percent of parents thought that caries could be prevented by proper nutrition, 15.2% of children still had night meals and sometimes used a feeding bottle.

Spearman's correlation was conducted between the dmft index and Wyne types, and the number of meals per day, the frequency of intake of sweets, the number of times they brush their teeth each day, the frequency of dentist visits, the frequency of night meals, the age when oral hygiene practices began, and their attitude to fluorides. A statistically significant positive correlation was observed between dmft and the age of beginning oral hygiene ($r=0.363$, $p=0.001$), the attitude towards the caries preventive effects of fluorides ($r=0.29$, $p=0.000$) and the Wyne class and the age of beginning oral hygiene ($r=0.28$, $p=0.005$).

Discussion

The mean value of dmft in the population studied is quite high according to WHO standards (11). A high percentage of preschool children had untreated carious lesions. Comparing these results with previous studies from the country, it is evident that the epidemiology of the studied population has not changed. In the survey conducted in 1999 the mean caries prevalence in preschool children in Bosnia and Herzegovina (BH) was reported as dmft 6.87 and the percentage of untreated caries 90.7%

(12). In 2001 the mean dmft was 6.8 and the percentage of untreated caries was 87.7% (13), and the latest available data showed no improvement, reporting a mean dmft of 6.7 and the percentage of untreated caries as 88.8% in 2004 (14).

The prevalence of early childhood caries is different around the world. In Croatia 30% of children aged 3-5 develop early childhood caries (9). Similar results were reported for some parts of Serbia (30.5%) (15), and in Bulgaria (32%) (16). The lowest prevalence of early childhood caries was reported in Canada, at 5% (17).

The classification of early childhood caries by Wyne (10) gives a better insight into the severity of the disease and the extent of the problem for health care workers. The distribution and severity are in line with the general prevalence of early childhood caries for the investigated population. Good oral hygiene, alongside other preventive measures, is the most economical, most accessible and most practical way to prevent tooth decay. A high percentage of parents/guardians, 90.9%, indicated that caries could be prevented by good oral hygiene, but epidemiological findings revealed that this was not properly applied in practice. The American Academy of Pediatric Dentistry (AAPD) recommends that oral hygiene should begin with the eruption of the first tooth, and that parents should assist children in tooth brushing until the age of 10 (18). Most of the respondents indicated brushing their children's teeth at least twice a day, but it is probable that in practice oral hygiene is not carried out thoroughly, which results in a high prevalence of dental caries. The importance of the frequency of tooth brushing, and the importance of parental involvement has been emphasized in many studies (19). In the present study, 70.3% of parents were aware of the importance of nutrition for good oral health, which is quite good progress compared to research from 2001, where only 25% of parents recognized the importance of nutrition (13). Besides the fact that most parents were aware of the importance of nutrition, the results showed that almost all children consumed sweet drinks and foods at least once a day. The importance of the frequency of consumption of less sweet food and fewer sugary drinks has been known for a long time. A study conducted in 1954 reported that sugar consumption less than 4 times per day during meals, does not favor the development of dental caries (19). The Scandinavian countries, which are very successful in preventive care and caries reduction in children of pre-school age, have a usual "day for sweets", thus their consumption is minimized to a weekly level; e.g. in Denmark 45% of children and in Finland 21% of children only consume sweets on a certain day of the week (19). Night meals are a very important risk factor for development of early childhood caries. The recommendation of AAPD is to stop breastfeeding when the child is one year old (18). The WHO recommends breastfeeding until the child is two years old, with the introduction of supplementary feeding at six months (19). Parental attitudes regarding this specific issue were in line with these guidelines, although most of the parents agreed with the AAPD recommendation to stop breastfeeding when the child is one year old. In comparison with previous investigations, levels of knowledge and awareness have been obviously raised, but practice of good oral health habits is still lacking.

Conclusion

The present study provides evidence of the relatively high caries prevalence in preschool children in the FBH, with mean dmft of 6.7 and the small percentage of children without caries (17%). The distribution of Wyne types revealed the presence of a higher progression and severity of early childhood

caries among the youngest examinees. The percentage of 3 year-olds classified as Wyne type 3 indicates that the focus on preventive measures has to be placed on education and motivation for proper oral hygiene and good nutrition practices as early as possible. A higher frequency of sugar intake, late onset of oral hygiene practices, lack of fluoride exposure and lack of knowledge about fluoride impact to oral health protection were behavioral factors related to higher values of dmft and scoring of Wyne types in examined population. The positive parental attitude regarding behavior and practice was not in line with the prevalence and severity of the disease. Community-based preventive programs have to be developed and implemented urgently in order to achieve the WHO goals and to improve oral health, health in general and the quality of life.

What is already known on this topic

There has been a considerable decrease in caries prevalence in many European countries in recent decades. Caries epidemiology involves the study of variables that may influence its occurrence and severity, including behavioral factors, such as knowledge of and attitude towards dietary and oral hygiene habits. Recent studies have shown the complex interaction of these factors and caries in preschoolers. The last epidemiological data on caries in preschool children in FBH were assessed in 2004.

What this study adds

It is the first epidemiological study in FBH where the severity of early childhood caries has been assessed and analyzed. In addition, this study assesses the behavioral variables and interaction with early childhood caries experience and severity in children in FBH.

Author`s contributions: Conception and design: LS and NM. Acquisition, analysis and interpretation of data: LS, NM and AZ; Drafting the article: LS and NM; Revising it critically for important intellectual content: NM, AAM and SK; Approved final version of the manuscript: LS, NM, AAM, AZ and SK.

Conflict of interest: The authors declare that they have no conflict of interest.

References

1. Drury TF, Horowitz AM, Ismail AI, Maertens MP, Rozier RG, Selwitz RH. Diagnosing and reporting early childhood caries for research purposes. A report of a workshop sponsored by the National Institute of Dental and Craniofacial Research, the Health Resources and Services Administration, and the Health Care Financing Administration. J Public Health Dent. 1999;59(3):192-7.
2. Kaste LM, Drury TF, Horowitz AM, Beltran E. An evaluation of NHANES III estimates of early childhood caries. J Public Health Dent. 1999;59:198-200.
3. Douglass JM, Douglass AB, Silk HJ. A practical guide to infant oral health. Am Fam Physician. 2004;70(11):2113-20.
4. Hale KJ; American Academy of Pediatrics Section on Pediatric Dentistry. Oral health risk assessment timing and establishment of the dental home. Pediatrics. 2003;111(5 Pt 1):1113-6.
5. Seow WK. Biological mechanisms of early childhood caries. Community Dent Oral Epidemiol. 1998;26(1 Suppl):8-27.
6. Lulić-Dukić O, Jurić H, Dukić W, Glavina D. Factors predisposing to early childhood caries (ECC) in children of pre-school age in the city of Zagreb. Coll Antropol. 2001;25:297-302.
7. Douglass JM. Response to Tinanoff and Palmer: Dietary determinants of dental caries and dietary recommendations for preschool children. J Public Health Dent. 2000;60(3):207-9.
8. Paes Leme AF, Koo H, Bellato CM, Bedi G, Cury JA. The role of sucrose in cariogenic dental biofilm formation--new insight. J Dent Res. 2006;85(10):878-87.
9. World Health Organization (WHO). Oral Health Surveys: Basic methods. 4th edition. Geneva: WHO; 1997.
10. Wyne AH. Early childhood caries: nomenclature and case definition. Community Dent Oral Epidemiol. 1999;27(5):313-5.
11. Hobdell M, Petersen PE, Clarkson J, Johnson N. Global goals for oral health 2020. Int Dent J. 2003;53(5):285-8.
12. Kobašlija S, Maglajlić N, Huseinbegović A, Tahmiščija H. The Prevalence of dental Caries in Children. Acta Stomatol Croat. 2000;34(1):83-5.
13. Huseinbegović A. Social and medical aspects of primary dentition caries in urban conditions. [master's dissertation]. Sarajevo: University of Sarajevo, School of Dentistry; 2001.
14. Marković N, Arslanagić Muratbegović A, Kobašlija S, Bajrić E, Selimović-Dragaš M, Huseinbegović A. Caries prevalence of children and adolescents in Bosnia and Herzegovina. Acta Med Acad. 2013;42(2):108-16.

15. Tušek I, Carević M, Tušek J. The Presence of early childhood caries among members of different ethnic groups of The South Bačka District [in Serbian].Vojnosanit Pregl. 2012;69(12):1046-51.
16. Markova N. Early childhood caries-caries infantiae. [PhD dissertation]. Sofia: University of Sofia; 2003.
17. Colak H, Dülgergil CT, Dalli M, Hamidi MM. Early childhood caries update: A review of causes, diagnoses, and treatments. J Nat Sci Biol Med. 2013;4(1):29-38.
18. American Association of Pediatric Dentistry (AAPD). Early childhood caries: unique challenges and treatment options. Pediatr Dent. 2000;22:21.
19. World Health Organization (WHO). Global strategy for infant and young child feeding. Geneva: WHO; 2003.

Original article

Acta Medica Academica 2016;45(1):26-33
DOI: 10.5644/ama2006-124.153

The business process management software for successful quality management and organization: A case study from the University of Split School of Medicine

Damir Sapunar*, Ivica Grković, Davor Lukšić, Matko Marušić

University of Split School of Medicine
Croatia

*Corresponding author:
ds@mefst.hr
Tel.: + 385 21 557 809
Fax.: +385 21 557 811

Received: 16 December 2015
Accepted: 6 April 2016

Key words: Medical education ▪ Medical school ▪ Organization ▪ Quality management.

Objective. Our aim was to describe a comprehensive model of internal quality management (QM) at a medical school founded on the business process analysis (BPA) software tool. **Methods.** BPA software tool was used as the core element for description of all working processes in our medical school, and subsequently the system served as the comprehensive model of internal QM. **Results.** The quality management system at the University of Split School of Medicine included the documentation and analysis of all business processes within the School. The analysis revealed 80 weak points related to one or several business processes. **Conclusion.** A precise analysis of medical school business processes allows identification of unfinished, unclear and inadequate points in these processes, and subsequently the respective improvements and increase of the QM level and ultimately a rationalization of the institution's work. Our approach offers a potential reference model for development of common QM framework allowing a continuous quality control, i.e. the adjustments and adaptation to contemporary educational needs of medical students.

Introduction

Medical education takes place in one of the most complex academic settings. This complexity is best envisaged by Flexner's triadic framework of education, research, and clinical care that has been a standard for the majority of medical schools for almost a century (1). Managing and providing support for these three major elements presents serious organizational challenges. In addition, the organization of medical schools and medical education faces general (e.g., continuous increase of demands) and specific (e.g., shortage of resources) problems of health care systems worldwide (2, 3). Today's health systems are struggling to keep up with increasing inequities in health care availability, new infectious agents, environmental, and behavioral risks, and rapid demographic and epidemiological transitions that threaten the health security of all (3).

All of these factors reflect on the cost of medical education, which is becoming increasingly demanding, complicated and expensive. According to an estimate for US medical schools, $62,877 USD is the annual variable cost of educating a medical student (4). These costs are significantly lower in less developed countries but still present a substantial burden for the communities (5).

These problems impose a necessity of organizing better and more cost-efficient management of medical schools. One of the

ways to achieve this is through the implementation of quality management (QM) system which become a prerequisite for high quality medical teaching, research and administration. The implementation should not only be limited to medical education but should encompass the overall organization of medical schools.

The QM approach initially emerged from industrial and commercial practices and gradually spread to other sectors (6). Universities and medical schools are now responsible for operating a quality management system that designs, delivers, monitors and assesses medical curricula to meet required standards (7, 8). These standards and requirements for QM in medical education are well defined (7, 8). However, there are no general guidelines for the implementation of these standards in medical education, including those defined by International Organization for Standardization (ISO) standard. As a consequence, numerous concepts of ISO standards implementation may exist in medical schools and health care institutions (9). Those standards often emphasize only the educational processes and neglect other important aspects of medical school organization.

Here we present our attempt to address the issue of QM in our medical school through implementation of the business process analysis (BPA) tool. The main aim was to document, analyze and streamline all business processes within our medical school as a first step in the IT-based development of a comprehensive QM system.

Here we describe the respective experience, the opportunities, the limits, and the perspectives that such a methodology allowed.

Methods

Setting

The University of Split School of Medicine is located in the city of Split, the second largest city in Croatia, and is one of four state owned medical schools in Croatia (10). All four schools are funded by the Ministry of Science, Education and Sports. The physician's education is based on a six-year integrated curriculum. The medical school in Split annually enrolls around 200 students in medicine, dental medicine and pharmacy courses.

The process management approach

With the objective of documenting and analyzing all business/work processes within the University of Split School of Medicine, a multidisciplinary work group was created, including health professionals, researchers, software engineers from the School's IT department and administrative staff members. The members of the work group were educated in business process management software by BPA professionals from Scheer GmbH Company (Saarbrucken, Germany). Upon training, all members of the work group were certified for business process modeling. The collaborative work was carried out in six phases: initial informative meetings, intensive training, process selection, definition of work method, process description by experts, and process modeling. Process description was prepared through interviews with the persons in charge of specific process by one member of the work team. The reduction of working hours was also estimated based on these interviews and was based on anticipated time saved by reducing number of unnecessary steps, documents and/or people involved.

Tools

BPA tools are primarily intended for users looking to document, analyze and streamline complex processes, thereby improving productivity, increasing quality and efficiency. These tools are also utilized by business

process architects and business process analysts, who want to gain a deeper understanding of business processes, events, workflows and data using proven modeling techniques. BPA tools permit users to illustrate their processes and validate this information using standard methodologies and best practices allowed by the software. Ideally, it can automate the models into deployable applications that leverage their analytical efforts and comply with the business process rules. The ARIS platform (Architecture of Integrated Information Systems, Scheer, Saarbrucken, Germany) is the leading platform for BPA. The platform allows description and documentation of all business processes performed in a particular institution. The resulting repository of business/work processes represents a basis for development of future IT solution with the aim of process automation. Two products were used; ARIS Business Server and ARIS Business Architect, which constitute a tool for modeling, analysis and displaying business processes. The Server module allows several ARIS Business Architect users to work simultaneously on the database.

Ethics statement

The Helsinki Declaration is not applicable to the research presented in the manuscript since the presented research describes the business processes and did not involve human subjects or human data.

Results

First we included definitions of the processes gained by the respective School's personnel in the ARIS flowchart, and then analyzed them for completeness and unambiguity. This approach identified weaknesses that should have subsequently been corrected by the School's administration and experts.

Structure and processes

The overall structure of the medical school was described by the "entry model" defined by the following: a) Organization structure, b) Processes, c) Applications, d) Documents and e) Products and services. These elements are presented in the form of a "virtual institution" schematic diagram in which business processes constitute a central point, while documents and applications are depicted as pillars supporting the structure of the institution (Figure 1). The organization of the School covers the whole structure, while the basis of the School structure is presented by its products and services (Figure 1).

All business processes within the School were divided into three main categories of interlinked processes (Figure 2). The first category comprises the "key" or "core" processes that are directly related to the main school's purpose, as expressed in the School's Mission (i.e. education, scientific and professional work) (Figure 2). Secondly, the "supportive" processes are not directly linked with teaching, research, and clinical work, but are essential for the successful execution of "key" processes (e.g. library management, IT service, administrative and lagal support) (Figure 2). The third category

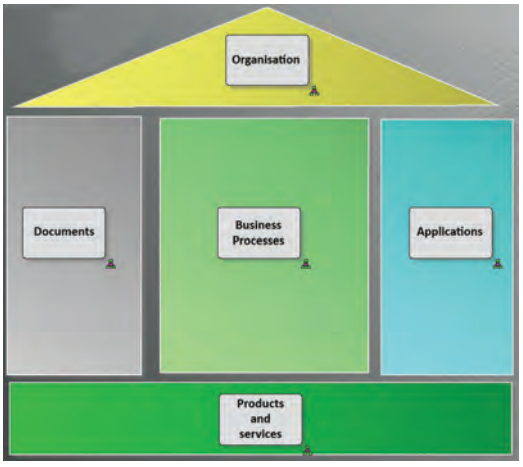


Figure 1 Entry model of medical school organization prepared according to the "business management approach".

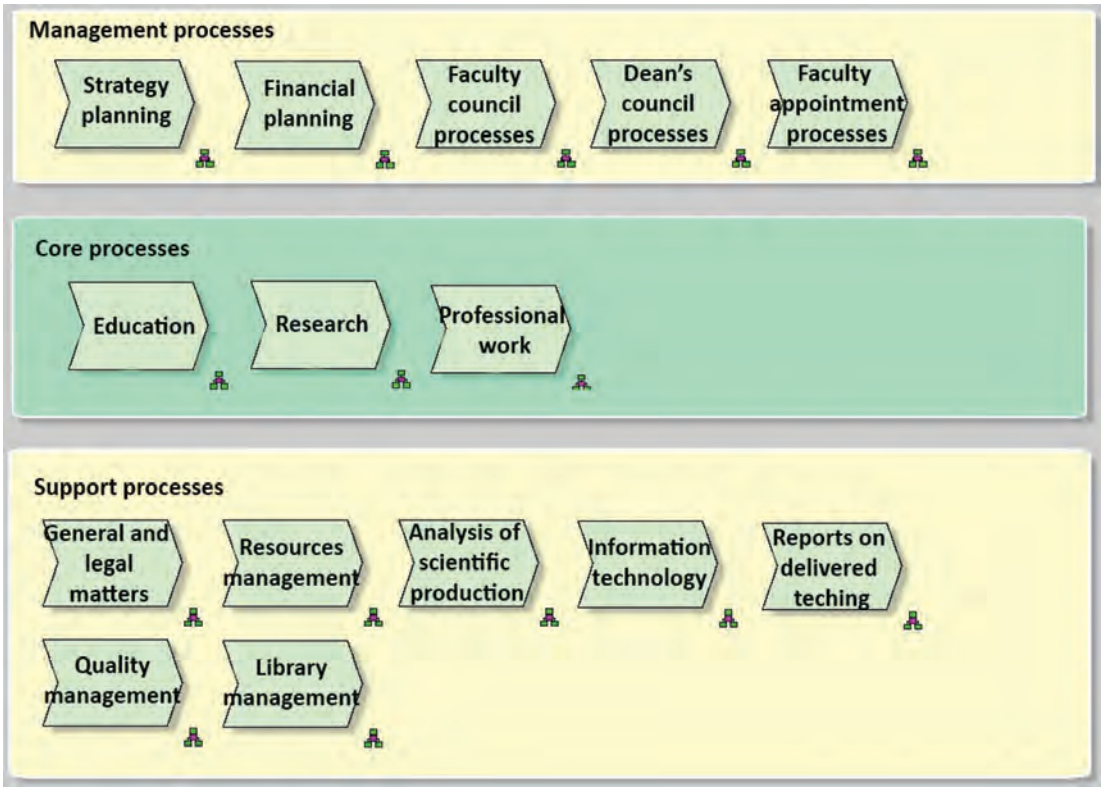


Figure 2 Three main categories of business processes within the medical school. Core processes encompass all activities directly related to the school's mission. The role of Supportive and Management processes is to allow successful execution of the core processes.

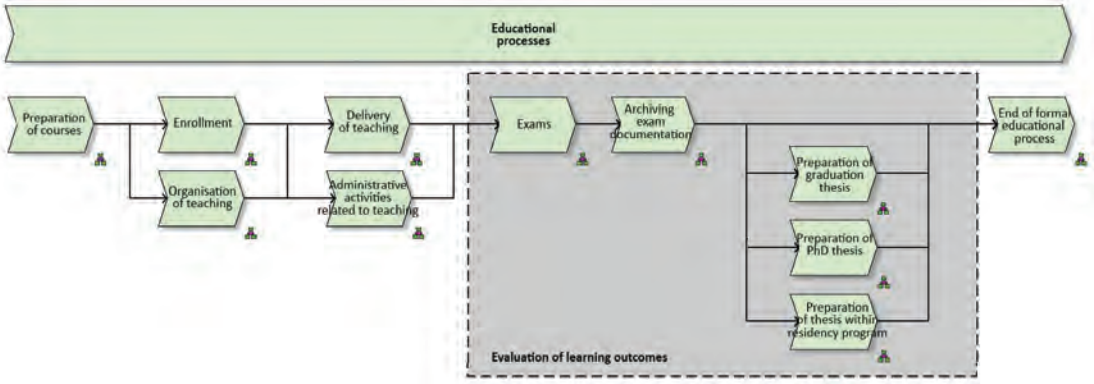


Figure 3 Example of Value added chain (VAC) diagram developed for educational processes.

encompasses institutional "management" processes (e.g., organization of the school council, or dean's cabinet meetings). The clustering was done according to the overall goal of the presented processes.

The business processes within each cluster were subdivided and presented through value added chain (VAC) diagrams, where each VAC diagram contained one or multiple sub-processes (Figure 3). Each element of the VAC ended up with the final process described through an "event driven process chain" (EPC) (Figure 4). In order to produce a detailed description of each EPC diagram,

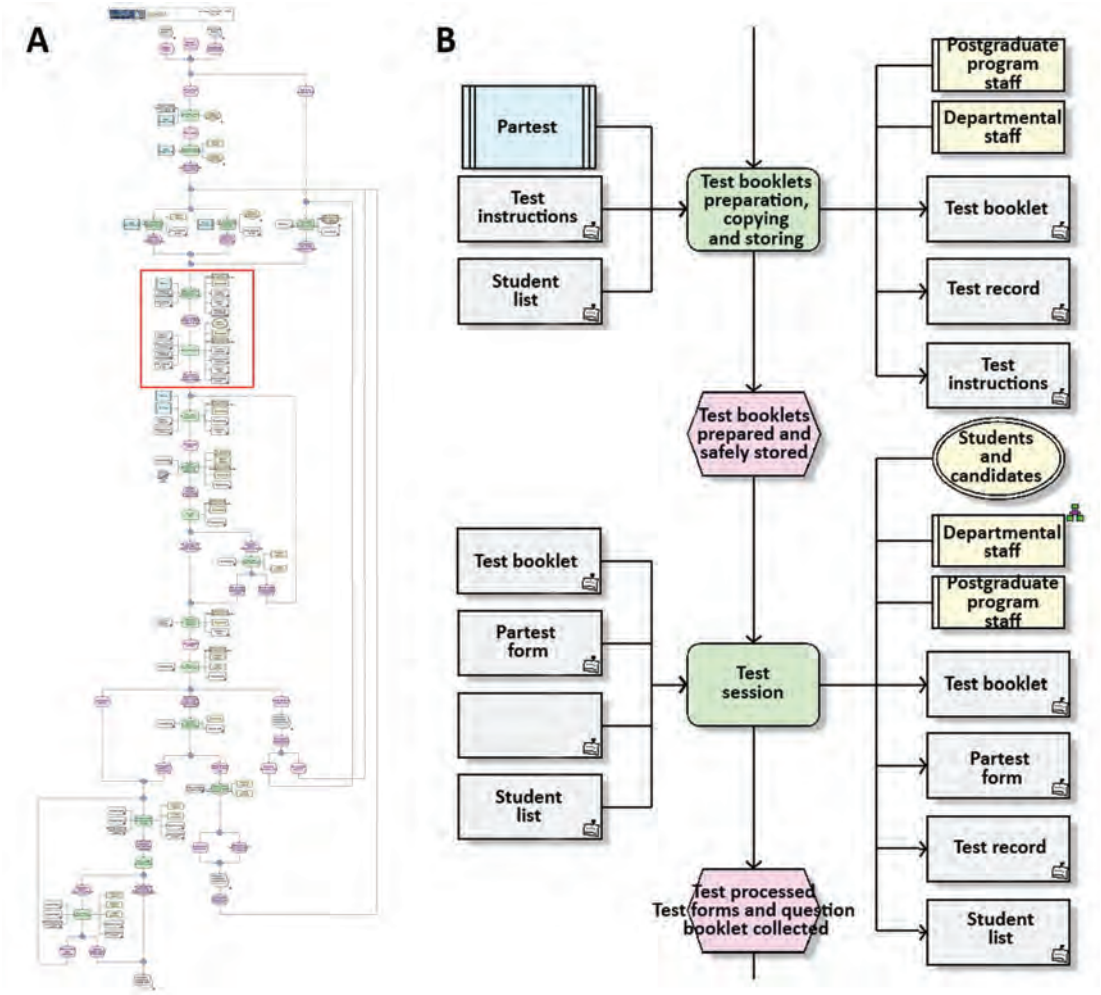


Figure 4 Example of Value added chain (VAC) diagram developed for the business process described as "Student testing". A) The left panel presents the whole structure of the business process. B) The selected part of the process represents a small segment marked with the red square on the left panel.

the processes were presented as series of attributes. The most important attributes were function, event, operators, responsible person or organizational unit, necessary documents or software application (Figure 4). The whole structure and all business processes can be accessed on the project website http://genom.mefst.hr/ARIS/.

Detection of failures and weak points

The analysis of the documented business processes revealed 80 weak points (WP, Table 1). The term weak point encompasses business processes that are missing or are deficient. The identified WPs were related to missing (n=13) or incomplete (n=19) processes, processes without defined deadlines (n=4) or even to processes which were in collision with current laws and institutional bylaws (n=14). The remaining weak points were identified in processes that lacked description of involved persons / institutional units (n=11), lack of necessary documents, archiving procedures or defined ways of making the results of the process available to stakeholders (n=15), as well as lack of equipment or necessary software (Table 1).

Table 1 The description and number of weak points encountered within the University of Split School of Medicine

Weak points	Core processes	Support processes				Management processes		Total
	Education	General and legal matters	Resources management	IT	Quality management	Strategy planning	Financial planning	
Lack of process	2	1	5	2	1	1	1	13
Lack of equipment / software	-	1	1	2	–	–	–	4
Incomplete process	10	2	5	2	-	-	-	19
Document / web management problem	4	2	-	2	7	-	-	15
Collision with laws / institutional bylaws	7	2	5	-	-	-	-	14
No defined deadline	-	1	1	2	-	-	-	4
Person or institutional unit not defined	10	-	1	-	-	-	-	11
Total	33	9	18	10	8	1	1	80

Analysis of weak points

The analysis of identified weak points revealed processes which could be substantially shortened by reducing number of unnecessary steps, documents and/or people involved. The analysis was performed by modeling and the comparison of current ("as is") and modeled ("as if") business processes. A precise analysis allowed us to determine the reduction of costs and/or working hours for specific processes upon improvement. As an example, the Figure 5 depicts the reduction of the working time necessary for purchasing procedures. Improvement of purchasing processes resulted in 53% reduction in working hours for that specific process.

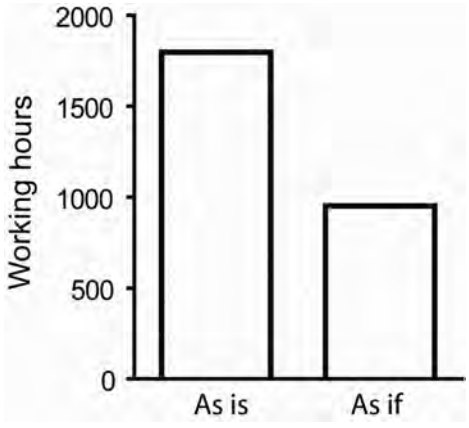


Figure 5 Example of improvement modeling of business processes related to purchasing procedures. Improvement is presented as reduction in working hours between "as is" and "as if" conditions.

The actual improvements based on implementation of the analysis of the weak points depended on the readiness of the school management to enforce these changes, attitude towards changes of the current school management, financial issues, and priorities set up by different school managements.

Discussion

The ARIS platform provides a suitable BPA tool for the medical school setting, and we believe that it may be used as a possible reference model for developing common QM frameworks according to the plan–do–study–act (PDSA) cycle of continuous improvement (11).

Our present work is the first step in QM implementation within the University of Split School of Medicine. Its main result was

the description and analysis of all business/work processes within the School. The application of the ARIS BPA tool helped the School start its own QM system as an initial step towards a comprehensive QM system.

There is no single (or simple) definition of quality, inasmuch as this term has different meanings to different professionals (12, 13). The issue of QM in higher and medical education has been the objective of many international organizations, including the European Association for QA in Higher Education (ENQA) and the World Federation for Medical Education (WFME) which developed a set of standards, procedures and guidelines on QM (7, 8, 14). QM of medical education implies a well-planned assessment of the structure, process and the outcome of education based on defined standards and objectives.

Published examples of business process modeling in medical education and health care practice are scarce (15-20), and none of them presents a comprehensive documentation and analysis of processes within the whole institution. In most cases these examples present a small segment of business processes generally oriented only towards educational processes, while neglecting other important processes such as management, research or support.

In our opinion this presents serious drawbacks because a segmented approach seriously limits the potential for the implementation of IT solutions that can manage business/work operations and customer satisfaction. We adopted a different, comprehensive, "business-oriented" approach, inasmuch as we have been aware that efficacy of the educational processes depend on the workflow and harmonization of all supporting processes in the medical school. However, to our knowledge, this notion has not been tested directly.

Quality management practices in the Croatian academic community have never been adopted in full. In 2005 the Croatian Parliament established the Agency for Science and Higher Education (AZVO) that has been organizing a system of quality assurance in higher education and science. AZVO is the key institution performing external accreditation of academic institutions according to ISO 9001:2008 standard. In 2009 the State Parliament introduced a legal act regarding quality assurance in science and higher education, (21) but academic institutions still did not adopt proper mechanisms of QM. However, most of the proposed activities are related to accreditation procedures and not to other aspects of QM.

In conclusion, we have shown that existing business process analysis tools can be important part of quality management implementation in medical schools. Precise analysis of medical school business processes allows identification of weak points for specific processes that need improvement. Our approach can be considered a possible reference model for the development of a common QM framework which will allow for continuous quality control, adjustments and adaptation in medical schools and other higher education institutions.

What is already known on this topic

The quality management is necessary for organizing better and more cost-efficient management of medical schools. The standards and requirements for quality management in medical education are well defined, but other important aspects like professional, scientific, support and management processes within medical school organization are completely neglected.

What this study adds

The study presents description and analysis of all business processes within our medical school. That analysis can be considered as a first step in the development of a comprehensive quality management system. The business process analysis tools are important part of quality management implementation in medical schools. Precise analysis of medical school business processes allows the rationalization of working hours for specific processes that need improvement.

Acknowledgements: The members of the project team that developed database of business processes at the University of Split School of Medicine were: Davor

Lukšić, Frane Mihanović, Vana Košta, Lana Barać, Josip Barić, Asija Petrašić and Mijo Kardum from the IDS Scheer. The head of the project team were Damir Sapunar and Katarina Dobronić from the IDS Scheer.

Authors' contribution: Conception and design: DS, IG, DL, and MM; Acquisition, analysis and interpretation of data: DS, IG, DL and MM Drafting the article: DS; Revising it critically for intellectual content: IG, DL and MM; Approval of final version to be published: DS, IG, DL and MM.

Conflict of interest: The authors declare that they have no conflict of interest.

References

1. Flexner A. Medical Education in the United States and Canada: A Report to the Carnegie Foundation for the Advancement of Teaching in Bulletin. Boston: The Merrymount Press; 1910.
2. Chen L, Berlinguer G. Health equity in a globalizing world. In: Evans T, Whitehead M, Diderichsen F, Bhuiya A, Wirth M, editors. Challenging inequities in health: from ethics to action. New York: Oxford University Press; 2001. p. 35-44.
3. Frenk J, Chen L, Bhutta ZA, Cohen J, Crisp N, Evans T, et al. Health professionals for a new century: transforming education to strengthen health systems in an interdependent world. Lancet. 2010;376(9756):1923-58.
4. Schieffler DA, Azevedo BM, Culbertson RA, Kahn MJ. Financial implications of increasing medical school class size: does tuition cover cost? Perm J. 2012;16(2):10-4.
5. Maslov Kruzicevic S, Barisic KJ, Banozic A, Esteban CD, Sapunar D, Puljak L. Predictors of attrition and academic success of medical students: a 30-year retrospective study. PLoS One. 2012;7(6):e39144.
6 Barrows H, Tamblyn R. Problem-based learning: an approach to medical education. Medical Education. New York: Springer Publishing Company; 1980.
7. WFME - World Federation for Medical Education. Postgraduate medical education - WFME global standards for quality improvement. Copenhagen: Kandrups Bogtrykkeri; 2003.
8. ENQA - European Association for Quality Assurance in Higher Education. Standards and Guidelines for Quality Assurance in the European Higher Education Area. Brussels: ENQA; 2015.
9. Sweeney J, Heaton C. Interpretation and variations of IS 9000 in acute health care. Int J Qual Health Care. 2000;12(3):203-9.
10. Grkovic I, Sapunar D, Marusic M. Ways to address the challenges of a modern medical curriculum: living academic medicine at the University of Split, School of Medicine. Acta Med Acad. 2012;41(1):7-17.
11. Moen RD, Norman CL. Clearing up myths about the Deming cycle and seeing how it keeps evolving. Quality Progress. 2010;11:22-8.
12. Tariq M, Ali SA. Quality assurance and its application in medical education. J Coll Physicians Surg Pak. 2014;24(3):151-2.
13. Joshi MA. Quality assurance in medical education. Indian J Pharmacol. 2012;44(3):285-7.
14. Eriksen SD. TQM and the transformation from an elite to a mass system of higher education in the UK. Qual Assur Educ. 1995;3(1):14-29.
15. Rojo MG, Rolon E, Calahorra L, Garcia FO, Sanchez RP, Ruiz F, et al. Implementation of the Business Process Modelling Notation (BPMN) in the modelling of anatomic pathology processes. Diagn Pathol. 2008;3(Suppl 1):S22.
16. Dieter PE. Quality management of medical education at the Carl Gustav Carus Faculty of Medicine, University of Technology, Dresden. Ann Acad Med Singapore. 2008;37(12):1038-40.
17. Dieter PE. A faculty development program can result in an improvement of the quality and output in medical educaton, basic science and clinical research and patient care. Med Tech. 2009;31(7):566-9.
18. Scheuerlein H, Rauchfuss F, Dittmar Y, Molle R, Lehmann T, Pienkos N, et al. New methods for clinical pathways-Business Process Modeling Notation (BPMN) and Tangible Business Process Modeling. Langenbecks Arch Surg. 2012;397(5):755-61.
19. McClintock DS, Lee RE, Gilbertson JR. Using computerized workflow simulations to assess the feasibility of whole slide imaging full adoption in a high-volume histology laboratory. Anal Cell Pathol (Amst). 2012;35(1):57-64.
20. Barbagallo S, Corradi L, de Ville de Goyet J, Iannucci M, Porro I, Rosso N, et al. Optimization and planning of operating theatre activities: an original definition of pathways and process modeling. BMC Med Inform Decis Mak. 2015;15:38.
21. Law on Quality Assurance in Science and Higher Education [in Croatian]. Narodne Novine; 45:2009.

Original article

Acta Medica Academica 2016;45(1):34-38
DOI: 10.5644/ama2006-124.154

Management of teaching processes using the Share point platform: A case study from the University of Split School of Medicine

Damir Sapunar*, Ivica Grković, Davor Lukšić, Matko Marušić

University of Split School of Medicine
Split, Croatia

*Corresponding author:
ds@mefst.hr
Tel.: + 385 21 557 809
Fax.: + 385 21 557 811

Received: 24 February 2016
Accepted: 12 April 2016

Key words: Medical education ▪ Medical school ▪ Organization ▪ Teaching load.

Objective. To develop a software tool that will combine teaching timetables with the generation of reports on teaching load. **Methods.** The University of Split School of Medicine project team and the external experts from the company LAMA, LLC. determined necessary functionalities and developed the software platform as an extension of the existing software solutions already in use by the Croatian academic community. **Results.** By combining comprehensive scheduling functionality with planned and performed teaching activities we determined the teaching load and realized automatic generation of payments for adjunct lecturers. The implementation required perfecting of the human resources services, brought about a manifold alleviation of the work of the entire school's administration and substantially increased the effectiveness of the quality management. The software is currently managing 54,676 teaching hours, 841 teaching staff member, 111 teaching rooms, 8 study programs, and 645 courses. **Conclusion.** The program resolved several administrative problems of the school and is an example of successful implementation of IT technology in medical school management.

Introduction

Medical education in Croatia is based on a six-year integrated program (1) offered in four medical schools at the Universities of Osijek, Rijeka, Split, and Zagreb. All four schools are a part of public universities and are funded by the Ministry of Science, Education and Sports. The process of budget allocation to an individual medical school is not a result of a defined funding system but is largely based on old practice inherited from times before Croatia became an independent country. Currently there are no clear monetary allocation principles, and the documents from which the schools' budgets can be determined are scarce (2). If the budget is considered a function of the cost per graduating student, the largest amount is spent at the medical school in Zagreb (US$ 90,000 per student, for the six-year study program). The amount per graduating student in US dollars in Rijeka is $ 40,000, $ 30,000 in Split, and $ 29,000 in Osijek (3). These amounts and the lack of budget allocation principles are still not provoking serious discussion and analysis in the respective professional circles.

The only fixed factor that directly affects the above mentioned costs is the number and structure of employed faculty members. Salaries make up an average of 50% to 60% of

the expenditures (54% at the medical school in Split in 2009, data in the possession of the authors). Because the main criterion for the opening of new positions is the teaching load, there is a serious need for the transparent determination of the teaching load for each academic staff member, department, and the school as a whole. One would therefore expect that schools, universities, and the relevant Ministry officials would seriously scrutinize teaching loads. The need for a precise analysis of the teaching load is additionally emphasized by the phenomenon of professorial "moonlighting" (the practice of academics teaching at several schools and receiving salaries from all of them), which has become a serious problem in the academic community (4).

Without a proper information technology (IT) solution it is quite difficult to determine the total teaching load at a particular school and, consequently the budget for the salaries. The budget calculation is further complicated by the additional cost of adjunct lecturers, mainly clinicians who teach part-time.

When confronted with this problem, we reckoned that the IT approach would be the right strategy to solve the proper allocation of salaries based on teaching load. The main software platform for the management of educational processes in Croatia is the Information System for Higher Education (ISVU) (5), and has been in use at the medical school in Split since 2007. However, this platform does not assist in determining either teaching loads or associated costs. Also, various software solutions used in other Croatian medical schools provide only scheduling capabilities without options for calculating the teaching load. The lack of this important functionality required an extremely tedious and relatively imprecise "manual" labor by the schools' administration to compose the reports required by the university and the Ministry of Science, Education and Sports, which subsequently led to the imprecise determination of budget allocation.

Methods

We decided to develop a software platform that will enable us to combine teaching timetables with the generation of reports on teaching load, planned and performed teaching activities, and the automatic generation of payments for adjunct lecturers. The project team at the University of Split School of Medicine determined the necessary functionalities for the platform and engaged LAMA, LLC, an external IT company, with the aim of developing new software that will be compatible with the existing ISVU software solution.

The requirements for the new program are from a business process analysis performed at our school (6) and divided into two main functionalities (Figure 1). The first functionality addressed planning and scheduling of teaching and extracurricular activities, generation of a web-based timetable of all teaching/space allocation modalities: room, teacher, student group, type of teaching (lecture, seminar, practical) and topic – all on an a daily and hourly basis.. The second functionality was related to the key problem of the calculation of teaching load, generation of the reports on planned and performed teaching activities and the automatic generation of payment contracts for adjunct lecturers or teachers (Figure 1).

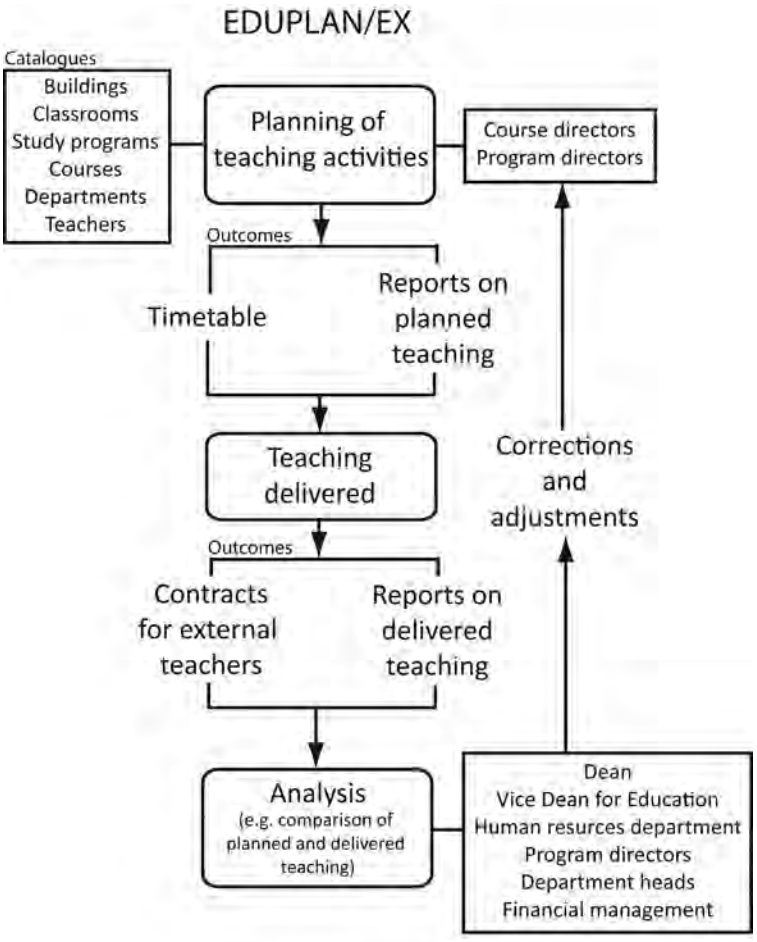


Figure 1 The functionalities of the software tool that combines teaching timetables with generation of reports on teaching load at the University of Split School of Medicine. By combining a comprehensive scheduling functionality with planned and performed teaching activities, we achieved the main goal of the program, i.e., determination of the teaching load and automatic generation of payments for adjunct lecturers or teachers.

Results

The result of the project was the development of the EduPlan/EX software based on Microsoft Sharepoint, SQL and ASP.NET technologies implemented through a virtualized environment on two Microsoft Windows Server. Usage of MS Active Directory repository allows authentication and authorization based on previously granted user rights by system administrator and distinguished user roles. Access to the EduPlan/EX application is through a web browser. The system has an internal fully functional interface for authenticated faculty staff, an external presentation interface with limited functionality and read only access at http://nastava.mefst.hr:10000/.

The first step in implementation of the program is completing the main catalogues (list or record of buildings, teaching rooms, departments and teachers). Administrators from the Office of Student Affairs and the IT Department entered catalogue data.

The teachers/administrators selected by a particular department execute the teaching

timetable. The planning, particularly in the block-based organization of the curriculum, is a demanding and complex task, which requires a specific user-friendly computer interface. Planning includes entry of all elements of the teaching based on one teaching hour as the core unit that comprises course, topic, time, teaching room, teacher, type of the teaching, and the student group. Based on entered data, the system provides real time availability information for all teaching locations. This functionality provides a key point of resource sharing and the efficient management of teaching resources.

Teaching reports can be automatically produced for all these entries: teaching load for an individual teacher, course, department, and for the school as a whole. Hours of lectures, seminars, and practical classes are all exportable as lists into different formats such as Portable Document Format (pdf), Microsoft (MS) Word, or MS Excel.

Our team entered the complete plan for all courses into the program before the start of the academic year. At the inception of this program (academic year 2011/12), planning and entering data required a lot of time and effort since we had to deal with a large number of teaching hours. However, in subsequent years the work was much less demanding, because the educational framework did not change and the program allows copy and paste changes of dates, teacher names, and lectures.

Currently, the program deals with 54,676 teaching hours distributed over four integrated programs (medicine, dental medicine, pharmacy, medical studies in English), and three postgraduate (doctoral) programs. However, the application of this program for the first time in 2011 had additional outcomes. First, we discovered discrepancies between the educational program of several subjects and their plans for the current school year, as well as numerous discrepancies between the teaching plans and data entered in the program. This clear-cut and quantitative insight enabled us to synchronize subsequently the data to a satisfactory level. Second, we were able to identify departments with high teaching loads from adjunct faculty, distribute that teaching load to employed faculty, and by doing so reduced the costs of adjunct lecturers.

Currently, the EduPlan/EX contains 841 teaching staff members, 111 teaching rooms, 8 study programs, and 645 courses. Notably, our business solution program had the highest business value recognition at the Windays 2012 conference (7).

Discussion

With EduPlan/EX we achieved all planned functionalities and resolved one of the main administrative problems in the management of resources at our school. The scheduling functionality allowed us to have precise timetables several months before the start of the academic year, to provide online access to timetables, and to avoid conflicts in classroom booking. The biggest tangible gain was the drastic reduction in administrative work to collect data on the teaching workload from all teachers all of whom have numerous variations in their contracts, academic status, planned and completed teaching hours. We also achieved a reduction in the automatic generation of contracts for adjunct lecturers or teachers (about 500 professionals). Weeks of exhausting and prone-to-error work by several offices to compose hundreds of employment contracts to achieve contractal payments are now shortened to a direct printing of the contracts from to the EduPlan/EX program. The satisfaction of the finance and education administrative staff is worth noting in this report. The lack of quantitative outcomes following the implementation of the EduPlan/EX program was a limitation of the study. However, the quantification can be considered unnec-

essary when we know that all presented outcomes were unavailable before implementation of the program.

The program allowed us to keep track of the changes in the planned teaching activities due to engagement of different teachers. This was necessary because all teachers cannot plan their extracurricular or other obligations the whole year in advance. The changes (replacing the names of absent teachers with those who substituted them) turned out to be relatively frequent and difficult to manage on time, mainly due to the lack of control of the communication between the teachers in question and persons in charge of the EduPlan/EX in a specific department. Endowing the teachers with personal electronic cards, which they would activate at the beginning of the lecture/seminar/practical class, so that subsequently the program automatically changes the names in its database, provides an elegant solution. An additional way of registering a teacher could be through logging into a classroom computer or by a smartphone, all with the ultimate goal of full automatization. The expansion of the currently used version of the program is aiming in that direction.

What is already known on this topic

Currently there are no well-defined principles for budget allocation to Croatian medical schools while salaries make up on average 50% to 60% of the expenditures. The teaching load is the main argument for opening new positions in the Croatian academic community. There are no information technology (IT) solutions for the automatic calculation of the teaching load.

What this study adds

This study describes the development of a software tool that combines teaching timetables with the generation of reports on teaching load. The combination of comprehensive scheduling functionality with planned and performed teaching activities allows the determination of the teaching load and automatic generation of payments for adjunct lecturers or teachers. The program resolved several administrative problems at the medical school. With the success of our resource saving software in medical school management, perhaps other medical schools in the region may benefit from this software as well.

Acknowledgement: The authors acknowledge the LAMA, LLC company (Split, Croatia) for providing technical support for the execution of the project, and Professor Ana Marušić for critical review of the report.

Authors' contribution: Conception and design: DS, IG, DL, and MM; Acquisition, analysis and interpretation of data: DS, IG, DL and MM; Drafting the article: DS; Revising it critically for intellectual content: IG, DL and MM; Approval of final version to be published: DS, IG, DL, and MM.

Conflict of interest: The authors declare that they have no conflict of interest.

References

1. Grkovic I, Sapunar D, Marusic M. Ways to address the challenges of a modern medical curriculum: Living academic medicine at the University of Split, School of Medicine. Acta Med Acad. 2012;41(1):7-17.
2. Maslov Kruzicevic S, Barisic KJ, Banozic A, Esteban CD, Sapunar D, Puljak L. Predictors of attrition and academic success of medical students: a 30-year retrospective study. PloS One. 2012;7(6):e39144.
3. Petrašić A, Janković S, Marušić M. Why is the price of a student education three times hights in Zagreb than in Split? [in Croatian]. Liječničke novine. 2011;(96):65.
4. Marušić M. The equilibrium of the low quality [in Croatian]. Školske novine. 2001;30(4):3.
5. Information system of higher education institutions - ISVU [homepage on the Internet]. Zagreb: University of Zagreb, University Computing Centre - SRCE [cited 2016 Feb 10]. Available from: http://www.isvu.hr/.
6. Sapunar D, Grković I, Lukšić D, Marušić M. The business process management software for successful quality management and organisation: A case study from the University of Split School of Medicine. Acta Med Acad. 2016;45;1:26-33.
7. EDUPLAN/EX – A solution with best business value [homepage on the Internet]. Split: Lama [cited 2016 Feb 10]. Available from: http://www.lama.hr/rjesenja/aplikativna-rjesenja/eduplan/.

Original article

Acta Medica Academica 2016;45(1):39-50
DOI: 10.5644/ama2006-124.155

Stethoscope vs. ultrasound probe - which is more reliable in children with suspected pneumonia?

Jovan Lovrenski[1*], Slobodanka Petrović[2], Svetlana Balj-Barbir[1], Radoica Jokić[3], Gordana Vilotijević-Dautović[2]

[1]Radiology Department, [2]Pulmonology Department and [3]Pediatric Surgery Department, Institute for Children and Adolescents Health Care of Vojvodina Serbia

*Corresponding author:
jolo221177@gmail.com
Tel.: + 381 641 436 030
Fax.: + 381 21 425 509

Received: 20 January 2016
Accepted: 1 April 2016

Key words: Pneumonia ▪ Children ▪ Ultrasound ▪ Auscultation.

Objective. To compare lung ultrasound (LUS) with auscultation findings in children with clinical suspicion of pneumonia. **Patients and methods**. A prospective study including 95 patients (age: from 2 months to 17.5 years; mean age: 5.1 y, SD 4.5 y) with referral diagnosis of suspected pneumonia. In all patients LUS and auscultatory examinations were performed within an hour. These findings were compared separately in each hemithorax. The radiologist performing LUS was blinded to the patient's clinical information. Positive auscultatory findings included: crackles and/or abnormal breath sounds (decreased, asymmetric, absent, or bronchial). For LUS examinations a combined transthoracic – transabdominal approach was used. A pneumonia-positive LUS finding included subpleural consolidation with air-bronchogram, or an adjacent area of interstitial edema. For each subpleural consolidation the cranio-caudal (CC) diameter was measured, and 95% confidence intervals (CI) of the sizes of subpleural consolidations for positive and negative auscultatory findings were compared. The p-value between LUS and auscultation was calculated using McNemar's test. **Results**. LUS and auscultation showed pneumonia-positive findings in 98 and 64 hemithoraces, i.e. in 67 and 45 patients respectively. In positive auscultatory findings the CI for CC diameters of subpleural consolidations ranged from 32.46 to 54.14 mm, and in negative auscultatory findings the CI was between 16.52 and 29.83 mm, which showed a statistically significant difference. McNemar's test showed a statistically significant difference between LUS and auscultation. **Conclusions.** LUS showed positive findings in more hemithoraces than auscultation in children with suspected pneumonia. A cranio-caudal size of subpleural consolidation of less than 30 mm significantly reduces the possibility of auscultatory detection.

Introduction

Lung ultrasound (LUS) has recently been recognized as an even more reliable imaging modality in detection and follow-up of pneumonia than chest X-ray (CXR), both in children and adults, and even to some extent rivaling computed tomography (CT) (1-11). However, it still cannot be claimed that it is a widely acknowledged imaging tool in everyday clinical practice. On the other hand, the stethoscope has been a broadly accepted diagnostic tool of every single medical student and doctor since the early 19th century, and represents a symbol of the medical profession.

Among a growing number of studies comparing LUS primarily with CXR, but also CT findings, we found only one comparing LUS and auscultatory findings, which was performed in adult patients with acute respiratory distress syndrome, and not a single one considering the pediatric population (12).

Therefore, the aim of this study was to compare LUS and auscultatory findings in children with a referral diagnosis of pneumonia.

Patients and methods

A prospective study was carried out at the Institute for Children and Adolescents Health Care of Vojvodina, Novi Sad, Serbia, in association with the Pediatric Emergency Department and Radiology Department, from 01 November 2012 to 30 May 2013. It included 95 outpatients with referral diagnosis of suspected pneumonia [59 males and 36 females; aged 2 months - 17.5 years, mean age 5.1 y (SD=4.5 y)] set at the Pediatric Emergency Department of the Institute. Inclusion criteria were as follows: 1) LUS and auscultatory examinations performed within an hour in the same child; 2) the availability of a pediatric radiologist (J.L.) with 7 years of experience in performing and interpreting LUS; 3) the radiologist performing LUS was blinded to all the patients' information, apart from the referral diagnosis (suspicion of pneumonia); 4) auscultatory examinations were performed by pediatricians (not pediatric residents); 5) only children with no former history of chronic lung disease (asthma, cystic fibrosis, bronchopulmonary dysplasia, etc.), immunosuppressive disorder, or malignant disease were included.

LUS examinations included both transthoracic (TT) and trans-abdominal (TA) approaches, using a linear probe of 9 MHz for TT, and a convex probe of 5 MHz for TA approach (Acuson S2000, Siemens, Erlangen, Germany). The average time needed for LUS examinations with standard deviation (SD) was calculated. The trans-thoracic approach comprised examination in supine and both lateral decubitus positions of the anterior (between the sternum and the anterior axillary line), lateral (between the anterior and posterior axillary lines) and posterior (between the posterior axillary line and the spine) lung areas, from the apex to the lung base. The US examination of each lung area consisted of longitudinal and transversal (intercostal) sections. The trans-abdominal approach included trans-hepatic and trans-splenic US scans in supine position to examine both lung bases. The US probe was angulated from the most anterior to the most posterior sections. A normal trans-abdominal US finding of the lung bases was presented with the acoustic phenomenon of "mirror image", which is a supra-diaphragmatic projection of liver or spleen (13).

Each US finding of subpleural consolidation, with or without air-bronchogram, as well as consolidation with the adjacent area of B lines (vertically oriented "comet-tail" artifacts arising from the pleural line, reaching the edge of the screen, erasing the A lines, and moving with lung sliding) was considered as pneumonia-positive. According to the current literature, these findings included children in the study with US features of both bacterial and viral pneumonia (14, 15). Positive auscultatory findings included: crackles and/or abnormal breath sounds (decreased, asymmetric, absent, or bronchial). Auscultatory and LUS findings were compared separately in each hemithorax. Moreover, US findings were compared with CT and video-assisted thoracoscopy (VATS) in two children.

Ethics statement

The Ethical Committee approved the research and informed consent was obtained

from the parents of each examined child, as well as from the older children and adolescents themselves.

Statistical analysis

Each subpleural consolidation had the cranio-caudal (CC) diameter measured by ultrasound, and 95% confidence intervals (CI) of the sizes of subpleural consolidations for auscultatory positive and auscultatory negative findings were compared. In hemithoraces with two or more subpleural consolidations, the largest was used for calculation of CI. McNemar's test was performed using IBM SPSS statistics for Windows software, version 21.0 (Inc., Chicago, IL, USA), with calculation of the P-value between the two diagnostic modalities (LUS and auscultation). A P-value below 0.05 was considered as statistically significant.

Results

Out of 95 children (i.e. 190 hemithoraces) included in the study, LUS and auscultation showed pneumonia-positive findings in 98 and 64 hemithoraces, i.e. in 67 and 45 patients respectively. There were no hemithoraces with an auscultatory positive and LUS negative finding of pneumonia (Table 1, Figure 1). In one patient, pneumonia was revealed using the trans-hepatic approach only, and proved afterwards by CXR (Figure 2).

Pleural effusion was detected by ultrasound in 14 hemithoraces. In two hemithoraces, LUS findings completely matched the VATS finding (Figure 3). In one child with CT performed within 24 hours after LUS, and before VATS, necrotizing pneumonia and pleural effusion initially detected by LUS were confirmed by CT examination (Figure 4). However, in the same patient, LUS detected loculated pleural effusion with multiple fibrin strands, indicating organization of the effusion, whilst CT did not recognize them.

In the group of patients with positive auscultatory findings, the CI for CC diameters of subpleural consolidations ranged from 32.46 mm to 54.14 mm, and in patients with negative auscultatory findings, the CI was between 16.52 mm and 29.83 mm, which showed a statistically significant difference, based on the absence of the overlap between the two CIs.

The two-tailed P-value between LUS and auscultation, calculated with McNemar's test, was less than 0.0001, which, by conventional criteria, is considered to be extremely statistically significant. The average time of LUS examination was 5.7 minutes (SD 1.63).

Table 1 Distribution of the number of hemithoraces with and without pneumonia diagnosed by ultrasound and auscultation

Ultrasound	Auscultation		Total
	Positive	Negative	
Positive	64	34	98
Negative	0	92	92
Total	64	126	190

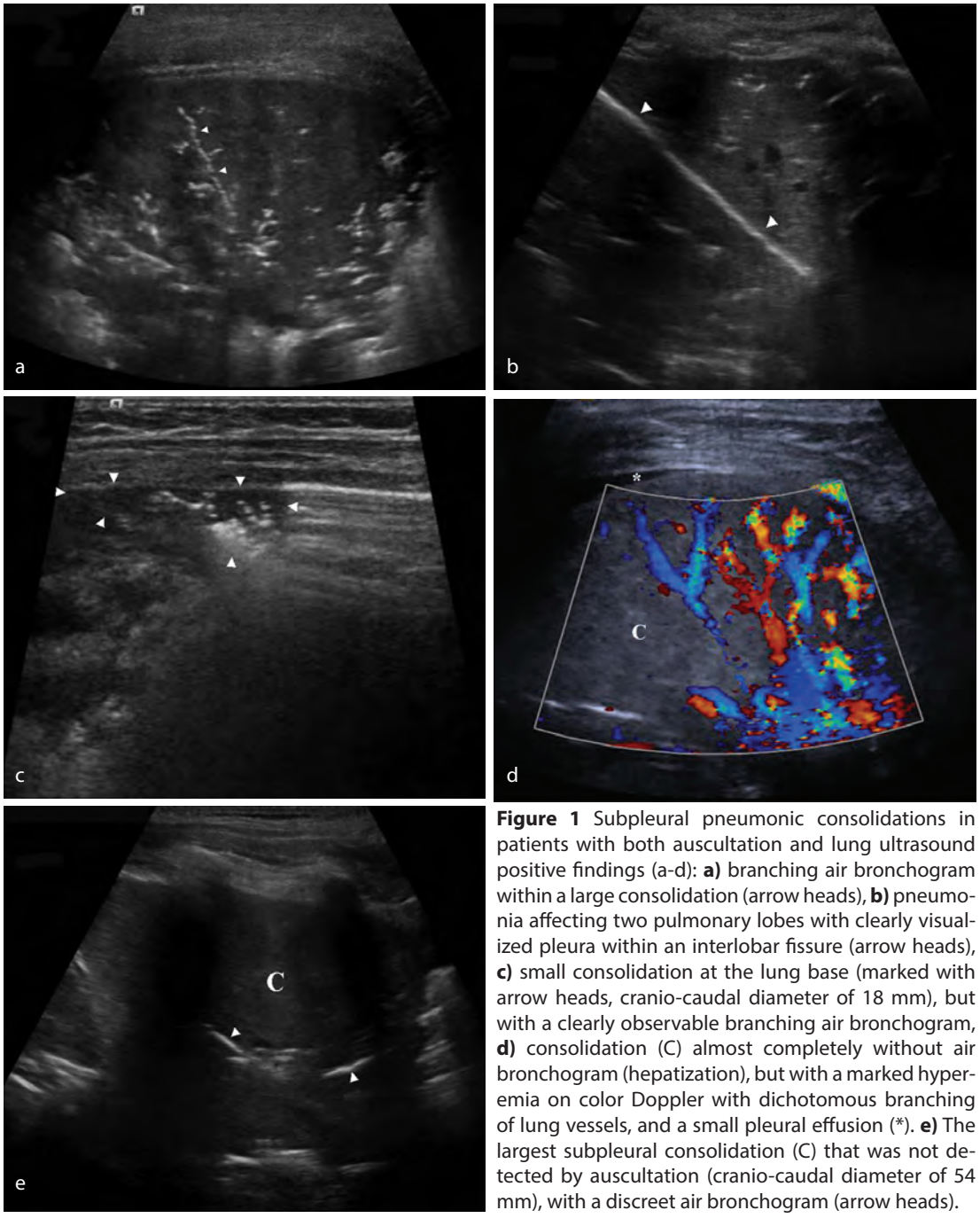


Figure 1 Subpleural pneumonic consolidations in patients with both auscultation and lung ultrasound positive findings (a-d): **a)** branching air bronchogram within a large consolidation (arrow heads), **b)** pneumonia affecting two pulmonary lobes with clearly visualized pleura within an interlobar fissure (arrow heads), **c)** small consolidation at the lung base (marked with arrow heads, cranio-caudal diameter of 18 mm), but with a clearly observable branching air bronchogram, **d)** consolidation (C) almost completely without air bronchogram (hepatization), but with a marked hyperemia on color Doppler with dichotomous branching of lung vessels, and a small pleural effusion (*). **e)** The largest subpleural consolidation (C) that was not detected by auscultation (cranio-caudal diameter of 54 mm), with a discreet air bronchogram (arrow heads).

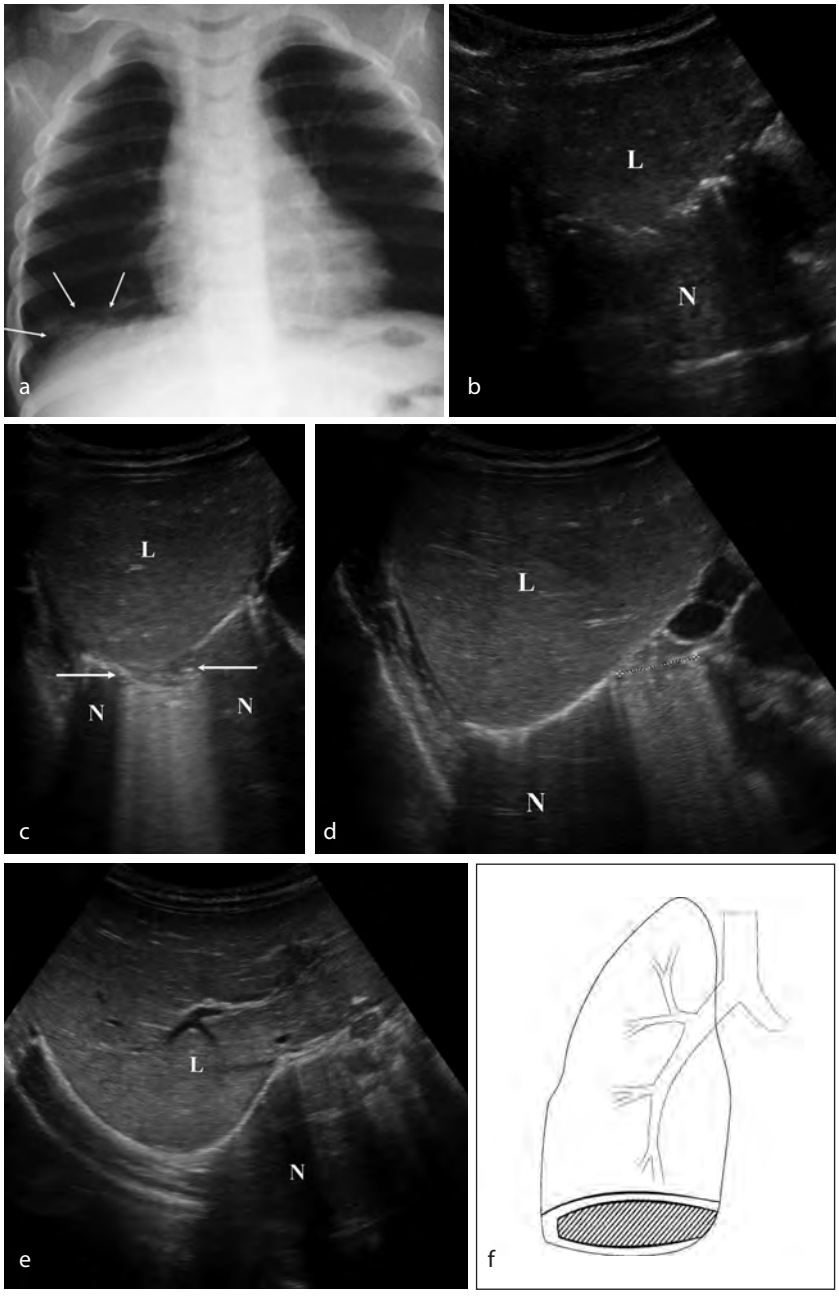


Figure 2 a) Chest X-ray showing a pulmonary consolidation within the right lung base (arrows). This consolidation went unmarked using a trans-thoracic lung ultrasound approach before CXR. However, trans-hepatic examination of the right lung base (**b - e**), from the most anterior (**b**) to the most posterior (**e**) section detected this pulmonary pathology. Images **b** and **e** show a normal ultrasound pattern of the "mirror image" phenomenon (N), while in the middle sections of the right lung base there are lung consolidations marked with arrows (**c**) and asterisks (**d**), with a discreet air-bronchogram. Note the normal lung ultrasound pattern adjacent to them (N), especially important laterally, because pneumonia does not abut on the lateral pleural surface which is accessible by a low trans-thoracic approach. L - liver. **f)** Scheme of the right lung with an area within the lung base (marked with oblique lines), which is only accessible to visualization by ultrasound when using the trans-hepatic approach. This area is not in contact with either anterior, or lateral, or posterior pleura, which is mandatory for trans-thoracic visualization, but only with basal pleura.

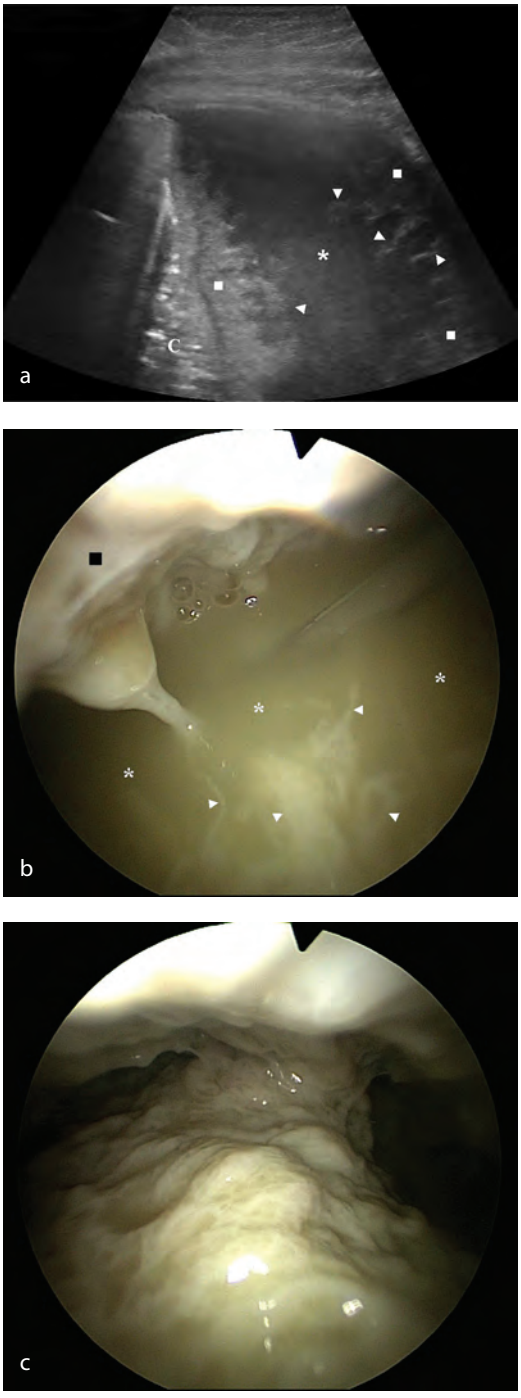


Figure 3 A 16-year old boy was provided with ambulatory care for 9 days and antibiotic therapy for a week. On admission he was dyspneic, febrile (38.7°C), and was coughing heavily, with oxygen saturation 91%-97%, and auscultatory finding of decreased breath sounds on the left. Lung ultrasound was performed on admission and video-assisted thoracoscopic surgery (VATS) the next day. There was a complete match of lung ultrasound **(a)** and VATS **(b)** findings of massive dense pleural effusion (*), with thick fibrin layers on both visceral and parietal pleural surfaces (□), and numerous fibrin filaments and strands floating within the pleural effusion (arrow heads). C - consolidation. **c)** VATS showing an extensive fibrinous coating of both visceral and parietal pleural surface after evacuation of the pleural effusion.

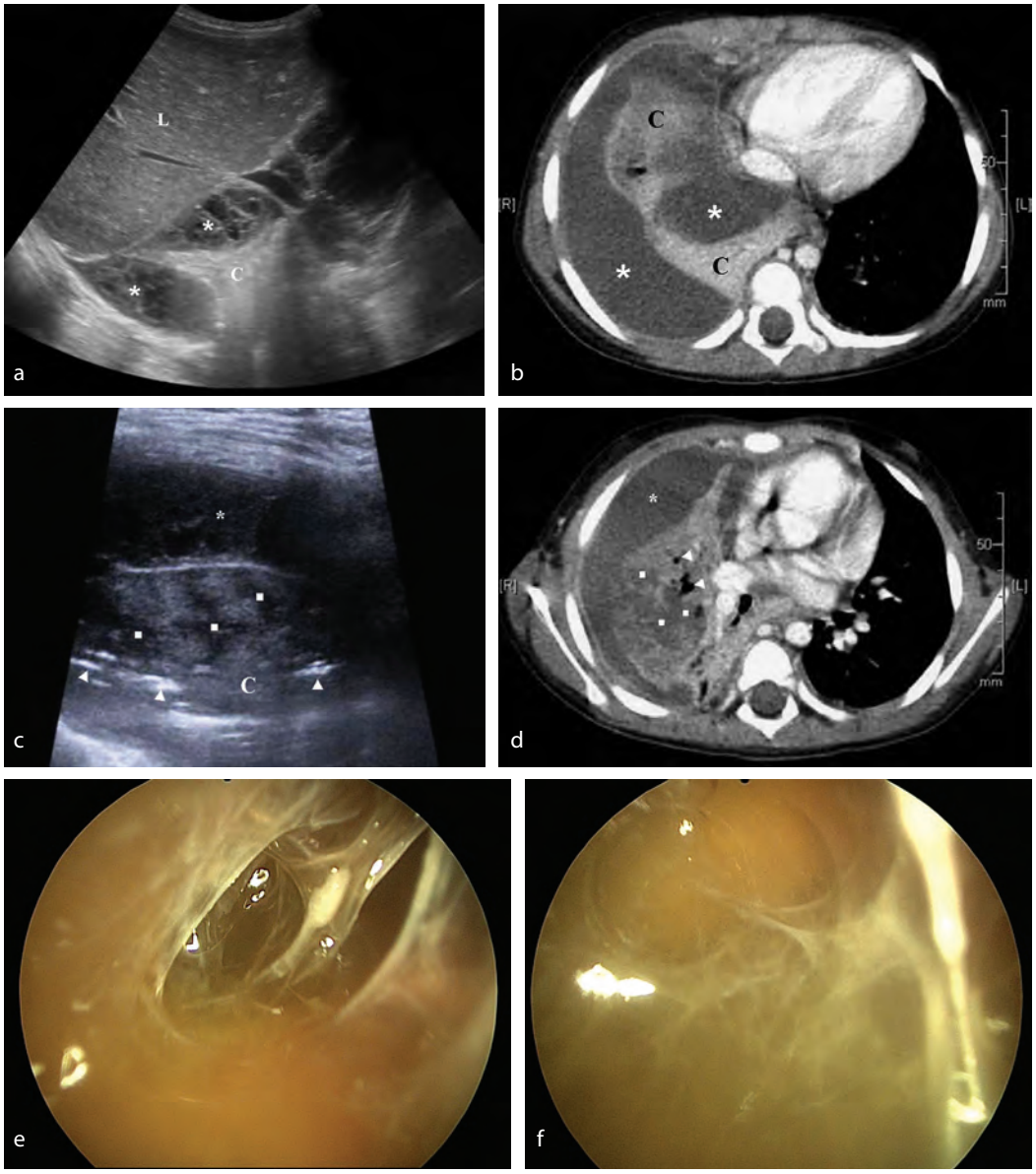


Figure 4 A 3-year old girl who was treated as an outpatient for 8 days by a local pediatrician, receiving antibiotic therapy for 5 days, was admitted to the Pediatric Emergency Department with tachypnea, tachycardia, and fever (38.3°C). Auscultation showed asymmetric breath sounds, and both early and late inspiratory crackles on the right. Lung ultrasound **(a, c)** and CT performed the next day **(b, d)** showed lung consolidations (C) with necrotic areas (□) and a small amount of air (arrow heads), as well as massive pleural effusion (*). However, lung ultrasound, unlike CT, detected numerous fibrin strands within the pleural effusion. L - liver. **e, f)** Video assisted thoracoscopy confirmed the ultrasound finding of multiple fibrin strands within the pleural space.

Discussion

Although LUS has been used for a shorter period of time than CT, and especially CXR, we cannot refer to it as a new diagnostic technique. It simply has not been as widely excepted as perhaps it should be. A large number of studies have already compared LUS with CXR, and proved its superiority in the evaluation of not only the pleural space, but also the lung parenchyma, especially in detecting pneumonia, both in adults and children (1-4, 6, 8, 9, 16-19). Only a few studies have compared LUS with CT findings, which is highly reasonable considering the ionizing radiation and consequent ethical issue (2, 4, 5, 7, 10, 11). However, we found only one study comparing LUS and auscultation findings, but not a single study comparing them in children with suspicion of pneumonia (12). In that one study, Lichtenstein et al. showed the higher diagnostic accuracy of LUS in comparison to auscultation and bedside CXR in detection of pleural effusion, alveolar consolidation and alveolar-interstitial syndrome (12). It is well known that the diagnosis of pneumonia simply by physical examination, history taking, and specific auscultatory findings is not reliable, even in expert hands (20). However, on the other hand, when there is a diagnostic modality such as LUS, which has still not been widely accepted, it is expected and understandable that clinicians are suspicious of positive US findings which they do not recognize using auscultation. This was the reason why we focused our study almost solely on a comparison of findings from an ultrasound probe and a stethoscope, in children with suspected pneumonia.

LUS has been used as a routine diagnostic procedure in our tertiary health care, regional children's hospital for seven years, and during this period it has served as a very reliable imaging method. We mostly use it in detecting pneumonia in children of all ages, and pulmonary diseases in preterm infants, as well as for their follow-up, which has been reported in three of our studies (18, 21, 22). The use of LUS in newborns was also reported by Copetti et al. (23, 24). On the basis of a number of studies showing the high sensitivity and specificity of LUS in detecting pneumonia, greater than CXR, as well as our substantial experience derived from everyday clinical practice, all patients with LUS positive findings are treated as having pneumonia.

Comparing the groups with positive and negative auscultatory findings with regard to the 95% CI of the CC diameter of lung consolidations, we determined that there is a 30 mm threshold size of the consolidation for auscultatory findings. This suggests that in 95% of auscultatory examinations it is not possible to determine the presence of the consolidation of lung parenchyma with a CC diameter less than 30 mm, which indicates the limited possibilities of physical diagnostics, predominantly in early pneumonic changes and those of smaller extent. McNemar's test showed a statistically significant difference in performance between LUS and auscultation.

We compared LUS with VATS and CT findings in only 2 children (1 VATS, 1 VATS and CT), and the match was almost perfect. In one child, LUS proved even more reliable in evaluating the internal components of pleural effusion in comparison to the CT, which was in concordance with the published data (5, 10, 11). This information had an important impact on the therapy, because a pediatric surgeon decided to perform VATS, instead of only placing a chest tube. In the second child, a 16-year old boy, information provided by US led directly to the VATS procedure, which was performed without a previous chest CT examination. LUS served here as an outstanding tool in avoiding the patient's exposure to a very

high effective dose of potentially harmful ionizing radiation.

We have already proposed the use of a combined, trans-abdominal and trans-thoracic approach (18, 21, 22). This was based on the observations made in our daily clinical practice, indicating that the TA approach can occasionally provide additional information about the extensiveness of pathological findings within the lung base. However, for the first time, in one child, we faced the situation where a positive US finding was detected using the trans-hepatic approach, whereas the TT approach showed a normal LUS pattern. The pathological finding within the right lung base was seen medially in its middle section when angulating the probe from the most anterior to the most posterior position. In entirely anterior and posterior sections of the right lung base, the US findings were normal, presenting with the acoustic phenomenon of "mirror image". The reason why these pulmonary changes were undetected by the TT approach is probably their position within the centre of the right lung base, not reaching the anterior, lateral, or posterior costal pleural surfaces (which would be mandatory for the trans-thoracic visualization), but only the basal pleura. This is the reason why the TT approach should be accompanied by the TA approach, although even recently published studies, both in children and adults, have reported only the TT approach as a sufficient LUS technique to diagnose pneumonia (1, 2, 16, 17). It is important to say that the low TT approach used in these studies is exactly the same as the TA approach with regard to the costo-phrenic angles, but should not be equated with regard to the lung base parenchyma, because using solely the TT technique would have resulted in one false-negative finding of pneumonia in our study, which is not negligible. This case of pneumonia was proved using CXR. The pathological US finding observed within the lung base by the TA approach only was completely resolved after antibiotics treatment. The regular use of the additional trans-abdominal US approach might increase the sensitivity of the LUS, which is already high. The implementation of the additional TA approach would decrease the delay, especially in the diagnosis of early stages of pneumonia in some patients, which is extremely important from the aspect of potential complications in children with pneumonia which is unrecognized at the time of the first LUS examination.

LUS imaging for the detection of pneumonia is highly reliable, but like most diagnostic tests, it is not perfect. It is very hard to strictly define a pneumonia-positive US finding, because there is a wide range of positive findings, depending on the stage of pneumonia caught at the time of examination. These findings may encompass the following: solely the areas of confluent B lines, subpleural consolidations, without an air bronchogram (so called hepatization), subpleural consolidations with adjacent areas of B lines, extremely small subpleural consolidations with sizes of less than 5 mm, and subpleural consolidation with an air-bronchogram as a most typical US finding (1-3, 14, 15, 25). It is also hard to distinguish bacterial pneumonic consolidation from subsegmental atelectasis due to viral pneumonia. Anyhow, we have to be aware that in some cases LUS findings are non-specific and have to be compared to and associated with clinical findings, so that we may determine the true etiology of pulmonary changes (21). Auscultation does, and will always have its place in diagnosing pulmonary diseases, especially those with a very limited or the still insufficiently explored role of LUS, such as acute bronchitis or bronchiolitis. Therefore, we propose the use of LUS whenever the physical finding is unclear, without exposing children to unnecessary CXRs.

Anyone accessing the world of lung ultrasonography has to be aware of its limitations, such as the inability to detect pulmonary changes not abutting pleura, pathological findings within hilar regions, and air-filled lung abscesses. However, the current literature suggests that most consolidations (up to 98%) will contact the pleura and are US detectable (26). As with any other US application, operator competency is very important, and error may occur if the operator is not properly trained and experienced. In our study, all LUS examinations were performed by a pediatric radiologist very experienced in this field. This fact probably resulted in the very short average time needed for LUS examination (5.7 minutes). However, this time can be quite variable, depending on the age of the child (older child - larger thorax surface to examine), the child's cooperation during the exam, as well as the complexity of the finding (more complicated finding - longer exam and report).

This study has several limitations. In the course of our study the greatest problem was the lack of a gold standard for diagnosis of pneumonia. It was not feasible to prove all the LUS and auscultatory findings by CT, which is considered to be the diagnostic gold standard in this field, but it cannot be used on a regular basis for ethical reasons, namely due to the high exposure to ionizing radiation. This was the reason why we could not calculate the sensitivity and specificity of LUS and auscultation. The pediatric radiologist performing LUS was aware of the clinical referral diagnosis. However, the great majority of children sent to the Radiology Department of our hospital for LUS have a clinician's referral diagnosis of pneumonia, so it is very easy to work it out even when this information is not immediately accessible. Furthermore, each LUS was performed and interpreted by a single pediatric radiologist, which creates a bias in the research. However, in real life, we believe that each clinician would prefer to have a finding from an experienced operator rather than from someone who is still becoming familiar with the technique, which is the case with other pediatric radiologists from our department. The operator tried to preserve objectivity by not knowing anything else about the patient, except the referral diagnosis. It was not possible to define bacterial and viral pneumonias clearly (blood culture, when obtained, was negative due to antibiotic treatment before admission to our hospital, and serology for respiratory viruses, *Chlamydia* and *Mycoplasma pneumoniae* when performed were negative). However, no distinction between bacterial and viral pneumonia has been made in most articles dealing with this topic (1-3, 4, 6). In clinical practice, especially in underdeveloped countries, it is often virtually impossible to distinguish between bacterial and viral pneumonia, so antibiotic treatment is mostly empirical, based on the age and current epidemiological situation (27).

Conclusion

In conclusion, in children with clinically suspected pneumonia, lung ultrasound showed a positive finding in more hemithoraces than auscultation. A cranio-caudal size of a subpleural consolidation of less than 30 mm significantly reduced the possibility of auscultatory detection. The use of an additional trans-abdominal US approach, along with the standard trans-thoracic approach, is expected to result in a further increase of ultrasound sensitivity in diagnosing pneumonia, which is already high. Lung ultrasound is a reliable diagnostic tool, and should be implemented in everyday clinical practice whenever physical findings need to be complemented with imaging findings. Its application might to a certain extent exclude the need for imaging modalities based on

ionizing radiation, which would strongly support the Image Gently campaign.

What is already known on this topic

Lung ultrasound is an extremely valuable diagnostic tool in detecting pneumonia in children of all ages, with higher sensitivity and specificity than chest X-ray, shown by a number of studies. However, only one study in the published literature has compared lung ultrasound and auscultation findings, but not in pediatric patients with suspicion of pneumonia.

What this study adds

Our study shows more positive lung ultrasound findings compared to auscultation in children with suspected pneumonia, and establishes the threshold size of subpleural consolidations below which it is highly unlikely that pneumonia will be detected by auscultation. This is very important from the aspect of expectations from both diagnostic methods, and their reliability in everyday clinical practice. When the physical finding is unclear, lung ultrasound can provide valuable information for the clinician, without using ionizing radiation in children, supporting the "Image gently" campaign.

Authors' contributions: Conception and design: LJ, PS and BBS; Acquisition, analysis and interpretation of data: LJ, PS, BBS, VDG and JR; Drafting the article: LJ; Revising it critically for important intellectual content: JR and PS. Approved final version of the manuscript: LJ, PS, BBS, VDG and JR.

Conflict of interest: The authors declare that they have no conflict of interest.

References

1. Caiulo VA, Gargani L, Caiulo S, Fisicaro A, Moramarco F, Latini G, et al. Lung ultrasound characteristics of community-acquired pneumonia in hospitalized children. Pediatr Pulmonol. 2013;48(3):280-7.
2. Reissig A, Copetti R, Mathis G, Mempel C, Schuler A, Zechner P, et al. Lung ultrasound in the diagnosis and follow-up of community-acquired pneumonia: a prospective, multicenter, diagnostic accuracy study. Chest. 2012;142(4):965-72.
3. Copetti R, Cattarossi L. Ultrasound diagnosis of pneumonia in children. Radiol Med. 2008;113(2):190-8.
4. Parlamento S, Copetti R, Di Bartolomeo S. Evaluation of lung ultrasound for the diagnosis of pneumonia in the ED. Am J Emerg Med. 2009;27(4):379-84.
5. Kurian J, Levin TL, Han BK, Taragin BH, Weinstein S. Comparison of ultrasound and CT in the evaluation of pneumonia complicated by parapneumonic effusion in children. AJR Am J Roentgenol. 2009;193(6):1648-54.
6. Cortellaro F, Colombo S, Coen D, Duca PG. Lung ultrasound is an accurate diagnostic tool for the diagnosis of pneumonia in the emergency department. Emerg Med J. 2012;29(1):19-23.
7. Nazerian P, Volpicelli G, Vanni S, Gigli C, Betti L, Bartolucci M, et al. Accuracy of lung ultrasound for the diagnosis of consolidations when compared to chest computed tomography. Am J Emerg Med. 2015;33(5):620-5.
8. Bourcier JE, Paquet J, Seinger M, Gallard E, Redonnet JP, Cheddadi F, et al. Performance comparison of lung ultrasound and chest x-ray for the diagnosis of pneumonia in the ED. Am J Emerg Med. 2014;32(2):115-8.
9. Esposito S, Sferrazza Papa S, Borzani I, Pinzani R, Giannitto C, Consonni D, et al. Performance of lung ultrasonography in children with community-acquired pneumonia. Ital J Pediatr. 2014;40:37.
10. Khalil M, Samy Diab H, Hosny H, Edward E, Thabet E, Emara W, et al. Chest ultrasound versus chest computed tomography for imaging assessment before medical thoracoscopy. Egypt J Bronchol. 2014;8(2):149-52.
11. El Sheikh H, Abd Rabboh MM. Chest ultrasound in the evaluation of complicated pneumonia in the ICU patients: Can be viable alternative to CT? The Egypt Journal of Radiology and Nuclear Medicine. 2014;45(2):325-31.
12. Lichtenstein D, Goldstein I, Mourgeon E, Cluzel P, Grenier P, Rouby JJ. Comparative diagnostic performances of auscultation, chest radiography, and lung ultrasonography in acute respiratory distress syndrome. Anesthesiology. 2004;100(1):9-15.
13. Cosgrove DO, Garbutt P, Hill CR. Echoes across the diaphragm. Ultrasound Med Biol. 1978;3(4):385-92.
14. Tsung JW, Kessler DO, Shah VP. Prospective application of clinician-performed lung ultrasonography during the 2009 H1N1 influenza A pandemic: distinguishing viral from bacterial pneumonia. Crit Ultrasound J. 2012;4(1):16.
15. Tsai NW, Ngai CW, Mok KL, Tsung JW. Lung ultrasound imaging in avian influenza A (H7N9) respiratory failure. Crit Ultrasound J. 2014;6(1):6.
16. Blaivas M. Lung ultrasound in evaluation of pneumonia. J Ultrasound Med. 2012;31(6):823-6.
17. Shah VP, Tunik MG, Tsung JW. Prospective evaluation of point-of-care ultrasonography for the diagnosis of pneumonia in children and young adults. JAMA Pediatr. 2013;167(2):119-25.

18. Lovrenski J, Petrović S, Varga I, Varga J. Pneumonias in children – comparison of lung ultrasonography findings with chest X-rays. Paediatr Croat. 2013;57(3):227-34.
19. Hu QJ, Shen YC, Jia LQ, Guo SJ, Long HY, Pang CS, et al. Diagnostic performance of lung ultrasound in the diagnosis of pneumonia: a bivariate meta-analysis. Int J Clin Exp Med. 2014;7(1):115-21.
20. Wipf JE, Lipsky BA, Hirschmann JV, Boyko EJ, Takasugi J, Peugeot RL, et al. Diagnosing pneumonia by physical examination: relevant or relic? Arch Intern Med. 1999;159(10):1082-7.
21. Lovrenski J. Lung ultrasonography of pulmonary complications in preterm infants with respiratory distress syndrome. Ups J Med Sci. 2012;117(1):10-7.
22. Lovrenski J, Sorantin E, Stojanović S, Doronjski A, Lovrenski A. Evaluation of surfactant replacement therapy effects - a new potential role of lung ultrasound? Srp Arh Celok Lek. 2015;143(11-12):669-75.
23. Copetti R, Cattarossi L. The 'double lung point': an ultrasound sign diagnostic of transient tachypnea of the newborn. Neonatology. 2007;91(3)203-9.
24. Copetti R, Cattarossi L, Macagno F, Violino M, Furlan R. Lung ultrasound in respiratory distress syndrome: a useful tool for early diagnosis. Neonatology. 2008;94(1):52-9.
25. Lichtenstein DA, Meziere GA. Relevance of lung ultrasound in the diagnosis of acute respiratory failure: the BLUE protocol. Chest. 2008;134(1):117-25.
26. Lichtenstein DA, Lascols N, Meziere G, Gepner A. Ultrasound diagnosis of alveolar consolidation in the critically ill. Intensive Care Med. 2004;30(2):276-81.
27. Virkki R, Juven T, Rikalainen H, Svedstrom E, Mertsola J, Ruuskanen O. Differentiation of bacterial and viral pneumonia in children. Thorax. 2002;57(5):438-41.

Original article

Acta Medica Academica 2016;45(1):51-60
DOI: 10.5644/ama2006-124.156

The ultrasonographic determination of the position of the mental foramen and its relation to hard tissue landmarks

Abdullah Ebrahim Laher*, Zeyn Mahomed

Division of Emergency Medicine
Charlotte Maxeke Johannesburg
Academic Hospital, University of
the Witwatersrand South Africa

*Corresponding author:
abdullahlaher@msn.com
Tel.: + 278 48 402 508
Fax.: + 271 18 430 646

Received: 14 January 2016
Accepted: 6 April 2016

Key words: Ultrasound ▪ Mental foramen ▪ Mental nerve ▪ Hard tissue landmarks.

Objective. The goal of this ultrasound based cross-sectional study was to make use of ultrasound to determine the position of the mental foramen in relation to hard tissue landmarks. **Material and methods.** One hundred Black and Caucasian subjects were included. An ultrasound transducer was used to locate the mental foramina. Distances to various landmarks were measured and compared. **Results.** All mental foramina were visualised ultrasonographically. The mean distances to various landmarks from the mental foramen for the entire group on the right and left sides respectively were as follows: a) 22.8 mm (SD 2.04 mm) and 22.8 mm (SD 2.0 mm) to the cusp of the related tooth, b) 13.2 mm (SD 1.6 mm) and 13.2 mm (SD 1.6 mm) to the inferior border of the mandible. The mean position of the mental foramen was found to be 63.4% (SD 1.8%) of the distance from the cusp of the related tooth to the inferior border of the mandible on the right and 63.3% (SD 1.7%) on the left. There were statistically significant differences between race groups and genders, but not between age groups. **Conclusion.** These results suggest that ultrasound is a sensitive modality to locate the mental foramen. There are minor, statistically significant (but clinically insignificant) differences in the position of the mental foramen with regard to various hard tissue landmarks.

Introduction

The mental foramen is located on either side of the mandible just below the corners of the lips, around the region of the root of the second premolar tooth (1). The mental nerve emerges from the mental foramen and provides sensation to the lower central portion of the face (1, 2).

Dentists, oral maxillofacial surgeons, emergency physicians, and plastic and reconstructive surgeons are required to be knowledgeable regarding the anatomy of the mental foramen and variations in its position, for the purpose of achieving local anaesthesia as well as planning various surgical procedures (3, 4). Procedures important to the anatomy of the mental foramen include: tooth extractions, root canal treatment, scaling, polishing, treatment of gingival disease, removal of cysts and tumors, repair of lower lip and chin lacerations, reconstructive soft tissue procedures, endodontic/orthogenetic surgery, fixation of bone fractures and implant placement (5-7). Variation in the anatomy and position of the mental foramen, with regard to race, age and gender, play an important role (8-12). The mental foramen and the various modalities useful in locating the mental foramen have been reviewed in detail elsewhere (13).

Local anaesthesia infiltration and surgical procedures in the vicinity of the mental nerve may be complicated by temporary or permanent sensory dysfunction and paraesthesia as a result of injury to the mental nerve (14, 15). Therefore the accurate determination of the position of the mental foramen is important to all clinicians concerned.

The aim of this ultrasound based cross sectional study was to determine the position of the mental foramen in relation to hard tissue landmarks using ultrasound.

Materials and methods

In the preparation prior to this study, ultrasound echogenic markers were placed at the mandibular border and cusp tip to ensure that the image limits seen on the monitor screen correlated with the distances measured without markers (Figure 1 and 2).

In this study we enrolled 100 Adult Black and Caucasian (White and Asian) patients, older than 18 years who presented to the CMJAH ED (Figure 3). Patients

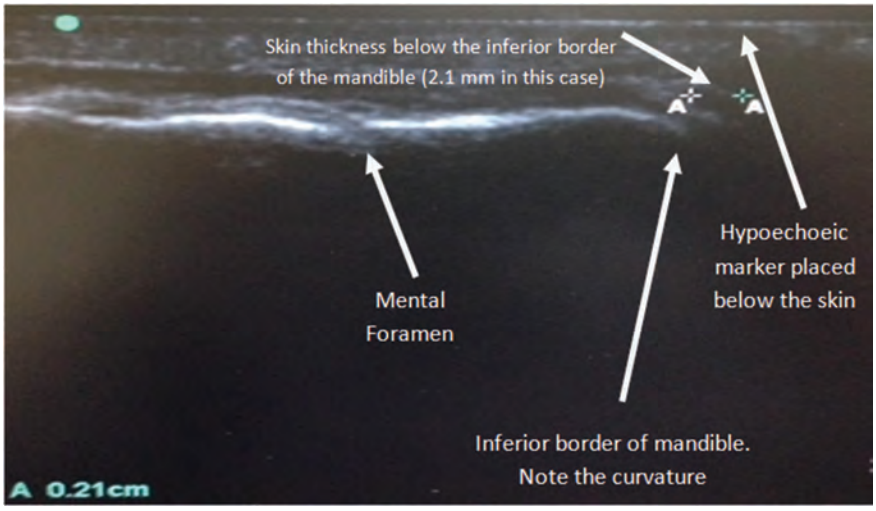


Figure 1 Ultrasound image showing the inferior border of the mandible and the mental foramen.

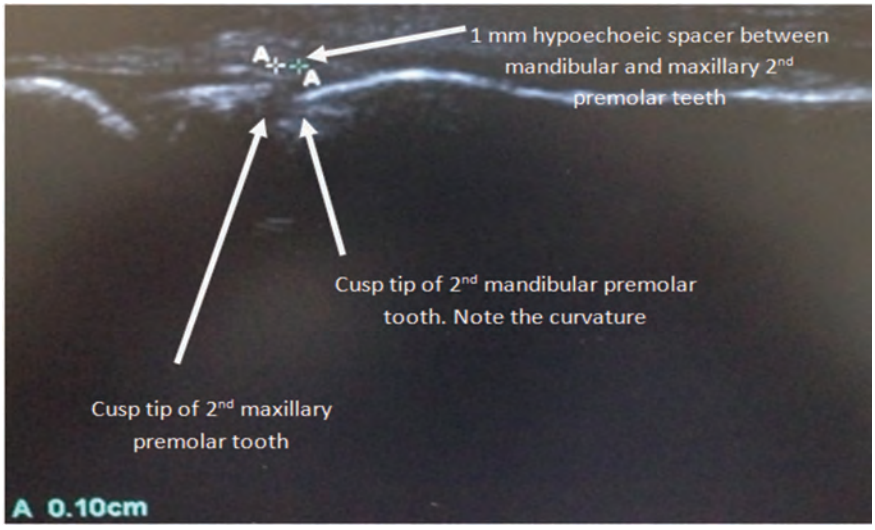


Figure 2 Ultrasound image showing cusp tips of the 2nd premolar teeth with interposing 1 mm hypoechoic spacer.

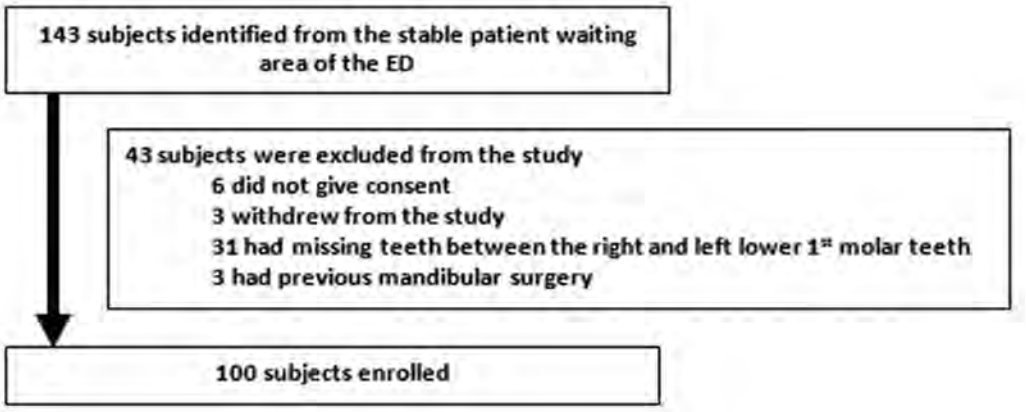


Figure 3 Exclusions and final sample for analysis.

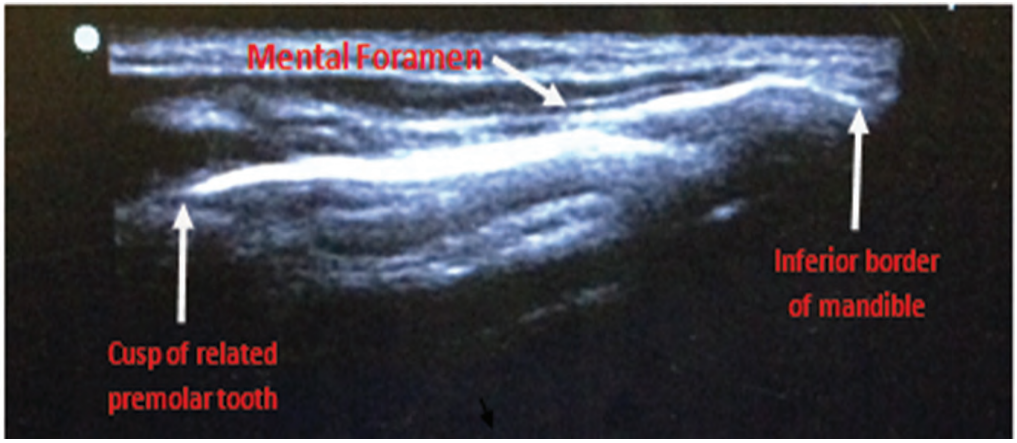


Figure 4 Ultrasound image of the mental foramen and its hard tissue relations. The mental foramen is easily identified as a break in the continuity of the bone in the vicinity just below the corner of the mouth.

were randomly selected from the ED queue at a time convenient to the researcher. The last patient waiting in the ED queue to see a doctor for his/her presenting complaint was approached first for participation in the study. Patients were approached in this manner so as not to lengthen their waiting time in the ED queue for the purpose of their visit. Potential participants were given an information leaflet. Eligible volunteers, who consented to participate in the study, were made to lie in the supine position in an examination cubicle. We used a Toshiba diagnostic ultrasound system (model SSA-510A) and a high frequency (8MHz) transducer (PLF.805ST) with the machine set on the "small parts" preset mode. The length of the transducer covered the distance between the related cusp tip and the inferior border of the mandible in all cases. Sonar gel (Konix ultrasound gel, Sanichem, Durban, South Africa) was applied to the ultrasound transducer once the machine was in running mode. The transducer, with the marker facing cranially, was gently applied just lateral to the mentum. The mental foramen was identified and the appropriate image frozen (Figure 4). The cusp to mental foramen and the inferior border of the mandible to mental foramen distances were measured and documented. Participants were asked to maintain a neutral facial ex-

pression during measurements. The above procedure was repeated on the opposite side of the face. After documenting relevant data, excess gel was gently cleaned off and the volunteer thanked. Any difficulties experienced during the investigation were documented. Individuals with congenital / acquired facial distortion, a history of mandibular surgery and patients who had mandibular teeth missing between the right and left lower 1st molars were excluded from the study. Details of patient recruitment and exclusion are listed in the flow diagram in figure 3.

Patient confidentiality was respected at all times. Data collection sheets did not include personal data. Only relevant demographic data was included. The information gathered was protected by a coded numbering system, which was stored in a password-protected computer that was only accessible to the researcher.

Ethics statement

Permission to conduct the study was obtained from the head of department (H.O.D) of the CMJAH ED and the hospital management. Clearance was obtained from the Human Research Ethics Committee of the University of the Witwatersrand (certificate no. M110920).

Statistical analysis

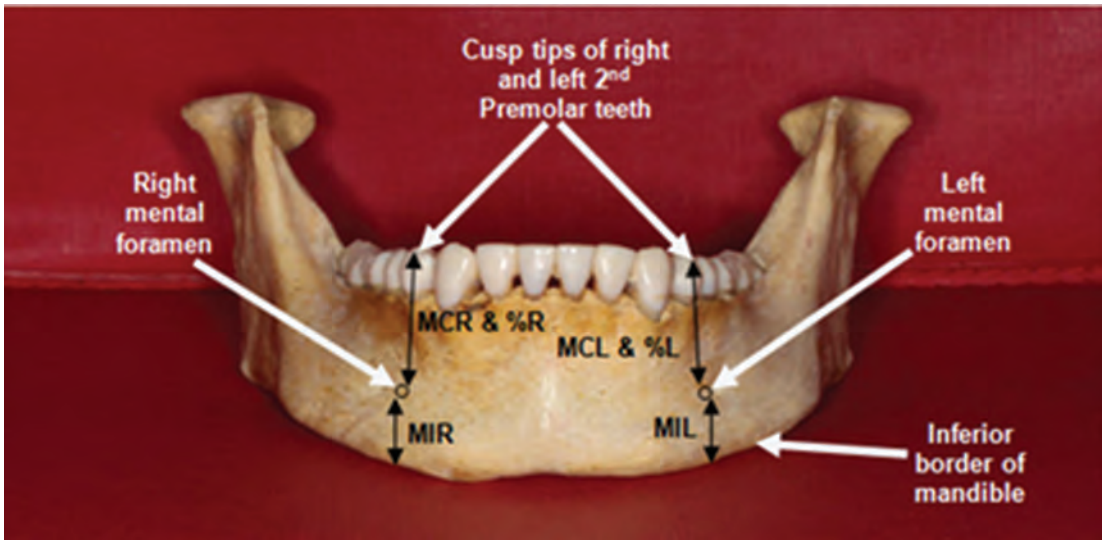
All data were captured from the data collection sheets by the primary investigator and entered into an electronic spreadsheet (Microsoft® Excel®). STATA® version12.1 software (StataCorp LP) was used to analyze all data. Each volunteer was placed into an age category: a) 18-30 yrs, b) 31-40 yrs, c) 41-50 yrs, d) 51-60 yrs, e) 61-70 yrs. Means and standard deviations were calculated for continuous variables (measurements obtained). The means of measurements obtained (continuous variable) for age group, gender and race (categorical variables) were compared. Normal (Gaussian) distribution and equal variance of the data were confirmed using the Kolmogorov–Smirnov and Barnett's tests, respectively. Data were statistically analyzed using one-way ANOVA. Where appropriate, the Student's-T-test and Bonferroni post hoc analysis were performed. The level of significance was set at α=0.05, CI=95%. Study reporting conformed to STROBE guidelines (16).

Results

The total sample of 100 subjects consisted of 50 Blacks (27 males and 23 females) and 50 Caucasians (23 males and 27 females). The Caucasians were further subdivided into 25 Asians (13 males and 12 females) and 25 Whites (10 males and 15 females). The overall sex distribution was equal and (50 males and 50 females). The overall mean age of the study population was 35.7 years (SD 1.9 years).

All mental foramina (100%) were ultrasonographically identified. Figures 5 and 6 respectively describe the hard tissue distances that were measured and the mean measurements for the entire group. Table 1 describes the age group frequencies of the various race groups studied and Table 2 describes the impact of race, gender and age on the position of the mental foramen, with regard to distances to hard tissue landmarks.

A significant difference was found between races and between genders for the distances from the mental foramen to the various hard tissue landmarks. However there were no statistically significant differences between age categories. This is presented in Table 2.



MCR=Vertical distance from the mental foramen to the cusp of the concerned tooth on the right. MIR=Vertical distance from the mental foramen to the inferior border of the mandible on the right. %R=The proportion of the distance (in percentage) of the position of the mental foramen from the cusp of the related tooth to the inferior border of the mandible on the right (i.e. MCR / MCR + MIR). MCL=Vertical distance from the mental foramen to the cusp of the concerned tooth on the left. MIL=Vertical distance from the mental foramen to the inferior border of the mandible on the left. %L=The proportion of the distance (in percentage) of the position of the mental foramen from the cusp of the related tooth to the inferior border of the mandible on the left (i.e. MCL / MCL + MIL).

Figure 5 Frontal view of the mandible showing horizontal hard tissue measurements.

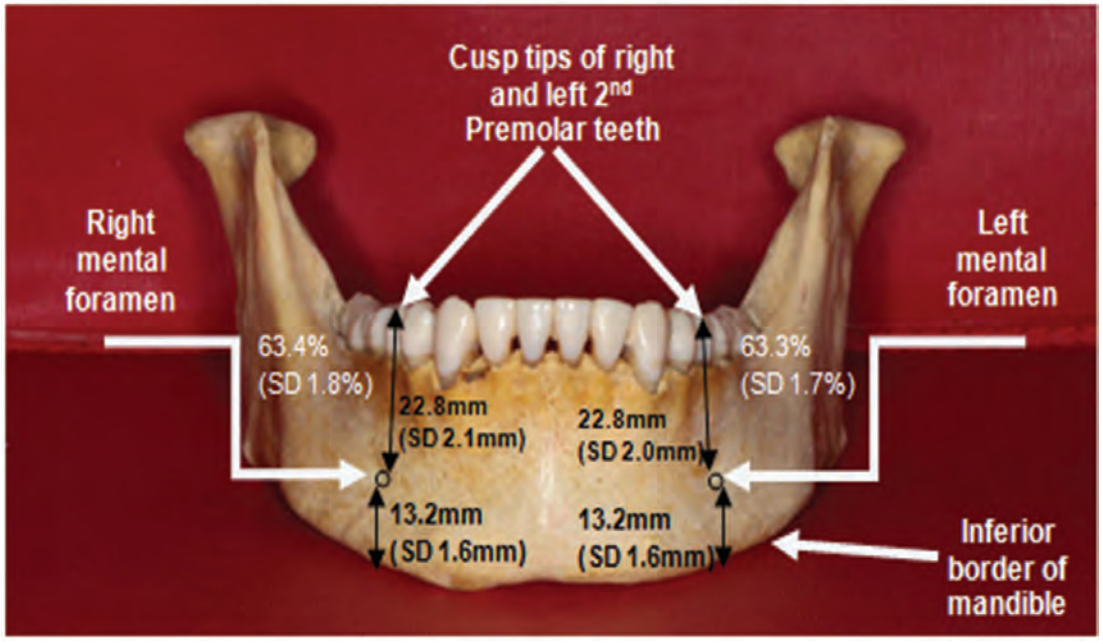


Figure 6 Frontal view of the mandible showing the various mean horizontal hard tissue measurements for the entire group of participants.

Table 1 Age group frequencies of the various race groups studied

Race	Age Group (yrs)					
	18-30	31-40	41-50	51-60	61-70	Mean (SD)
Black	18	20	8	3	1	34.7 (10.4)
Asian	13	6	3	3	-	33.5 (11.6)
White	9	3	5	7	1	39.9 (11.6)
Total	40	29	16	13	2	35.7 (11.1)

Table 2 The impact of race, gender and age with regard to the distance from the mental foramen to various hard tissue landmarks

Distances		All patients	Race			Gender		Age group (years)				
			Black	Asian	White	Female	Male	18-30	31-40	41-50	51-60	61-70
MCR (mm)	Mean	22.8	23.5	22.1	21.9	21.5	24.0	22.3	23.4	23.3	22.2	20.9
	SD	2	2.0	1.8	1.7	1.5	1.7	1.7	1.9	2.4	2.4	0.6
			ANOVA (p=0.0009)			T test (p=0.0000)		ANOVA (p=0.0671)				
MCL (mm)	Mean	22.8	23.5	22.1	22.1	21.6	24.0	22.4	22.4	23.4	22.3	20.8
	SD	2	1.9	1.7	2.0	1.4	1.7	1.7	1.9	2.3	2.4	0.6
			ANOVA (p=0.0023)			T test (p=0.0000)		ANOVA (p=0.0842)				
MIR (mm)	Mean	13.2	13.9	12.2	12.8	12.1	14.2	12.6	13.7	13.4	12.9	12.4
	SD	1.6	1.4	1.5	1.6	1.2	1.3	1.6	1.6	1.7	1.9	0.4
			ANOVA (p=0.0000)			T test (p=0.0000)		ANOVA (p=0.2487)				
MIL (mm)	Mean	13.2	13.9	12.2	12.7	12.1	14.2	12.8	13.7	13.3	12.9	12.5
	SD	1.6	1.4	1.4	1.6	1.2	1.3	1.5	1.5	1.8	1.8	0.8
			ANOVA (p=0.0000)			T test (p=0.0001)		ANOVA (p=0.2263)				
%R (mm)	Mean	63.4	62.9	64.5	63.4	63.9	62.9	63.6	63.2	63.6	63.2	62.8
	SD	1.8	1.3	2.0	2.0	1.9	1.5	2.0	1.4	1.8	1.9	0.0
			ANOVA (p=0.0007)			T test (p=0.0037)		ANOVA (p=0.8039)				
%L (mm)	Mean	63.3	62.8	64.3	63.4	63.9	62.8	63.6	63.1	63.5	63.1	62.4
	SD	1.7	1.5	1.8	1.9	1.8	1.6	1.9	1.6	1.8	1.6	1.0
			ANOVA (p=0.0020)			T test (p=0.0019)		ANOVA (p=0.6668)				

MCR=Vertical distance from the mental foramen to the cusp of the concerned tooth on the right; MIR=Vertical distance from the mental foramen to the inferior border of the mandible on the right; %R=The proportion of the distance (in percentage) of the position of the mental foramen from the cusp of the related tooth to the inferior border of the mandible on the right (i.e. MCR MCR + MIR); MCL=Vertical distance from the mental foramen to the cusp of the concerned tooth on the left; MIL=Vertical distance from the mental foramen to the inferior border of the mandible on the left. %L=The proportion of the distance (in percentage) of the position of the mental foramen from the cusp of the related tooth to the inferior border of the mandible on the left (i.e. MCL/MCL+MIL).

Discussion

This was a prospective, cross-sectional observational study of patients who presented to a single center ED (Charlotte Maxeke Johanesburg Academic Hospital (CMJAH), Johannesburg, South Africa) between February 2012 and March 2013. CMJAH is a tertiary care facility in a large urban environment, and is affiliated with the University of the Witwatersrand.

In this study, we identified 100% of mental foraminae by ultrasound. By applying the ultrasound probe just lateral to the mentum, the mental foramen is easily recognized as a break in the continuity of the bone. There are no other similar ultrasonographic structures that may be confused with the mental

foramen in this region. Jacobs et al. reported detection of the mental foramen in 94% of panoramic radiographs, and only 49% were clearly visible (17), whilst the mental foramen was visualized in only 84.2% of cases in an Iranian study that also assessed panoramic radiographs (18). An earlier study that assessed periapical films reported detection rates of the mental foramen in only 46.8% of cases (19). Therefore the use of ultrasonography to identify the mental foramen may be regarded as superior to panoramic and periapical films. It is also a safer option, with no known side effects or risk of radiation exposure (20).

Sixty-nine percent of subjects were under the age of 40 years and only 2% of subjects were older than 60 years. The reason that most of our subjects were under 40 years of age was due to the fact that with advancement in age, the incidence of missing teeth between the right and left mandibular 1st molars is higher. Therefore, many potential subjects that were approached to participate in the study were excluded as they had missing teeth between the right and left 1st mandibular molars.

The mean vertical distance of the entire group of subjects from the buccal cusp tip of the concerned tooth to the mental foramen was 22.8mm (SD 2.0 mm) on the right and 22.8 mm (SD 2.0 mm) on the left side. Differences between all race groups were minimal at around 1 mm. Although these differences are statistically significant, they are however minimal and are not regarded significant from a practical or clinical point of view. In males, the mean distances were about 2.5 mm longer than in females ($p<0.05$). Average distances of 23.34mm and 25.69mm have been recorded in Chinese and Korean populations respectively (21, 22).

The mean vertical distance of the entire group of subjects from the inferior border of the mandible to the mental foramen was 13.2 mm (SD 1.6 mm) on the right and 13.2 mm (SD 1.6 mm) on the left side. The mean difference between racial groups was approximately 1 mm ($p<0.05$). In males the mean distances were about 2 mm longer than in females. In studies on American and Indian subjects, the mean distance has been reported as 12.9 mm and 16.5mm respectively (9, 23). Other studies documented distances between the above (10, 21, 22, 24-28).

No previous published studies have compared differences between race groups, between genders or between age groups with regard to the buccal tip to mental foramen distance or the inferior border of the mandible to mental foramen distance. However the distance from the mental foramen to the symphysis menti, and from the mental foramen to the posterior border of the ramus has been previously studied and compared between population groups (10, 29, 30).

The mean position of the mental foramen for the entire group of subjects in this study was 63.4% (SD 1.8%) of the distance from the cusp of the related tooth to the inferior border of the mandible on the right (%R) and 63.3% (SD 1.7%) on the left (%L) side. The mean position of the mental foramen was lowest in Asians, then Whites and then Blacks. They were all however within 2% of each other. The mental foramen was located about 1 mm lower in females compared to males ($p<0.05$). An American study located the mental foramen at an average of approximately 60% of the distance between the buccal cusp tip and the inferior border of the mandible (31). A Korean study compared dry skulls with panoramic radiographs, and concluded that the average distance ratio from the buccal cusp tip to the inferior border of the mandible was 60.6% on dry skulls and 63.6% on panoramic radiographs (22). A study using panoramic X-ray images looked at ideally positioned and systematically mis-positioned skulls, to evaluate for errors in linear measurements and symmetry ratios. The study concluded that panoramic radiographs should be in-

terpreted with caution for absolute measurements or relative comparisons, even when internal fiducial calibration for image distortion of anatomy is used (32). Ultrasonographic techniques make use of direct measurement and do not have the negative effect of radiographs, where angles and curves are not taken into account.

A limitation to the use of ultrasound includes the fact that ultrasonography is operator dependent. Therefore, all ultrasound examinations and data collection were conducted by the primary investigator, who is certified for emergency ultrasound by the College of Emergency Medicine of South Africa. The study was fully supervised by a faculty member of the division of emergency ultrasound of the College of Emergency Medicine of South Africa. Another limitation to our study is that we excluded patients with congenital / acquired facial distortions, patients with a history of mandibular surgery, and patients who had mandibular teeth missing between the right and left lower 1st molars. Perhaps the mental foramen may not have been as easily found with ultrasonography in these patients as a result of positional change or distortion of the mental foramen. Studies have reported a change in the position of the mental foramen with regard to hard tissue landmarks in subjects with advanced age, tooth wear and loss of teeth (8, 11, 12, 33). We did not find any statistically significant differences between age groups in our study. A likely reason is that more than two thirds of the subjects in our study were under 40 years old, and only 2% of the subjects were older than 60 years. Further studies using ultrasonography and hard tissue landmarks will be required to see if the same holds true in patients with advanced age, tooth wear and tooth loss.

Conclusion

Ultrasonography, regarded as the 21st century stethoscope in the Emergency Department (34), is a cost effective, time saving, non-invasive, safe modality, with no risk of radiation exposure (20). It has many uses in the Emergency Department, including regional nerve block anesthesia, and can be used as a diagnostic, as well as an interventional tool (35). Theoretically, the use of ultrasonography for mental nerve blocks would decrease the need for local anesthesia, increase first time success rates and decrease complication rates. Traxler et al. used ultrasound in 1992 to determine the alveolar ridge width for purposes of dental implants. They also commented that ultrasound provided accurate information about the position of the mental foramen, as a secondary finding (36). Recently, Møystad and colleagues used ultrasound to evaluate the size of the mental foramen in patients with unilateral neurosensory dysfunction after third molar removal (37). More recently, Chan and colleagues, in a proof of concept study, compared CBCT scans with real-time ultrasound. They commented that hard tissue surfaces, including enamel, root dentin, and bone, as well as soft tissues and the mental foramen, were easily visualized. Various ultrasonographic measurements correlated well with the measurements obtained from CBCT scans (38). Point of care / hand held ultrasound devices, as well as recent advances in 3D ultrasonography, have the potential to revolutionize the practice of dento-maxillofacial surgery. A limitation to the use of ultrasonography is that it is operator dependent (34).

What is already known on this topic

The mental foramen is an important landmark for dentists, oral maxillofacial surgeons, emergency physicians, and plastic and reconstructive surgeons. The position of the mental foramen and nerve has been well reported in the dento-maxillofacial setting on cadaver specimens, intra-operatively and radiologically. The literature regarding the role of ultrasound in finding the mental foramen and other oro-facial structures is rather sparse.

What this study adds

Ultrasound has 100% sensitivity in accurately locating the mental foramen in normal human mandibles. There were mi-

nor, statistically significant (but clinically insignificant) differences in the position of the mental foramen across race, gender and age, with regard to various hard tissue landmarks. Point of care / hand held ultrasound devices have the potential to revolutionize the practice of dento-maxillofacial surgery.

Acknowledgements: We are grateful to the Charlotte Maxeke Johannesburg Academic Hospital for allowing us to use the ultrasound machine.

Authors' contributions: Conception and design: AL and ZM; Acquisition, analysis and interpretation of data: AL and ZM; Drafting the article: AL and ZM; Revising it critically for important intellectual content: AL and ZM; Approved final version of the manuscript: AL and ZM.

Conflict of interest: The authors declare that they have no conflict of interest.

References

1. Haghanifar S, Rokouei M. Radiographic evaluation of the mental foramen in a selected Iranian population. Indian J Dent Res. 2009;20(2):150-2.
2. Hell B, Freitag V. Lower lip carcinoma. Infiltration of the mandible along the mental nerve. J Craniomaxillofac Surg. 1988;16(2):76-9.
3. Song WC, Kim SH, Paik DJ, Han SH, Hu KS, Kim HJ, et al. Location of the infraorbital and mental foramen with reference to the soft-tissue landmarks. Plast Reconstr Surg. 2007;120(5):1343-7.
4. von Arx T, Friedli M, Sendi P, Lozanoff S, Bornstein MM. Location and dimensions of the mental foramen: a radiographic analysis by using cone-beam computed tomography. J Endod. 2013;39(12):1522-8.
5. Gianni AB, D'Orto O, Biglioli F, Bozzetti A, Brusati R. Neurosensory alterations of the inferior alveolar and mental nerve after genioplasty alone or associated with sagittal osteotomy of the mandibular ramus. J Craniomaxillofac Surg. 2002;30(5):295-303.
6. Juodzbalys G, Wang H-L, Sabalys G. Anatomy of Mandibular Vital Structures. Part II: Mandibular Incisive Canal, Mental Foramen and Associated Neurovascular Bundles in Relation with Dental Implantology. J Oral Maxillofac Res. 2010;1(1):e3.
7. Song Q, Li S, Patil PM. Inferior alveolar and mental nerve injuries associated with open reduction and internal fixation of mandibular fractures: A Seven Year retrospective study. J Craniomaxillofac Surg. 2014;42(7):1378-81.
8. Al-Khateeb T, Al-Hadi Hamasha A, Ababneh KT. Position of the mental foramen in a northern regional Jordanian population. Surg Radiol Anat. 2007;29(3):231-7.
9. Sankar DK, Bhanu SP, Susan PJ. Morphometrical and morphological study of mental foramen in dry dentulous mandibles of South Andhra population of India. Indian J Dent Res. 2011;22(4):542-6.
10. Santini A, Alayan I. A comparative anthropometric study of the position of the mental foramen in three populations. Br Dent J. 2012;212(4):E7.
11. Chrcanovic BR, Abreu MHNG, Custódio ALN. Morphological variation in dentate and edentulous human mandibles. Surg Radiol Anat. 2011;33(3):203-13.
12. Soikkonen K, Wolf J, Ainamo A, Xie Q. Changes in the position of the mental foramen as a result of alveolar atrophy. J Oral Rehabil. 1995;22(11):831-3.
13. Laher AE, Wells M, Motara F, Kramer E, Moolla M, Mahomed Z. Finding the mental foramen. Surg Radiol Anat. Epub 2015 Oct 13.
14. Loudon J. Beware the mental foramen. Br Dent J. 2011;210(7):293.
15. Smith MH, Lung KE. Nerve injuries after dental injection: a review of the literature. J Can Dent Assoc. 2006;72(6):559-64.
16. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007;370(9596):1453-7.
17. Jacobs R, Mraiwa N, Van Steenberghe D, Sanderink G, Quirynen M. Appearance of the mandibular incisive canal on panoramic radiographs. Surg Radiol Anat. 2004;26(4):329-33.
18. Jalili MR, Esmaeelinejad M, Bayat M, Aghdasi MM. Appearance of anatomical structures of mandible on panoramic radiographs in Iranian population. Acta Odontol Scand. 2012;70(5):384-9.
19. Fishel D, Buchner A, Hershkowith A, Kaffe I. Roentgenologic study of the mental foramen. Oral Surg Oral Med Oral Pathol. 1976;41(5):682-6.
20. Claudon M, Guillaume L. Diagnostic imaging and radiation hazards [in French]. Rev Prat. 2015;65(1):79-81.
21. Guo JL, Su L, Zhao JL, Yang L, Lv DL, Li YQ, et al. Location of mental foramen based on soft- and hard-tissue landmarks in a chinese population. J Craniofac Surg. 2009;20(6):2235-7.

22. Kim IS, Kim SG, Kim YK, Kim JD. Position of the mental foramen in a Korean population: a clinical and radiographic study. Implant Dent. 2006;15(4):404-11.
23. Smith JD, Surek CC, Cortez EA. Localization of the supraorbital, infraorbital, and mental foramina using palpable, bony landmarks. Clin Anat. Epub 2010 Feb 18.
24. Smajilagić A, Dilberović F. Clinical and anatomy study of the human mental foramen. Bosn J Basic Med Sci. 2004;4(3):15-23.
25. Gupta T. Localization of important facial foramina encountered in maxillo-facial surgery. Clin Anat. 2008;21(7):633-40.
26. Igbigbi PS, Lebona S. The position and dimensions of the mental foramen in adult Malawian mandibles. West Afr J Med. 2005;24(3):184-9.
27. Mbajiorgu EF, Mawera G, Asala SA, Zivanovic S. Position of the mental foramen in adult black Zimbabwean mandibles: a clinical anatomical study. Cent Afr J Med. 1998;44(2):24-30.
28. Oguz O, Bozkir MG. Evaluation of location of mandibular and mental foramina in dry, young, adult human male, dentulous mandibles. West Indian Med J. 2002;51(1):14-6.
29. Santini A, Land M. A comparison of the position of the mental foramen in Chinese and British mandibles. Acta Anat (Basel). 1990;137(3):208-12.
30. Koppe T. Summary of: A comparative anthropometric study of the position of the mental foramen in three populations. Br Dent J. 2012;212(4):188-9.
31. Phillips JL, Weller RN, Kulild JC. The mental foramen: 1. Size, orientation, and positional relationship to the mandibular second premolar. J Endod. 1990;16(5):221-3.
32. Laster WS, Ludlow JB, Bailey LJ, Hershey HG. Accuracy of measurements of mandibular anatomy and prediction of asymmetry in panoramic radiographic images. Dentomaxillofac Radiol. 2005;34(6):343-9.
33. Green RM, Darvell BW. Tooth wear and the position of the mental foramen. Am J Phys Anthropol. 1988;77(1):69-75.
34. Coşkun F, Akıncı E, Ceyhan MA, Sahin Kavaklı H. Our new stethoscope in the emergency department: handheld ultrasound. Ulus Travma Acil Cerrahi Derg. 2011;17(6):488-92.
35. Wells M. Local and Regional Anaesthesia in the Emergency Department Made Easy - Elsevier. 1st ed. London: Churchill Livingstone Elsevier; 2010.
36. Traxler M, Ulm C, Solar P, Lill W. Sonographic measurement versus mapping for determination of residual ridge width. J Prosthet Dent. 1992;67(3):358-61.
37. Møystad A, Bjørnland T, Friedland B, Donoff RB. Ultrasonographic pilot study of mental foramen size, with and without postoperative neurosensory dysfunction. Oral Surg Oral Med Oral Pathol Oral Radiol. 2015;120(2):275-80.
38. Chan HL, Wang HL, Fowlkes JB, Giannobile WV, Kripfgans OD. Non-ionizing real-time ultrasonography in implant and oral surgery: A feasibility study. Clin Oral Implants Res. Epub 2016 Mar 19.

Review article

Acta Medica Academica 2016;45(1):61-69
DOI: 10.5644/ama2006-124.157

Transition from paternalism to shared decision making – a review of the educational environment in Bosnia and Herzegovina and Croatia

Marta Vučemilović[1], Mersiha Mahmić-Kaknjo[2*], Ivančica Pavličević[3]

[1]School of Medicine, University of Split, Croatia, [2]Department of Clinical Pharmacology, Zenica Cantonal Hospital Zenica, Bosnia and Herzegovina
[3]Department of Family Medicine, School of Medicine, University of Split, Split Croatia

*Corresponding author:
mmahmickaknjo@gmail.com
Tel.: + 387 32 405 133
Fax.: + 387 32 226 576

Received: 7 September 2015
Accepted: 22 February 2016

Key words: Shared decision making ▪ Ethics ▪ Communication skills ▪ Medical schools

In this article we will review the benefits of a system built on partnership of physicians and their patients, highlight some of the factors which impede this transition, and propose ways to address these factors. Also, we are going to analyze the educational environment in Bosnia and Herzegovina and Croatia concerning ethics and communication skills. Personal responsibility of patients for their health should be reflected in their joint involvement in health decisions with their physicians. Patients, insecure about their individual competence surrounding their health decisions, tend to shy away from responsibility, whereas physicians, pressured by the responsibilities of the profession, do not always show sensitivity to all of the patient's concerns. They often treat illnesses instead of patients. A more open and collaborative relationship between the patient and the physician through shared decision making would be a better alternative. In the end, the patient ultimately decides whether a health intervention was satisfactory in fulfilling his or her specific needs. Transition from a paternalistic to a mutual relationship between doctors and patients has already begun. In an era of intense information sharing, shared decision making is a sensitive, ethical, legal, and political concept which needs empathic doctors with well-developed communication skills to integrate their clinical knowledge with patient-centered care. **Conclusion.** Transition from paternalistic to partner relation between physicians and patients is moving slowly ahead in Croatia and Bosnia and Herzegovina. Educational environment is improving but needs intense efforts to develop further.

Introduction

Over the last several decades, medicine has undergone a paradigm shift from a model based on paternalism to one based on partnership (1). This transition from a paternalistic system to a system built on partnership has not been uniform across the globe. Different countries have different cultural, historical, and political factors which affect the speed and shape of this transition.

In this article we will review the benefits of a system built on partnership, highlight some of the factors which impede this transition, and propose ways to address these factors.

Factors and benefits of the transition

As technology improves and is used more frequently, a feeling of distance between the

patient and the doctor emerges (2). This can cause patients to become confused or overwhelmed, leading to a loss of trust toward both the doctor and the healthcare system. Consequently, this can result in low adherence to the prescribed regimens by patients. Conversely, a new concept known as shared decision-making (SDM) can effectively limit confusion and dissatisfaction surrounding health decisions, lead thus often to better compliance, improved health outcomes, fewer lawsuits, and more meaningful interactions with health care professionals (2).

The SDM concept is defined as "an approach where clinicians and patients share the best available evidence when faced with the task of making decisions, and where patients are supported, while considering their options, to achieve informed preferences" (3). It is a patient-centered system which aims for a better means of communication and trust. Its implementation includes options, discussion, and decision making (4). The patient must feel free to discuss personal goals or concerns, and find a way to align them with available treatments that are supported through evidence-based medicine (EBM) (5).

Furthermore, the concept of SDM aligns well with today's legal requirements. As early as 1978, the Declaration of Alma-Ata recognized that "people have a duty and a right to become involved participants in their healthcare" (1). Additionally, the Declaration highlighted that health is not only the "absence of disease" but, rather, is "the state of complete physical, mental, and social wellbeing" (6).

Through SDM, both the physician and the patient feel more assured that they have established an accurate diagnosis and subsequent follow-up procedures. With this improved decisiveness, there is a reduction in avoidable costs for specialty care visits and diagnostic tests (7). Furthermore, more engaged patients tend to decide against costly invasive treatments. In fact, according to a 2014 Cochrane systematic review, more engaged and properly informed patients tend to decide against costly invasive treatments which can lessen costs and hospital burdens (RR 0.79; 95% CI 0.68 to 0.93) (8). Understandably, physicians are most concerned with the eradication of illness, whereas the patients are more concerned about their well-being and will consequently be more concerned with potential side effects of procedures than the physicians (9).

Challenges to shared decision making

Although the interest in supporting the adoption of SDM is growing, actual implementation is slow, and faces many challenges. There are extensive systemic barriers which prevent physicians from being able to champion SDM (10). The three most often reported barriers to SDM are: time constraints, lack of applicability due to patient characteristics, and the clinical situation (11). Additionally, patients may be initially reluctant to fully participate in the decision making process. Strong emotions such as anxiety, fear, and anger may interfere with the patient's ability to process information for good decision making; low health literacy, cultural and religious differences may cause disagreement with the physician (12).

Decision aids provide pertinent information for selected patient conditions, supported by credible research through EBM. The information can be provided through videos or audiotapes, workbooks, pamphlets, etc. (13). Decision aids are used as an addition to discussions with physicians, and, therefore, are provided in a distinctly neutral and informative manner. It is important to note that they are not a method of acquiring informed consent. Their purpose is to equip the patient with pertinent material for future discussion during doctor visits (13).

It has been demonstrated in multiple randomized control trials that their use:

1) improves patient knowledge; 2) lowers decisional conflict; and 3) increases active patient decision making (14). A 2014 Cochrane review of 115 studies (8) highlighted that, when compared with patients who received usual care, those who used decision aids had increased knowledge, more accurate risk perceptions, reduced internal conflict about decisions, and a greater likelihood of receiving care aligned with their values. Moreover, fewer patients were undecided or passive in the decision-making process – changes that are essential for patients' adherence to therapies. However, despite this evidence, decision aids are still not being sufficiently implemented. Their distribution remains relatively low due to the slow progress of physician adaptation to patient involvement and a lack of proper education in decision aids (15). Therefore, in order to successfully begin SDM, it is imperative that decision aids are correctly administered and implemented, with constant adjustment to new relevant science.

During the War for Independence, Croatia and Bosnia and Herzegovina (BH) faced devastating losses to their health infrastructures, funding, and professional personnel, and have been forced to make more efficient use of now severely limited resources (16). The concept of patient-centered medicine through active SDM has great benefits in the form of reduced overall workload, making it a natural fit for a health care system that still faces many burdens.

Unfortunately, although sufficient legislature is in place, implementation is lacking in Croatia and BH, where the culture of physician omnipotence has just recently been challenged. Concerning patients' health concerns, many patients may feel that their physicians are not open to discussion. Many of the patients do not even object to this one-sided relationship because they fear the effort would be fruitless and would simply cause more strain. It is, therefore, important that both physicians and patients are better informed of their rights and responsibilities regarding their collaboration.

Regret is a common consequence of decisions and greatly influences overall participation in SDM, yet the instruments to measure this are still undeveloped (17). Although there has been the development of many scales in English and other languages, which indicates growing research efforts in various countries (18), the methodological guidelines that could improve future preference-match studies of the patient-physician interaction are still missing. Adoption of patient-match assessment and intervention strategies are both necessary, and should be used as an addition to patient-centered and shared decision-making approaches (19). However, the latest Cochrane review revealed uncertainty in whether interventions to improve the adoption of SDM were effective, given the low quality of the evidence (20). However, the authors conclude that any intervention that actively targets patients, healthcare professionals, or both, is "better than none".

Public notion of SDM in Croatia and BH does not seem to be very high and academic research on SDM in these regions remains fairly rare. Only recently have some studies started to address the benefits of SDM. In 2013 and in 2014, two studies argued its benefits in respect to flu vaccination and cardiovascular health in female patients respectively (21, 22). The few studies introducing the practice of SDM to the Croatian community mirror those conducted in Brazil or Chile, where actual research in SDM remains in its infancy (23, 24).

A call to action: Proper training and decision aids

In order for patients to become more involved in health decisions, it is essential that they are treated as equal partners, meaning

that physicians are required to create a pleasant environment where the patient would feel that his or her input is welcome. Physicians need to be trained in advance on how to create a rapport with patients surrounding health decisions. Consequently, medical education and training should include both communication skills and ethics focusing on patient-centeredness (20). These topics should be emphasized more in undergraduate medical studies where students would become more familiar with possible scenarios and adequate and sensitive reactions to patient needs (25). This training would provide better skilled and empathetic clinicians. In order to better prepare future physicians, undergraduate and postgraduate training should integrate a more patient-centered approach.

Table 1 gives an overview of ethics and communication courses in medical schools in Croatia, BH, Macedonia, Montenegro, Serbia, Kosovo, and Albania, and represents the picture of continuous efforts for improvement. This data was obtained from primary care physicians gathered in an initiative called the "Split Initiative", which consists of a series of conferences attended by representatives from each of the regional family medicine departments from their respective schools of medicine (26). These conferences, held so far in Split, Ljubljana, Zagreb, and Podgorica, allowed sharing of knowledge and experiences regarding family medicine teaching methods, patient-doctor relations, and international research collaboration. In total, data from 14 schools of medicine were analyzed; 4 from Croatia (all), 5 from BH (all), 1 from Macedonia, 1 from Montenegro, 1 from Serbia (the oldest and largest university), 1 from Kosovo, and 1 from Albania.

Both ethics and communication skills classes are already available in the majority of medical schools included in this analysis. However, they are not equally emphasized in each of the curricula. When comparing the availability of either ethics or communication skills courses in neighboring countries, such as in Italy, there is also a similar lack of emphasis in such courses (27). Overall, it is clearly necessary for these universities to offer more credit hours on these subjects. Communication skills should be more than an elective course, and should provide students with more real life practice, including training in both face-to-face and electronic communication. The way to improve patient-doctor communication is by understanding the theory behind good doctor-patient communication, and by practicing these skills while maintaining the capability of modifying communication styles in accordance to specific situations (28).

In the similar light of encouraging ethics and communication classes, related SDM training could also be provided through the use of several specialized toolkits. These include: face-to-face encounters for physician training purposes, on-the-fly coaching and feedback to health care providers during training, as well as reminder cards, cue posters and decision aids (29). While this sort of training has the potential to benefit health care providers at any stage of their professional career, ideally it would be implemented as an elective undergraduate class, in order to introduce the aspiring physicians to the concept of SDM as early as possible.

Croatian medical professionals have generally recognized the value of applying data supported by EBM. In fact, Cochrane Croatia was established by the medical school in Split with the aim to promote the development and usage of EBM for physicians, students, and patients. More than 1,000 Cochrane summaries have already been translated into Croatian and further translation activities are currently being planned (30, 31). In 2013, the 5th annual Croatian Cochrane Symposium was dedicated to lay users, e.g., patients. Efforts in popularizing

Table 1 Details from ethics and communication skills curricula at medical schools in Croatia, Bosnia and Herzegovina, Macedonia, Montenegro, Serbia, Kosovo and Albania (data from 2014)*

Medical School	Ethics			Communication skills		
Split University (HR)	Subject: Ethics in "Medical humanistic science"			Subject: "Psychological medicine"		
				Years	Hours/Year	Type
				3rd	25	S
				Subject: "Family medicine"		
				Years	Hours/Year	Type
				6th	2	S
				Elective subject: "Communication skills"		
	Years	Hours/Year	Type	Years	Hours/Year	Type
	2nd, 3rd, 4th, 5th, 6th	15	L6, S9	4th	25	-
Zagreb University (HR)	Subject: "Medical Ethics"			Subject: "Basics of physicians' knowledge"		
	Years	Hours/Year	Type	Years	Hours/Year	Type
	5th	45	L4, S41	1st-6th	30	P
Rijeka University (HR)	Subject: "Medical Ethics"			None		
	Years	Hours/Year	Type			
	6th	45	L15, S 30			
Osijek University (HR)	Subject: "Medical Ethics"			Subject: "Family medicine"		
	Years	Hours/Year	Type	Years	Hours/Year	Type
	6th	40	L20, S20	6th	2	S
	Elective subject: "How to apply Hippocrates oath"			Elective subject: "Communication skills"		
	Years	Hours/Year	Type	Years	Hours/Year	Type
	1st	-	-	4th	25	L15, S10
Mostar University (BA)	Subject: "Medical Ethics and bioethics"			Elective subject: „Communication skills"		
	Years	Hours/Year	Type	Years	Hours/Year	Type
	1st-6th	10	L5, S5	1st	-	-
Tuzla University (BA)	Subject: "Introduction to medicine"			Subject: "Psychology of communication"		
	Years	Hours/Year	Type			
	1st	3	L2, P 1			
	Subject: "Family medicine"					
	Years	Hours/Year	Type	Years	Hours/Year	Type
	6tth	2	L2	1st	3	L2, P1
Sarajevo University (BA)	Subject: "Medical Ethics and sociology"			None		
	Years	Hours/Year	Type			
	1st	45	L30, P15			
Eastern Sarajevo University (BA)	Subject: "Ethics"			Subject: "Clinical Praxis II"		
	Years	Hours/Year	Type	Years	Hours/Year	Type
	1st	25	-	2nd	30	L15 + P15
Banja Luka University (BA)	None			Subject: "Family Medicine"		
				Years	Hours/Year	Type
				6th	2	S
Skopje University (MK)	Subject: "Medical Ethics"			Subject: "Medical Psychology and Sociology"		
	Years	Hours/Year	Type	Years	Hours/Year	Type
	1st	60	-	1st	-	-

Continuation of Table 1 Details from ethics and communication skills curricula at medical schools in Croatia, Bosnia and Herzegovina, Macedonia, Montenegro, Serbia, Kosovo and Albania (data from 2014)*

Medical School	Ethics			Communication skills		
Podgorica University (ME)	Subject: "Medicine and Society"			Subject: "Family Medicine"		
	Years	Hours/Year	Type			
	1st	-	-			
	Subject: "Family Medicine"					
	Years	Hours/Year	Type	Years	Hours/Year	Type
	4tth	1	L	6th	1	L
Beograd University (RS)	Subject: "Medicine and Society"			Elective subject: "Communication in Medicine"		
	Years	Hours/Year	Type			
	-	20	S			
	Elective subject: "Bioethics 3"					
	Years	Hours/Year	Type			
	3rd	30	L15, P15			
	Elective subject: "Bioethics 5"					
	Years	Hours/Year	Type	Years	Hours/Year	Type
	5th	30	L15, P15	-	30	L15, P15
Priština University (RKS)	Subject: "Medical Ethics"			Subject: "Medical Psychology and communication skills"		
	Years	Hours/Year	Type	Years	Hours/Year	Type
	1st			1st	-	-
Tirana University (AL)	Subject: "Medical Ethics"			Subject: "Communication in health care"		
	Years	Hours/Year	Type	Years	Hours/Year	Type
	1st	25	L13, S 12	1st	35	L15, S20

*Types of classes: L=Lectures, S=Seminars, P=Practicals. HR=Croatia; BA=Bosnia and Herzegovina; MK=Macedonia; ME=Montenegro; RS=Serbia; AL=Albania; RKS-=Kosovo.

Cochrane have been started in BH, where a conference about the perspectives of Cochrane and EBM was organized at the Sarajevo Medical School in October 2015, and although this symposium was targeted at academia and decision makers, the efforts will be continued to better present evidence to the lay public.

Due to the fairly regular media coverage of such events and programs that raise awareness about EBM, professional meetings in both countries seem to be a fairly effective method of relaying the importance of EBM to health care system policy-makers and regulatory officials (such as the top officials at ministries and institutes of public health and heads of hospital departments). As such events become more frequent, perhaps their message could be disseminated through a top-down movement resulting in a systemic change toward the implementation of SDM and EBM.

Aside from physician education, patients should also be better educated regarding their health. Demand for patient education is demonstrated by the involvement of the Croatian Patient Association in the International Association of Patient Organizations. Through this organization, patients have expressed demands for greater involvement in decision making on the health policy level (32). Patients should be both properly informed about their condition and about associated risks of each treatment, so that they could be involved in effective conversations. The issues of time constraint and insufficient

patient medical literacy can be overcome by utilizing decision aids. Yet, there is a lack of translated material, which is an issue that Cochrane Croatia will tackle by pursuing the translation of decision aids in cooperation with the Patient Decision Aids Research Group. This research group in Canada is exemplary, being famous for its Ottawa Personal Decision Guide and various toolkits, along with other materials available online for free (33). Overall, the current level of development of decision aids in Croatia again seems to be similar to the situation in neighboring Italy, where there are still insufficient examples of decision aids structured around SDM. One critical point which prevents a stronger movement in Croatia and BH toward their production is a lack of specific evaluation tools which can track SDM progress. This is in contrast to the progress in Italy where versions of the OPTION scale and the SDM-Q are already instilled, which supply reliable outcome measures (27).

Some attempts to give public lectures and workshops with the aim of introducing the concept of SDM have already been made in Split, but have so far failed due to a lack of resources. Another way to put SDM into the spotlight with the general public might be through the media, such as local TV, radio stations, or newspapers, especially in programs or news articles which focus on health information and advice.

Conclusion

Transitioning to SDM has become a global initiative because it gives any growing health care system a more efficient method for providing the highest quality care. In addition, the physician has the obligation, both legal and moral, to stop practicing medicine in a paternalistic manner. Patients have expressed their desire to become more involved in the decision making process, and are unsatisfied when their input is underestimated. The physician can no longer rely only on professional opinion, but must become open to accepting patients' choices. This trend, although definitely present, has been developing more slowly in Croatia and BH. However, with the help of international collaborations, academic research done by scientists from Croatia and BH, decision aids, and proper training of ethics and communication skills in medical schools, SDM will become more widely practiced. Soon, this culture of productive collaboration will provide the many benefits necessary to improve the health care system.

What is already known on this topic

Shared decision making is becoming more and more important, as there is a lot of medical information publicly available. Not all patients are capable or willing to share all the decisions all the time. The greatest challenge is to communicate information and willingness to share with the individual patient.

What this study adds

In this paper we aimed at defining risks, benefits and barriers to shared decision making. As physicians' communication skills seem to be the corner stone of quality SDM, we collected data on teachings on ethic and communication skills at medical schools in Croatia, BH, Macedonia, Montenegro, Serbia, Kosovo and Albania Universities.

Acknowledgements: The authors thank Matko Marušić and Ana Marušić for their suggestions and support in writing this manuscript and Dalibora Behmen and Shelly Pranić for language editing.

Authors' contributions: Conception and design: MV, MMK and IP; Acquisition, analysis and interpretation of data: IP and MMK; Drafting the article MV, MMK and IP; Revising it critically for important intellectual content: IP and MMK; Approved final version of the manuscript: MV, MMK, IP.

Conflict of interest: The authors declare that they have no conflict of interest.

References

1. Pavlicevic I, Simi S. It is important what patients think: patients should decide on their treatment together with their doctors. [in Croatian]. Medix. 2014;20:109-110.

2. Talanga J. Doctors' and patients' attitude towards medical ethics. [in Croatian]. BS. 2006;76:47-59.
3. Elwyn G, Laitner S, Coulter A, Walker E, Watson P, Thomson R. Implementing shared decision making in the NHS. BMJ. 2010;341:c5146.
4. Elwyn G, Frosch D, Thomson R, Joseph-Williams N, Lloyd A, Kinnersley P, et al. Shared decision making: a model for clinical practice. J Gen Intern Med. 2012;27(10):1361-7.
5. Ferrer RL, Gill JM. Shared decision making, contextualized. Ann Fam Med. 2013;11(4):303-5.
6. WHO. Declaration of Alma-Ata. International Conference on Primary Health Care [monograph on the internet]. Alma-Ata, USSR, 1978. [cited 2016 Apr 10]. Available from: http://apps.who.int/medicinedocs/documents/s21369en/s21369en.pdf
7. Caffarini K. Patient- centered care found to reduce medical costs. American Medical News. 2011 Jul [cited 2015 Jul 23]; [about 2 p.]. Available from: http://www.amednews.com/article/20110718/business/307189961/7/.
8. Stacey D, Légaré F, Col NF, Bennett CL, Barry MJ, Eden KB, et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev. 2014 28;1:CD001431.
9. Turkovic K. Right to refuse medical treatment in Republic of Croatia [in Croatian]. Medicina. 2008;44(2):158-70.
10. Durand MA, Carpenter L, Dolan H, Bravo P, Mann M, Bunn F, et al. Do interventions designed to support shared decision-making reduce health inequalities? A systematic review and meta-analysis. PloS one. 2014;9(4):e94670.
11. Légaré F, Ratté S, Gravel K, Graham ID. Barriers and facilitators to implementing shared decision-making in clinical practice: update of a systematic review of health professionals' perceptions. Patient Educ Couns. 2008;73(3):526-35.
12. American Heart Organization [homepage on the Internet]. Dallas: Overcoming Barriers to Shared Decision Making. 2014 [updated 2015 Jun 4; cited 2015 Dec 10]; [about 2 screens]. Available from: http://www.heart.org/HEARTORG/Conditions/HeartFailure/LivingWithHeartFailureAndAdvancedHF/Overcoming-Barriers-to-Shared-Decision-Making_UCM_441939_Article.jsp#.Vmni2dLhC00.
13. O'Connor A. Using patient decision aids to promote evidence-based decision making. ACP J Club. 2001;135(1):A11-2.
14. O'Connor AM, Stacey D, Entwistle V, Llewellyn-Thomas H, Rovner D, Holmes-Rovner M, et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev. 2003;(2)CD001421.
15. Robert Wood Johnson Foundation. People actively involved in their health and health care tend to have better outcomes- and, some evidence suggests, lower costs. Health Policy Brief [serial on the Internet]. 2013 Feb [cited 2015 Jan 5]; [about 6 p.]. Available from: http://healthaffairs.org/healthpolicybriefs/brief_pdfs/healthpolicybrief_86.pdf.
16. Bagaric I. Medical services of Croat people in Bosnia and Herzegovina during 1992-1995 war: losses, adaptation, organization, and transformation. Croat Med J. 2000;41(2):124-40.
17. Joseph-Williams N, Edwards A, Elwyn G. The importance and complexity of regret in the measurement of 'good' decisions: a systematic review and a content analysis of existing assessment instruments. Health Expect. 2011;14(1):59-83.
18. Scholl I, Koelewijn-van Loon M, Sepucha K, Elwyn G, Légaré F, Härter M, et al. Measurement of shared decision making - a review of instruments. Z Evid Fortbild Qual Gesundhwes. 2011;105(4):313-24.
19. Kiesler DJ, Auerbach SM. Optimal matches of patient preferences for information, decision-making and interpersonal behavior: evidence, models and interventions. Patient Educ Couns. 2006;61(3):319-41.
20. Légaré F, Stacey D, Turcotte S, Cossi MJ, Kryworuchko J, Graham ID, et al. Interventions for improving the adoption of shared decision making by healthcare professionals. Cochrane Database Syst Rev. 2014;9:CD006732.
21. Pavlicevic I, Skrabic S, Malicki M, Mercep AH, Marusis A, Marusic M. Decisional Conflict and Vaccine Uptake: Cross-Sectional Study of 2012/2013 Influenza Season in Croatia. Arch Med Sci. 2015;11(4):788-95.
22. Pavlicevic I, Malicki M, Mrduljas-Dujic N, Curcic L, Dosen Jankovic S, Skrabic S, et al. Shared decision making in life style and nutrition for intervention in women with risk factors in cardiovascular health. RECOOP 5th TriNet Meeting Wroclaw, Poland, October 17-19th 2014.
23. Abreu MM, Battisti R, Martins RS, Baumgratz TD, Cuziol M. Shared decision making in Brazil: history and current discussion. Z Evid Fortbild Qual Gesundhwes. 2011;105(4):240-4.
24. Bravo P, Cabieses B, Bustamante C, Campos S, Stacey D. Shared decision making in Chile: supportive policies and research initiatives. Z Evid Fortbild Qual Gesundhwes. 2011;105(4):254-8.
25. Stacey D, Bennett CL, Barry MJ, Col NF, Eden KB, Holmes-Rovner M, et al. Decision aids for

people facing health treatment or screening decisions. Cochrane Database Syst Rev. 2011;(10): CD001431.

26. Pavlicevic I, Svab I. Family medicine defines its academic niche: The Split Initiative. Acta Med Acad. 2012;41(1):1-3.
27. Goss C, Mosconi P, Renzi C, Deledda G. Participation of patients and citizens in healthcare decisions in Italy. Z Evid Fortbild Qual Gesundhwes. 2011;105(4):277-82.
28. Ha JF, Longnecker N. Doctor-patient communication: a review. Ochsner J. 2010. Spring;10(1):38-43.
29. Association of American Medical Colleges [homepage on the Internet]. Washington: The Asscociation; c1995-2015 [updated 2013 May 10; cited 2015 Dec 15]. Shared Decision-Making (SDM) Toolkit: Train-the-Trainer Tools for Teaching SDM in the Classroom and Clinic; [about 2 screens]. Available from: https://www.mededportal.org/publication/9413.
30. Puljak L. Using social media for knowledge translation, promotion of evidence-based medicine and high-quality information on health. J Evid Based Med. 2015;9(1):4-7.
31. Cochrane [homepage on the Internet]. London: Cochrane; c2015 [cited 2015 Dec 8]. Najpopularniji Cochrane dokazi; [about 2 screens]. Available from:http://www.cochrane.org/hr/evidence.
32. International Alliance of Patients' Organizations. Patient involvement in all aspects of healthcare decision-Making [cited 2015 Oct 29]; [about 2 screens]. Available from: https://www.iapo.org.uk/iapo-members.
33. Légaré F, Stacey D, Forest PG, Coutu MF. Moving SDM forward in Canada: milestones, public involvement, and barriers that remain. Z Evid Fortbild Qual Gesundhwes. 2011;105(4):245-53.

Case report

Acta Medica Academica 2016;45(1):70-73
DOI: 10.5644/ama2006-124.158

The feasibility of transradial laser atherectomy for chronic total occlusion using the 5 Fr sheath system

Khaled Sherif*, Yasir Yaqub, Jose A Suarez

Internal Medicine Department-Texas Tech University Health Sciences Center Lubbock, TX, USA

*Corresponding author:
k_a_sherif@hotmail.com
Tel.: + 1 806 743 3155
Fax.: + 1 806 743 3143

Received: 13 January 2016
Accepted: 25 March 2016

Key words: Chronic total occlusion ▪ LASER endovascular intervention ▪ Coronary artery disease.

Objective. We present a case of chronic total occlusion (CTO) approached with LASER endovascular intervention by radial artery approach using a 5 French sheath. **Case report.** A 57-year-old man presented to our hospital having had retrosternal chest pain for two days. Physical examination was normal at the time of presentation. The laboratory tests were within normal limits, including cardiac enzymes except the lipid panel which showed hypertriglyceridemia. The patient underwent a myocardial perfusion scintigraphy stress test that revealed inferior wall ischemia, with normal left ventricular ejection fraction. A 5-French vascular sheath was placed in the right radial artery. Selective coronary artery angiography was performed, which showed right coronary artery (RCA) CTO. A 5-French JR4 guide catheter successfully engaged the RCA and Laser angioplasty was performed across the CTO into the RCA. A marked improvement of flow was evident thereafter. **Conclusion**. To best of our knowledge this is the first case report showing the feasibility of laser atherectomy using the 5 French sheath system in a coronary arterial CTO.

Introduction

Chronic total occlusion of the coronary (CTO) artery is defined as occlusion longer than 3 months after a clinical event, or sometimes of an unknown duration (1). A successful CTO revascularization is associated with improved long term survival, especially in the case of a viable myocardium supplied by the occluded vessel, fewer symptoms, improved left ventricular function, and reduced need for coronary artery bypass surgery (2). Even though the femoral artery is the usual route for percutaneous coronary intervention for CTO in most cardiac laboratories, the transradial route is now becoming more popular, with the main advantages of early mobilization of patients post procedure and less vascular complications when compared to the transfemoral route. (3). Most arterial sheets involved in percutaneous coronary intervention (PCI) for CTO are the 6-7 Fr sheath system.

We report a patient with CTO who had PCI with the 5Fr system transradial system.

Case report

A 57-year-old man with a history of diabetes mellitus, hypertension, coronary artery disease, peripheral vascular disease, and obstructive sleep apnea, presented to our hospital with retrosternal chest pain over the previous two days. The pain was exertional, with episodes lasting 5 minutes, and it was relieved by nitroglycerine. He had no history of diaphoresis, nausea, or peripheral

edema. The patient had a history of coronary angiography two years before this presentation that showed diffuse right coronary (RCA) disease. The physical examination was normal at the time of presentation. The laboratory tests were within normal limits, including cardiac enzymes, except the lipid panel which showed hypertriglyceridemia. Transthoracic echocardiography showed an ejection fraction of 45% with no regional wall motion abnormalities with normal left ventricular pressure. The patient underwent a myocardial perfusion scintigraphy stress test that revealed inferior wall ischemia with a normal left ventricular ejection fraction. On the basis of these findings and given his history of RCA disease, the decision was made to perform coronary angiography.

Access to the right radial artery was achieved by a modified Seldinger technique, and a 5-French vascular sheath was placed. A pigtail catheter was used to engage the left ventricle. Left ventriculogram, left ventricular end diastolic pressure and pullback pressures were performed. The Tiger catheter was used to engage the left coronary artery. Another Tiger catheter was used to engage the right coronary artery. Selective coronary artery angiography was performed in multiple projections, and it showed distal RCA CTO (Figure 1).

The 5-French EBU 3.0 guide catheter was unable to engage the RCA. Therefore, it was exchanged by a 5-French JR4 guide. A Pilot-200 cm guide wire was advanced into the distal posterior left ventricular branch (PLV) after some effort, with utilization of a quick cross catheter (Figure 2).

We could not advance the 2.0×30 mm over-the- wire Sprinter balloon for angioplasty and the decision to perform excimer laser coronary angiography was made. Laser angioplasty was performed across the CTO into the distal RCA, and a marked improvement of flow was evident thereafter. A 2×40 mm Apex Flex balloon was advanced into the distal RCA and inflations were performed at 6 atmospheres (ATMs) 40 seconds, 12 ATMs for 40 seconds, 16 ATMs for 40 seconds and finally 20 ATMs for 40 seconds. Check angiography showed significantly improved flow. A Medtronic 1.5×20 mm Sprinter balloon was inflated further distally at 7 ATMs for 60 seconds. A Taxus Atom 2.25×32 mm stent was advanced without any difficulty in the distal RCA, and another Taxus Atom 2.25×28 mm was overlapped proximally at 14 ATMs for

Figure 1 Diagnostic angiogram showing CTO of the distal RCA.

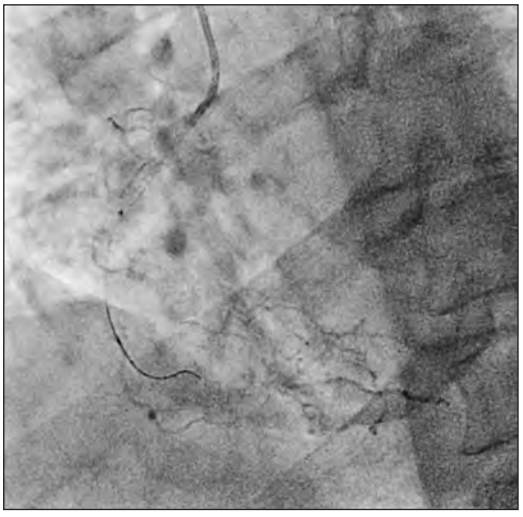


Figure 2 The Pilot 200 guide wire passed into the distal RCA with the help of a quick cross catheter.

30 seconds. Then, the Taxus Liberté 2.5×32 mm stent was overlapped more proximally and inflated at 14 ATMs for 33 seconds. Finally, the Taxus Liberté 2.75×16 mm stent was inflated more proximally at 16 ATMs for 30 seconds. The final angiography demonstrated an excellent result with TIMI III flow in the RCA (Figure 3) showing the feasibility of the transradial 5 French system in LASER endovascular intervention (EVI) in coronary CTO's.

Figure 3 Final angiographic image showing successful CTO PCI, with flow visible in PLV and PDA.

Discussion

CTOs are more complex and time consuming to revascularize, but successful revascularization of CTOs may lead to a ten-year survival advantage compared to failed treatment (4). PCI for CTO has been limited due to low success and high restenosis rates. However, the success has increased in recent years as the result of improvement of procedural techniques and devices. The femoral artery is the usual vascular route used in PCI for CTOs in most cardiac catheterization laboratories. However, there has been growing interest in transradial PCI because of its fewer complications at the puncture site, patient convenience, early discharge, and short hospitalization (5). The factors that affect success of PCI for CTO include the chronicity of the lesion, the presence or absence of side branches and bridging collateral vessels, occlusion length, reference diameter less than 3 mm and occlusion morphology (5).

Most cardiac catheterization laboratories use 6 and 7 Fr sheaths and related guiding catheters for PCI in patients with CTOs (6). However, there are benefits from using a 5 Fr system guiding catheter instead. First, it reduces the amount of contrast used during the procedure. This is an important strategy in patients with chronic kidney disease, to reduce the risk of acute kidney injury in those patients. The second reason is the favorable impact of using a 5 Fr guiding catheter on vascular complications (6). Finally, as in our case, the 5Fr guiding catheter is used to finish a difficult laser atherectomy for CTO in patients with small radial vessels. There are difficulties that may occur from a small size guide catheter in radial access, such as crossing the lesion with the balloon. Here, it may be necessary to use another therapeutic strategy such as laser atherectomy, as in our patient.

Conclusion

To best of our knowledge this is the first case report describing successful LASER EVI of a coronary CTO with a 5 French radial sheath. This approach shows that smaller sheath sizes can be used despite the procedural complexities that come with LASER EVI in the coronary arterial system.

What is already known on this topic

Chronic total occlusion intervention in the coronary artery is both complex and time consuming, but has been associated with better long term outcomes. The femoral artery is the usual route for percutaneous coronary intervention for CTO in most cardiac laboratories, and most arterial sheets involved in PCI for CTO are from the 6-7 Fr sheath system.

What this case adds

We report a patient with CTO who had PCI using a 5Fr system transradial system.

Authors' contributions: Conception and design: KS, YY and JAS; Acquisition, analysis and interpretation of data: KS, YY and JAS; Drafting the article: KS, YY and JAS; Revising it critically for important intellectual content: KS, YY and JAS; Approved final version of the manuscript: KS, YY and JAS.

Conflict of interest: The authors declare that they have no conflict of interest.

References

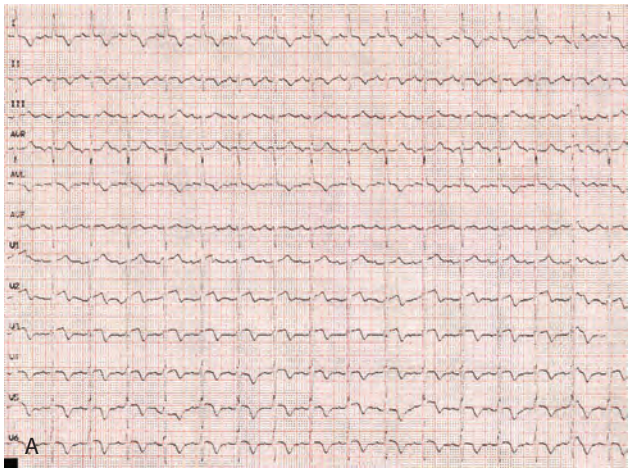
1. Lamm G, Auer J, Berent R, Eber B. Chronic total occlusion--a definite state? Int J Cardiol. 2005;102(1):155-6.
2. Olivari Z, Rubartelli P, Piscione F, Ettori F, Fontanelli A, Salemme L, et al. Immediate results and one-year clinical outcome after percutaneous coronary interventions in chronic total occlusions: data from a multicenter, prospective, observational study (TOAST-GISE). J Am Coll Cardiol. 2003;41(10):1672-8.
3. Lim VY, Chan CN, Kwok V, Mak KH, Koh TH. Transradial access for coronary angiography and angioplasty: a novel approach. Singapore Med J. 2003;44(11):563-9.
4. Falk E, Shah PK. Ischemic Heart Disease. In: Crawford MH, DiMarco JP, Paulus WJ, editors. Cardiology. 2nd ed. New York: Mosby; 2004. p. 451-3.
5. Bahl VK, Chandra S, Goswami KC, Manchanda SC. Crosswire for recanalization of total occlusive coronary arteries. Cathet Cardiovasc Diagn. 1998;45(3):323-7.
6. Cheng-Hsueh Wu, Zu-Yin Chen, Lung-Ching Chen. Use of 5 French Guiding Catheters in Transradial Coronary Intervention Procedures. Acta Cardiol Sin. 2011;27:21-8.

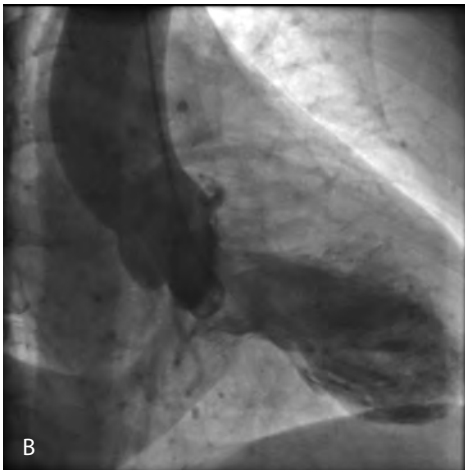
Acta Medica Academica 2016;45(1):74-75
DOI: 10.5644/ama2006-124.159

The Takotsubo cardiomyopathy caused by the family drama

Mehmed Kulić[1], Elnur Tahirović[2*]

Cardiology clinic[1], Cardiosurgery clinic[2], University Clinical Center Sarajevo, Sarajevo, Bosnia and Herzegovina





A 61 year old woman was admitted to our hospital for acute anginal pain which had occurred two hours before she was admitted. The symptoms started after she experienced psychological stress, due to her daughter's divorce. Her personal anamnesis was negative for coronary artery disease. An electrocardiogram (ECG) showed sinus rhythm with ST-segment elevation of 2 mm in leads V2-V3 and negative T waves in leads DI, DII, AVL, and V2-V6 (Panel A). Her troponin I level was 1196 pg/ml (normal range <30 pg/ml). A transthoracic echocardiogram estimated the left ventricular ejection fraction at 35%, with evidence of segmental motion abnormalities in the medioapical segments of the anterior, septal, inferior wall, with moderate mitral regurgitation. Coronary angiography was performed and we found normal coronary arteries, with left ventricular apical ballooning and hypercontraction of the basal segment (Panel B; (http://ama.ba/index.php/ama/article/view/264/264-845-1-PC.HTML2). On the basis of these findings and anamnesis, Takotsubo cardiomyopathy or broken heart syndrome (1) was diagnosed. She was treated with medical therapy (diuretics, beta blockers, anticoagulant therapy, ACE-inhibitors) and after one month her echocardiogram was without any abnormalities. Also, the ECG normalized without any sign of myocardial ischemia. Although it has unclear pathogenesis, studies have shown that this cardiomyopathy is associated with a large quantity of catecholamines produced as a response to stress (2).

Therefore, it is very important for physicians to recognize this very rare and frequently unrecognized cardiomyopathy, which can often mimic acute coronary syndrome.

Key words: Takotsubo cardiomyopathy ▪ Acute coronary syndrome.

Authors' contributions: Conception and design: MK and ET; Acquisition, analysis and interpretation of data: ET and MK; Drafting the article: ET and MK; Revising it critically for important intellectual content: MK and ET; Approved final version of the manuscript: ET and MK.

Conflict of interest: The authors declare that they have no conflict of interest.

*Corresponding author
elnur.tahirovic@gmail.com
Tel.: + 387 33 298 219
Fax.: + 387 33 268 791

Received: 15 February 2016; Accepted: 17 March 2016

References

1. Virani SS, Khan AN, Mendoza CE, Ferreira AC, de Marchena E. Takotsubo Cardiomyopathy, or Broken-Heart Syndrome. Tex Heart Inst J. 2007;34(1):76-9.
2. Komamura K, Fukui M, Iwasaku T, Hirotani S, Masuyama T. Takotsubo cardiomyopathy: Pathophysiology, diagnosis and treatment. World J Cardiol. 2014;6(7):602-9.

Commentary

Acta Medica Academica 2016;45(1):76-77
DOI: 10.5644/ama2006-124.160

Lung ultrasonography: A new imaging approach in diagnosis of pneumonia in children

Damjana Ključevšek*

University Medical Center, Children's Hospital
Radiology Unit, Ljubljana, Slovenia

*Corresponding author:
damjana.kljucevsek@gmail.com
Tel.: + 386 1 522 92 64
Fax.: + 386 1 522 29 93

Received/Accepted: 2 May 2016

Key words: Lung ultrasonography ▪ Pneumonia ▪ Children.

Respiratory tract infections are a significant cause of pediatric morbidity and mortality. Chest radiography is the most common diagnostic imaging. Current guidelines suggest that a diagnosis of pneumonia can only be made considering clinical history, respiratory rate, fever, respiratory signs and symptoms limited the use of radiography to severe or complicated cases only (1). Up till now lung ultrasound (LUS) has not been mentioned as a diagnostic tool in current guidelines.

Although LUS is not in the guidelines, it has gained a value in the clinical practice in the last 15 years. It moved from the traditional assessment of pleural effusions and thoracic masses towards the imaging of the pulmonary parenchyma, mainly as a point-of-care technique (2). As a technique LUS has many advantages. It is quick to preform, repeatable, and radiation-free compared to chest radiography or computer tomography. It has been proved that the learning curve of LUS is relatively short ("easy-to-learn technique"), less technically demanding than other sonographic examinations. In addition, the main advantage of LUS in children is related to the small size of the chest, which allows quite optimal (still indirect) visualization of the lungs by the point-of-case technique. However, ultrasonographers should be aware of its limitations. US waves are reflected by alveolar air and bones of the thoracic cage. Pulmonary changes are detected only when the lesion reaches the lung surface. Pathological findings within hilar regions are missed, and there is a problem in detection of air-filled lung abscesses. Despite these limitations LUS has proved to be useful in the evaluation of many clinical pulmonary conditions, acute or chronic, in children and adults.

Most of the published studies compared chest radiography with LUS in pediatric population. It was shown that LUS is especially valuable in detecting pneumonia in children, with sensitivity even higher than that of chest radiography. A meta-analysis including 8 pediatric studies comparing LUS with X-ray was performed by Pereda et al. (3); LUS had a sensitivity of 96% and specificity of 93%, and positive and negative likelihood ratios were 15.3 and 0.06, respectively.

Lovrenski et al. (4) presented a unique prospective study comparing LUS and lung auscultation using stetoscope, a widely accepted diagnostic tool. The technique of LUS is a well described, standardized using trans-thoracic and transabdominal approach. In experienced hands the examination is relatively short (average time 5.7 minutes). Of course, the examination time depends on the size of the thorax, a child's cooperation and the complexity of the findings. The wide range of positive findings depending on the stage of pneumonia at the time of examination is also well described and explained. LUS has proved to show more positive findings compared to auscultation in children with suspected pneumonia. A very important scientific contribution is the determination of the threshold size of subpleural consolidations below which it is highly unlikely that pneumonia will be detected by auscultation: a cranio-caudal size of subpleural consolidation of less than 30 mm significantly reduced the possibility of an auscultatory detection. The limitations of LUS and study were discussed.

How can LUS be introduced in diagnostic algorithm in children with suspected pneumonia? Is its place in diagnostical algorithms? Iorio et al. proposed LUS as initial imaging in children with suspected pneumonia (5). According to the published data by Lovrenski et al. (4) LUS should be used whenever physical findings are unclear and in cases with a negative auscultation and strong clinical suspicion of pneumonia. Consequently, children would not be exposed to unnecessary chest radiography.

In conclusion, LUS is a promising method in the evaluation of children with suspected pneumonia, with many advantages and some limitations, which should be respected. LUS has a great potential to be implemented in everyday clinical practice in detecting and following pneumonia and some of its complications. Its role should be further evaluated. Every study from that field contributes a piece in the mosaic. In the future, there is hope that the introduction of LUS in diagnostic algorithm will diminish the use of radiation to a certain degree, which is in concordance with the nowadays strategy regarding radiation in children.

Conflict of interest: The author declares that she has no conflict of interest.

References

1. Bradley JS, Byington CL, Shah SS, Alverson B, Carter ER, Harrison C et al. Executive summary: the management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis. 2011; 53(7):617-30.
2. Volpicceli G. Lung Sonography. J Ultrasound Med. 2013;32:165-71.
3. Pereda MA, Chavez MA, Hooper-Miele CC, Gilman RH, Steinhoff MC, Ellington LE et al. Lung ultrasound for the diagnosis of pneumonia in children: a meta-analysis. Pediatrics. 2015;135(4):714-22.
4. Lovrenski J, Petrović S, Balj-Barbir S, Jokić R, Vilotijević-Dautović G. Stetoscope vs. ultrasound probe – which is more reliable in children with suspected pneumonia? Acta Med Acad. 2016;45(1):39-50.
5. Iorio G, Capasso M, De Luca G, Prisco S, Mancusi C, Laganà B et al. Lung ultrasound in the diagnosis of pneumonia in children: proposal for a new diagnostic algorithm. PeerJ. 2015;3:e1374.

Commentary

Acta Medica Academica 2016;45(1):78-79
DOI: 10.5644/ama2006-124.161

Lung ultrasound in children with pneumonia

Mark C. Liszewski*

Montefiore Medical Center and
Albert Einstein College of Medicine
111 East 210th Street, Bronx, NY 10467, USA

*Corresponding author:
markcliszewski@gmail.com
Tel.: + 718 920 7748
Fax.: + 718 798 7983

Received/Accepted: 27 April 2016

Key words: Ultrasound ▪ Pneumonia ▪ Children.

Chest radiography is the primary imaging modality utilized for the evaluation of pneumonia in children. When cross sectional imaging is needed, CT and increasingly MRI are the preferred modalities. Ultrasound has received increasing attention in recent years as a tool to evaluate the lungs given its lack of ionizing radiation, portability, and ease of use (1). Advances in ultrasound imaging technology including higher resolution transducers and harmonic-imaging have made high quality sonography of the chest more feasible. Children tend to have better sonographic windows than adults, and factors including unossified costal cartilage, less subcutaneous fat, and the ability to use the thymus as a sonographic window make chest ultrasound an attractive consideration in children.

Chest ultrasound is most commonly utilized to evaluate an opacity that is first seen on chest radiographs, and has a long-established role in the evaluation of the completely opacified hemithorax, pleural effusion, diaphragmatic motion, and chest wall lesions (2). Though radiographs are most commonly the first imaging test performed in the evaluation of suspected pneumonia, ultrasound may be performed before chest X-ray in some critical and emergency settings. When pneumonia is peripherally located, and not covered by aerated lung, consolidation can frequently be visualized. Unlike in normal lung, where sound waves are immediately reflected back to the transducer by the aerated lung, consolidated lung will transmit sound waves through fluid-filled alveoli causing an appearance similar to the liver, leading to the term *hepatization* (2). Branching echogenic air will often be seen within the bronchi, leading to sonographic air-bronchograms. Investigations in adults have shown that ultrasound without chest radiography can be fairly sensitive and specific for the diagnosis of pneumonia (3). Ultrasound may even be equivalent to CT in the detection of several complications of pneumonia including loculated pleural effusion, lung necrosis, and lung abscess (4). Though the results of these studies are encouraging, ultrasound of the central portions of the lungs is subject to acoustic shadowing from overlying aerated lung, which is a major technical limitation. This limited ability to assess central portions of the lung make it unlikely that ultrasound will ever completely replace chest X-ray as the prima-

ry imaging test for evaluating pneumonia, however ultrasound can play an important role.

In the current issue of *Acta Medica Academica* Lovrenski et al. (5) take an interesting approach to the role of lung ultrasound in pneumonia by comparing it with lung auscultation. They found that in children with suspected pneumonia, lung ultrasound was positive in more cases than chest auscultation. The authors also found that in those cases with normal auscultatory findings and abnormal ultrasound findings, the ultrasound findings tended to be smaller. This suggests that if one is suspicious for pneumonia but auscultation is negative, ultrasound could be considered as a method that will detect findings of pneumonia more often than chest auscultation alone.

This study is limited because other modalities, such as chest radiographs or CT, were not incorporated into the analysis. Though ultrasound is being utilized with increased frequency and several studies have demonstrated its utility in the diagnosis of pneumonia, most practitioners still consider chest X-ray to be the standard first-line imaging test for the evaluation of suspected pneumonia and CT to be the gold standard. It is difficult to know how many cases in this study were true-positives and if any cases may have been false-positives due to another entity such as atelectasis. It is also unknown how many cases were false negatives, if for instance breath sounds were normal and a centrally-located consolidation was obscured by overlying aerated lung on ultrasound. Though ultrasound does have the benefit of utilizing no ionizing radiation, chest radiographs use a very low amount of ionizing radiation, ranging from 0.01-0.02 mSv for a standard PA chest radiograph, and most consider them relatively safe. As the authors point out, chest CT utilizes a larger amount of radiation and it would not be appropriate to perform CT in the entire patient population.

Pneumonia is a common disease in children, and ultrasound can play a role in its diagnosis as a non-invasive imaging test which does not utilize ionizing radiation. As Lovrenski et al. (5) found, ultrasound may detect findings of pneumonia in a larger number of patients than auscultation alone, and may play a role in detecting small abnormalities that are too small to cause abnormal breath sounds.

Conflict of interest: The author declares that he has no conflict of interest.

References

1. Mong A, Epelman M, Darge K. Ultrasound of the pediatric chest. Pediatr Radiol. 2012;42(11):1287-97.
2. Coley BD. Chest sonography in children: current indications, techniques, and imaging findings. Radiol Clin North Am. 2011;49(5):825-46.
3. Chavez MA, Shams N, Ellington LE, Naithani N, Gilman RH, Steinhoff MC, et al. Lung ultrasound for the diagnosis of pneumonia in adults: a systematic review and meta-analysis. Respir Res. 2014;15:50.
4. Kurian J, Levin TL, Han BK, Taragin BH, Weinstein S. Comparison of ultrasound and CT in the evaluation of pneumonia complicated by parapneumonic effusion in children. AJR Am J Roentgenol. 2009;193(6):1648-54.
5. Lovrenski J, Petrović S, Balj-Barbir S, Jokić R, Vilotijević-Dautović G. Stethoscope vs. ultrasound probe – which is more reliable in children with suspected pneumonia? Acta Med Acad. 2016;45(1):39-50.

Commentary

Acta Medica Academica 2016;45(1):80-81
DOI: 10.5644/ama2006-124.162

Is lung ultrasound the stethoscope of the new millennium? Definitely yes!

Roberto Copetti*

Emergency Department Latisana
General Hospital Latisana, Italy

*Corresponding author:
robcopet@gmail.com
Tel.: + 39 043 152 9328
Fax.: + 39 043 152 9461

Received/Accepted: 2 May 2016

Key words: Lung ultrasound ▪ Pneumonia ▪ Children.

Children with community acquired pneumonia may present with a wide spectrum of different clinical signs and symptoms as fever, tachypnoea, breathlessness or difficulty in breathing, cough, wheeze, chest pain, tachycardia, rales, rhonchi, crackles, decreased breath sounds, low oxygen saturation. These findings, especially in infants, are highly specific and greatly increase the likelihood of pneumonia when present. However, their absence does not rule out pneumonia, and the accuracy of any individual sign or symptom is limited (1).

According to current guidelines, chest radiography should not be routinely performed in an ambulatory setting, and diagnosis is therefore frequently committed to clinical evaluation alone (2). Recently, current evidences have been included in a meta-analysis which confirmed the high accuracy of lung ultrasound in the diagnosis of pneumonia in children (3).

Lovrenski and colleagues (4), compared lung ultrasound with auscultation findings in children with clinical suspected pneumonia and demonstrated that lung ultrasound showed positive findings in more hemithoraces than auscultation. These data are very interesting and impose a serious reflection about the objective limits of classic semeiotics. The stethoscope is the symbol of doctors, and palpation, percussion and auscultation represented for nearly two centuries the art of the physical examination. The doctor who was exploring the patient's body in the nineteenth century and the first decades of the twentieth century, probably thought to have the sensibility of an artist, and perhaps the ear of a musician. This semeiotics has been the essence of the so called "medical art". The explosive growth of medical technology in the last fifty years has limited the use of the senses for patients' examination and has stripped its limits.

Lovrenski and colleagues (4) demonstrated that in about 95% of auscultatary examinations it is not possible to determine the presence of the consolidation of the lung parenchyma with a cranio-caudal diameter less than 30 mm. These measures are often found in the early stage of pneumonia. This means that we need to fill the gap between semeiotics and its limits. Another interesting point of the paper of Lovrenski and colleagues (4), is the suggestion to perform

lung examination with a combined trans-abdominal and trans-thoracic approach. In one child trans-hepatic examination of the lung base detected a consolidation not visible only with the trans-thoracic approach. Doubtless this recommendation might increase the sensitivity of lung ultrasound.

Ultrasound is a radiation free technique and this is an undoubted advantage in the pediatric population in which serious concerns about radiation exposure have been raised. It is high time to consider ultrasound the best stethoscope in our hands. It is high time to include lung ultrasound in the international guidelines and in our clinical practice.

The basic form of the stethoscope was invented by the French physician René-Théophile-Hyacinthe Laënnec who published a description of the instrument in 1819. In 1821 Laënnec's book was translated into English by sir Johan Forbes that in the preface wrote: "... notwithstanding its value, I am extremely doubtful; because its beneficial application requires much time, and gives a good deal of trouble both to the patient and the practitioner ..." (5).

It makes me smile to think that today there is still someone who think the same about the using of lung ultrasound in the routinely clinical practice. It's time to change!

Conflict of interest: The author declares that he has no conflict of interest.

References

1. Lynch T1, Platt R, Gouin S, Larson C, Patenaude Y. Can we predict which children with clinically suspected pneumonia will have the presence of focal infiltrates on chest radiographs? Pediatrics. 2004;113(3 Pt 1):e186-9.
2. Harris M, Clark J, Coote N, Fletcher P, Harnden A, McKean M, Thomson A; British Thoracic Society Standards of Care Committee. British Thoracic Society guidelines for the management of community acquired pneumonia in children: update 2011. Thorax. 2011;66 Suppl 2:ii1-23.
3. Pereda MA, Chavez MA, Hooper-Miele CC, Gilman RH, Steinhoff MC, Ellington LE, et al. Lung ultrasound for the diagnosis of pneumonia in children: a meta-analysis. Pediatrics. 2015;135(4):714-22.
4. Lovrenski J, Slobodanka Petrović S, Balj-Barbir S, Jokić R, Vilotijević-Dautović G. Stethoscope vs. ultrasound probe – which is more reliable in children with suspected pneumonia? Acta Med Acad. 2016;45(1):39-50.
5. Forbes J. A treatise on diseases of the chest in which they are described according to their anatomical characters, and there diagnosis established on a new principle by means of acoustic instruments. London: T & G Underwood. 1821.

Commentary

Acta Medica Academica 2016;45(1):82-83
DOI: 10.5644/ama2006-124.163

Lung ultrasound in the diagnosis of pediatric pneumonia: Are we ready for routine use?

Goran Roić*

Children's Hospital Zagreb, Department of Pediatric Radiology, Zagreb, Croatia

*Corresponding author:
goran.roic@kdb.hr
Tel.: + 385 1 460 0274
Fax.: + 385 1 460 0113

Received/Accepted: 25 April 2016

Key words: Children ▪ Pneumonia ▪ Lung ▪ Ultrasonography.

The interest in lung ultrasound (LUS) for the use in the diagnosis and follow-up of pediatric pneumonia increased during the last few years. However, it still has not been widely excepted routine imaging tool in every day clinical practice as it should be in my opinion.

Pediatric pneumonia is the leading cause of illness and death in children worldwide and still remains a diagnostic challenge (1). Clinical signs and symptoms of pneumonia vary depending on a child's age and the etiology of infection. Presenting signs and symptoms have poor diagnostic specificity, which may further complicate the diagnosis. Traditionally, the diagnosis of pneumonia is mainly based on physical examination including auscultation, chest radiograph and laboratory evaluation. Within the physical examination, the stethoscope is broadly accepted diagnostic tool in every day clinical practice (2).

Although chest radiography has been widely used for the diagnosis of pneumonia because of its convenience and ease of access, some studies have shown substantial variability in the interpretation of chest radiographs. On the other hand, the fact is that a negative chest radiograph does not eliminate the possibility of having pneumonia. Thoracic CT scan is considered the "gold standard" for detection of pneumonia and other pulmonary lesions in adults, but due to high radiation dose it cannot be used as a first-line radiological examination in pediatric patients with suspected pneumonia (3).

The lung is not an ideal target for ultrasonography, but once fluid or solid material has accumulated in the lung it can more easily be visualized on an ultrasound scan. That is the reason that lung ultrasonography is being increasingly utilized in the diagnosis of pediatric pneumonia. Furthermore, advances in ultrasound technology have made lung ultrasound an attractive, safe, portable and inexpensive option for the diagnosis of pneumonia (4). To identify pneumonia by LUS, a consolidation needs to reach the pleura and be within an intercostal window. In children, the former is offset by the relative small lung size, and may explain the relative high sensitivity. The characteristic so-

nographic sign of lung consolidation is a sub pleural, echo-poor region with air or fluid bronchograms, comet-tail reverberation artifacts at the far-field margin, and a vascular pattern within the consolidation (2, 5, 6). It is also useful in following up the progress of pneumonia. Multiple studies have shown LUS is sensitive diagnostic imaging tool to identify pneumonia in children, more accurate in comparison with conventional chest radiography. LUS is suggested as complementary tool to chest radiography in the diagnosis of pneumonia in children and that the follow up of pneumonia, which can reduce the exposure of children to ionizing radiation. According to a meta-analysis, LUS had high specificity and sensitivity in the hands of trained clinicians (7). As with any other ultrasound applications, LUS is operator-dependent and correct diagnosis cannot be made if the operator is insufficiently trained or inexperienced. Fortunately, it appears that the learning curve for LUS is easier and faster than for other ultrasound applications. Recommendations to train general pediatricians on LUS for the diagnosis of childhood pneumonia could have an important impact in different clinical settings, especially in limited resources countries and small primary care clinics where radiography may not be commonly available (7). Furthermore, it is very important that its application might to a certain extent exclude the need for imaging modalities based on ionizing radiation, strongly supporting the Image Gently campaign (8).

In Conclusion at the current stage, LUS is a complementary tool to chest radiography and physical examination in the diagnosis and the follow-up of pneumonia in children, allowing reduction of exposure to ionizing radiation, which is exceptionally important. Lung ultrasound is a reliable, safe, inexpensive and portable diagnostic tool, and should be implemented in everyday clinical practice whenever physical findings need to be complemented with imaging findings.

Conflict of interest: The author declares that he has no conflict of interest.

References

1. Liu L, Oza S, Hogan D, Perin J, Rudan I, Lawn JE, et al. Global, regional, and national causes of child mortality in 2000-13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet. 2015; 31;385(9966):430-40.
2. World Health Organization. Pneumonia. Fact Sheet No. 331. Available at: www. who.int/mediacentre/factsheets/fs331/en/. 2014.
3. Lovrenski J, Petrović S, Balj-Barbir S, Jokić R, Vilotijević-Dautović G. Stethoscope vs. ultrasound probe – which is more reliable in children with suspected pneumonia? Acta Med Acad. 2016;45(1):39-50.
4. Ye X, Xiao H, Chen B, Zhang SY. Accuracy of Lung Ultrasonography versus Chest Radiography for the Diagnosis of Adult Community Acquired Pneumonia: Review of the Literature and Meta-Analysis. PLoS One. 2015;10(6):e0130066.
5. Blaivas M. Lung Ultrasound in Evaluation of Pneumonia. J Ultrasound Med. 2012;31(6):823-6.
6. Caiulo VA, Gargani L, Caiulo S, Fisicaro A, Moramarco F, Latini G, et al. Lung ultrasound characteristics of community-acquired pneumonia in hospitalized children. Pediatr Pulmonol. 2013;48(3):280-7.
7. Copetti R, Cattarossi L. Ultrasound diagnosis of pneumonia in children. Radiol Med. 2008;113(2):190-8.
8. Pereda MA, Chavez MA, Hooper-Miele CC, Gilman RH, Steinhoff MC, Ellington LE, et al. Lung ultrasound for the diagnosis of pneumonia in children: a meta-analysis. Pediatrics. 2015;135(4):714-22.
9. Ho MC, Ker CR, Hsu JH, Wu JR, Dai ZK, Chen IC. Usefulness of lung ultrasound in the diagnosis of community-acquired pneumonia in children. Pediatr Neonatol. 2015;56(1):40-5.

Acta Medica Academica 2015;44(2):84-88
DOI: 10.5644/ama2006-124.164

International publications of authors from Bosnia and Herzegovina in Current Contents indexed publications in the second half of 2015*

Ačkar Đ, Babić J, Jozinović A, Miličević B, Jokić S, Miličević R, Rajič M, Šubarić D. Starch Modification by Organic Acids and Their Derivatives: A Review. Molecules. 2015 Oct 27;20(10):19554-70. doi: 10.3390/molecules201019554.

Barišić T, Šutalo N, Letica L, Kordić AV. Rupture of splenic artery aneurysm in primipara five days after cesarean section: case report and review of the literature. Wien Klin Wochenschr. 2015 Nov;127(21-22):896-8. doi: 10.1007/s00508-015-0856-x. Epub 2015 Sep 15.

Bergsland J, Mirtaheri P, Hiorth N, Fosse E. Review of the endovascular approach to mitral valve disease. Minim Invasive Ther Allied Technol. 2015;24(5):282-8. doi: 10.3109/13645706.2015.1065891. Epub 2015 Jul 23.

Bjelanović V, Babić D, Hodžić D, Bjelanović A, Krešić T, Dugandžić-Šimić A, Orešković S. Correlation of psychological symptoms with cortisol and CRP levels in pregnant women with metabolic syndrome. Psychiatr Danub. 2015 Dec;27 Suppl 2:578-85.

Bugiardini R, Cenko E, Ricci B, Vasiljevic Z, Dorobantu M, Kedev S, Vavlukis M, Kalpak O, Puddu PE, Gustiene O, Trninic D, Knežević B, Miličić D, Gale CP, Manfrini O, Koller A, Badimon L. Comparison of Early Versus Delayed Oral β Blockers in Acute Coronary Syndromes and Effect on Outcomes. Am J Cardiol. 2016 Mar 1;117(5):760-7. doi: 10.1016/j.amjcard.2015.11.059. Epub 2015 Dec 13.

Bukvić N, Marinović M, Bakota B, Veršić AB, Karlo R, Kvesić A, Gusić N, Čoklo M, Bukvić F. Complications of ESIN osteosynthesis--Experience in 270 patients. Injury. 2015 Nov;46 Suppl 6:S40-3. doi: 10.1016/j.injury.2015.10.042. Epub 2015 Nov 10.

Campos CM, Stanetic BM, Farooq V, Walsh S, Ishibashi Y, Onuma Y, Garcia-Garcia HM, Escaned J, Banning A, Serruys PW; SYNTAX II Study Group. Risk stratification in 3-vessel coronary artery disease: Applying the SYNTAX Score II in the Heart Team Discussion of the SYNTAX II trial. Catheter Cardiovasc Interv. 2015 Nov 15;86(6):E229-38. doi: 10.1002/ccd.25907. Epub 2015 May 6.

Catic T. Access to Biological Therapies and Consumption Trends in Bosnia and Herzegovina. Value Health. 2015 Nov;18(7):A655. doi: 10.1016/j.jval.2015.09.2364. Epub 2015 Oct 20.

Catic T. Differences In Reimbursement Prices And Inequalities To Access Most Commonly Prescribed Medicines In Bosnia And Herzegovina. Value Health. 2015 Nov;18(7):A527. doi: 10.1016/j.jval.2015.09.1630. Epub 2015 Oct 20.

Choe JY, Prodanovic N, Niebrzydowski J, Staykov I, Dokoupilova E, Baranauskaite A, Yatsyshyn R, Mekic M, Porawska W, Ciferska H, Jedrychowicz-Rosiak K, Zielinska A, Choi J, Rho YH, Smolen JS. A randomised, double-blind, phase III study comparing SB2, an infliximab biosimilar, to the infliximab reference product Remicade in patients with moderate to severe rheumatoid arthritis despite methotrexate therapy. Ann Rheum Dis. 2015 Aug 28. pii: annrheumdis-2015-207764. doi: 10.1136/annrheumdis-2015-207764. [Epub ahead of print]

Ćurguz Z, Stojanovska Z, Žunić ZS, Kolarž P, Ischikawa T, Omori Y, Mishra R, Sapra BK, Vaupotič J, Ujić P, Bossew P. Long-term measurements of radon, thoron and their airborne progeny in 25 schools in Republic of Srpska. J Environ Radioact. 2015 Oct;148:163-9. doi: 10.1016/j.jenvrad.2015.06.026. Epub 2015 Jul 12.

Damjanov I, Vranic S, Skenderi F. Does everything a surgeon takes out have to be seen by a pathologist? A review of the current pathology practice. Virchows Arch. 2016 Jan;468(1):69-74. doi: 10.1007/s00428-015-1801-0. Epub 2015 Jul 9.

*Data for this survey were collected from PubMed/MEDLINE using the keywords Bosnia and Herzegovina and 2015.

Damjanovska M, Cvetko E, Hadzic A, Seliskar A, Plavec T, Mis K, Vuckovic Hasanbegovic I, Stopar Pintaric T. Neurotoxicity of perineural vs intraneural-extrafascicular injection of liposomal bupivacaine in the porcine model of sciatic nerve block. Anaesthesia. 2015 Dec;70(12):1418-26. doi: 10.1111/anae.13189. Epub 2015 Sep 4.

Debeljak M, Toplak N, Abazi N, Szabados B, Mulaosmanović V, Radović J, Perko D, Vojnović J, Constantin T, Kuzmanovska D, Avčin T. The carrier rate and spectrum of MEFV gene mutations in central and southeastern European populations. Clin Exp Rheumatol. 2015 Nov-Dec;33(6 Suppl 94):S19-23. Epub 2015 Sep 24.

Denislic M, Tiric-Campara M, Resić H, Al-Hashel JY, Zorec R, Gojak R, Ravnik J. A neurophysiological study of large- and small-diameter nerve fibers in the hands of hemodialysis patients. Int Urol Nephrol. 2015 Nov;47(11):1879-87. doi: 10.1007/s11255-015-1117-7. Epub 2015 Oct 3.

Dujic T, Causevic A, Bego T, Malenica M, Velija-Asimi Z, Pearson ER, Semiz S. Organic cation transporter 1 variants and gastrointestinal side effects of metformin in patients with Type 2 diabetes. Diabet Med. 2016 Apr;33(4):511-4. doi: 10.1111/dme.13040. Epub 2015 Dec 24.

Džoić Dominković M, Ivanac G, Kelava T, Brkljačić B. Elastographic features of triple negative breast cancers. Eur Radiol. 2016 Apr;26(4):1090-7. doi: 10.1007/s00330-015-3925-7. Epub 2015 Aug 1.

Fan T, Grychtol P, Knut R, Hernández-García C, Hickstein DD, Zusin D, Gentry C, Dollar FJ, Mancuso CA, Hogle CW, Kfir O, Legut D, Carva K, Ellis JL, Dorney KM, Chen C, Shpyrko OG, Fullerton EE, Cohen O, Oppeneer PM, Milošević DB, Becker A, Jaroń-Becker AA, Popmintchev T, Murnane MM, Kapteyn HC. Bright circularly polarized soft X-ray high harmonics for X-ray magnetic circular dichroism. Proc Natl Acad Sci U S A. 2015 Nov 17;112(46):14206-11. doi: 10.1073/pnas.1519666112. Epub 2015 Nov 3.

Gyberg V, De Bacquer D, De Backer G, Jennings C, Kotseva K, Mellbin L, Schnell O, Tuomilehto J, Wood D, Rydén L, Amouyel P, Bruthans J, Conde AC, Cifkova R, Deckers JW, De Sutter J, Dilic M, Dolzhenko M, Erglis A, Fras Z, Gaita D, Gotcheva N, Goudevenos J, Heuschmann P, Laucevicius A, Lehto S, Lovic D, Miličić D, Moore D, Nicolaides E, Oganov R, Pająk A, Pogosova N, Reiner Z, Stagmo M, Störk S, Tokgözoğlu L, Vulic D; EUROASPIRE Investigators. Patients with coronary artery disease and diabetes need improved management: a report from the EUROASPIRE IV survey: a registry from the EuroObservational Research Programme of the European Society of Cardiology. Cardiovasc Diabetol. 2015 Oct 1;14:133. doi: 10.1186/s12933-015-0296-y.

Hadziabdic N, Kurtovic-Kozaric A, Pojskic N, Sulejmanagic N, Todorovic L. Gene-expression analysis of matrix metalloproteinases 1 and 2 and their tissue inhibitors in chronic periapical inflammatory lesions. J Oral Pathol Med. 2016 Mar;45(3):224-30. doi: 10.1111/jop.12347. Epub 2015 Aug 21.

Hadžimehmedagić A, Gavrankapetanović I, Vranić H, Šunje M, Gavrankapetanović F, Papović A, Granov N, Begović B, Omerović Đ. Haemodynamic assessment in simulated operative positions before knee arthroplasty can be useful in deep vein thrombosis prediction. Int Orthop. Hodzic E, Rasic S, Klein C, Covic A, Unsal A, Cunquero JM, Prischl FC, Gauly A, Kalicki RM, Uehlinger DE. Clinical Validation of a Peritoneal Dialysis Prescription Model in the PatientOnLine Software. Artif Organs. 2016 Feb;40(2):144-52. doi: 10.1111/aor.12526. Epub 2015 Jul 6.

Hagl M, Powell S, Rosner R, Butollo W. Dialogical Exposure with Traumatically Bereaved Bosnian Women: Findings from a Controlled Trial. Clin Psychol Psychother. 2015 Nov;22(6):604-18. doi: 10.1002/cpp.1921. Epub 2014 Sep 24.

Hermans LE, Svicher V, Pas SD, Salpini R, Alvarez M, Ben Ari Z, Boland G, Bruzzone B, Coppola N, Seguin-Devaux C, Dyda T, Garcia F, Kaiser R, Köse S, Krarup H, Lazarevic I, Lunar MM, Maylin S, Micheli V, Mor O, Paraschiv S, Paraskevis D, Poljak M, Puchhammer-Stöckl E, Simon F, Stanojevic M, Stene-Johansen K, Tihic N, Trimoulet P, Verheyen J, Vince A, Weis N, Yalcinkaya T, Lepej SZ, Perno C, Boucher CA, Wensing AM; HEPVIR Working Group of the European Society for Translational Antiviral Research. Combined Analysis of the Prevalence of Drug-Resistant Hepatitis B Virus in Antiviral Therapy-Experienced Patients in Europe (CAPRE). J Infect Dis. 2016 Jan 1;213(1):39-48. doi: 10.1093/infdis/jiv363. Epub 2015 Jul 1.

Hodzic E, Rasic S, Klein C, Covic A, Unsal A, Cunquero JM, Prischl FC, Gauly A, Kalicki RM, Uehlinger DE. Clinical Validation of a Peritoneal Dialysis Prescription Model in the PatientOnLine Software. Artif Organs. 2016 Feb;40(2):144-52. doi: 10.1111/aor.12526. Epub 2015 Jul 6.

Jakovljević M, Ostojić L. Person-centered medicine and good clinical practice: disease has to be cured, but the patient has to be healed. Psychiatr Danub. 2015 Dec;27 Suppl 2:546-9.

Janković J, Marinković J, Stojisavljević D, Erić M, Vasiljević N, Janković S. Sex inequalities in cardiovascular health: a cross-sectional study. Eur J Public Health. 2016 Feb;26(1):152-8. doi: 10.1093/eurpub/ckv161. Epub 2015 Sep 14.

Kajić M, Tomić V, Martinac M, Mikulić-Kajić M, Orlović M. Medical students' attitudes towards contraception. Psychiatr Danub. 2015 Dec;27 Suppl 2:590-2.

Kasum M, von Wolff M, Franulić D, Čehić E, Klepac-Pulanić T, Orešković S, Juras J. Fertility preservation options in breast cancer patients. Gynecol Endocrinol. 2015;31(11):846-51. doi: 10.3109/09513590.2015.1081684. Epub 2015 Sep 15.

Kiss O, Tőkés AM, Vranic S, Gatalica Z, Vass L, Udvarhelyi N, Szász AM, Kulka J. Expression of miRNAs in adenoid cystic carcinomas of the breast and salivary glands. Virchows Arch. 2015 Nov;467(5):551-62. doi: 10.1007/s00428-015-1827-3. Epub 2015 Aug 21.

Korda-Vidić V, Vasilj I, Babić D. The stress of war and breast cancer incidence. Psychiatr Danub. 2015 Dec;27 Suppl 2:571-7.

Kučinić M, Previšić A, Graf W, Mihoci I, Šoufek M, Stanić-Koštroman S, Lelo S, Vitecek S, Waringer J. Larval description of Drusus bosnicus Klapálek 1899 (Trichoptera: Limnephilidae), with distributional, molecular and ecological features. Zootaxa. 2015 May 13;3957(1):85-97. doi: 10.11646/zootaxa.3957.1.7.

Kujundzic B, Zeljic K, Supic G, Magic M, Stanimirovic D, Ilic V, Jovanovic B, Magic Z. Association of vdr, cyp27b1, cyp24a1 and mthfr gene polymorphisms with oral lichen planus risk. Clin Oral Investig. 2016 May;20(4):781-9. doi: 10.1007/s00784-015-1572-7. Epub 2015 Aug 26.

Kurtovic-Kozaric A, Hasic A, Radich JP, Bijedic V, Nefic H, Eminovic I, Kurtovic S, Colakovic F, Kozaric M, Vranic S, Bovan NS. The reality of cancer treatment in a developing country: the effects of delayed TKI treatment on survival, cytogenetic and molecular responses in chronic myeloid leukaemia patients. Br J Haematol. 2016 Feb;172(3):420-7. doi: 10.1111/bjh.13843. Epub 2015 Nov 11.

Lipovac K, Tešić M, Marić B, Đerić M. Self-reported and observed seat belt use--A case study: Bosnia and Herzegovina. Accid Anal Prev. 2015 Nov;84:74-82. doi: 10.1016/j.aap.2015.08.010. Epub 2015 Aug 31.

Lukenda A, Dotlic S, Vukojevic N, Saric B, Vranic S, Zarkovic K. Expression and prognostic value of putative cancer stem cell markers CD117 and CD15 in choroidal and ciliary body melanoma. J Clin Pathol. 2016 Mar;69(3):234-9. doi: 10.1136/jclinpath-2015-203130. Epub 2015 Aug 19.

Mahmić-Kaknjo M, Kadić D, Hodžić H, Spahić-Sarajlić S, Hadžić E, Ademović E. Awareness, knowledge, use, and attitudes toward evidence based medicine in a developing country: survey of physicians in a canton in Bosnia and Herzegovina. Croat Med J. 2015 Dec;56(6):558-66.

Marković-Peković V, Škrbić R, Petrović A, Vlahović-Palčevski V, Mrak J, Bennie M, Fadare J, Kwon HY, Schiffers K, Truter I, Godman B. Polypharmacy among the elderly in the Republic of Srpska: extent and implications for the future. Expert Rev Pharmacoecon Outcomes Res. 2015 Dec 15:1-10. [Epub ahead of print]

Meisrimler CN, Menckhoff L, Kukavica BM, Lüthje S. Pre-fractionation strategies to resolve pea (Pisum sativum) sub-proteomes. Front Plant Sci. 2015 Oct 19;6:849. doi: 10.3389/fpls.2015.00849. eCollection 2015.

Milicevic R, Jaksic N, Aukst-Margetic B, Jakovljevic M. Personality traits and treatment compliance in patients with type 2 diabetes mellitus. Psychiatr Danub. 2015 Dec;27 Suppl 2:586-9.

Mirjanic-Azaric B, Stojakovic-Jelisavac T, Vukovic B, Stojanovic D, Vujnic M, Uletilovic S. The impact of time of sample collection on the measurement of thyroid stimulating hormone values in the serum. Clin Biochem. 2015 Dec;48(18):1347-9. doi: 10.1016/j.clinbiochem.2015.08.020. Epub 2015 Aug 20.

Mišigoj-Duraković M, Sorić M, Matika D, Jukić I, Duraković Z. Which is more important for reducing the odds of metabolic syndrome in men: Cardiorespiratory or muscular fitness? Obesity (Silver Spring). 2016 Jan;24(1):238-44. doi: 10.1002/oby.21264. Epub 2015 Dec 6.

Namy S, Heilman B, Stich S, Crownover J, Leka B, Edmeades J. Changing what it means to 'become a man': participants' reflections on a school-based programme to redefine masculinity in the Balkans. Cult Health Sex. 2015;17 Suppl 2:206-22. doi: 10.1080/13691058.2015.1070434.

Novokmet N, Galov A, Marjanović D, Škaro V, Projić P, Lauc G, Primorac D, Rudan P. Genetic structure and admixture between Bayash Roma from northwestern Croatia and general Croatian population: evidence from Bayesian clustering

analysis. Anthropol Anz. 2015;72(3):321-34. doi: 10.1127/anthranz/2015/0485. Epub 2015 Aug 3.

Obradovic B, Obradovic M. Triple V-Y Vermilion Augmentation of the Upper Lip. J Craniofac Surg. 2015 Nov;26(8):e736-8. doi: 10.1097/SCS.0000000000002246.

Petric I, Mustafić N. Dynamic modeling the composting process of the mixture of poultry manure and wheat straw. J Environ Manage. 2015 Sep 15;161:392-401. doi: 10.1016/j.jenvman.2015.07.033. Epub 2015 Jul 24.

Pilav A, Rudić A, Branković S, Djido V. Perception of health risks among adolescents due to consumption of cigarettes, alcohol and psychoactive substances in the Federation of Bosnia and Herzegovina. Public Health. 2015 Jul;129(7):963-9. doi: 10.1016/j.puhe.2015.05.004. Epub 2015 Aug 6.

Pojskic L, Haveric S, Lojo-Kadric N, Hadzic M, Haveric A, Galic Z, Galic B, Vullo D, Supuran CT, Milos M. Effects of dipotassium-trioxohydroxytetrafluorotriborate, K(2)[B(3)O(3)F(4)OH], on cell viability and gene expression of common human cancer drug targets in a melanoma cell line. J Enzyme Inhib Med Chem. 2015 Aug 26:1-6. [Epub ahead of print]

Prohic A, Jovovic Sadikovic T, Krupalija-Fazlic M, Kuskunovic-Vlahovljak S. Malassezia species in healthy skin and in dermatological conditions. Int J Dermatol. 2016 May;55(5):494-504. doi: 10.1111/ijd.13116. Epub 2015 Dec 29.

Rajič B, Arapović J, Raguž K, Bošković M, Babić SM, Maslać S. Eradication of Blastocystis hominis prevents the development of symptomatic Hashimoto's thyroiditis: a case report. J Infect Dev Ctries. 2015 Jul 30;9(7):788-91. doi: 10.3855/jidc.4851.

Rašić S, Rebić D, Hasić S, Rašić I, Delić Šarac M. Influence of Malondialdehyde and Matrix Metalloproteinase-9 on Progression of Carotid Atherosclerosis in Chronic Renal Disease with Cardiometabolic Syndrome. Mediators Inflamm. 2015;2015:614357. doi: 10.1155/2015/614357. Epub 2015 Oct 11.

Rebić D, Matovinović MS, Rašić S, Kes P, Hamzić-Mehmedbašić A. The Effect of Preserved Residual Renal Function on Left Ventricular Structure in Non-Anuric Peritoneal Dialysis Patients. Kidney Blood Press Res. 2015;40(5):500-8. doi: 10.1159/000368526. Epub 2015 Oct 4.

Rebić D, Rašić S, Hamzić-Mehmedbašić A, Džemidžić J, Kurtalić E. Valvular calcification and left ventricular modifying in peritoneal dialysis patients. Ren Fail. 2015;37(8):1316-22. doi: 10.3109/0886022X.2015.1073495. Epub 2015 Aug 14.

Salkic NN, Cickusic E, Jovanovic P, Denjagic MB, Iljazovic-Topcic S, Bevanda M, Ahmetagic S. Online combination algorithm for non-invasive assessment of chronic hepatitis B related liver fibrosis and cirrhosis in resource-limited settings. Eur J Intern Med. 2015 Oct;26(8):628-34. doi: 10.1016/j.ejim.2015.07.005. Epub 2015 Jul 18.

Santrac V, Nedic DN, Maric J, Nikolic S, Stevanovic O, Vasilev S, Cvetkovic J, Sofronic-Milosavljevic L. The first report of Trichinella pseudospiralis presence in domestic swine and T. britovi in wild boar in Bosnia and Herzegovina. Acta Parasitol. 2015 Sep;60(3):471-5. doi: 10.1515/ap-2015-0066.

Sartelli M, Abu-Zidan FM, Catena F, Griffiths EA, Di Saverio S, Coimbra R, Ordoñez CA, Leppaniemi A, Fraga GP, Coccolini F, Agresta F, Abbas A, Abdel Kader S, Agboola J, Amhed A, Ajibade A, Akkucuk S, Alharthi B, Anyfantakis D, Augustin G, Baiocchi G, Bala M, Baraket O, Bayrak S, Bellanova G, Beltràn MA, Bini R, Boal M, Borodach AV, Bouliaris K, Branger F, Brunelli D, Catani M, Che Jusoh A, Chichom-Mefire A, Cocorullo G, Colak E, Costa D, Costa S, Cui Y, Curca GL, Curry T, Das K, Delibegovic S, Demetrashvili Z, Di Carlo I, Drozdova N, El Zalabany T, Enani MA, Faro M, Gachabayov M, Giménez Maurel T, Gkiokas G, Gomes CA, Gonsaga RA, Guercioni G, Guner A, Gupta S, Gutierrez S, Hutan M, Ioannidis O, Isik A, Izawa Y, Jain SA, Jokubauskas M, Karamarkovic A, Kauhanen S, Kaushik R, Kenig J, Khokha V, Kim JI, Kong V, Koshy R, Krasniqi A, Kshirsagar A, Kuliesius Z, Lasithiotakis K, Leão P, Lee JG, Leon M, Lizarazu Pérez A, Lohsiriwat V, López-Tomassetti Fernandez E, Lostoridis E, Mn R, Major P, Marinis A, Marrelli D, Martinez-Perez A, Marwah S, McFarlane M, Melo RB, Mesina C, Michalopoulos N, Moldovanu R, Mouaqit O, Munyika A, Negoi I, Nikolopoulos I, Nita GE, Olaoye I, Omari A, Ossa PR, Ozkan Z, Padmakumar R, Pata F, Pereira Junior GA, Pereira J, Pintar T, Pouggouras K, Prabhu V, Rausei S, Rems M, Rios-Cruz D, Sakakushev B, Sánchez de Molina ML, Seretis C, Shelat V, Simões RL, Sinibaldi G, Skrovina M, Smirnov D, Spyropoulos C, Tepp J, Tezcaner T, Tolonen M, Torba M, Ulrych J, Uzunoglu MY, van Dellen D, van Ramshorst GH, Vasquez G, Venara A, Vereczkei A, Vettoretto N, Vlad N, Yadav SK, Yilmaz TU, Yuan KC, Zachariah SK, Zida M, Zilinskas J, Ansaloni L. Global validation of the WSES Sepsis Severity Score for patients with complicated intra-

abdominal infections: a prospective multicentre study (WISS Study). World J Emerg Surg. 2015 Dec 16;10:61. doi: 10.1186/s13017-015-0055-0. eCollection 2015.

Stankovic MS, Turuntas V, De Luka SR, Jankovic S, Stefanovic S, Puskas N, Zaletel I, Milutinović-Smiljanic S, Trbovich AM. Effects of Il-33/St2 pathway on alteration of iron and hematological parameters in acute inflammation. Exp Mol Pathol. 2015 Dec;99(3):687-92. doi: 10.1016/j.yexmp.2015.11.016. Epub 2015 Nov 11.

Šabanagić-Hajrić S, Suljić E, Kučukalić A. Fatigue during multiple sclerosis relapse and its relationship to depression and neurological disability. Psychiatr Danub. 2015 Dec;27(4):406-12.

Šutalo N, Šoljić M, Kozomara D, Petričević J, Glibo DB, Bošnjak A, Čuljak V. The influence of dreinage in the treatment of chronic pilonidal sinus disease using midline closure. Psychiatr Danub. 2015 Dec;27 Suppl 2:593-5.

Veličković V, Jović M, Nalić E, Višnjić A, Radulović O, Šagrić Č, Ćirić M. Knowledge, Attitudes Toward, and Acceptability of Genetic Modification among Western Balkan University Students of Life Sciences (AGREE Study). J Am Coll Nutr. 2016 Feb-Mar;35(2):150-62. doi: 10.1080/07315724.2014.1003115. Epub 2015 Jun 1.

Vodenčarević AN, Terzić S, Terzić A. Endophthalmitis After Intravitreal Injections: Incidence, Presentation, Management, and Visual Outcome. Am J Ophthalmol. 2015 Oct;160(4):843-4. doi: 10.1016/j.ajo.2015.07.003. Epub 2015 Jul 30.

Weltermann BM, Gerasimovska-Kitanovska B, Thielmann A, Chambe J, Lingner H, Pirrotta E, Buczkowski K, Tekiner S, Czachowski S, Edirne T, Zielinski A, Yikilkan H, Koskela T, Petrazzuoli F, Hoffman RD, Petek Šter M, Guede Fernández C, Uludağ A, Hoffmann K, Mevsim V, Kreitmayer Pestic S. Self-Care Practices for Common Colds by Primary Care Patients: Study Protocol of a European Multicenter Survey-The COCO Study. Evid Based Complement Alternat Med. 2015;2015:272189. doi: 10.1155/2015/272189. Epub 2015 Sep 2.

Yahia ME, Tolba RE, El-Bedwehy NA, El-Labany SK, Moslem WM. Rogue waves lead to the instability in GaN semiconductors. Sci Rep. 2015 Jul 24;5:12245. doi: 10.1038/srep12245.

Zerem E, Imširović B, Loga-Zec S, Kunosić S, Hujdurović A, Zerem O. Treatment of Recurrent Pancreatic Pseudocysts with Proven Communication between Pseudocyst and Pancreatic Duct by Long-term Percutaneous Drainage. Ann Acad Med Singapore. 2015 Nov;44(11):542-4.

Zerem E, Lincender-Cvijetić L, Kurtčehajić A, Samardžić J, Zerem O. Symptomatic Gallbladder Sludge and its Relationship to Subsequent Biliary Events. J Clin Gastroenterol. 2015 Oct;49(9):795-6. doi: 10.1097/MCG.0000000000000361.

Zerem E, Omerović M, Zerem O. What is the optimal treatment for hepatic abscess and infected biloma? Gastrointest Endosc. 2015 Nov;82(5):971-2. doi: 10.1016/j.gie.2015.06.011.

Zielinski C, Lang I, Beslija S, Kahan Z, Inbar MJ, Stemmer SM, Anghel R, Vrbanec D, Messinger D, Brodowicz T. Predictive role of hand-foot syndrome in patients receiving first-line capecitabine plus bevacizumab for HER2-negative metastatic breast cancer. Br J Cancer. 2016 Jan 19;114(2):163-70. doi: 10.1038/bjc.2015.419. Epub 2015 Dec 10.

Zvorničanin J, Zvorničanin E. The Diagnostic Accuracy of Bedside Ocular Ultrasonography for the Diagnosis of Retinal Detachment: A Systematic Review and Meta-analysis. Ann Emerg Med. 2015 Sep;66(3):342-3. doi: 10.1016/j.annemergmed.2015.05.011.

by Nerma Tanović

PEER REVIEWERS FOR ACTA MEDICA ACADEMICA IN 2015

The Editorial Board of Acta Medica Academica (Acta Med Acad) wishes to acknowledge and thank the reviewers who volunteered their time and expertise to read and evaluate the submissions for Acta Med Acad. The following individuals provided such expert assistance to Acta Med Acad in 2015:

Mark Agius, UK
Cenk Demirdöver, TR
Krzysztof Tomaszewski, PL
Jana Kučerova, CZ
Rafael Guimarães dos Santos, BR
Vincenzo Micale, CZ
Jerzy Walocha, PL
Funda Aksu, TR
Franciszek Burdan, PL
B. V. Murlimanju, IN
Gordan Vujanić, UK
Cemal Cingi, TR
Goran Imamović, BA
Maria Victoria Delpino, AR
Selma Ates Guler, TR
Dubravka Matanić, HR
Ljerka Ostojić, BA
Lucia Silva-Fernández, ES
Francesca Romana Spinelli, IT
Carol Haigh, UK
Rajko Igić, US
Daniela D'Angelo, IT
Fiona Duncan, UK
Jan Novak, CZ
Srđa Janković, RS
Ozren Polašek, HR
Ivan Damjanov, US
Dario Sambunjak, HR
Nermin Salkić, BA
Marta Čivljak, HR
Robin Köck, DE
Alex Friedrich, NL
Jacek Tomczyk, PL
Maria Piagkou, GR
Stella Fatović-Ferenčić, HR
Bogdan Bošković, RS
Ljubomir Berberović, BA
Luigi Camporota, UK
Ariel Shiloh, US
Wilhelm Jahnen-Dechent, DE
János Nemcsik, HU
Mariana Figueiroa Careta, BR
Fernanda Falcini, IT
Fernando Alfageme, ES
Peppino Mirabelli, IT
Gangping Wang, CN
Mariarosaria Incoronato, IT
Sofia Jonasson, SE
Elisabeth Wigenstam, SE
Linda Svensson-Elfsmark, SE
Dwarakanath Srinivas, IN
Mahmood Dhahir Al-Mendalawi, IQ
Niels Nørskov-Lauritsen, DK
Chandrashekar Nagarathna, IN
Kenji Iwaku, JP
Irene Campi, IT
Jan Calissendorff, SE
Ming Lim, UK
Ben Wakerley, UK
Robert Hadden, UK
Livia Puljak, HR
Jordi Almirall Pujol, ES
Jacobo Sellarés, ES
Michael R. Gionfriddo, US
Lara Mihaljević, AU
Franz Wiedermann, AT
Yong Chan Ahn, KR
Jianji Pan, CN
Peng Sun, CN
Tadashi Nakamura, JP
Gisele Zandman-Goddard, IL
Gleb Slobodin, IL
Roland C. Francis, DE
Ivančica Pavličević, HR
Zdenko Sonicki, HR
Michael Tai, TW
Edward J. Burger, US
Anant Mehrotra, IN
Girolamo Crisi, IT
George Mendes, FR
Zijad Duraković, HR
Molly Howard, US
Petra A. Thürmann, DE
Robert McKelvie, CA
Mojca Čižek Sajko, SI
Tomasz Jacek Lis, PL
Husnija Kamberović, BA
Stojan Berber, RS
Srećko Severinski, HR
Mira Samardžić, ME
Irena Bralić, HR
Mojca Zerjav Tansek, SI
Maria Pia De Carolis, IT
Cinzia Auriti, IT
Darja Paro Panjan, SI

Instructions to authors

Scope

Acta Medica Academica is a biannual, peer-reviewed journal that publishes: (1) reports of original research, (2) original clinical observations accompanied by analysis and discussion, (3) analysis of philosophical, ethical, or social aspects of the health profession or biomedical sciences, (4) critical reviews, (5) statistical compilations, (6) descriptions of evaluation of methods or procedures, (7) case reports, and (8) images in clinical medicine. The fields covered include basic biomedical research, clinical and laboratory medicine, veterinary medicine, clinical research, epidemiology, phramacology, public health, oral health, and medical information.

Manuscript submission

Manuscript can be submitted electronically, as an email attachment, to one of the following addresses: amabih@anubih.ba; amaanubih@hotmail.com; info@ama.ba. All manuscripts submitted to AMA will be regularly analysed by plagiarism detection software.

All parts of the manuscript, including title page, abstract, text, tables, figures, etc., have to be available in electronic format. The recommended formats are: Microsoft Word, Excel, JPEG, GIF, TIFF. Always keep a backup copy of the electronic file for reference and safety. All electronically submitted files are to be scanned by the authors for viruses immediately prior to submission with appropriate current software, and submitted in good faith that the files are free of viruses.

Cover letter

Manuscripts must be accompanied by a cover letter, which should include the following information:

- A statement that the paper has not been sent to or accepted for publication in any other journal;
- A statement of financial or other relationships that might lead to a conflict of interest, if that information is not included in the manuscript itself; Conflict of Interest Statement is available at www.ama.ba;
- A statement that the manuscript has been read and approved for publication by all authors;
- Copies of all permissions to reproduce published material, to use illustrations or report information about identifiable people;
- Opinion of the authors about the category of the article;
- Contact information and addresses of three potential reviewers, as well as names of the persons you would not like to be reviewers of your manuscript;
- A statement of authorship by all listed authors about their contribution in the drafting of the paper which needs to include the text in accordance with one of the following sentences: (a) A substantial contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) Drafting the article or revising it critically for important intellectual content; (c) Final approval of the version to be published. (eg. Authors' contributions: Conception and design: XX and YY; Acquisition, analysis and interpretation of data: YY and ZZ; Drafting the article: XX, YY and ZZ; Revising it critically for important intellectual content: XX, ZZ; Approved final version of the manuscript: XX, YY and ZZ.

Copyright assignment

All authors must complete and sign the Copyright Assignment form upon acceptance of the manuscript and return it to the editorial office. The Copyright Assignment form can be found at www.ama.ba. Accepted papers will not be sent for publication until this form has been completed and submitted.

Manuscript preparation

Manuscripts have to be written according to the rules stated in "Uniform Requirements for Manuscripts Submitted to Biomedical Journals". The full document is available from www.icmje.org

Language. Manuscripts must be written in clear, concise, grammatical English. Authors

from non-English speaking countries are requested to have their text translated by a professional, or thoroughly checked by a native speaker with experience in writing scientific and medical manuscripts in English. Revision of the language is the responsibility of the author. All manuscripts should be spellchecked using a Microsoft Word or Dorland's spellchecker before they are submitted. Spelling should be US English or British English, but not a mixture. On the grounds of poor English manuscripts may be sent back to an author for rewriting or language correction.

Font and spacing. The manuscript should be prepared in Microsoft Word format (for PC, 6.0 or a later version). Paper version should be typewritten on white bond paper of A4 size, with margins 3 cm each. Write on one side of each sheet, using a font not smaller than 12 points, preferably Times New Roman or Arial. All pages must be numbered. Prepare texts with double spacing (except those of tables, which are made with table tools in Word or in Excel). Double spacing of all portions of the manuscript (including the title page, abstract, text, acknowledgments, references, and legends), makes it possible for editors and reviewers to edit the text line by line, and add comments and queries, directly on the paper copy.

Length. The length of a manuscript depends on its type. On the title page, author should specify total word count and/or character count. Microsoft Word can count them for you. With **double spacing** (2000 characters with spaces per page), the limits are as follows:

- **Editorial** – up to 3 pages (maximum count 6000 characters with spaces) and maximum 15 references.
- **Review article** – from 12 to 20 pages (maximum count 30000 characters with spaces) and maximum 40 references.
- **Original research study** – from 12 to 15 pages (maximum count 30000 characters with spaces).
- **Original (scientific and professional) article** – from 12 to 15 pages (maximum count 30000 characters with spaces).
- **Short communication** – up to 5 pages (maximum count 10000 characters with spaces), only two graphical display (figure or table) and up to 5 references and up to 3 authors.
- **Statistical and methodological compilations** – up to 16 pages (maximum count 32000 characters with spaces).
- **Case reports and letters** – up to 3 pages (maximum count 10000 characters with spaces), a maximum of 2 figures or tables and no more than 15 references.
- **Images in clinical medicine** – is an article providing one or two fascinating pictures in black and white or in color. It can be clinical or technical on a patient or part of a patient, for instance an x-ray or MRI image or a histological document. The picture is accompanied by a short text (a maximum of 300 words), up to 3 authors, and if necessary 1 to 3 references can be included.
- **Letter to the editor** – up to 3 pages (maximum count 2000 characters with spaces), and up to 5 references.

Organization of the text. The text of original articles is usually divided into sections with the following headings: Introduction, Materials (Patients) and methods, Results, Discussion and Conclusion. This structure is not simply an arbitrary publication format, but rather a direct reflection of the process of scientific discovery. Long articles may need subheadings within some sections (especially the Results and Discussion sections) to clarify their content. Other types of articles, such as case reports, reviews, and editorials, are likely to need other more flexible structure of the text. If possible, use standard abbreviations. Non-standard abbreviations should be defined when first used in the text.

Title page (the first page)

The title page should carry the following information:

1. Type of the article.
2. Title of the article, which should be as short and concise as possible. Authors should include all information in the title that will make electronic retrieval of the article both sensitive and specific.
3. A short title (up to 50 characters with spaces), which will appear in the heading of an article in the journal.
4. Authors' names and institutional affiliations (full first name followed by family name, separated by a comma from the next name; us-

ing Arabic numerals in superscript format relate names and institutions).

5. The name of the department(s) and institution(s) to which the work should be attributed.

6. Corresponding authors. The name, mailing address, telephone and fax numbers, and e-mail address of the author responsible for correspondence about the manuscript. The name and address of the author to whom requests for reprints should be addressed (if different from the corresponding author), or a statement that reprints will not be available from the authors.

7. Specify sources of support in the form of grants, equipment, drugs, or others, if any and a statement about existence or non-existence of the conflict of interests.

8. Total number of pages, words and characters with spaces (Microsoft Word enables the simple acquisition of these data), number of figures and tables. A word count for the text only (excluding abstract, acknowledgments, figure legends, and references) allows editors and reviewers to assess whether the information contained in the paper warrants the amount of space devoted to it, and whether the submitted manuscript fits within the journal's word limits. A separate word count for the Abstract is also useful for the same reason.

Second page

Abstract and Key words are written on the second page. Because abstracts are the only substantive portion of the article indexed in many electronic databases, and the only portion many readers read, authors need to be careful that abstracts reflect the content of the article accurately. An abstract (250 words) is written without authors' names and institutional affiliations. Its structure should be similar to that of the text. For original articles, the abstract needs to have the structure with the following subtitles: Objective, Materials and methods, Results and Conclusion. Abstracts for Case reports also need to have the following subtitles: Objective, Case report, and Conclusion and for Review articles: Objective, Background, Methods, Discussion and Conclusion. Abstracts for Short communication (150 words) should not be structured but should end with Conclusion. Following the abstract, authors provide, and identify as such, 3 to 5 key words or short phrases that capture the main topics of the article. The key words should not repeat the title of the manuscript. Terms from the Medical Subject Headings (MeSH) list of Index Medicus should be used; MeSH terms are available from: www.nlm.nih.gov/mesh/.

Third page

Should carry the manuscript of article. Text should be under the following headings:

Introduction. Needs to be short and to specify to the reader, clearly and with arguments, reasons for the research presentation, and the novelties that the article brings. In Introduction maximum 3 to 4 pertinent and directly related works need to be cited. At the end of Introduction, an author needs to clearly specify the set aim of the research.

Methods. This part needs to provide the following information: selection and description of participants, precise technical information about all methods (describe the methods, apparatus, and procedures in sufficient detail to allow other workers to reproduce the results; give references to established methods, including statistical methods; identify precisely all drugs and chemicals used, including generic names, doses, and routes of administration and other specificities related to the presented research). Upon reporting about humane experiments, an author needs to indicate if the used procedures were in accordance with the Declaration of Helsinki from 1975 and its amendments from 1983. In addition, there needs to be stated if and which ethical committee gave consent for carrying out the research. A separate subtitle is Statistical Analysis. Authors need to indicate all statistical tests that were used. In addition, there needs to be stated the level of significance selected beforehand (p), that is which value p the authors considered to be statistically important (ex. 0.05 or 0.01, or some other). The results should be stated with pertaining confidence intervals (CI).

The editorship recommends to the authors to follow STARD instructions published in 2003 in the researches of diagnostic accuracy. At the end of the paragraph authors need to state which computer statistical program they have been us-

ing, as well as indicate the manufacturer and version of the program.

Results. Present your results in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. Restrict tables and figures to those needed to explain the argument of the paper and to assess its support. Use graphs as an alternative to tables with many entries; do not duplicate data in graphs and tables. The text must contain a clear designation as to where the tables and illustrations are to be placed relative to the text. Do not duplicate data by presenting it in both a table and a figure.

Discussion. Emphasize the new and important aspects of the study and the conclusions that follow from them. Do not repeat in detail data or other material given in the Introduction or the Results section. For experimental studies it is useful to begin the discussion by summarizing briefly the main findings, then explore possible mechanisms or explanations for these findings, compare and contrast the results with other relevant studies, state the limitations of the study, and explore the implications of the findings for future research and for clinical practice.

Conclusion. Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not adequately supported by the data. In particular, authors should avoid making statements on economic benefits and costs unless their manuscript includes the appropriate economic data and analyses. Avoid claiming priority and alluding to work that has not been completed. State new hypotheses when warranted, but clearly label them as such.

Acknowledge. Anyone who contributed towards the study by making substantial contributions to conception, design, acquisition of data, or analysis and interpretation of data, or who was involved in drafting the manuscript or revising it critically for important intellectual content, but who does not meet the criteria for authorship. List the source(s) of funding for the study and for the manuscript preparation in the acknowledgements section.

Authors' contributions (eg. Authors' contributions: Conception and design: XX and YY; Acquisition, analysis and interpretation of data: YY and ZZ; Drafting the article: XX, YY and ZZ; Revising it critically for important intellectual content: XX, ZZ; Approved final version of the manuscript: XX, YY and ZZ.

Conflict of interest (eg.): The authors declare that they have no conflict of interest.

References. Need to be on a separate page. Small numbers of references to key original papers will often serve as well as more exhaustive lists. Avoid using abstracts as references. References to papers accepted but not yet published should be designated as "in press" or "forthcoming"; authors should obtain written permission to cite such papers as well as verification that they have been accepted for publication. If the paper has been published in electronic form on PubMed the confirmation of acceptance is not needed. Information from manuscripts submitted but not accepted should be cited in the text as "unpublished observations" with written permission from the source. Avoid citing a "personal communication" unless it provides essential information. For scientific articles, authors should obtain written permission and confirmation of accuracy from the source of a personal communication.

References should be numbered consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and legends by Arabic numerals in parentheses at the end of a sentence. Use the same number in the reference list. References cited only in tables or figure legends should be numbered in accordance with the sequence established by the first identification in the text of the particular table or figure.

The titles of journals should be abbreviated according to the style used in PubMed. Consult NLM Catalogue: Journals referenced in the NCBI Databases available at: http://www.ncbi.nlm.nih.gov/nlmcatalog/journals.

Tables. Need to be submitted separate from the main text. The preferred software for tables is Microsoft Excel (save each table in a file with single worksheet). Only tables made with table tools in Microsoft Word are acceptable. For the paper version, type or print each table on a separate sheet of paper. Number tables consecutively in the order of their first citation in the text. Use Arabic numerals. Each table needs to have an explanatory title. Place the title above the table. Give each column a short or abbreviated heading. Also, visibly indicate the position of each table in the text, using its assigned numeral at the end of the

sentence which is relevant to the table(s). Tables should be positioned in the text where the author feels is appropriate but the Editor reserves the right to reorganize the layout to suit the printing process. Authors need to place explanatory matter in footnotes, not in the heading. Explain in footnotes of the table all nonstandard abbreviations. For footnotes use the following symbols, in sequence: *, †, ‡, §, ||, ¶, **, ††, ‡‡. Identify statistical measures of variations, such as standard deviation and standard error of the arithmetic mean. *Be sure that each table is cited in the text.* If you use data from another published or unpublished source, obtain permission and acknowledge them fully.

Figures. (illustrations: diagram, photograph, photomicrograph, radiograph, drawing, sketch, picture, outline, design, plan, map, chart, etc.). Need to be submitted separate from the main text. They need to be submitted as photographic quality digital prints or, exceptionally, as professionally drawn and photographed original illustrations. Figures should be in a digital format that will produce high quality images. Formats recommended include: JPEG, GIF, TIFF, Microsoft Word, Excel. Sending original photographs and slides is permissible when they cannot be digitized without professional help. In this case, send an explanation in the cover letter. Using Arabic numerals, number figures consecutively in the order of their first citation in the text. Also, visibly indicate the position of each figure in the text, using its assigned numeral in parentheses. Figures should be positioned in the text where the author feels is appropriate but the Editor reserves the right to reorganize the layout to suit the printing process.

Supply a legend for each figure. Titles and detailed explanations belong in the legends, however, not on the figures themselves. Figures should be made as self-explanatory as possible. Letters, numbers, and symbols on figures should therefore be clear and even throughout, and of sufficient size that when reduced for publication each item will still be legible. Photomicrographs should have internal scale markers. Symbols, arrows, or letters used in photomicrographs should contrast with the background. If photographs of people are used, either the subjects must not be identifiable or their pictures must be accompanied by written permission to use the photograph.

Legends for Figures need to be included in the main manuscript text file, on a separate page immediately following the references. Type or print out legends using double spacing. For each figure, the following information should be provided: figure number (in sequence, using Arabic numerals – i.e. Figure); title of the figure; all necessary explanations. When symbols, arrows, numbers, or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

Units of measurement

Measurements of length, height, weight, and volume should be reported in metric units (meter, kilogram, or liter) or their decimal multiples. Temperatures should be in degrees Celsius. Blood pressures should be in millimeters of mercury, unless other units are specifically required by the journal.

Abbreviation, Acronyms and Symbols

If possible for metric units use standard abbreviations. Non-standard abbreviations should be defined when first used in the text.

Sample references

Articles in journals

Standard journal article (*List the first six authors followed by et al.*):

Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002;347(4):284-7.

More than six authors:

Rose ME, Huerbin MB, Melick J, Marion DW, Palmer AM, Schiding JK, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res. 2002;935(1-2):40-6.

Organization as author:

Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. Hypertension. 2002;40(5):679-86.

No author given:

21st century heart solution may have a sting in the tail. BMJ. 2002;325(7357):184.

Volume with supplement:

Geraud G, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. Headache. 2002;42(Suppl 2):S93-9.

Issue with supplement:

Glauser TA. Integrating clinical trial data into clinical practice. Neurology. 2002;58(12 Suppl 7):S6-12.

Issue with no volume:

Banit DM, Kaufer H, Hartford JM. Intraoperative frozen section analysis in revision total joint arthroplasty. Clin Orthop. 2002;(401):230-8.

Letters or abstracts:

Tor M, Turker H. International approaches to the prescription of long-term oxygen therapy [letter]. Eur Respir J. 2002;20(1):242.;

Lofwall MR, Strain EC, Brooner RK, Kindbom KA, Bigelow GE. Characteristics of older methadone maintenance (MM) patients [abstract]. Drug Alcohol Depend. 2002;66 Suppl 1:S105.

Article republished with corrections:

Mansharamani M, Chilton BS. The reproductive importance of P-type ATPases. Mol Cell Endocrinol. 2002;188(1-2):22-5. Corrected and republished from: Mol Cell Endocrinol. 2001;183(1-2):123-6.

Article with published erratum:

Malinowski JM, Bolesta S. Rosiglitazone in the treatment of type 2 diabetes mellitus: a critical review. Clin Ther. 2000;22(10):1151-68; discussion 1149-50. Erratum in: Clin Ther. 2001;23(2):309.

Article published electronically ahead of the print version:

Yu WM, Hawley TS, Hawley RG, Qu CK. Immortalization of yolk sacderived precursor cells. Blood. 2002 Nov 15;100(10):3828-31. Epub 2002 Jul 5.

Books and other monographs

Personal author(s):

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

Editor(s), compiler(s) as author:

Gilstrap LC 3rd, Cunningham FG, VanDorsten JP, editors. Operative obstetrics. 2nd ed. New York: McGraw-Hill; 2002.

Organization(s) as author:

Royal Adelaide Hospital; University of Adelaide, Department of Clinical Nursing. Compendium of nursing research and practice development, 1999-2000. Adelaide (Australia): Adelaide University; 2001.

Chapter in a book:

Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93-113.

Conference paper:

Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer; 2002. p. 182-91.

Dissertation:

Borkowski MM. Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]. Mount Pleasant (MI): Central Michigan University; 2002.

Other published material

Newspaper article:

Tynan T. Medical improvements lower homicide rate: study sees drop in assault rate. The Washington Post. 2002 Aug 12;Sect. A:2 (col. 4).

Dictionary and similar references:

Dorland's illustrated medical dictionary. 29th ed. Philadelphia: W.B. Saunders; 2000. Filamin; p. 675.

Electronic material

CD-ROM:

Anderson SC, Poulsen KB. Anderson's electronic atlas of hematology [CD-ROM]. Philadelphia: Lippincott Williams & Wilkins; 2002.

Audiovisual material:

Chason KW, Sallustio S. Hospital preparedness for bioterrorism [videocassette]. Secaucus (NJ): Network for Continuing Medical Education; 2002.

Journal article on the Internet:

Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [serial on the Internet]. 2002 Jun [cited 2002 Aug 12];102(6):[about 3 p.]. Available from: http://www.nursingworld.org/AJN/2002/june/Wawatch.htm.

Monograph on the Internet:

Foley KM, Gelband H, editors. Improving palliative care for cancer [monograph on the Internet]. Washington: National Academy Press; 2001 [cited 2002 Jul 9]. Available from: http://www.nap. edu/books/0309074029/html/.

Homepage/Web site:

Cancer-Pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources, Inc.; c2000-01 [updated 2002 May 16; cited 2002 Jul 9]. Available from: http://www.cancer-pain.org/.

Part of a homepage/Web site:

American Medical Association [homepage on the Internet]. Chicago: The Association; c1995-2002 [updated 2001 Aug 23; cited 2002 Aug 12]. AMA Office of Group Practice Liaison; [about 2 screens]. Available from: http://www.ama-assn.org/ama/pub/category/1736.html.

Database on the Internet:

Who's Certified [database on the Internet]. Evanston (IL): The American Board of Medical Specialists. c2000 – [cited 2001 Mar 8]. Available from: http://www.abms.org/newsearch.as.

ISSN 1840-1848