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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 2 November 2016 ISSN 1840-2879 (Online)

Online First www.ama.ba

Acta Medica Academica

Contents
2016 Vol. 45, No. 2

Acta Medica Academica

www.ama.ba

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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

Omer Mujadžić (1903-1991), "A family", 1960, oil on plywood, 495x570 mm. Courtesy of the International gallery of portrait Tuzla.

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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(2):97-103
DOI: 10.5644/ama2006-124.165

Predictive value of SAPS II and APACHE II scoring systems for patient outcome in a medical intensive care unit

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Received: 6 April 2016
Accepted: 30 September 2016

Key words: SAPS II ▪ APACHE II ▪ Medical intensive care unit.

Objective. The aim is to determine SAPS II and APACHE II scores in medical intensive care unit (MICU) patients, to compare them for prediction of patient outcome, and to compare with actual hospital mortality rates for different subgroups of patients. **Methods.** One hundred and seventy-four patients were included in this analysis over a one-year period in the MICU, Clinical Center, University of Sarajevo. The following patient data were obtained: demographics, admission diagnosis, SAPS II, APACHE II scores and final outcome. **Results.** Out of 174 patients, 70 patients (40.2%) died. Mean SAPS II and APACHE II scores in all patients were 48.4±17.0 and 21.6±10.3 respectively, and they were significantly different between survivors and non-survivors. SAPS II >50.5 and APACHE II >27.5 can predict the risk of mortality in these patients. There was no statistically significant difference in the clinical values of SAPS II vs APACHE II (p=0.501). A statistically significant positive correlation was established between the values of SAPS II and APACHE II (r=0.708; p=0.001). Patients with an admission diagnosis of sepsis/septic shock had the highest values of both SAPS II and APACHE II scores, and also the highest hospital mortality rate of 55.1%. **Conclusion.** Both APACHE II and SAPS II had an excellent ability to discriminate between survivors and non-survivors. There was no significant difference in the clinical values of SAPS II and APACHE II. A positive correlation was established between them. Sepsis/septic shock patients had the highest predicted and observed hospital mortality rate.

Introduction

There are many intensive care unit (ICU) scoring systems, and many new ones are being developed to achieve an objective and quantitative description of the degree of organ dysfunction and evaluation of morbidity in ICU patients. Scoring systems such as: Acute Physiology and Chronic Health Evaluation (APACHE) II, III and IV, Simplified Acute Physiology Score (SAPS), Sepsis-related Organ Failure Assessment Score (SOFA), Mortality Prediction Model (MPM), Multiple Organ Dysfunction Score (MODS), and Logistic Organ Dysfunction Score (LODS) have become a necessary tool to describe ICU populations and to explain differences in mortality (1).

The Acute Physiology and Chronic Health Evaluation II (APACHE II) is the

most commonly used severity-of-disease scoring system in ICUs around the world (2). Within the first 24 hours of patient admittance, the worst value for each physiological variable is calculated into an integer score from 0 to 71. Higher scores represent a more severe disease and a higher hospital mortality risk. The first APACHE model was presented by Knaus et al. in the 1980's (3). It has not been validated for use in patients under the age of 16. Even though newer scoring systems have been developed, APACHE II still continues to be used because so much documentation is based on it. The relationship between APACHE II scores and approximate mortality interpretation in medical (non-surgical) patients is shown in Table 1.

The Simplified Acute Physiology Score II (SAPS II) was first described in 1984 as an alternative to the APACHE scoring system (4). The SAPS II score is calculated from the worst value of 12 routine physiological measurements during the first 24 hours of patient admisson, information about previous health status and some information obtained at admission. 24 hours after admission to the ICU, the measurement is completed and this results in an integer point score between 0 and 163, and predicted hospital mortality between 0% and 100%. There is a sigmoidal relationship between SAPS II score and mortality rate. SAPS II score and mortality rate interpretation are shown in Table 2.

Table 1 APACHE II score and hospital mortality interpretation for non-surgical patients (3)

APACHE II score	Hospital mortality*
0-4	4%
5-9	8%
10-14	15%
15-19	24%
20-24	40%
25-29	55%
30-34	73%
35-100	85%

*Approximate interpretation (non-surgical patients).

Table 2 SAPS II score and hospital mortality interpretation (4)

SAPS II score (points)	Mortality
29	10%
40	25%
52	50%
64	75%
77	90%

Previous studies have reported the varying performance of these scoring systems in predicting hospital mortality. Several studies had reported better performance by APACHE II (5, 6). Other studies on different patient populations validated SAPS II as a good prediction scoring system (7, 8). Juneja et al. (9) reported that the difference in performance of the scoring systems was not significant and depends on local preferences. Newer scoring systems have been developed, such as APACHE III and IV, to refine the previous APACHE II. However, APACHE II and SAPS II as the simplest and inexpensive scoring systems are still used in our medical intensive care unit (MICU).

The aim of this study is to determine the SAPS II and APACHE II scores in patients admitted to the MICU and compare them for prediction of the outcome in these patients (survivors i.e. patients who were discharged from the hospital, and non-survivors i.e. patients who died during the same hospitalization). Predictive scores were calculated and actual hospital mortality rates were compared for different subgroups of MICU patients.

Materials and methods

Study design and data collection

The Clinical Center of the University of Sarajevo is a 1952-bed tertiary university hospital, with a 7-bed closed MICU with a

nurse/patient ratio of 1:3.5. One hundred and eighty-nine (189) patients were admitted to the MICU in the Clinical Center of the University of Sarajevo from October 2014 to September 2015. Patients were either admitted from the emergency department or transferred from a hospital ward. There were 15 patients who had exitus letalis in the first 24 hours of hospitalization in the MICU, for which SAPS II and APACHE II scores could not be calculated. The remaining 174 patients that were hospitalised for more than 24 hours in the MICU were included in the study. Out of 174 patients, 89 were admitted from the emergency department and 85 were transferred from a hospital ward. For patients with multiple admissions, only the first data set was included in the data analysis. For each patient the following data were obtained: demographic data, admission diagnosis, parameters for SAPS II and APACHE II scores and the final outcome (survivors i.e. patients who were discharged from the hospital, and non-survivors i.e. patients who died during the same hospitalization). The reasons for admission were grouped into five categories: sepsis / septic shock (based on the presence of systemic inflamatory response syndrome and a source of infection with/without hypotension and hypoperfusion despite adequate fluid resuscitation), respiratory failure (hypoxemia and/or hypercarbia requiring non-invasive ventilation or me.chanical ventilation), cardiovascular (based on clinical, laboratory and ECG and/or echocardiography findings), neurological (based on clinical and diagnostic findings of central nervous system damage) and other causes. Surgical, burns, coronary care and cardiac surgery patients were not admitted to this MICU. When multiple diagnoses were present, the leading one, with the worst prognosis was selected as the main reason for admission. SAPS II and APACHE II were calculated 24 hours after admission to the MICU. The SAPS II score was calculated from the following parameters: age, heart rate, systolic blood pressure, temperature, Glasgow Coma Scale, mechanical ventilation or continuous positive airway pressure (CPAP), PaO2/FiO_2, urine output, urea, sodium, potassium, bicarbonate, bilirubin, leucocyte count, chronic diseases, type of admission. The APACHE II score was calculated from the patient's age and 12 parameters: PaO_2, temperature, mean arterial pressure, arterial pH, heart rate, respiratory rate, sodium, potassium, creatinine, hematocrit, leucocyte count and Glasgow Coma Scale. Also, information about previous health status (surgery, history of organ insufficiency, immunocompromised state) was calculated into the result. The worst parameters in the first 24 hours of hospitalization were selected for calculation of the scores.

Statistical analysis

Data were presented for continuous variables as means and standard deviation, and for categorical variables as absolute and relative frequencies. The data were analysed using t-test, Fisher's exact and chi-square test. A receiver operating characteristic (ROC) curve was used to determine a cut-off value for mortality, and the sensitivity and specificity of each scoring system for prediction of mortality. Pearson's correlation was used for evaluating the correlation between the scoring systems. Statistical significance was interpreted as $p \leq 0.05$. Graphically, data were presented in the form of tables and figures. Data were analysed using SPSS for Windows version 20.0 (SPSS Inc., Chicago, IL, USA).

Results

Out of 174 patients included in the study, 104 patients (59.8%) survived and 70 patients (40.2%) died. One hundred patients were male (57.5%). Their mean age was 61.7±16.3 years (range 19-87). When survi-

vors v. non-survivors were compared, there was no statistical difference in patient age (59.6±14.7 vs. 62.3±15.9; p=0.654) or gender (61 males vs. 43 females in the survivor group and 39 males vs. 31 females in the non-survivor group; p=0.232). Mean SAPS II and APACHE II scores in all admitted patients were 48.4±17.0 and 21.6±10.3 respectively. The mean SAPS II score was 41.2±14.1 in survivors and 63.9±11.2 in non-survivors (p<0.0001). The mean APACHE II score was 16.9±6.4 in survivors and 31.5±10.2 in non-survivors (p<0.0001). The receiver operating characteristics curve results of SAPS II and APACHE II scores in prediction of fatal outcome are shown in Figure 1.

The area under the ROC curve was calculated to evaluate the predictive value of the scoring systems. The SAPS II scoring system represents a statistically significant predictive marker of fatal outcomes of patients (area under the curve of 0.892, CI 0.84-0.94, p=0.001). Cut off value for SAPS II was 50.5, with the sensitivity of 90.2% and specificity of 75.7%. The APACHE II scoring system represents a statistically significant predictive marker of fatal outcomes of patients (area under the curve of 0.920, CI 0.87-0.97, p=0.001). Cut off value for APACHE II was 27.5, with sensitivity of 74.5% and specificity of 93.4%. When the ROC curves were compared, that there was no statistically significant difference in the clinical values of SAPS II vs APACHE II (p=0.501). By using Pearson's correlation, a statistically significant positive correlation was established between the values of SAPS II and APACHE II (r=0.708; p=0.001). This means that when SAPS II value increases, so does the value of APACHE II, as shown in Figure 2.

SAPS II and APACHE II scores and hospital mortality for patients based on their admission diagnoses, are shown in Table 3.

Respiratory failure was the leading cause for ICU admission (62 patients, 35.6%), followed by sepsis /septic shock (49 patients, 28.1%) and cardiovascuar failure (31 patients, 17.8%). Patients with admission diagnosis of sepsis/septic shock had the highest values of both SAPS II and APACHE II scores, and also the highest hospital mortality rate of 55.1%. Patients in the group admitted for other causes had the lowest SAPS II score. Patients with respiratory failure had the lowest APACHE II score and lowest hospital mortality rate.

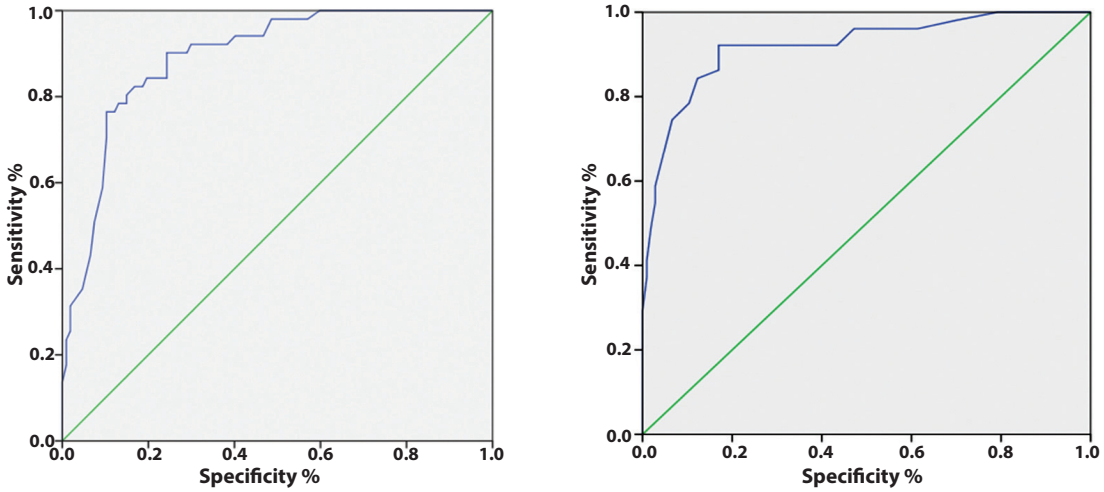

Figure 1 Receiver operating curve for predicting fatal outcome according to SAPS II and APACHE II scoring systems.

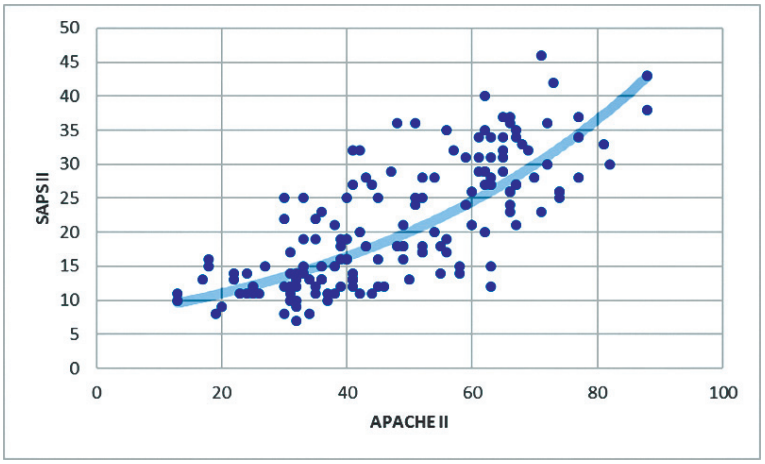

Figure 2 Correlation between SAPS II and APACHE II scores.

Table 3 Predictive scoring systems and hospital mortality rate in studied patients according to admission diagnosis

Characteristics	Patients admitted to the ICU with the primary admission diagnosis (n=174)				
	Respiratory failure (n=62)	Sepsis/septic shock (n=49)	Cardiovascular failure (n=31)	Neurological causes (n=16)	Other causes (n=16)
SAPS II ($\bar{x} \pm SD$)	42.4±14.9	58.4±15.0	47.6±17.8	55.4±17.0	40.9±15.0
APACHE II ($\bar{x} \pm SD$)	17.5±7.5	27.0±11.9	21.5±9.8	26.0±11.0	20.1±9.1
Hospital mortality rate (%)	17.7	55.1	51.6	50.0	25.0

Discussion

According to our results, a SAPS II score higher than 50.5 can predict the MICU patients' mortality rate with good sensitivity (90.2%) and lower specificity (75.7%). An APACHE II score higher than 27.5 can predict the MICU patients' mortality rate with good specificity (93.4%) but with lower sensitivity (74.5). Based on further analysis, there was no significant difference in the clinical values of SAPS II and APACHE II. Haq et al. (10) also showed similar performance by SAPS II and APACHE II. Sathe et al. (11) and Mosenson et al. (12) showed that APACHE II had better discrimination than SAPS II.

APACHE II was a less sensitive predictor than SAPS II, but with higher specificity. The specificity of APACHE II was 93.4% which is higher than reported by Sekulic et al. (13).

In a study of 11,300 patients from 35 hospitals in California, the authors noted that only the APACHE II scoring system showed good discrimination for predicting ICU mortality (14). However, Sekulic et al. (13) concluded that SAPS II was a better predictor for hospital mortality in ICU patients. In a study by Ho et al. (15) SAPS II was confirmed to have the best performance overall.

As different subpopulations of critically ill patients are admitted to our MICU every day, there was a need to evaluate which subgroup had the worst expected and actual prognosis. The way in which the patients were divided is in accordance with the study by Breslow et al. where the diagnosis was documented within the first ICU day; it reflected the primary reason for ICU admission; and, when multiple diagnoses were relevant, the diagnosis with the worst prognosis (e.g., sepsis rather than hyper-

glycemia) was the leading one (16). When our patients were divided into subgroups according to their admission diagnosis, the leading cause of admission was respiratory failure, followed by sepsis / septic shock. Severe sepsis and septic shock were shown to be major reasons for ICU admission and also the leading causes of mortality in non-coronary ICUs (17). Hospital mortality in patients with sepsis was 55.1% which is in accordance with the results by Mohan et al. study (18). In our study, patients with respiratory failure had a hospital mortality rate of 17.7% which is lower than 30.7% as reported by Evran et al. (19).

Juneja et al. (9) indicated that the newer scoring systems performed better than their older counterparts, and were more accurate. Nevertheless, the difference in performance was not statistically significant and the choice of scoring system may depend on the ease of use and local preferences.

Limitations of study

The present study has some limitations. First, our small sample size is a limiting factor in analysis. Also, being a single center study, there is possibly some amount of bias due to differences in ICU admission policies.

Advantages of study

The results of this study and of past studies suggest ambiguous and inconclusive results regarding outcome, and they are heavily dependent on patient populations and medical interventions used on those patients. This must be taken into consideration when it comes to the interpretation of results. The existence of a large number of scoring systems suggests that the ideal model has yet to be found. Differences in the performance of scoring systems reinforce the need to validate them using data from independent samples from different ICUs in different countries due to variations in the structure and quality of medical care, as well as genetic differences between populations.

Conclusion

In conclusion, both APACHE II and SAPS II have an excellent ability to discriminate between survivors and non-survivors. ROC curve analysis showed that there was no significant difference in the clinical values of SAPS II vs APACHE II in MICU patients. Also, a positive correlation was established between the values of SAPS II and APACHE II scores. Sepsis/septic shock patients had the highest predicted and observed hospital mortality rate.

What is already known on this topic

Scoring systems predict patient outcomes in intensive care units. Over the years, many studies have evaluated the predictive ability of various scoring systems, and conflicting data have been reported so far. Although there are newer scoring systems, some of the most widely used are SAPS II and APACHE II. There is a need for more studies evaluating various scoring systems to predict mortality in different patient populations.

What this study adds

To the best of our knowledge, this is the first study to evaluate predictive scoring systems of patient outcome in a medical intensive care unit in Bosnia and Herzegovina.

Authors' contributions: Conception and design: AG and SJ; Acquisition, analysis and interpretation of data: AK, IT and AR; Drafting the article: AA and AG; Revising it critically for intellectual content: AI and AK; Approved final version of the manuscript: AG and IT.

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

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Original article

Acta Medica Academica 2016;45(2):104-120
DOI: 10.5644/ama2006-124.166

Factors influencing pain therapy for metastatic cancer patients in Bosnia and Herzegovina

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Received: 10 February 2016
Accepted: 24 August 2016

Key words: Pain ▪ Cancer ▪ Analgesics.

Objective. To investigate cancer pain management and evaluate factors that could be addressed and lead to potential improvement of pain therapy. **Materials and methods.** Two hundred patients with metastatic cancer pain at the Department of Oncology, University Hospital Mostar, completed questionnaires about cancer pain treatment. Thirty oncologists from the Cancer Institute, University of Sarajevo and the Department of Oncology, Clinical Hospital, Mostar were asked to complete the questionnaire about cancer pain management. **Results.** Compliance for analgesics was statistically better (p=0.013) for patients who were regularly asked about pain than for those patients who were asked periodically. Nearly twice as many patients, whom the doctor always asked about pain, regularly took medication (65.5% versus 32.8%). There was a statistically significant, positive relationship between regular use of analgesics and the interest of the doctor about pain reduction after initiation of analgesic therapy (p=0.008). Almost half of the patients, 47%, stated that their doctor did not devote enough time to their pain problems during the interview. Statistically significantly more patients took analgesic medication regularly if they were not afraid of narcotics (p=0.006). Numerical or VAS scales in description of cancer pain were used by only 30% of interviewed oncologists. The vast majority of doctors, 86.7%, used opiates for the terminal phase of the illness. **Conclusion.** Assessment and the treatment of cancer pain in Bosnia and Herzegovina remains inadequate, emphasizing the need for changes to cancer pain patient care.

Introduction

Unfortunately cancer has become a major public health problem and an increasingly important factor in the burden of disease. Based on the most recent available data for 2012, there were an estimated 3.45 million new cases of cancer (excluding non-melanoma skin cancer) and 1.75 million deaths from cancer in Europe (1, 2). Cancer pain is a multifactorial phenomenon that results in complex interactions between physical, psychological, cognitive, social and other factors. The prevalence of acute and chronic pain in cancer patients is high: about 30% in patients with newly diagnosed cancer, 50-70% in patients receiving active anticancer therapy, and 60-80 % in patients with advanced disease (3-5). Untreated and poorly treated pain affects physical and mental health, functional status

and quality of life, and is associated with an increased incidence of medical complications, increased use of medical services, decreased patient satisfaction, and unnecessary suffering (5-9).

A decrease in the intensity of the pain is one of the fundamental tasks in clinical practice, so identification of factors that influence the outcome of pain treatment is of great importance for improving the quality of life of cancer patients. It has been shown that pain can be controlled in close to 90% of patients when proper guidelines for pain management are used (10). Unfortunately, despite universal advances in cancer-pain management through better anticancer therapy in general and better pain management as well, there is widespread evidence that cancer pain remains inadequately treated (11-13).

Inadequate treatment of cancer pain is often caused, especially in countries in development, by barriers to the use of analgesics, opioids in particular (14). In this respect, patient, health care professional-related and institutional barriers have been identified (15-22). The most significant patient-related barriers are the patient's reluctance to report pain and adhere to treatment recommendations (15).

Effective doctor-patient communication is the cornerstone of successful pain treatment; however, poor communication between patients and their physicians remains a pervasive problem (16). Several studies have investigated cancer patients' communication with healthcare providers concerning their pain experience (17-20). Few of these studies have focused on the quality of the communication between cancer patients and physicians regarding the subject of the patient's pain. The quality of the patient-physician communication was not satisfactory in general (17-20). Patients want to be more active in the process of information exchange by expressing their own needs; they also want their providers to have better communication skills and to address their fears regarding cancer pain management as well.

Insufficient knowledge and education of physicians in cancer pain management has been regarded as one of the main factors causing inadequate pain relief in cancer patients all over the world (21). There are institutional barriers in many countries, such as complicated bureaucratic regulations governing the supply, regulations on prescription and administration of opioids, as well as problems related to continuity of care, when the patient is seen by a number of different physicians, across a number of different health care settings, with no one capable or willing to take responsibility for the overall pain management (22). Furthermore, it has been shown that changes to legal requirements concerning opioid prescription have had less influence on the outcomes of pain treatment, if compared with patient or physician-related barriers (23).

Although there have been numerous studies on the topic of quality of treatment of pain in various countries of the world, this is the first study in the area of Bosnia and Herzegovina, whose poor socio-economic situation in general contributes to poorer health care for patients, compared to developed countries. In most parts of Bosnia and Herzegovina patients must buy analgesics, which hinders correct medical decisions when prescribing analgesics for pain. Also, an additional problem is the lack of an adequate number of clinics for pain treatment, which makes it difficult for oncologists in specific oncological treatment.

The aim of this study was to describe the current state of cancer pain management in Bosnia and Herzegovina, and to identify barriers that may be contributing to improper pain management. Additionally, our goal was to compare cancer-related pain control between compliant and non-compliant pa-

tients, in order to provide new guidelines for pain management in Bosnia and Herzegovina, since this could have a significant impact on the quality of life of cancer patients and give physicians directions in their future practice.

Materials and methods

Study design

This was a non-interventional study of 200 metastatic cancer patients (88 females and 112 males) with cancer pain who were treated at the Department of Oncology, University Hospital, Mostar in the period from September 2011 to April 2012. In the same time interval the oncologists who treated these patients at the same Department (8 oncologists) as well as oncologists from the largest cancer institution in Bosnia and Herzegovina, The Cancer Institute, University of Sarajevo (22 oncologists), were given questionnaires about pain management. The questionnaire used in this study was adapted from the questionnaire used to test the quality of pain treatment in Ankara, Turkey. The adapted questionnaire was validated and translated to Croatian and back translated to English. In the appendix of this study are the questionnaires for patients and doctors that were used in study.

Participants

The predefined inclusion criteria for patients were as follows: age >18 years, diagnosed with metastatic cancer and existence of cancer pain. None of the patients refused to participate in the research. Patients were screened to determine whether they met the inclusion criteria. They were provided with study information, and after the patients consented, we enrolled them in the study. The patients' data were marked with a code, and anonymous patient data were collected and analyzed.

Questionnaire

The patient questionnaire covered the socioeconomic characteristics of the patients, including age, gender, marital status, number of children, education level, number of household members, and personal monthly income. The "extended family" was regarded as a patient living with children and parents / with children and husband-wife / with husband-wife and parents. Also, the questionnaire covered the level of satisfaction with the information received from doctors about pain, its causes and treatment, the type of analgesic therapy they received, availability of analgesics, satisfaction with treatment, physical and mental state after prescribed therapy, fear of morphine preparations and the most common reason for stopping taking analgesics.

The patient's compliance (regularity of analgesic usage) was determined in relation to gender, education, family monthly income and the number of family members. Concerning questions about pain, patients were asked whether their doctor asked them about pain, if they reported pain, how much time the doctor spent with them talking about pain, if the doctor used instruments for pain measurement, whether the analgesics were free or if doctors asked them about pain relief after pain treatment. Additionally, patients were asked about side effects, fear of analgesic addiction and satisfaction about pain management.

In the oncologists' questionnaires we asked these questions: the usage of instruments for pain measurement, preferred analgesics for treatment of strong, medium and weak pain, the influence of the poor economic situation on the choice of analgesic treatment, the availability of analgesics, the level of knowledge about the treatment of the pain, the importance of training in the treatment of the pain, their relationship to morphine preparations, and the existence of centers for pain treatment.

Ethics statement

The study was approved by the Ethics Committee of the School of Medicine in Mostar.

Statistical analysis

For data processing we used Excel 2000 (Microsoft, USA) and SPSS Statistics 16.0 (IBM, USA). A Kolmogorov-Smirnov test confirmed the normal distribution of data. To compare two sets of numeric data, an appropriate parametric test (student t-test) was used. Qualitative and quantitative data were processed by the appropriate measurement scales(nominal and ordinal) and analyzed using the chi-squared test. To view the results of the survey we used methods of relative numbers, such as percentages and proportions. Statistically significant values were defined as $p<0.05$.

Results

The characteristics of the 200 patients included in the study are shown in Table 1.

Table 1 The characteristics of patients enrolled in the study

Characteristics	
Total (n)	200
Median age (years; min-max)	58.5 (31-79)
Gender, n (%)	
Male	112 (56)
Female	88 (44)
Who do you live with, n (%)	
Alone	12 (6)
With children	38 (19)
With husband/wife	60 (30)
With parents	12 (6)
With extended family	78 (39)
Education level, n (%)	
Elementary school	94 (47)
High school	84 (42)
University	22 (11)
Personal monthly financial income, n (%)	
No allowances	4 (2)
< 500 EUR	132 (66)
500 – 1500 EUR	54 (27)
>1500 EUR	10 (5)

The median age of patients who regularly took medication was 59.5 years (min-max 44-79 years) and this was higher than in the group of patients who did not regularly take medication, whose median age was 56 years (min-max 31-70 years) ($p=0.032$).

The results of the patients' questionnaire in terms of compliance to analgesic therapy are shown in Table 2.

One hundred and sixteen (58%) patients regularly took medication. There was statistically positive correlation between patients who reported pain during the interview with doctors and regularity of taking medication ($p=0.023$): In the group of patients who regularly used medication, 96 patients (82.8 %) reported pain during the interview with a doctor, while only 20 patients (17.2%) did not reported pain during the same interview. Twice as many patients (n=76, 65.5%), whose doctors always asked about pain, were taking analgesics regularly ($p<0.001$) in comparison to the patients whose doctors never asked about pain. In terms of whether the doctor used a scale for pain measurement, only 18 patients reported that the doctor used this scale, while 182 did not ($p=0.026$). Also, there is a statistically significant relationship between analgesic compliance and when oncologists asked cancer patients about the reduction in the intensity of the pain after administration of analgesic in further interviews ($p<0.001$): when the doctor asked patients about cancer pain relief after administration of analgesics 108 patients took them regularly (93.1%). Only 8 patients (6.9%) took analgesics regularly if the doctor did not ask about the cancer pain relief after ordination of pain therapy.

Table 2 Results of the metastatic cancer patients' questionnaire according to compliance to analgesic therapy

Question		All patients n=200	Regularity of taking drug		p*
			Yes	No	
			n=116	n=84	
Was your doctor interested in your pain?	Always	106	76 (65.5)	30 (35.7)	<0.001
	Sometimes	90	38 (32.8)	52 (61.9)	
	No interest	4	2 (1.7)	2 (2.4)	
Have you reported pain during the interview?	Yes	154	96 (82.8)	58 (69)	0.023
	No	46	20 (17.2)	26 (31)	
Did your doctor have enough time during the conversation with you?	Yes	106	68 (58.6)	38 (45.2)	0.061
	No	94	48 (41.4)	46 (54.8)	
Did your doctor use a scale for pain measurement?	Yes	18	6 (5.2)	12 (14.3)	0.026
	No	182	110 (94.8)	72 (85.7)	
Did your doctor inform you about analgesic side effects?	Yes	86	56 (48.3)	30 (35.7)	0.077
	No	114	60 (51.7)	54 (64.3)	
Were analgesics free of charge?	Yes	78	50 (43.1)	28 (33.3)	0.162
	No	122	66 (56.9)	56 (66.7)	
How much did they cost per month of therapy (EUR)?	<10	52	26 (22.4)	26 (31)	0.215
	10- 4	50	32 (27.6)	18 (21.4)	
	25-34	12	6 (5.2)	6 (7.1)	
	35-49	6	2 (1.7)	4 (4.8)	
	>50	2	0 (0)	2 (2.4)	
Were you prescribed analgesic relief pain?	Yes	120	74 (63.8)	46 (54.8)	0.198
	No	80	42 (36.2)	38 (45.2)	
Was the doctor interested in the reduction in pain after treatment with analgesics?	Yes	168	108 (93.1)	60 (71.4)	<0.001
	No	32	8 (6.9)	24 (28.6)	
Were you afraid of addiction to prescribed pain medication?	Yes	80 (40.0)	32 (27.6)	48 (57.1)	<0.001
	No	120	84 (72.4)	36 (42.9)	

Data are absolute frequencies (%); *$\chi 2$ test.

Mostly due to the shortness of the interview and poor communication, 94 patients (47%) said that they were not able to inform the doctor clearly about their pain (Table 2). Eighty-four patients (42%) were taking analgesics irregularly because of fear of the adverse effects, they did not believe in the effect of the drug, or they did not believe in it because the drug did not work effectively from the start, so they did not continue taking the medication. Sixty-one percent of patients had to buy the medication, but this did not affect the regularity of taking it (p=0.162). Almost twice (1.7 times) as many patients who were not afraid of becoming addicted to analgesics were in the group of patients who regularly took medication, compared to those patients who did not regularly take them. There were twice as many of those who were afraid of addiction to drugs in the group of those who did not use analgesics regularly (p<0.001).

All the other data about the doctors' questionnaires about pain can be found in Table 3. Twenty-one doctors (70%) had more than five years' work experience, and nineteen believed that the poor economic situation in the country had a great influence on pain

Table 3 Results of the oncologists' questionnaire about pain treatment

Question		All doctors (n=30)
Price of analgesics	Asked patients of the possibility of paying	22 (73.3)
	Did not ask about payment	8 (26.7)
Most commonly used analgesics	NSAR	17 (56.7)
	Paracetamol	4 (13.3)
	Tramadol	8 (26.7)
	Fenacetin	1 (3.3)
Preferred form of administration of opioids	Oral	19 (63.3)
	Transdermal	9 (30)
	Other	2 (6.6)
Need for free analgesics	Yes	27 (90)
	No	3 (10)
Use of adjuvant drugs	Yes	26 (86.7)
	No	4 (13.3)
How often do you ask patients about pain?	Always	22 (73.3)
	Sometimes	8 (26.7)
Methods of measuring pain	Do not use instruments to measure pain	21 (70)
	VAS scale	2 (6.7)
	Numerical scale	7 (23.3)
Interested about pain reduction after ordination of analgesics	Always	27 (90)
	Sometimes	3 (10)
Satisfaction with existing education about pain	No	26 (86.7)
	Yes	4 (13.3)
How much time has passed since your last education about pain management?	<6 months	5 (16.7)
	6 - 12 months	7 (23.3)
	>12 months	14 (46.7)
	I've never had any education about pain treatment	4 (13.3)

Data are absolute frequencies (%); NSAR=Non steroid Anti-rheumatic Drugs; VAS= Visual analogue scale.

treatment of cancer patients. Twenty-six doctors (86.7%) preferred administration of opioids (fentanyl, buprenorphine) only in the terminal phase of the disease, when other analgesics were not effective. Numerical or VAS scales for pain measurement were used by only 9 (30%) doctors. Twenty-two doctors (73.3%) reported that they always educated patients about pain and treatment, while 8 physicians (26.7%) educated them only periodically. Seventy percent of doctors believed that brochures were the best way to educate patients about pain, while 23 % preferred oral or written forms of patient education. Nearly half of the physicians (46.7 %) had been trained and educated on the subject of pain management for a period of time which lasted over a year, while 40% had finished their most recent training within one year of completing the questionnaire. On the other hand, 13.3% of doctors had never had any education on the subject of cancer pain management.

Discussion

Despite the fact that many types of cancer are now diagnosed early and treated successfully, unfortunately there are still large

numbers of cancer patients, especially with metastatic disease, who suffer from pain associated with cancer (3, 4). Among European countries, wide differences in the quality of oncology care are observed, especially when comparison is made between «old» and «new» EU members, or between developed and developing countries (24). The cancer problem in general, and cancer pain management in particular, is the worst and fastest growing among transitional and middle income countries, and consequently cancer survival is significantly lower in transitional European countries than in the developed ones (24). While there have been numerous studies in various countries of the world on the subject of quality of the pain treatment in cancer patients, the factors that make treatment of pain inadequate and studies from transitional, developing countries are still lacking. This is the first study on the subject of cancer pain management carried out in the territory of Bosnia and Herzegovina. Barriers that hinder adequate pain treatment are classified as barriers related to health care professionals, patients and the health care system (8, 15, 21). The most common barriers to adequate pain treatment relating to patients and doctors are poor communication and fear of opioids (15). Similarly, in our study, 47% of patients had the opinion that their conversation regarding the causes and treatment of pain with their doctor did not last long enough. Most patients attributed this problem to the length of time which doctors dedicate to patients, which leads to the fact that half of the patients are not familiar with the cause of the pain they are suffering from. Quality of communication did impact compliance with the prescribed analgesics, as we found that there were twice as many compliant patients in the group whose doctor always asked about pain.

It is interesting to mention that in the group of patients who regularly used medication, 96 patients (82.8 %) reported pain during the interview with a doctor, while only 20 patients (17.2%) did not report pain during the same interview. According to the results of the study by Anderson et al. concerning doctor-patient communication, patients testified that 93%-100% of doctors had asked about the presence of the pain, which is not the case in our study, where only 53% of patients stated that their doctor had asked them about the presence of pain (17). The reason why our results are worse probably lies in the fact that there is only a small number of oncologists, who care for a large number of patients. Moreover, the primary focus of most oncologists is often on the treatment of the cancer, which often results in lower commitment to supportive medicine in general, including pain treatment. Besides this, other possible reasons are the lack of proper education in cancer pain management, the lack of cancer pain clinics and adequate multidisciplinary work, the limited availability of analgesic drugs, and the negative opinion of society in general about narcotic drugs, and social and cultural barriers in general. Patients are often denied adequate medication for pain due to fear of opioids among physicians, nurses, patients and family members (25). Coward and his colleagues found that most patients do not take regular medication because of fear of opioids (19), which is similar to our results, where we found a statistically and clinically significant correlation between the regularity of taking analgesics and fear of opioids. Knowledge of the principles of medical pain treatment among physicians varies greatly in different countries of the world, from 25%-30% to almost 100% (26, 27).

Oncologists are generally poorly educated when it comes to the administration of opioid analgesics. In line with this, our doctors used a scale for pain measurement only in 18 out of 200 patients. Studies show that physicians in Western Europe have bet-

ter knowledge about opioid analgesics than their counterparts in the southern parts of Asia (28). In a study by Peker at al. (29) they showed that education is a substantial problem in cancer pain management in Turkey, where only 35% of doctors had some form of pain management education during their residency training. Similarly, in our study, only slightly more than 10% of the oncologists interviewed considered their pain care education adequate.

In many countries, as is the case in Bosnia and Herzegovina, institutional barriers, such as the intricate bureaucratic regulations related to distribution and administration of opioids, create barriers to effective analgesic care (22, 23). Unfortunately, in most counties of Bosnia and Herzegovina, patients are not covered by insurance for the majority of analgesic drugs, particularly transdermal opioids (buprenorphine, fentanyl). All of this creates a major obstacle in the medical decision-making process when prescribing adequate analgesics, or limits the freedom of doctors in good clinical practice in the treatment of pain. According to our research, 60% of patients had to buy medicine themselves and therefore most doctors prescribe analgesics with the financial background of the patients in mind. All doctors believe that the unsatisfactory socio-economic situation of the country greatly affects the quality of treatment of pain, and that one of the first steps in the improvement of pain treatment should be the introduction of a free analgesics list. It is considered to be of great importance to note the need to organize a pain treatment clinic, as suggested by oncologists, for these do not exist in any institution where the study was conducted.

Although the World Health Organization has had a tremendous impact in changing policies relating to cancer pain management, still in many parts of the world even simple analgesics, particularly morphine, are not available for cancer pain (17, 30, 31), which is also visible from the results of our survey. It is worth noting that Bosnia and Herzegovina is at the bottom of European opiate consumption for morphine (0.6750 mg/per capita) compared to the neighboring country Croatia (2.6303 mg/per capita) or a developed country such as Denmark (55.9 mg /per capita) (32).

It is essential in each country to determine the severity of barriers to the effective treatment of cancer pain, and to set priorities for their elimination, in order to improve the treatment of cancer pain and to create the conditions for implementation of guidelines for the treatment of pain, which unfortunately we do not have in Bosnia and Herzegovina.

Limitation of study

A potential limitation of our study was the relatively small absolute number of patients and oncologists included in research. Nevertheless, this is a relatively high number for a small country like Bosnia and Herzegovina, especially when the number of oncologists considered, since more than 50% of the country's oncologists were enrolled in the study. Also, in our research we used the questionnaire only to define the patients' satisfaction with the quality of pain therapy and compliance to the therapy, and not other methods to check adherence to pain therapy. Many methods have been used to measure adherence, each of which is limited by biases and methodological flaws (33). The potential effect of the measurement itself, termed the "Hawthorne effect," must be considered (34, 35). This is the effect (often beneficial or positive) on the outcome of observation itself.

Conclusion

Between patients who regularly take medication and those that do not, we did not find any statistically significant difference in terms of gender, education, monthly income,

nor in terms of the number of members in the household. In the group of patients that the doctor always asks about pain, almost twice as many take regular therapy for pain, so doctors need to focus on this important part of therapy. Information about the regularity of the use of analgesics in patients treated for malignant diseases indicates the need for better cooperation between doctors and patients (47% of patients reported that their doctor did not have enough time for the conversation about pain therapy). Therefore, state policies should aim to increase the number of oncologists in Bosnia and Herzegovina. This would give oncologists more time to spend with their patients, which would increase patient compliance in pain management. Since no uniform guidelines about pain management in our country exist, they should be drawn up in order to help oncologists in their everyday practice. In order to establish uniform guidelines, doctors need to have better education about the treatment of cancer pain. This can be achieved through the organization of pain clinics, which would be accessible and available to cancer patients. Additionally, basic analgesics should be freely available on the general hospital list to all patients suffering from cancer. We recommend that lectures related to pain management in cancer patients should be included in the curriculums of all Medical Schools, and be part of physicians' training in all training establishments in Bosnia and Hercegovina.

What is already known on this topic

The first pain clinic was established in 1961 in the USA. Pain clinics are an important part of health care, specialized in pain management. Among European countries wide differences are observed in the quality of oncology care, especially when a comparison is made between developed and developing countries. Cancer pain management is worst, but the fastest growing among transitional and middle income countries. In many countries, as is the case in Bosnia and Herzegovina, institutional barriers, such as the intricate bureaucratic regulations related to distribution and administration of opioids, hinder effective analgesic care. This is the first study about pain management in Bosnia and Herzegovina. Pain clinics in Bosnia and Herzegovina mostly employ only physicians and nurses. Many treatments available in the pain clinics analyzed are not evidence-based.

What this study adds

According to results from our study we need better pain management in our country through education of doctors, organization of pain clinics and free analgesics available on the general hospital list.

Authors' contributions: Conception and design: ITS and EV; Acquisition, analysis and interpretation of data: SC, MP, AP, JJ, ITS and EV; Drafting the article: ITS and EV; Revising it critically for important intellectual content: EV; Approved final version of the manuscript: ITS.

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

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Appendix

1. Questionnaire for patients

1. Age: _____

2. Gender
   A. Female
   B. Male

3. Education:
   A. Illiterate
   B. Elementary school
   C. High school
   D. University

4. Family financial benefits
   A. No allowances
   B. < 500 EUR
   C. 500 – 1 500 EUR
   D. > 1 500 EUR

5. Number of household members
   A. Single
   B. With children
   C. With husband/wife
   D. With parents
   E. With extended family

6. Diagnosis
   A. Breast cancer
   B. Colon cancer
   C. Gynecological cancer
   D. Lung cancer
   E. Urogenital cancer
   F. Melanoma
   G. Head and neck cancer

7. Does your doctor ask you about pain?
   A. Always
   B. Sometimes
   C. Never

8. If pain is present do you report it to the doctor every time?
   A. Yes
   B. No

9. If the answer is NO, why do you not tell the doctor about your pain?
   A. I can bear the pain
   B. Because of the fear that I will not receive oncological treatment
   C. Because of the fear that the disease has worsened
   D. I wait for the doctor to ask me about pain

10. Do you have enough time in conversations with the doctor about pain, its causes and treatments?
   A. Yes
   B. No

11. If the answer is no, what you think is the most important reason for that?
   A. The doctor does not have enough time
   B. I do not insist on talking about pain
   C. I don't know.

12. Do you know what causes your pain?
   A. Yes
   B. No

13. Does the doctor use a scale for pain measurement?
   A. Yes
   B. No

14. Does your doctor prescribe analgesics, when you mention pain?
   A. Yes
   B. No

15. Do you know the most important side effects of the analgesics?
   A. Yes
   B. No

16. Do you pay for the drugs yourself?
   A. Yes
   B. No

17. How much do they cost per month of therapy?
    A. < 10 EUR
    B. 10 - 25 EUR
    C. 25- 35 EUR
    D. 35 - 50 EUR
    E. >50 EUR

18. Do you take the medication regularly?
    A. Yes
    B. No

19. If the answer is no, why do you not take the medication regularly?
    A. I do not believe in medication.
    B. Because of the adverse effects of the drug
    C. Because the drug did not act immediately
    D. Because of fear of addiction

20. Was the drug effective?
    A. Yes
    B. No

21. Was your doctor interested in pain reduction after treatment with analgesics?
    A. Yes
    B. No

22. Do you have any side effects?
    A. Yes
    B. No

23. Which side effects do you have?

_____

24. Do you believe in analgesic addiction?
    A. Yes
    B. No

25. If you use other forms of treatment for pain, what are they?
    A. Acupuncture
    B. Yoga
    C. Psychological treatment
    D. Physical therapy
    E. Propolis, honey, tea…

27. How satisfied are you with the prescribed medications?
    A. Very satisfied
    B. Satisfied

C. Slightly satisfied
D. Unsatisfied

28. What is your general health like when you take analgesics?
A. Very good
B. Good
C. Moderate
D. Bad
E. Very bad

32. How satisfied are you with your doctor?
A. Very satisfied
B. Not very satisfied
C. Dissatisfied

33. Are you satisfied with education about pain treatment?
A. Very satisfied
B. Not very satisfied
C. Dissatisfied

34. Does your family participate in treatment of pain?
A. Always
B. Sometimes
C. Never

2. Questionnaire for doctors

1. You are a:
A. Medical oncologist
B. Radiation oncologist
C. Medical and radiation oncologist

2. Where are you working?
_____

3. How long have you been treating oncological patients?
A. < 5 years
B. 5 - 10 years
C. > 10 years

4. Do you have radiotherapy in your institution?
A. Yes
B. No

5. If the answer is no, how much does this affect treatment of pain?
   A. No influence
   B. Some
   C. A great deal

6. How often do you ask patients about pain?
   A. In 100% cases
   B. 75 - 99% cases
   C. 50 - 75% cases
   D. 25 - 49%
   E. 0 - 25%
   F. No one

7. What is your preferred way to test intensity of pain?
   A. Through conversation
   B. VAS scale
   C. Numerical scale
   D. Macgill questionnaire
   E. Other……..

8. Do you ask your patients how much their therapy costs per month?
   A. Always
   B. Never

9. Which analgesics do you prescribe for low level pain?
   A. NSAR
   B. Paracetamol
   C. Tramal
   D. Aspirin
   F. Other…….

10. What do you do when a patient has strong pain initially?
    A. I immediately use opioids
    B. I first use weak opioids then gradually increase
    C. It depends on the patient and diagnosis

11. Which is your preferred route of drug administration?
    A. Oral
    B. Subcutaneous
    C. Intravenous
    D. Intramuscular
    E. Transdermal

12. Are transdermal analgesics free in your canton?
    A. Yes
    B. No

14. Do you think it is necessary to improve the list of free analgesics?
    A. Yes
    B. No

15. Do you have an out-patients' pain clinic in your hospital?
    A. Yes
    B. No

16. If no, do you think that is necessary to have an out-patients' pain clinic?
    A. Yes
    B. No

17. Do you use adjuvant drugs for treatment of pain?
    A. Yes
    B. No

18. Are you interested in pain reduction after treatment with analgesics?
    A. Always
    B. Never

19. Do you educate patients about pain and analgesics?
    B. Always
    C. Sometimes, especially when the patient insists
    D. Never

20. What you think is the best way to educate patients?
    A. By word of mouth
    B. Brochures
    C. Cds
    D. Other

21. Do you think that patients should receive strong opioids in the terminal phase of their illness?
    A. Yes
    B. It depends on their general condition and diagnosis
    C. No

22. Do you think that education about pain is necessary for other medical workers than doctors?
    A. Yes
    B. No

23. Do you think that the bad economic situation affects treatment of pain?
    A. Yes
    B. No

24. Are you satisfied with your education about pain?
    A. No
    B. Yes

25. How much time has passed since you had training about pain?
    A. <6 months
    B. 6-12 months
    C. >12 months
    D. I have never had any education about pain

26. If you use some nonmedical forms of treatment of pain, they are:
_____

Original article

Acta Medica Academica 2016;45(2):121-127
DOI: 10.5644/ama2006-124.167

Risk factors for post-colectomy adhesive small bowel obstruction

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Received: 14 January 2016
Accepted: 6 April 2016

Key words: Small bowel ▪ Obstruction ▪ Colorectal cancer.

Objective. The purpose of this study was to assess the risk factors for adhesive small bowel obstruction (SBO) following colectomy for colorectal cancer. **Patients and methods.** In this retrospective study we analyzed 284 patients who underwent surgery for colorectal cancer at the Department of Surgery University Clinical Center Tuzla in the period from 1st January 2009 until 31st December 2014. All patients underwent open colectomy. The length of follow up was from 6 months to 6 years (median follow up 3 years and 6 months). The study included all patients who underwent surgery due to colon cancer. The study excluded patients with postoperative small bowel obstruction after colon cancer surgery with different comorbidities. **Results.** In the analyzed sample of 284 patients, a small bowel obstruction occurred in 13.7% patients after surgery for colon cancer. The highest correlation of risk factors and the occurrence of postoperative small bowel obstruction after colectomy for colorectal cancer in multivariate regression analysis was found to be for Tumor-Node-Metastasis ≥3 (or =3.680), and postoperative complications (or =30.683). **Conclusions.** Postoperative SBO have many causes, but in this study the highest risk factors were the Tumor-Node-Metastasis ≥3, and postoperative complications.

Introduction

Postoperative abdominal adhesions are associated with significant morbidity and mortality, placing a substantial burden on healthcare systems worldwide. It is estimated that in 93%-100% of patients undergoing transabdominal surgery, the operation results in postoperative adhesions. These widespread adhesions differ from patient to patient, depending on the type of surgery and possible postoperative complications (1). Small bowel obstruction (SBO) is caused mainly by postoperative adhesions (more than 75% of all cases) (2-6), and is a common postoperative morbidity of colectomy for colorectal cancer (7). It leads to markedly lower patient quality of life, longer hospital stays and increased hospitalization costs (8). Postoperative SBO is one of the major concerns in surgery, and the appearance of early postoperative SBO symptoms is a serious issue because it affects the long-term prognosis of patients with colorectal cancer. Patients with clinical deterioration or with a CT scan evoking strangulated SBO need urgent surgery (9-10).

Patients undergoing surgical management for SBO had a reduced risk of recurrence requiring hospitalization, as well as SBO symptoms, as compared to those

with conservative treatment (11). Acute SBO is still considered by many a relative contraindication for laparoscopy. However, laparoscopy is a feasible and effective treatment for acute SBO with acceptable morbidity but laparotomy remains the standard approach (12).

This study was designed to evaluate the risk factors for postoperative SBO after colectomy for colorectal cancer from our database, which contains 284 colectomy cases over 5 years.

Patients and methods

From January 1st 2009 to December 31st 2014 (6 years) at the Department of Surgery, University Clinical Centre, Tuzla, 284 patients underwent surgery for colorectal cancer (213 males, and 71 females). This retrospective study included all patients who underwent surgery for colorectal cancer. The study excluded patients under 40 years, patients with inflammatory bowel disease, abdominal abscess and associated abdominal cancer. The factors studied regarding adhesive postoperative SBO were as follows: age, gender, American Society of Anesthesiologists (ASA) score, operation time, elapsed time from the latest operation, the presence of foreign material and intra-abdominal drain, tumor size and location, operative procedures, Tumor-Node Metastasis stage, the urgency of the surgery, application of radiation and/or chemotherapy, and postoperative surgical and medical complications.

Data collected through a pre-established questionnaire were included. Patients were divided in two groups. The SBO group (39 patients), were the patients who underwent surgery one or more times due to postoperative SMO. The non SMO group (245 patients) were patients who underwent surgery due to colorectal cancer without clinical signs of postoperative SMO. All patients underwent open colectomy surgery. The duration of follow up ranged from 6 months to 6 years (median follow up: 3 years and 6 months). We treated patients with subocclusion interference conservatively, and we treated patients surgically who had clear clinical and radiological signs of intestinal obstruction. This is usually performed by adhesiolysis, but in two cases we had to perform resection of the small intestine due to intestinal obstruction. Adhesions as the cause of postoperative small bowel obstruction were detected by clinical and radiological examinations and intraoperatively.

Statistical analysis

Statistical analysis was done using the biomedical application software MedCalc 12.3 statistical software. Categorical variables were analyzed by the $\chi 2$-test, the $\chi 2$-test contingency, and by comparing proportions and the odds ratio (OR) for each variable, with 95% confidence intervals (CI). Nonparametric correlation by Spearman was used to test the significant relationships between the variables. Utilizing univariate and multivariate logistic regression analysis, the level of impact of certain variables on the presence of a postoperative small bowel obstruction caused by adhesion was tested. The difference between samples was considered significant if $p<0.05$.

Results

In the analyzed sample of 284 patients, small bowel obstruction after surgery for colorectal cancer was found in 39 patients. The majority of patients in the SBO group (56.4%), were over 60 years of age, and in the non SMO group the majority of patients were 40-60 years of age. There were similar percentages of male and female patients in both study groups. An ASA score of ≥III was most common in patients in the SMO group, that is in 74.3%. The number of previous surgi-

Table 1 Preoperative characteristics of patients with colectomy for colorectal cancer

Characteristic	Groups		p
	SMO n (%)	non SMO n (%)	
Age (year)			
40-60	17 (43)	208 (84)	<0.0001
>60	22 (56)	34 (13)	
Gender			
Male	30 (76)	183 (74)	>0.05
Female	9 (19)	62 (25)	
ASA score			
II	10 (25)	143 (58)	
III	20 (51)	93 (38)	<0.0001
IV	9 (23)	9 (3)	
No. of previous procedures			
1	32 (82)	215 (87)	
2	5 (12)	30 (12)	0.0017
3-5	2 (5)	0 (0.0)	

SBO=Small bowel obstruction.

cal procedures was about the same for both groups of patients (Table 1).

A median laparotomy was the only access in both groups of patients. Operation time exceeded three hours in 69.2% patients in the SMO group, and in 69% patients in the non SMO group the operation time was less than 3 hours. Intra-abdominal drains and foreign material were present in all patients in both groups. The most common surgical procedure in both groups was Miles' operation, followed by anterior rectal resection, Hartmann's procedure and left hemicolectomy. TNM stage 3 colorectal tumors were found in 76.5% in the SMO group, and in 53.9% in the non SMO group. TNM stage 2 was significantly more represented in patients in the non SMO group (37.1%), in relation to the SMO group (12.8%) (Table 2).

On the basis of the analysis of the preoperative and intraoperative risk factors for postoperative small bowel obstruction after colectomy due to colorectal cancer, it was determined that the following parameters significantly increased the likelihood of postoperative small bowel obstruction caused by adhesions: postoperative complications (OR: 38.3), TNM ≥3 (OR: 7.94), operating time (OR: 5.0), and age group 40-60 (OR: 0.126). Male gender, ASA score ≥3, emergency surgery, the application of radiation and/or chemotherapy and tumor location did not significantly increase the likelihood of the occurrence of postoperative obstruction of the small bowel in patients after colectomy for colorectal cancer (Table 3).

By multivariate regression analysis of preoperative and intraoperative risk factors for postoperative small bowel obstruction after colectomy for colorectal cancer, we found that TNM ≥3 (OR-30.68) and postoperative complications (OR-3.68) are the best predictive risk factors for postoperative small bowel obstruction (Table 4).

Table 2 Intraoperative risk factors for small bowel obstruction after colectomy for colorectal cancer

Characteristic	Groups		p
	SMO n (%)	non SMO n (%)	
Operating time (min)			
<180	12 (30.8)	169 (69.0)	<0.0001
>180	27 (69.2)	76 (31.0)	
The presence of foreign material	39 (100)	245 (100)	NS
The presence of an intra-abdominal drain	39 (100)	245 (100)	NS
Tumor location			
Colon	2 (5.1)	49 (20.0)	0.0926
Rectum	37 (94.9)	196 (80.0)	
Tumor size (cm)			
>5	19 (48.7)	115 (47.0)	0.9728
<5	20 (51.3)	130 (53.0)	
Operative procedure			
Miles' operation	15 (38.5)	99 (40.4)	0.1845
Anterior rectal resection	13 (33.3)	108 (44.0)	
Hartmann's procedure	9 (23.1)	27 (11.0)	
Left hemicolectomy	2 (5.1)	11 (4.6)	
Tumor-Node Metastasis stage			
II	5 (12.8)	132 (37.1)	<0.0001
III	30 (76.5)	91 (53.9)	
IV	4 (10.3)	22 (9.0)	

SBO=Small bowel obstruction.

Table 3 The probability ratio of preoperative and intraoperative risk factors for postoperative small bowel obstruction after colectomy for colorectal cancer in univariate analysis

Risk factor	Groups		OR	95% CI	p
	SMO n	non SMO n			
The age group 40-60 (years)	17	208	0.126	0.060-0.262	<0.0001
Male sex	30	183	1.129	0.508-2.510	>0.05
ASA score ≥3	29	102	1.222	0.548-2.727	>0.05
Number of previous surgeries ≥2	11	30	2.815	1.271-6.236	>0.05
The urgency of the surgery	2	15	0.828	0.182-3.77	>0.05
Operating time >3 h	27	76	5.000	2.406-10.402	<0.0001
Tumor location					
Colon	13	49	0.500	0.239-1.043	>0.05
Rectum	26	196			
Tumor-Node Metastasis ≥3	34	113	7.943	3.005-20.992	<0.0001
Application of radiation and/or chemotherapy	36	58	2.134	0.625-7.293	>0.05
Postoperative complications	26	12	38.833	16.057-93.914	<0.0001

SBO=Small bowel obstruction.

Table 4 Multivariate regression analysis of preoperative and intraoperative risk factors for postoperative small bowel obstruction after colectomy for colorectal cancer

Risk factor	OR	95% CI	p
Number of previous surgery ≥2	0.915	0.214-3.907	0.9050
Operating time >3 h	1.0109	0.303-2.522	0.8029
Tumor-Node Metastasis ≥3	3.680	1.036-13.072	0.0439
Postoperative complications	30.683	10.183-92.455	<0.0001

Discussion

In our study, postoperative small bowel obstruction caused by adhesions after colectomy for colorectal cancer was determined in 13.7% of patients, and in similar studies, the percentage of postoperative adhesions after surgery colon tumors ranged from 5.5% (13) to 9.5% (14-17).

In our study, most patients (81.2%) with SMO after colectomy due to colorectal cancer were older than 60 years, as in Manilich's study (18). In the same study, gender was classified as a less significant risk factor for postoperative adhesions.

In our study, the proportion comparison also did not show gender as a risk factor for postoperative adhesions of the small intestine after colectomy for colorectal cancer (Table 1). The results of similar studies are very contradictory, perhaps because few studies have mentioned the role of gender in the development of complications associated with intra-abdominal adhesions.

Various factors, other than inflammatory responses, may play a role in early postoperative SBO. In our study, the highest correlation of risk factors and the occurrence of postoperative small bowel obstruction after colectomy for colorectal cancer was determined in relation to the TNM ≥3 (OR: 3.68), and postoperative complications (OR: 30.683) (Table 4). Those factors are considered to contribute to the increased incidence of SBO. Postoperative complications were determined as Grade II-Grade IIIb, using the Clavien-Dindo Classification of Surgical Complications. Early postoperative SBO reduces patient quality of life and also alters consecutive therapies. For instance, SBO leads to delay in introduction of chemotherapy in patients with advanced colorectal cancer. For patients with rectal cancer, which is considered to be a risk factor for postoperative SBO, attention must be paid to the choice of surgical procedure, taking operating time into account. Adhesions are the most common complication in abdominal surgery, and represent one of the greatest unsolved problems of contemporary medicine. Many surgeons are still not aware of this problem and its serious consequences (19).

Limitation of study

The limitations of this study are that it is a retrospective study, our sample does not include the group of patients treated with preventive measures for postoperative adhesions, and in our study there are no patients treated by laparoscopy-assisted colectomy. We could not measure the mean age or the corresponding dispersion measures because we did not take the exact age of the patients, we had already divided the patients into age groups.

Conclusion

Postoperative small bowel obstruction after colectomy for colorectal cancer is more likely to occur in patients with TNM ≥3, and in patients who have postoperative complications.

What is already known on this subject

Small bowel obstruction is caused mainly by postoperative adhesions (more than 75% of all cases) and is a common postoperative morbidity of colectomy for colorectal cancer. It leads to markedly lower patient quality of life, longer hospital stays and increased hospitalization costs. SBO accounts for as many as 12% to 16% of surgical admissions and more than 300,000 operations annually in the United States. This represents more than 2.3 billion dollars in health care expenditures. Peritoneal trauma and inflammation always lead to the formation of acquired adhesions and they may also occur following surgery and exposure to infection or intestinal content, ischemia, irritation or foreign materials. Acute small bowel obstruction is still considered a relative contraindication for laparoscopy. Laparotomy remains the standard approach.

What this study adds

In the analyzed sample of 284 patients, small bowel obstruction after surgery for colorectal cancer was found in 39 patients. In our study, the highest correlation of risk factors and the occurrence of postoperative small bowel obstruction after colectomy for colorectal cancer was determined in relation to TNM ≥3 (OR-3.68), and postoperative complications (OR-30.68). TNM ≥3 increases the likelihood of the occurrence of SMO by 4, while postoperative complications increase the likelihood of the occurrence of SMO 31 times. We believe that the results of our study should be viewed as an overview of the current status and a good basis for future research in application of different methods to prevent postoperative adhesions and consequent obstruction of the small intestine.

Authors' contributions: Conception and design: EH; Acquisition, analysis and interpretation of data: AH, NH, ŠH and IH; Drafting the article: SH; Revising it critically for important intellectual content: EH, NH, AH and ŠH; Approved final version of the manuscript: EH.

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

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Original article

Acta Medica Academica 2016;45(2):128-134
DOI: 10.5644/ama2006-124.168

Skeletal maturity assessment using mandibular canine calcification stages

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Received: 6 July 2016
Accepted: 30 September 2016

Key words: Orthodontics ▪ Mandibular canine ▪ Calcification stage ▪ Cervical vertebrae ▪ Skeletal maturation.

Objective. The aims of this study were: to investigate the relationship between mandibular canine calcification stages and skeletal maturity; and to evaluate whether the mandibular canine calcification stages may be used as a reliable diagnostic tool for skeletal maturity assessment. **Materials and methods.** This study included 151 subjects: 81 females and 70 males, with ages ranging from 9 to 16 years (mean age: 12.29±1.86 years). The inclusion criteria for subjects were as follows: age between 9 and 16 years; good general health without any hormonal, nutritional, growth or dental development problems. Subjects who were undergoing or had previously received orthodontic treatment were not included in this study. The calcification stages of the left permanent mandibular canine were assessed according to the method of Demirjian, on panoramic radiographs. Assessment of skeletal maturity was carried out using the cervical vertebral maturation index (CVMI), as proposed by the Hassel-Farman method, on lateral cephalograms. The correlation between the calcification stages of mandibular canine and skeletal maturity was estimated separately for male and female subjects. **Results.** Correlation coefficients between calcification stages of mandibular canine and skeletal maturity were 0.895 for male and 0.701 for female subjects. **Conclusions.** A significant correlation was found between the calcification stages of the mandibular canine and skeletal maturity. The calcification stages of the mandibular canine show a satisfactory diagnostic performance only for assessment of pre-pubertal growth phase.

Introduction

Timing plays a crucial role in the outcomes of treatment for skeletal disharmonies in growing patients. Successful treatment of skeletal disharmonies may be achieved by growth modification in patients that have a certain amount of growth remaining (1-3). There are wide individual variations in the timing, duration and velocity of growth, and therefore we need to assess individual development stages (4). Skeletal maturity may be assessed by means of several more or less reliable parameters: chronological age (5), increases in body height and weight (6), secondary sexual characteristics (6), dental maturity (calcification stages) (7), hand and wrist maturational stages (8), cervical vertebral maturation (3, 9) and biochemical markers (10, 11).

Dental development is one of the important indicators of skeletal maturity. There are two possibilities for assessment of skeletal maturity. One of them is tooth erup-

tion, which is not a reliable parameter of skeletal maturity. Franchi et al. (12) showed a poor correlation between the phases of dentition and skeletal maturity. In addition to tooth eruption, dental maturity is estimated through the stages of calcification, and this is a much more reliable parameter for assessment of skeletal maturity (13-16). For all these reasons, dental maturity is recommended as a clinically useful diagnostic tool for assessment of skeletal maturity. Assessment of skeletal maturity, based on the stages of tooth calcification, has certain advantages, as it allows assessment based on panoramic radiographs that are routinely used for diagnosis, and assessment may be carried out by analysing retroalveolar radiographs. Stages of teeth development are associated with growth and development, which means that dental maturity may be used as a parameter for assessment of skeletal maturity, as has been shown by numerous studies (13-16). Some authors noted that the developmental stages of certain teeth, for example canines (17, 18) and second molars (19), show a high correlation with skeletal maturity.

The aims of this study were: (1) to investigate the relationship between mandibular canine calcification stages and skeletal maturity; and (2) to evaluate whether the mandibular canine calcification stages may be used as a reliable diagnostic tool for skeletal maturity assessment.

Subjects and methods

This study included 151 subjects: 81 females and 70 males, with ages ranging from 9 to 16 years (mean age: 12.29±1.86 years). The mean age of the males was 12.05 (±1.83), and for females 12.31 (±1.89) years. Chronological age was recorded according to the date of birth, confirmed by the parents. The inclusion criteria for subjects were as follows: age between 9 and 16 years, and good general health without any hormonal, nutritional, growth or dental development problems. Subjects who were undergoing or had previously received orthodontic treatment were not included in this study. Assessment of mandibular canine calcification and cervical vertebral maturation stages were performed using good quality panoramic radiographs and lateral cephalograms. All analyses were conducted by an experienced orthodontist.

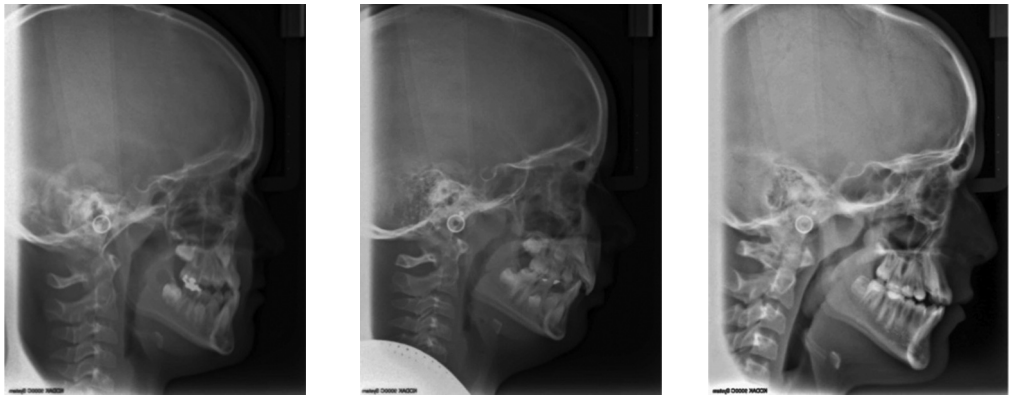
Assessment of mandibular canine calcification stages

The calcification stages of the left permanent mandibular canine were assessed according to the method of Demirjian et al. (7) (stages E to H), on panoramic radiographs. These stages are defined as:

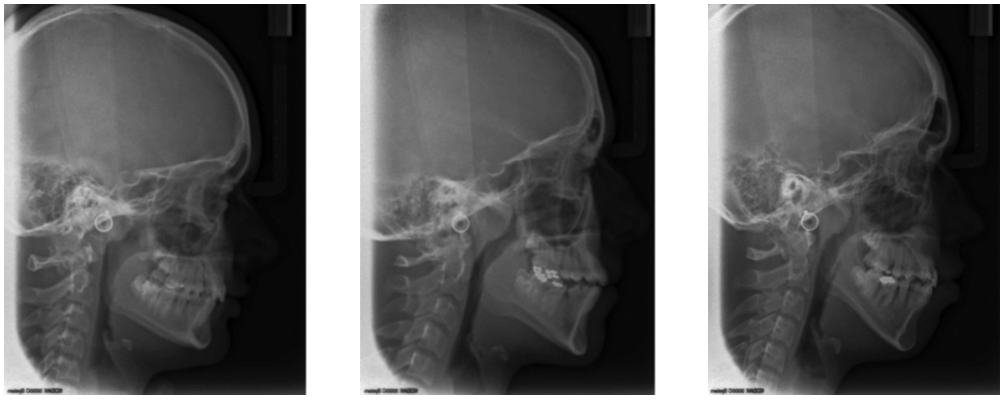
- Stage E – The walls of the pulp chamber form straight lines, the continuity of which is broken by the presence of the pulp horn, which is larger than in the previous stage and the root length is less than the crown height.
- Stage F – The walls of the pulp chamber form an isosceles triangle, with apex ending in a funnel shape, and the root length is equal to or greater than the crown height.
- Stage G – The walls of the root canal are parallel and its apical end is still partially open.
- Stage H – the apical end of the root canal is completely closed, and the periodontal membrane has a uniform width around the root and the apex.

Assessment of individual skeletal maturity

Assessment of skeletal maturity was carried out using the cervical vertebral maturation index (CVMI), as proposed by the Hassel-Farman method (9), on lateral cephalograms. This method requires that the second, third and fourth cervical vertebrae



a) CVMI 1 - Initiation b) CVMI 2 - Acceleration c) CVMI 3 – Transition



d) CVMI 4 - Deceleration e) CVMI 5 - Maturation f) CVMI 6 - Completion

Figure 1 The stages of cervical vertebral maturation according to the Hassel-Farman method.

(C2, C3 and C4) are analysed according to their shape and classified into one of the six stages, which are defined as follows:

- CVMI 1 *Initiation:* The lower borders of the second, third and fourth cervical vertebrae (C2, C3 and C4) are flat. The bodies of C3 and C4 are trapezoid in shape and the superior vertebral borders are tapered from posterior to anterior (Figure 1a).
- CVMI 2 *Acceleration:* Concavities develop on the inferior borders of C2 and C3, and the inferior border of C4 is flat. The bodies of C3 and C4 are nearly rectangular in shape (Figure 1b).
- CVMI 3 *Transition:* Distinct concavities develop on the inferior borders of C2 and C3, and concavity begins to develop on the inferior border of C4. The bodies of C3 and C4 are rectangular (Figure 1c).
- CVMI 4 *Deceleration*: Distinct concavities are seen on the inferior borders of C2, C3 and C4. The vertebral bodies are becoming more square in shape (Figure 1d).
- CVMI 5 *Maturation:* More accentuated concavities are seen on the inferior borders of C2, C3 and C4. The bodies of C3 and C4 are nearly square in shape (Figure 1e).
- CVMI 6 *Completion:* Deep concavities are seen on the inferior borders of C2, C3 and C4. The bodies of C3 and C4 are square or greater in vertical dimension than in horizontal dimension (Figure 1f).

Ethics statement

The study was approved by the Ethical Committee of the School of Dental Medicine, University of Sarajevo.

Statistical analysis

SPSS software, version 20 was used to perform the statistical analyses. The frequency and the percentage distribution of the CVMI stages and mandibular canine calcification stages were calculated separately for male and female subjects. Correlation between CVMI and the mandibular canine calcification stage was presented through Spearman's correlation coefficient. The level of significance was defined as $p<0.001$.

Results

The distributions of the different calcification stages of the mandibular canine for male subjects are shown in Table 1.

Calcification stages E (42.9%) and F (57.1%) of the mandibular canine were found at stage 1 of CVMI. At stage 2 of CVMI 82.6% of subjects were in calcification stage F and 17.4% of subjects were in stage G, while at stage 3 of CVMI only 11.1% of subjects were in stage F, 66.7% were in stage G and 22.2% were in stage H. At stage 4 of CVMI 17.4% of subjects were in stage G and 82.6% of subjects were in stage H. All subjects in stage 5 of CVMI were in calcification stage H of the mandibular canine. However, none of the male subjects was at stage 6 of CVMI. Spearman's correlation was used to assess the correlation between CVMI stages and mandibular canine calcification stages.

Table 1 Contingency table showing distributions between the different calcification stages of mandibular canine and CVMI stages for male subjects

CVMI	Stages of calcification of mandibular canine				Total
	E	F	G	H	
	n (%)	n (%)	n (%)	n (%)	n (%)
1	3 (42.9)	4 (57.1)	-	-	7 (100)
2	-	19 (82.6)	4 (17.4)	-	23 (100)
3	-	1 (11.1)	6 (66.7)	2 (22.2)	9 (100)
4	-	-	4 (17.4)	19 (82.6)	23 (100)
5	-	-	-	8 (100)	8 (100)
Total	3 (4.3)	24 (34.3)	14 (20.0)	29 (41.4)	70 (100)

CVMI=Cervical Vertebral Maturation Index (Spearman's rho correlation coefficient between calcification stages of mandibular canine and CVMI is 0.895, $p<0.001$).

Table 2 Contingency table showing distributions between the different calcification stages of mandibular canine and CVMI stages for female subjects

CVMI	Stages of calcification of mandibular canine			Total
	F	G	H	
	n (%)	n (%)	n (%)	n (%)
1	1 (100)	0	0	1 (100)
2	8 (66.7)	4 (33.3)	0	12 (100)
3	0	7 (46.7)	8 (53.3)	15 (100)
4	0	6 (31.6)	13 (68.4)	19 (100)
5	0	1 (3.7)	26 (96.3)	27 (100)
6	0	0	7 (100)	7 (100)
Total	9 (11.1)	18 (22.2)	54 (66.7)	81 (100)

CVMI=Cervical Vertebral Maturation Index (Spearman's rho correlation coefficient between calcification stages of mandibular canine and CVMI is 0.701; $p<0.001$).

Among the female subjects calcification stages F, G and H of the mandibular canine were found. Only one subject was at stage 1 (100%) of CVMI, with calcification stage F of the mandibular canine. At stage 2 of CVMI 66.7% of subjects were in calcification stage F, and 33.3% of subjects were in stage G. At stages 3, 4 and 5 of CVMI, the subjects were in calcification stages G and H of the mandibular canine. At stage 6 of CVMI all subjects were in calcification stage H of the mandibular canine. The correlation between CVMI and the calcification stage of the mandibular canine for female subjects was analysed by Spearman's correlation coefficient.

Discussion

In the present study, tooth calcification stages were preferred rather than eruption because tooth formation is proposed as a more reliable parameter. The method according to Demirjian was used, because this method is based on shape criteria and the proportion of root length, using the relative values of crown height rather than the absolute length (7). Therefore, foreshortened or elongated projections of developing teeth will not affect the reliability of assessment (20).

Among all the tested teeth, mandibular canines showed a significant association with the stages of development (17-21). In addition, hypodontia of permanent canine is extremely rare, and the prevalence ranges from 0.18 to 0.29% (22). Also, mandibular permanent canine rarely show morphological variations in their development (23).

Assessment of skeletal maturity was carried out using the cervical vertebral maturation index (CVMI), as the proposed Hassel-Farman method, on lateral cephalograms (9), is a routine diagnostic radiograph for orthodontic treatment. Studies have found that CVMI is a reliable method for skeletal maturity assessment (9, 13, 15, 19, 21). Some studies report high correlations between calcification stages of teeth (dental maturity) and skeletal maturity indicators (13-16). Some authors investigated correlations between calcification stages of some teeth (canines, second and third molars), and they found that the calcification stage of mandibular canine showed a significant correlation with skeletal maturity (17, 18, 21). In this study, the correlation coefficients between calcification stages of mandibular canine and skeletal maturity were 0.895 for male and 0.701 for female subjects, and all correlation coefficients were statistically significant, at $p<0.001$. These results indicate that the calcification stages of mandibular canine are a reliable parameter for skeletal maturity assessment.

CVMI stage 2 indicates the beginning of the pubertal growth spurt (9). In our study, calcification stage F of the mandibular canine coincided well with the CVMI stage 2, for both sexes (Table 1 and 2). Mittal et al. (15) and Goyal et al. (21) reported similar results in their studies. This means that calcification stage F of the mandibular canine could be used for assessing the pre-pubertal growth phase. According to the Hassel and Farman method, at CVMI stage 3 growth is still accelerating toward peak velocity; while at CVMI stage 4 adolescent growth begins to decelerate (9). Calcification stage G of the mandibular canine coincided well with CVMI stage 3, and stage H with CVMI stage 4 for the male subjects in our study. However, for female subjects calcification stage H of the mandibular canine showed the highest percentage distribution at CVMI stages 3 and 4. For both genders, canine root formation was complete (stage H) in the majority of subjects at CVMI stages 5 and 6. These results are consistent with the results of other similar studies (15, 16, 21).

In this study, dental maturation of the mandibular canine occurred earlier in female subjects than in male subjects, which

was in accordance with a previous study (21). In contrast, the results of the studies by Chertcow (13) and Uysal et al. (17) showed advanced dental maturation in male subjects. These results indicate that the calcification stages of mandibular canines may be considered as a reliable parameter to assess pre-pubertal growth phases.

Conclusions

A significant correlation between the calcification stages of the mandibular canine and skeletal maturity was found. The calcification stages of the mandibular canine show satisfactory diagnostic performance only for assessment of pre-pubertal growth phases.

What is already known on this topic

Successful treatment of the skeletal disharmonies may be achieved by growth modification, in patients that have a certain amount of growth remaining. There are wide individual variations in the beginning, amount and duration of pubertal growth acceleration, and therefore an assessment of individual development stages is needed. Individual skeletal maturity may be assessed by means of several, more or less reliable parameters.

What this study adds

The calcification stages of mandibular canine show satisfactory diagnostic performance for assessment of pre-pubertal growth phase.

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

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

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Original article

Acta Medica Academica 2016;45(2):135-144
DOI: 10.5644/ama2006-124.169

Medical futility treatment in intensive care units

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Received: 4 November 2016
Accepted: 21 November 2016

Key words: Intensive care unit ▪ Medical futility ▪ End-of-life ▪ Decision making ▪ Ethics.

Objective. To investigate cases of potential medical futility treatment in intensive care unit (ICU). **Materials and Methods.** Retrospective review of 1567 charts of patients treated during the three-year period (2012 - 2014) in the ICU of the University Hospital Centre Split, Croatia, was conducted. More detailed analysis of the deceased patients' (n=429) charts was performed to identify cases of potential medical futility treatment. There were 99 patients for which ICU treatment was questionable due to their low Glasgow coma scale (GCS) score. For those patients types and duration of treatment were analyzed. **Results.** Among patients who were treated during that period, 27% had died. Treatment of 99 patients (6.3% of the deceased) was considered a potential medical futility. Mean age of those 99 patients was 68±14 years and the mean stay in the ICU was 14±11 days. They spent 1302 patient days in the ICU, of which 52% days they had GCS 3 score. They were treated with catecholamines during 40% of the patient days. Minimal therapy was provided during 44% of the patient days. **Conclusions.** Analysis of the deceased patients' charts in the ICU indicated that a certain percentage of patients did not need prolonged ICU treatment. Instead, they were supposed to be treated in a palliative care unit. To avoid medical futility treatment in ICUs, palliative care unit needs to be established, as well as protocols for determining medical futility cases and ethical committee that will decide which patients will be transferred to palliative care.

Introduction

Intensive care units (ICU) are units for treatment of patients with severely impaired organ function and life-threatening conditions. With expert and aggressive treatment, a patient's life may be saved, disability reduced and a patient may fully recover (1). There are different ICUs – general, surgical, infectious diseases, internal medicine, cardiac, gastrointestinal, pediatric, psychiatric, neurological, trauma, etc. If there is an adequate space, equipment and expert health workers, the same level of medical care can be provided on different clinics and departments (2, 3). Due to rational care, high costs of treatment and lack of highly qualified medical personnel, smaller hospitals have central ICU where all patients who need mechanical ventilation, cardiovascular support and intensive care are treated (3). The aim of the ICU treatment is recovery of a failed organ function or of multiorgan failure, such as heart-, kidney- or liver failure, septic conditions, polytrauma, severe brain damage and metabolic disorders (4).

All treatments that physicians and other medical personnel provide to patients should primarily target prevention and maintenance of health, and when a patient

presents with disease and injury, the main goal is to help the ill (1, 5). Emphasis should be on maintaining and, if possible, enhancing patients' quality of life and, at the same time, reducing physical and emotional pain and suffering (5, 6). Prolonging life in critically ill patients is not the goal in itself and it should not be the main goal of the treatment except when it is medically justified (7).

Palliative medicine is a new branch of medicine, caring for patients in end of life stage and patients for which medicine has exhausted all curative options and is unable to help a patient to restore health. Palliative care is an approach that helps patients faced with life-threatening illness and their families to improve their quality of life (8). This can be enabled via prevention and alleviation of symptoms using methods of early detection, assessment and pain management, and alleviating other physical, psychosocial and spiritual problems (8). Palliative care is necessary for chronic patients in acute progressive phases of disease, with life expectancy under 6 months, at a time when medical curative treatment is no longer effective (9). Considering ethical dilemmas faced by physicians daily, it is important to emphasize that physicians are not obliged to suggest or start treatment measures for which they believe will not improve patients' condition, but can prolong patients' suffering (4).

Dysthanasia is a concept opposite to the concept of "euthanasia", and it covers practice of extending biological life of a dying patient using medical treatments and technology without regard to the patient's quality of life. This term is now associated with medical futility. Although medical futility is a widely known concept, we still do not have a single definition of such procedures (6, 10, 11). It has been reported previously that different institutions have different approaches to what is considered a medical futility treatment (2).

The factors associated with differences in the utilization of ICU resources between institutions are the decision-making process about when to start and complete treatment, the patient's condition at the moment of ICU admission, the number of staff employed and the possibility of transferring patients to other organizational units after completed treatment (2). Existing evidence indicates that providing proactive palliative care in the ICU, using either consultative or integrative palliative care interventions, may decrease hospital and ICU length of stay. Furthermore, it does not affect satisfaction, and neither decreases or affects patients' mortality (5). Therefore, it is important to continue discussion about medical futility treatment in order to prevent practice of dysthanasia and to provide patients with the best care without unnecessarily prolonging their life.

The aim of the study was to explore potential cases of medical futility treatment in the ICU and to encourage establishment of palliative care unit in the hospital, algorithms for recognizing patients that may be subjected to medical futility and working protocols for the ICU. The goal was also to point out the necessity of forming ethical committee that could be involved in decision-making, regarding potential medical futility and provide recommendations or decisions about further proceedings.

Materials and methods

Patients

Retrospective review of 1567 charts of patients treated during the three year period (2012-2014) in ICU of the University Hospital Split, Croatia, was conducted.

Setting

This is a central-type ICU in a tertiary hospital, organized within the Department of anesthesiology and intensive care. The ICU

operates on two locations, one with 10 and another one with 8 beds. The hospital has a total of 1530 beds, with 23 beds for intensive treatment (18 beds in the general ICU and 5 beds for the postoperative cardiosurgical ICU). Heads of the ICUs are anesthesiologists with a subspecialty in intensive treatment.

Data analysis

Patient records and daily charts of deceased patients (429/1567; 27%) were analyzed in detail. The following data were recorded: diagnosis, therapy and procedures received in the ICU (resuscitation, type of pharmacological treatment, minimal therapy), duration of treatment in the ICU before death, Glasgow coma scale (GCS) score for assessment of impairment of consciousness in response to defined stimuli, disease severity according to the Acute Physiology and Chronic Health Evaluation II (APACHE II) classification and hospital mortality estimate using Simplified Acute Physiology Score II (SAPS II) criteria. Additionally, bed occupancy in the ICU during a year was analyzed and indicated in percentages. Deceased patients with potential medical futility treatment were defined using the GCS (GCS <8 during ICU stay) and using those criteria 99 patients (6.3% of the total number of treated patients) were identified.

For evaluating whether their treatment in the ICU was justified, those 99 patients were divided into the 4 groups: the first group were the patients with GCS 3 who received minimal therapy in the ICU (5% glucose or saline and mechanical ventilation); the second group were those with GCS <6, who received vasopressor support with catecholamines (epinephrine, norepinephrine, dobutamine, dopamine); in the third group patients had GCS <6 and did not receive catecholamine treatment, while in the fourth group patients had GCS above 6 and received support with catecholamines (norepinephrine, dobutamine, dopamine). Data were shown separately for two different ICU locations. Economical aspects of treatment were not analyzed considering inadequate reimbursement system mandated by the Croatian Health Insurance Fund, which is not commensurate with the actual expenses.

Ethics

The study was approved by the University Hospital Split Ethical Committee. The study was conducted in accordance with the Declaration of Helsinki from 1975 and its amendments from 1983.

Statistics

For testing normality of data we used Kolmogorov-Smirnov test. Data were analyzed using descriptive statistics and shown as frequencies, percentages, means, standard deviation, median and range. For data analysis GraphPad program was used (GraphPad Software, La Jolla, CA, USA).

Results

In the two ICUs of the University Hospital Split, 1567 patients were treated during the analyzed period of three years (2012-2014), of which 429 patients died (27%). Detailed analysis was conducted for 99 patients (6.3%) that were potential cases of medical futility treatment (59 patients in Unit I and 40 patients in Unit II). Among them, there were 66 men and 33 women. Considering the four different groups in which they were categorized, according to their condition, most of the patients were in the group 2 (Table 1).

Patient characteristics are shown in Table 2. Mean age of patients with potential medical futility treatment was 68±14 years and their mean stay in the ICU was 14±11

Table 1 Number of patients in ICU* in different categories of potential medical futility (n=99)

Groups	GCS†	Vasopressor support	Number of patients in both units	n (%)
First	3	Yes‡	9	9 (9)
Second	<6	Yes	62	62 (63)
Third	<6	No	15	15 (15)
Fourth	<8	Yes	13	13 (13)

*Intensive care unit; †Glasgow Coma Scale; ‡Initially afterwards minimal therapy.

days. Duration of patients' stay in the ICU is shown in Table 2 for each group, as well as their APACHE II and SAPS II scores.

Total number of days patients were treated in the ICU is shown in Table 3. Patients spent 1302 patient days (1 to 79) in the ICU. GCS score of 3 was observed during 675 (52%) patient days of their ICU stay, and catecholamines were administered to those patients for 520 (40%) days. Nine patients received minimal therapy for a total of 55 days (4% of the total days that those patients spent in the ICU).

In 9 patients who received minimal therapy during the ICU stay, that therapy was administered during 33% of patient days spent in the ICU. They had GCS 3 during 65% of the patient days (Table 4).

Bed occupancy in the ICU during the year 2012 is shown in Table 5. Beds in the Unit I were occupied from 80 to 100% during 198 days in the year (54%), while the bed

Table 2 Characteristics of patients in ICU* with potential medical futility treatment (n=99)

Variables	Group 1	Group 2	Group 3	Group 4
	GCS† =3 min. th.‡	GCS† <6 + VP§	GCS† <6	GCS† >6 + VP§
Number of patients	9	62	15	13
Median age in years (range)	62 (35 – 84)	66.5 (22 – 84)	73 (52 – 82)	73 (24 – 86)
Median stay in ICU* (days; range)	16 (4 – 48)	9.5 (1 – 79)	7 (3 – 51)	9 (4 – 33)
APACHE II‖	24.5	24.2	24.6	23
SAPS II¶	67.1	68.3	72.3	63.5

*Intensive care unit; †Glasgow Coma Scale; ‡Minimal therapy; §Vasopressor support ‖Acute Physiology and Chronic Health Evaluation II, ¶Simplified Acute Physiology Score II.

Table 3 Number of patient days in ICU* and therapy (n=99)

Groups	Days in the ICU*	Days with GCS†=3	Days receiving VP§	Days receiving min. th.
	n	n (%)	n (%)	n (%)
First (Minimal therapy)	166	108 (65)	55 (33)	55 (33)
Second (GCS† < 6 + VP§)	794	445 (56)	338 (43)	0
Third (GCS† < 6)	168	122 (73)	0	0
Fourth (GCS† = < 8 + VP§	174	0	127 (73)	0
Total	1302	675 (52)	520 (40)	55 (4)

*Intensive care unit; †Glasgow Coma Scale; §Vasopressor support; ‡Minimal therapy.

Table 4 Patients receiving minimal therapy during their ICU* stay

Patient number	Age	Days of ICU* stay	Days of GCS† =3	Days of VP§	Days of min. th.‡
1	35	16	16	0	10
2	55	21	16	4	5
3	62	4	4	1	2
4	82	8	8	0	5
5	84	48	16	20	13
6	71	23	6	17	6
7	56	7	7	0	7
8	66	13	9	9	3
9	40	26	26	4	4
Total		166 (100%)	108 (65%)	55 (33%)	55 (33%)

*Intensive care unit; †Glasgow Coma Scale; §Vasopressor support; ‡Minimal therapy.

occupancy in Unit II was above 80% during 119 (33%) of days during that year. Similar data were observed for years 2013 and 2014.

Among 99 selected patients, 75% of them stayed for up to 9 days in the ICU, while 16% of patients in UNIT I and 11% of patients in UNIT II stayed for 10 to 19 days in the ICU. There was 1% of patients who were treated in the ICU longer than 20 days (Table 6).

Table 5 Bed occupancy in the Unit I and Unit II during year 2012

Unit I (10 beds)		
Beds	Days	%
10	45	100
9	73	90
8	80	80
7	62	70
6	50	60
5	31	50
Unit II (7 beds + one bed for burns)		
Beds	Days	%
7 +1	4	100
7	41	100
6	74	85.7
5	89	71.4
4	87	57.1
3	43	42.8
2	28	28.5

Table 6 Duration of patient stay in the Unit I and Unit II during year 2012

Number of days in the ICU*	Unit I	Unit II
	n (%)	n (%)
1 to 9	262 (74)	128 (76)
10 to 19	58 (16)	19 (11)
20 to 29	21 (5.9)	8 (4.7)
30 to 39	4 (1.2)	5 (3.0)
40 to 49	6 (1.7)	3 (1.8)
50, 52	1 (0.3)	1 (0.6)
75, 76	1 (0.3)	2 (1.2)
85, 86	0 (0)	2 (1.2)
141	0 (0)	1 (0.6)
Total	353 (100)	169 (100)

*Intensive care unit.

Details about 6 patients with GCS 3 who were resuscitated and received catecholamines are shown in Table 7. Due to GCS 3 results, these patients were resuscitated without expecting recovery. On average, they had GCS 3 during 56% of patient days spent in the ICU. During 56% of days spent in the ICU, they received catecholamine support.

The most common diagnoses of the 99 patients for which it was estimated that they received medical futility treatment were respiratory failure, injuries – most commonly

Table 7 Patients that were resuscitated without expecting recovery (6 patients)

Patient number	Days in ICU	Days with GCS 3	Days with vasopressor support	Times resuscitated (n)
1	24	10	18	3
2	5	3	0	2
3	6	2	4	1
4	5	5	4	1
5	4	2	2	1
6	6	6	0	1
Total	50 (100%)	28 (56%)	28 (56%)	-

Table 8 Patients' diagnoses (n=99)

Main diagnosis	n
J96 (Respiratory failure)	20
S02, S06 and S09 (Head injuries)	19
I61 (Intracerebral haemorrhage)	13
I21, I60, I62, I63 and I71 (Acute myocardial infarction and Cerebrovascular diseases)	11
I46 (Cardiac arrest)	8
A41,9 (Sepsis)	8
C15, C16 - C20, C34, C71 and C93 (Malignant neoplasms of digestive organs, bronchus and lungs, brain and laeukemias)	8
I26 and I72 (Pulmonary embolism and aneurysm)	3
J80 and J95 (ARDS* and postprocedural respiratory disorders)	2
X61 (Intentional self-poisoning)	2
G06 and G37,3 (Intracranial abscess and granuloma and acute transverse myelitis)	2
A39,9 (Meningococcal infection)	1
K56 (Paralytic ileus and intestinal obstruction)	1
T31,5 (Burns)	1

*Adult respiratory distress syndrome; Codes for diagnoses shown according to the International Classification of Diseases (ICD-10). Available at: http://apps.who.int/classifications/icd10/browse/2010/en.

from traffic accidents, circulation failure, sepsis and postoperative care of patients suffering from malignant diseases (Table 8).

Discussion

We conducted a retrospective chart review to investigate cases of potential medical futility treatment among deceased patients in intensive care unit. Our analysis indicated that a certain percentage of patients did not need prolonged ICU treatment. Instead, they were supposed to be treated in a palliative care unit.

Technology has revolutionized all aspects of our lives, and medicine is not an exception. Diagnostic procedures and interventions that can be done today were once unthinkable. By using technology and new knowledge from research, intensive care of patients is now on a very high level (10). However, technological advancement has brought along a number of questions in the field of medical ethics (4, 12). Due to

the complexity of decision-making in life-threatening conditions, ethical committees are being established. Their purpose is to provide help in solving ethically complex situations and to give recommendations about managing certain cases (11). Based on the objective medical factors, a good assessment of treatment outcomes can be made and further medical procedures directed (13). Likewise, decision-making about further treatment should always take into account patients' quality of life (10). When everything possible has been done, and when there is no chance of patient's recovery and further treatment is useless, certain complex medical interventions should no longer be conducted (12, 14). A patient without chances of recovery will be medically treated, but extraordinary treatment measures should not be taken in the case of organ failure (1). Certain institutions have protocols for terminating treatment in specific situations, when patient is disconnected from the mechanical ventilation and resuscitation procedures are not conducted. Such protocols can be devised in the hospital ICUs where working protocols are adopted, where ethical committees give consent for ending further intensive treatment because it is futile, and when there are no objective chances that patient will recover in a way he/she will have an acceptable quality of life (15, 16).

In our analysis of one ICU over three years (2012-2014), based on the criteria set for medical utility, 6.3% of deceased patients received treatment which was probably medical futility. That number is probably even greater, considering that data from literature describe that physicians consider 8.6% of ICU patients receive potentially futile treatment, and 11% definitely receive futile treatment (7). Average age of our patients considered potential medical futility was 68 years. They spent a total of 1302 days in the ICU, 14 days on average. According to the ETHICUS study, average ICU stay of patients considered potential medical futility was 18 days, and 15 days for patients considered definitive medical futility (7). Among patients considered as potential medical futility, 87% had GCS score under 6, and some of them had that score on the admission to the ICU. Patients had GCS 3 during 675 patient days (52% of their ICU stay). Only 9% of patients received minimal therapy. Catecholamine support was given to 76% of the potential medical futility patients during 40% of their ICU patient days. Considering that their need for further intensive care was questionable, it is unclear why potential medical futility patients received catecholamine support (7, 17).

In the analyzed ICU, 9 patients that were considered potential medical futility received minimal therapy, which means that their active treatment was withdrawn during their ICU stay (33% of their ICU stay). Those patients had GCS 3 during 65% of the ICU time. These data are in accordance with the corresponding data in other settings. Study from UK reported that active treatment was withdrawn for 9% of patients admitted to ICU (12). Time between ICU admission and decision about ending active treatment should be as short as possible. A large study of more than 80,000 ICU admissions in England and Wales showed that if that time could be shortened for just one day, it was estimated that 100 patients could be saved in that region annually (12, 18).

Capacities of ICU units are limited and treating patients whose recovery is not expected is not justified. Bed occupancy in the two analyzed ICU units were over 80% during 54% of the year for UNIT I and during 33% of the year for UNIT II, respectively. That should never be above 85% to allow admission of acute patients. Therefore, it is important to establish criteria for ICU admission. If the ICU receives and treats patients that cannot profit from that care, this practice reduces available beds and resources for

treating patients that really need intensive treatment (19). In adition to clear admission criteria, protocols for determining medical futility treatment should also be established as well as palliative care unit (11, 19).

Our data indicate that 25% of patients considered as potential cases of medical futility treatment were treated in the ICU longer than 10 days; 11% of those patients spent more than 20 days in the ICU. On average, those patients spent 13 days in the ICU. For comparison, average duration of ICU stay in Finland is 4 days and in Poland 14 days (2).

Data from the United States of America indicate that length of stay increases costs of intensive treatment, while not necessarily prolonging survival. Stricker et al. showed that caring for 11% of patients who were treated in the ICU longer than 7 days accounts for 50% of ICU costs (20). Several studies indicated a 50% mortality of patients who stay in ICU longer than 14 days, while 70% of those patients achieve less than 50% of functional recovery (21, 22). These data are additional support for arguments that medical futility treatments in the ICU should be reduced to minimum. Patients with GCS 3 that were resuscitated and received catecholamines on average had GCS 3 during 56% of days during their ICU stay and 56% of days received catecholamines. Since recovery objectively was not expected, it is reasonable to question decision to attempt resuscitation, especially considering that some patients were resuscitated multiple times. Furthermore, it is unclear why patients with no chances of improvement receive catecholamine support. There is no professional, ethical or economical justification for attempting resuscitation and giving catecholamines to patients without chances of recovery (17, 23).

Various reasons may explain why those patients were resuscitated. Firstly, it could be due to insufficient communication among staff and between patients and patients' family. Secondly, a physician might feel that his or her duty is to do "everything for a patient". One of the reasons is probably insufficient knowledge of patients' wishes, i.e. lack of official forms for resuscitation that patients can sign and his family can use when a patient is no longer capable of making decisions (23, 24).

One of the reasons that may explain such prevalence of medical futility is lack of palliative care unit in the analyzed hospital. Such units could receive medical futility patients once their intensive treatment is no longer considered sensible (10). The second reason is the lack of working protocols, algorithms and guidelines that will help physicians to decide that further treatment is futile (2). Furthermore, in the analyzed hospital there is no ethical committee in charge of making decisions about medical futility and helping physicians with decision-making about potential medical futility cases. Introduction of such guidelines and an ethical committee would help physicians and nurses in their daily work. Until such instruments become available, health care workers are forced to provide advanced treatments to ICU patients, knowing that they are futile (10, 11, 14). This practice prolongs suffering of patients and their family, and it also contributes to increased cost of health care. Physicians are burdened with conflict between their understanding of situation and requirements for treatments and they are growing dissatisfied. Futile medical care is provided because of fear of legal consequences, limited and unsatisfactory communication between physicians, patients and their family, and insufficient knowledge of palliative care principles (10, 14). Tools such as SAPS II and APACHE II have an excellent ability to discriminate between survivors and non-survivors so they can be used to guide medical decisions (25).

Death is natural and final part of life. Medicine can not prolong that process in-

definitely. When it is clear that inevitable death is imminent, it is legitimate for a physician to refuse or limit treatment options that would only secure a precarious and burdensome prolongation of life, for as long as basic humane, compassionate care is not interrupted (14). It is also accepted and ethically justified to refuse forms of treatment that are useless and not beneficial to a patient or in situations when it is not possible to offer such treatment (11).

Intensive treatment is very expensive and should be used rationally. Cost of treatment was not calculated in the study because calculation of medical expenses in Croatia is very specific and determined by the Croatian Health Insurance Fund, and therefore it cannot be compared to costs of treatment in other high-income countries. However, based on the published data, costs of ICU treatment account for 15% – 20% of hospital expenses, i.e. more than one third of expenses of the entire health system (15). After taking into account that a part of those funds was spent on medical futility treatments, on patients that should not be treated in the ICU at all, it is clear that this is a significant financial consideration. By treating in the ICU patients that cannot benefit from that treatment, other patients who may benefit from intensive care may be refused such treatment (1). Considering that ICUs are usually of limited capacities and often fully booked, from a medical, ethical and economical point of view it is not justified to use it for medical futility treatments (1).

All patients analyzed in the study as potential medical futility treatment cases died in the ICU. Their transfer to palliative care unit was not possible because there was no such unit, not in that hospital nor anywhere nearby in that geographical region. Likewise, there were no protocols to conduct in situations when ICU treatment was useless, or protocols for detaching a patient from mechanical ventilation when such treatment was no longer sensible.

Conclusions

Analysis of patient charts of patients who died in the ICU indicates that around 6% of patients were not supposed to be treated in the ICU – those patients belonged to the palliative care unit. Since this hospital does not have palliative care unit, nor such unit exists nearby, it is necessary to establish such unit for appropriate patient care. Besides establishing palliative care unit and a team, the hospital also needs to establish ethical committee that will consider all cases of potential medical futility treatment. Furthermore, clear working protocols for ICU are necessary. Such guidelines would help patients make decisions about resuscitation and providing vasoactive support. Additionally, physicians should receive education about medical futility.

What is already known on this topic

Emphasis of a medical treatment in intensive care units should be on maintaining and, if possible, enhancing patients' quality of life and, at the same time, reducing physical and emotional pain and suffering. Prolonging life in critically ill patients is not the goal in itself and it should not be the main goal of treatment except when it was medically justified.

What this study adds

A certain percentage of deceased patients did not need prolonged treatment in intensive care unit. Such patients should be treated in a palliative care unit instead. To avoid medical futility treatment, palliative care unit needs to be established, as well as protocols for determining medical futility cases and ethical committee that will decide which patients will be transferred to the palliative care.

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

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

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Short communication

Acta Medica Academica 2016;45(2):145-151
DOI: 10.5644/ama2006-124.170

Influence of gender and selection procedures on the academic performance of undergraduate medical students

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Received:19 June 2016
Accepted: 17 November 2016

Key words: Gender ▪ Medical School ▪ Selection ▪ Undergraduate academic success.

Objectives. To determine the impact of gender on success of students studying Medicine in Belgium from the first year (MED1) to the sixth year (MED6) of training, in the context (or not) of a selection process after three years at university. **Subjects and method.** Data were evaluated from two cohorts of medical students: students of the first group (n=88) were not submitted to a selection process and students of the second group (n=76) were submitted to a selection process after MED3. Students were enrolled in Brussels Medical School. The variables studied were the grades obtained after the first session of exams, and the student's gender. Variables were put into perspective in relation to the cohort/study year. STATA software was used for statistical analysis. **Results.** Linear regression showed the significant predictability of the grade obtained in MED2 for the grade obtained in MED6 for males and females only in the context of selection ($r=0.51$; $p<0.001$). The impact of grades after three years on those after six years was negative in the first group of students ($r=-0.17$; $p=0.005$) and positive in the second group ($r=0.54$; $p<0.001$). **Conclusion.** These results show a moderate link between success in MED1 and success in MED6, as long as the students undergo selection. A selection system after MED1, based on medical courses, inter alia, could speed up the maturation of students. Further studies with a higher number of candidates are necessary to confirm these results.

Introduction

The likelihood of success in the first years at university is 1.6 times higher for female than for male students (1). Moreover, studies addressing the impact of gender on undergraduate medical school (MS) success in the context of early selection (2, 3) have reported a more stable trajectory for female than male students in the course of medical studies (4).

The aim of this research was to study: i) the trajectory of success of medical students in the French Community of Belgium (FCB) during undergraduate medical studies, and ii) the impact of gender on success in the context of a selection system conducted at the end of three years of medical studies.

Subjects and methods

The medical school system in Belgium

The MS system in the FCB has a predefined number of courses amounting to the aca-

demic year (AY); first year = MED1, second year = MED2, etc., with a total of seven academic years (MED1-7) (Figure 1). To be able to progress to the following AY, students must pass all courses with an average of 12/20. MED1 consists of basic science courses, such as physic, chemistry and mathematics, while MED2 and MED3 consist of medical science courses including anatomy, physiology, histology, histopathology, semiology, etc. (Figure 1).

The first year (MED1) curriculum consists of basic sciences, while MED2 and MED3 include basic medical courses. From MED4 to MED7, the training program consists of medical courses and a practical program in some fields, such as surgery, pediatrics, gynecology and internal medicine. The selection process is based on the cumulated grades of the first three academic years (MED1, 2 and 3) and only a predefined number of students are able to continue the medical program. Only the students who attained their degree after 7 AY were considered. Thus, students who failed one or more AYs were excluded.

Concerning the selection system, the FCB healthcare system has been characterized by a selection system (secondary selection) for access to the various medical resident training programs (surgery, otolaryngology, general practice, etc.) after the last

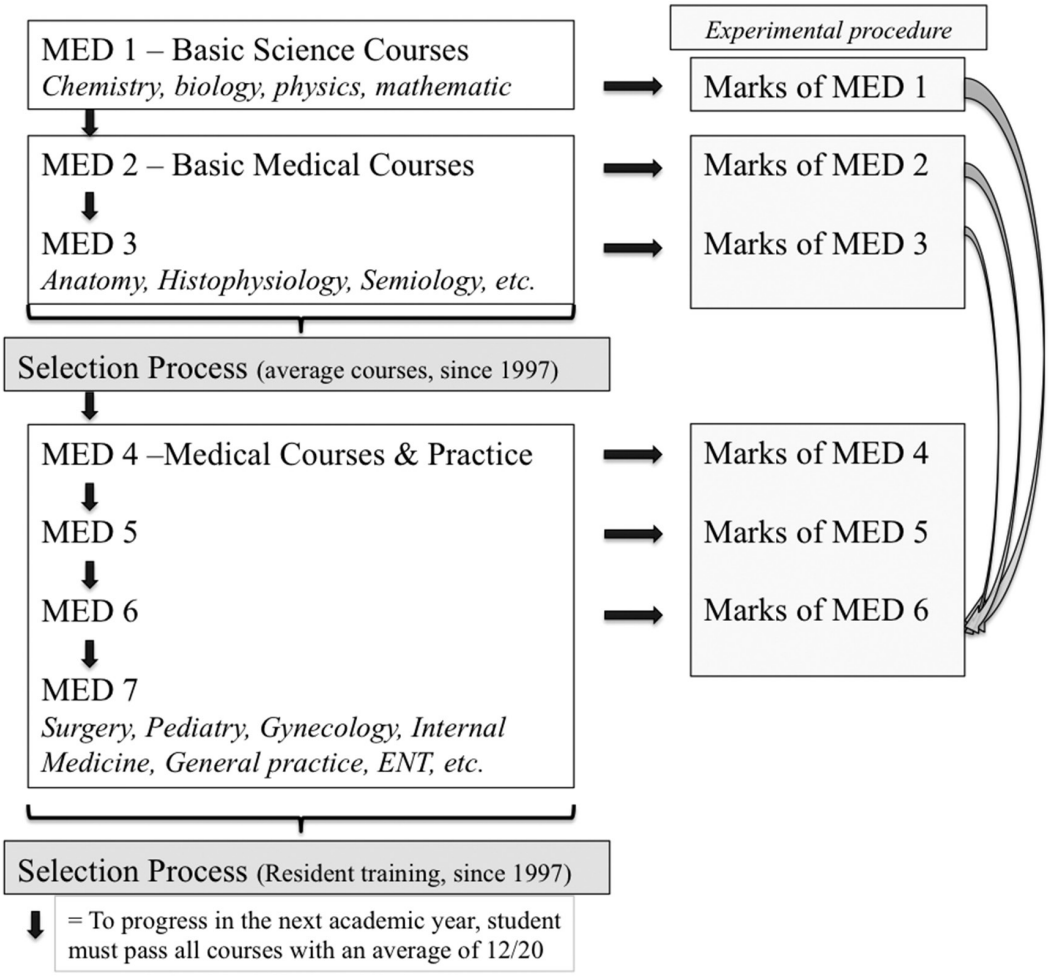

Figure 1 Medical school curriculum in Belgium.

AY (MED7) since 1997. Each resident training program has a predefined number of training places. To ensure a match between the total number of residency places available and the total number of candidates at the end of MED7, FCB established a primary selection system at the end of MED3. The selection process consisted of grading the students based on the average of all courses of MED1, MED2 and MED3. All students who pass the primary selection are guaranteed access to a resident training program. Students who began their medical studies before 1997 were not subject to the selection. By contrast, students beginning since 1997 have been selected at the end of MED3, and only a predefined number are authorized to continue the medical program (Figure 1). To date, FCB is the only region in the world to use delayed selection at the end of MED3, since the classical European selection system concerns entry selection or selection after the first year of medical studies (3).

Subjects and inclusion criteria

We retrospectively studied two cohorts of students at the Medical School of the Free University of Brussels (Ethical Committee N2012/06). The first cohort consisted of students who enrolled in MED1 in 1996-1997 (n=88) who were not subject to the selection system. The second cohort was composed of students who enrolled in MED1 in 1997-1998, and they were subject to the selection system after MED3 (n=76) (Figure 1 and Table 1).

Variables of interest

The following variables were analyzed: gender and grades (%) obtained by the students at the end of each AY. These variables were studied according to the cohort and the year of medical studies (MED1, MED2, MED3, MED6).

Statistical analysis

The statistical analysis was performed using STATA v13.1 software. Comparisons of the two cohorts regarding the distribution of gender, AY success, and comparison of the grades by gender were done using the univariate Chi square test or Fisher's Student t test. The contribution of each AY separately (MED1-3) to the success of MED6 (dependent variable) was assessed in a multivari-

Table 1 Cohort characteristics

Gender	Cohort 1	Grades mean	Cohort 2	Grades mean	Total	Grades mean
	n	± SD	n	± SD	n	± SD
Male						
MED1	26	65.9±9.3	26	70.2±9.0	52	68.0±9.3
MED2	26	72.2±7.2	26	73.4±10.0	52	72.8±8.6
MED3	26	75.3±7.5	26	73.7±8.5	52	74.5±7.9
MED6	26	82.2±7.5	26	81.7±8.7	52	82.0±8.0
Female						
MED1	58	67.7±9.4	48	68.7±9.6	106	68.2±9.6
MED2	62	74.0±9.2	50	72.4±8.5	112	73.3±8.9
MED3	62	75.3±10.7	50	71.0±8.9	112	73.4±10.2
MED6	62	83.2±6.4	50	82.6±5.4	112	83.0±5.9

MED=Year of studying medicine. SD=Standard deviation. There were 70% female students in the first cohort versus 66% in the second cohort.

ate way with multiple regression analysis of the gender, cohort, and their interactions with the grades obtained in MED1, MED2 or MED3. The regression coefficients of the grades obtained in MED1 to 3 are presented separately by cohort or gender. The conditions of applicability of multiple regressions were checked by residue analysis. The significance level was set at of α=0.05.

Results

Average grades according the gender and the cohort

The average grades did not differ significantly between the cohorts, except for the average grades of MED3 since they were lower in the second cohort (p<0.05). There was no difference in the average grades by gender (p=0.407).

Success of MED6 according to successful MED1

We did not find any significant interaction between the cohorts, the MED1 grades and those of MED6 (p=0.130). In other words, the MED1 grades predicted the MED6 grades similarly in both cohorts. The interaction between the grades in MED1 and gender was statistically significant (p=0.045). The effect was slightly stronger among male students (regression coefficient: female students: 0.30; male students: 0.51) (Table 2). The model explains the 29% variance in MED6.

Success of MED6 according to successful MED2

In the model analyzing the impact of the MED2 grades on those of MED6, no statistically significant association was observed between gender and the grades obtained in MED2, whereas the interaction between this result and the cohort was highly statistically significant (p<0.001). Indeed, as shown by the regression coefficients (Table 2), the grades in MED2 did not significantly impact the grades in MED6 in the first cohort (regression coefficient: -0.09; p=0.237). In the second cohort, the grades in MED2 significantly impacted the grades obtained in MED6 (regression coefficient: 0.51, p<0.001). The model shows 23% variance for MED6.

Success of MED6 according to successful MED3

In this model, we observed a statistically significant interaction between each cohort and the impact of the grades of MED3 on those of MED6. As shown in the regression coefficient values (Table 2), the impact of the MED3 grades on the grades of MED6 was negative in the first cohort (regression coefficient: -0.17; p=0.005), and positive in the second cohort (regression coefficient: 0.54; p<0.001) (Table 2).

The interaction between the grades in MED1, 2, 3, 6, and gender was presented in this Table. In a context of selection, the grades obtained in MED1, 2 and 3 significantly impacted the grades obtained in MED6 (p<0.001).

Table 2 Results of multiple regression models.

Variable	ß regression coefficient (95% confidence interval)	p value
MED1 grade		
Female	0.30 (0.18 to 0.42)	<0.001
Male	0.51 (0.34 to 0.68)	<0.001
MED2 grade		
Cohort 1	-0.09 (-0.23 to 0.06)	0.237
Cohort 2	0.51 (0.36 to 0.66)	<0.001
MED3 grade		
Cohort 1	-0.17 (-0.30 to -0.05)	0.005
Cohort 2	0.54 (0.39 to 0.69)	<0.001

MED=Year of studying medicine.

Discussion

The classical factors involved in the academic success of students in MS relate to high school education, social background, intrinsic motivation, IQ, EQ, regularity of work, sense of self-efficacy and hours of study (5). Some of them may specifically characterize the behavior of males and females, leading to substantial gender differences in success at MS (2).

A few studies have shown a path, evolution, and gender sensitivity towards academic success at MS, and in selection systems (6). Most of the studies observed that females have significantly better grades than males in first AY, while still being under-represented in management functions and academic posts (2, 6). These authors suggested that the gender differences in academic performance may be explained by females having a more positive attitude to academic work than the males, as males are generally less engaged in their studies, and perhaps less well adapted to the university environment (2, 7). It is important to emphasize that some studies did not find significant gender differences in adaptation to university life, notably regarding the development of working methods (8).

Regarding success in the last AY of medical studies, some studies showed that women are more efficient in non-cognitive skills, such as empathy and communication. This point gives them an advantage, in terms of overall performance in the last years of training, since these AY are characterized by clinical training where the non-cognitive skills are well used (9).

The present report fuels the current controversy regarding the effect of gender on overall performance. The impossibility of drawing clear conclusions from related studies is probably secondary to the methodological and epistemological differences between the studies. For example, in the present study, only students who had succeeded in their studies were included in the analysis, and those who had failed one or more AY were excluded. The latter included a large number of male students in MED1. Other studies did not approach the analysis in a similar manner, which may have resulted in a comparison bias (2, 9).

Secondly, our results reported the existence of a moderate relationship between the grades of the first year students (MED1, 2 and 3) and the grades of MED6, especially a weak link between the grades of MED1 and MED6, which is the AY corresponding to clinical internships. These observations are consistent with the current literature, since it has been repeatedly demonstrated that the grades obtained in the basic sciences at the start of the medical program, or at the end of MED1, are not predictive of success in the final AY and the clinical skills of the future physician (10, 11).

Thirdly, our results highlight that students subjected to selection after year three adapted better to the university environment than students who did not undergo the selection process. A better prediction of final year grades was observed from the "selection group's" first year grades, especially for male students. This may be explained by suggesting that males may have reached their full potential quicker than females in the context of selection.

Recent investigations have shown that early selection could promote competition, leading to higher positive anxiety in female than in male students, and, in this context, female students are more motivated to achieve their goals. As for male students, they may perceive failure as a loss of personal worth and are more likely to avoid any risk of failure, unless they are particularly confident or intrinsically motivated (2). Psychological studies reported that the fear of failure, procrastination and self-confidence, are particular male characteristics,

especially in less or unmotivated students, while anxiety and the value attributed to performance could be higher among female students (2). These theoretical differences could explain the results, reducing the difference between female and male students for MED2 grades predicting MED6 grades, if that filter is used. Indeed, it may be postulated that in MED2, male students have already undergone initial selection, simply related to their success in MED1, and the remaining males represent a group of motivated and relatively confident students. Our results could also suggest that the awareness of the existence of the filter after MED3 discouraged some male students to enroll in the MS program, out of fear of failure. Thus, the residual males engaged in the MS program could represent confident, mature and very motivated students. Another bias that may occur is the fact that professors could differently assess students who are subject to selection than students who are not, leading to subtle differences in their grades.

Limitation of study

The first weakness of the present study concerns the relatively low numbers of students included. The second weakness concerns the single-center aspect, which reduces its ability for generalization to other medical schools.

Conclusion

The debate about success in medical studies, and its predicting factors in the case of selection, makes sense in the world context of regulation of health care supply. The present study suggests that, in a case where a selection process is needed, an early selection system could accelerate the maturation of many candidates, including males, who adapt better to the academic environment and quickly adopt their final mode of working. If selection is needed, our findings also support the importance of using it on medical courses.

What is already known on this topic

A growing number of females are enrolling in medical school programs in European countries. It seems that they are able to succeed better than male students, especially in the context of early selection systems. To date, no study has been interested in the impact of gender on medical program success, particularly in the context of selection after the third year of the undergraduate medical school program.

What this study adds

The students who were subject to a filter system after three years at medical school adapted better to the university environment when compared with the group of students that did not undergo the selection process. Better prediction of final year grades in the medical school program was observed using the first year grades, especially for male students. The awareness of the existence of a filter after three years at medical school could discourage some male candidates from enrolling in the medical school program, out of fear of failure.

Acknowledgments: Professor Janet Tuškan, native English speaker for her collaboration in proofreading of the article.

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

Conflict of interest: JRL is a former student representative who has worked on the topic of selection in medical school. The authors declare that they have no conflict of interest.

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Essay

Acta Medica Academica 2016;45(2):152-157
DOI: 10.5644/ama2006-124.171

The forthcoming era of precision medicine

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Received: 20 October 2016
Accepted: 13 November 2016

Key words: Personalized medicine ▪ Precision medicine.

The aim of this essay is to present the definition and principles of personalized or precision medicine, the perspective and barriers to its development and clinical application. The implementation of precision medicine in health care requires the coordinated efforts of all health care stakeholders (the biomedical community, government, regulatory bodies, patients' groups). Particularly, translational research with the integration of genomic and comprehensive data from all levels of the organism ("big data"), development of bioinformatics platforms enabling network analysis of disease etiopathogenesis, development of a legislative framework for handling personal data, and new paradigms of medical education are necessary for successful application of the concept of precision medicine in health care. **Conclusion.** In the present and future era of precision medicine, the collaboration of all participants in health care is necessary for its realization, resulting in improvement of diagnosis, prevention and therapy, based on a holistic, individually tailored approach.

Introduction

Understanding of human genomes has given rise to the concept of personalized medicine, in which individual data on genomics, proteomics and the environment are integrated and applied to personal health care: diagnosis, prevention and treatment (1). Personalized medicine is widely accepted, but only superficially realized, mostly as the application of molecular (genomic, proteomic) biomarkers in prevention, diagnosis and therapy. On the basis of prognostic and predictive factors, patients are divided into subgroups that have a greater likelihood of an accurate diagnosis or favorable outcome. The choice of treatment for breast cancer (chemotherapy or hormonal therapy), according to the content of steroid receptors in the breast was one of the earliest such methods. It was introduced, in our country too, long before the concept of personalized medicine was launched (2). Until now, there have only been a few cases when the proper diagnosis was established on the basis of personal genomes, and appropriate and successful treatment applied (3). There is no doubt that medicine has always been personalized, at least to some extent. Physicians approach their patients as integral personalities, with inherent biological, psychological, mental and social characteristics and values. Therefore, the term "personalized medicine" is increasingly being replaced by the term "precision medicine".

The aim of this essay is to present a definition and the principles of personalized or precision medicine, its perspectives and the ways it may be implemented in health care.

Precision medicine: definition and implementation in health care

In the Precision Medicine Initiative Cohort Project, precision medicine is defined as follows:

"*We define precision medicine as an approach to disease treatment and prevention that seeks to maximize effectiveness by taking into account individual variability in genes, environment, and lifestyle. Precision medicine endeavors to redefine our understanding of disease onset and progression, treatment response, and health outcomes through the more precise measurement of potential contributors – for example, molecular measurements as captured through DNA sequencing technologies or environmental exposures, or other information captured through increasingly ubiquitous mobile devices. A precise delineation of the molecular, environmental, behavioral, and other factors that contribute to health and disease will lead to more accurate diagnoses, more rational disease prevention strategies, better treatment selection, and the development of novel therapies* "(4).

The adage "easy to write, difficult to implement" best describes the current circumstances regarding the realization of the concept of personalized or precision medicine; there are countless obstacles on its path (5). Overcoming them requires, amongst other things, the development of personal genomics, translational research that will transfer basic knowledge to clinical applications, a new taxonomy of disease, based on molecular disorders, auditing of clinical trials with the subsets of patients selected according to new prognostic and predictive factors, the creation of genomics, proteomics and tissue biobanks, collecting comprehensive uniform clinical data ("big data") and the development of bioinformatics systems that will integrate clinical data with the comprehensive knowledge of the pathogenic factors (6, 7) and build a functional network of disease etiopathogenesis at the population and individual levels. Also, the legal basis of the use of individual data should be added, which will be required for the realization of the concept of precision medicine (8). All these

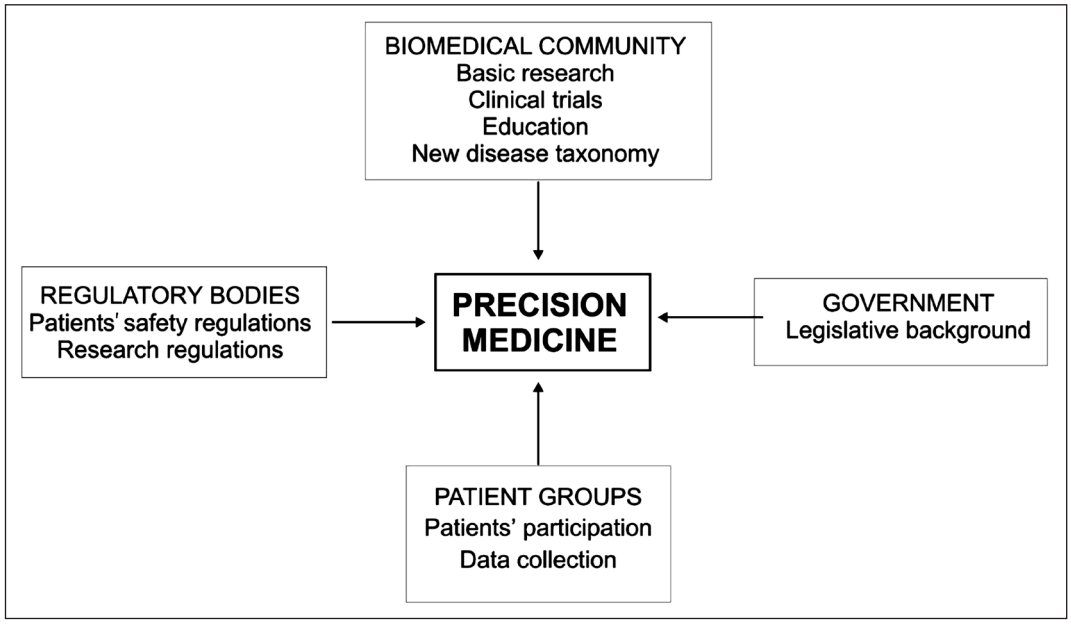

Figure 1 The major tasks of health care stakeholders involved in the progress of precision medicine.

present a major challenge to all health care stakeholders (Figure 1) (9).

In the world, particularly in the United Kingdom and the United States, encouraged by parliaments and governments, great exploratory, financial and organizational efforts are being made to realize the concept of personalized or precision medicine. In the United Kingdom, in 2009 the House of Lords conducted an investigation on the state of the application of genomics in medicine, and in 2012 there followed an action plan on the application of genomics in health care (10).

In the United States, in 2008 the President's council of advisors on science and technology submitted to President Bush a report on the priorities of personalized medicine (11). The personalized medicine acts which followed in 2008 and 2010 had the aim of personalizing medicine in health care, so that it would be available to every American. The acts determined an action program, program management, the role of government agencies and financing (about 50,000,000 $ per year) (12). President Obama, in his address to the nation in January 2015, announced the precision medicine initiative with a fund of 215 million $ in 2016, with the aim to "*pioneer a new model of patient-powered research that promises to accelerate biomedical discoveries and provide clinicians with new tools, knowledge, and therapies to select which treatments will work best for which patients*"(13). In September 2015 the cohort structure program was published, comprising a million or more patients, and to be followed for 10 or more years (Precision Medicine Initiative Cohort Project, PMI-CP). "*PMI-CP will be powered to identify biomarkers that are predictive of future development of a large number of diseases, affording new opportunity for disease prevention and therapy, as well as to provide new understanding of the factors that predict variation in response to current therapies for prevalent disease. Moreover, a design that allows participants to be recontacted for further study based on individual findings provides an invaluable opportunity to understand biological mechanisms that link biomarkers to traits in individuals* "(4).

Genomics stands as the foundation of personalized or precision medicine (14). DNA sequencing technology is developing rapidly; the price of sequencing is rapidly decreasing and the speed increasing (15). This enables the implementation of the personal genome project in which a global network is planned of institutions providing genome sequencing of 100,000 people, with the collection of the detailed demographic and health data necessary for research of genotype - phenotype relationships (16).

The huge amount of very diverse data from all hierarchical levels of the organization of the organism (molecular, subcellular, cellular, humoral, organic, organismic), functional totalities (genome, trascriptome, proteome, metabolome, microbiome, phenome and other "omics"), and the mental, spiritual, social, environmental domains should be united at population and individual levels in systems that will explain disease etiopathogenesis in general and individually, allowing an individual approach to each person in all aspects of health care. For such an analysis it is necessary to develop bioinformatics systems by applying systems of medicine that build a functional networks. They will explain in detail the interaction between these factors in integrative ways, combining the functional networks of different organizational levels in a complete, functional system (17). The enormous number of factors, links and nodes of these networks make it difficult to understand them without bioinformatics support. However, it is sufficient to identify essential nodes (about 20%) to define the function network (18). The interactions of important nodes can be displayed in a simplified network which summarizes

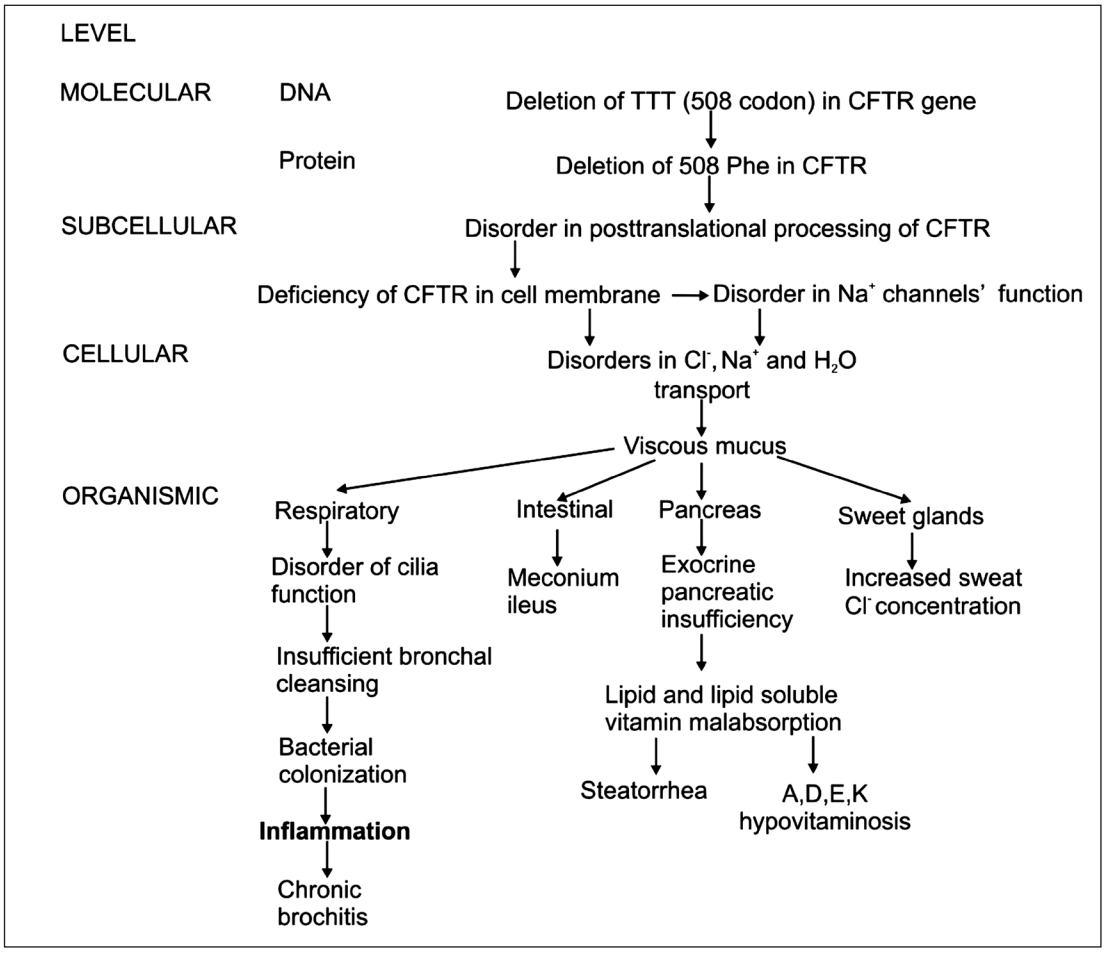

Figure 2 Vertical analysis of cystic fibrosis pathogenesis, for details see (20).

the detailed basic network allowing an overview of disease etiopathogenesis. Analyzing the disease etiopathogenes on this way, it is important to recognize the pathogenetic processes on the subsequent levels of organization of the organism, and integrate them vertically (along hierarchical levels) and horizontally (within the levels) (Figure 2) (19, 20).

The vertical analysis of disease pathogenesis integrates the basic genomic level with all subsequent levels and "omics", enabling interpretation of the influence of genomics on pathogenesis, and its application in clinical medicine.

Precision medicine: its impact on medical education

In order to be able to understand personalized or precision medicine, and accept and apply it, new paradigms in medical education (undergraduate, postgraduate, continuous) are required. Problem-solving education, including network analysis is appropriate for the complexity of the subject. Such an educational method has been developed at the School of Medical of the University of Zagreb, for problem-solving teaching of pathophysiology (21-23). Exercises are based on data presentation and

their algorithmic analysis in terms of etiopathogenetic mechanisms, leading to manifestation of signs and symptoms. In this way students gain competence in vertical analysis, enabling them to understand the disease mechanisms, from the basic molecular level to the whole body level, expressing disease manifestations. Appropriate adjusted algorithmic analysis also enables analysis of the individual variability of personal characteristics, causal factors, therapeutic procedures and consequent outcomes, providing the path to understanding personalized or precision medicine.

Conclusion

Realization of the concept of personalized or precision medicine requires the coordinated effort of all health care stakeholders. Among other things, it requires translational research, with integration of personal as well as population genomics and comprehensive data from all organization levels of the organism ("big data"), the development of an appropriate bioinformatics platform, enabling the building of functional networks of the detailed etiopathogenesis of the disease, and the development of a legislative framework governing the establishment of personal data databases, which would be used in global networks involved in the implementation of precision medicine. Also new paradigms in medical education are required, enabling students to understand, accept and apply an integrative approach to health care, in accordance with precision medicine.

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Case report

Acta Medica Academica 2016;45(2):158-162
DOI: 10.5644/ama2006-124.172

Successful thrombolytic therapy in a patient with congenital corrected transposition of the great arteries

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Received: 19 February 2016
Accepted: 16 June 2016

Key words: Congenitally corrected transposition of the great vessels ▪ Myocardial infarction ▪ Thrombolytic therapy.

Objective. The aim of this report is to emphasize the importance of thrombolytic therapy in selected patients, such as those with congenital heart defects in whom a coronary artery anomaly can be observed. **Case report.** We present here a 63 year-old female patient who was admitted to our emergency department with ST segment elevation myocardial infarction and a history of a congenital heart defect. We treated the patient successfully with thrombolytic therapy instead of primary percutaneous intervention, because of the suspicion of a coronary artery anomaly. On the following day, we performed coronary angiography on the patient, which revealed the anomalous origin of the coronary arteries, with the left and right coronary arteries originating from the right sinus of Valsalva and the circumflex artery originating from the left sinus of Valsalva. This anomaly in this patient group is described for the first time. **Conclusion.** Coronary artery anomaly may be observed in patients with congenitally corrected transposition of the great arteries, and in the case of requiring emergency reperfusion, thrombolytic treatment can be an alternative strategy in this patient group.

Introduction

Congenitally corrected transposition of the great arteries (ccTGA) is an unusual congenital anomally which is often diagnosed in adulthood. In ccTGA, the right atrium is connected to the morphologic left ventricle, which drains blood to the pulmonary artery, and the left atrium is linked with the morphologic right ventricle, which drains blood to the aorta (1). Its prevelance varies from approximately 0.5% to 1.4% of all congenital cardiac anomalies. Ventricular septal defect, pulmonary stenosis, atrial septal defect, situs inversus, heart blocks and arrythmias usually accompany ccTGA (2).

In ccTGA, the anatomy of the coronary arterial system is complex and the coronary arteries show a mirror-image spread. The morphological right coronary artery (RCA) originates from the left posterior sinus and the morphological left main coronary artery originates from the right anterior sinus (3). The possibility of progression of coronary artery disease is low in congenitally corrected TGA patients because these patients do not survive to old age due to the existing comorbidities (3). In the medical literature there is no evidence of any patient with ccTGA and ST segment elevation myocardial infarction (STEMI) which needs emergency reperfusion treatment. In this report, we describe a case of a ccTGA and STEMI patient, whom we treated successfully with thrombolytic therapy and in whom we detected

a coronary artery anomaly in the coronary angiography, which has not been mentioned in this patient group previously.

Case report

A 63 year-old female patient presented in the emergency room complaining of chest pain which had started three hours before. She had no risk factors for coronary artery disease, except mild hypercholesterolemia. Physical examination revealed a heart rate of 96 beats/min, blood pressure of 110/80 mmHg, S3 gallop with S1, S2 and 3/6 systolic murmur in the cardiac apex. Electrocardiography (ECG) showed ST segment elevation in V 1-4 and depression in the reciprocal leads (Figure 1A).

Initial laboratory analyses revealed the following: troponin I was 0.9 ng/ml (normal range: 0-0.06 ng/ml) and the creatine kinase-MB was 85.7 U/l (normal range: 0-24 U/l). The remaining blood count and biochemistry results were within normal ranges. It was learned from the patient's history that she had a congenital cardiac anomaly, but she had no report or hospital records confirming this condition. The patient received 300 mg acetylsalicylic acid, 300 mg clopidogrel orally and 5000 U unfractionated heparin intravenously, and she was transferred to the coronary intensive care unit. A bedside transthoracic echocardiography was performed, and transposition of the aorta and the pulmonary artery with transposition of the right and left ventricles were shown. The ejection fraction of the morphological right ventricle was slightly depressed (45%) and the apical region was observed to be hypokinetic. Due to the suspicion of a coronary artery anomaly, thrombolytic therapy was planned for the patient instead of primary percutaneous coronary intervention. After receiving the patient's consent, thrombolytic therapy (alteplase) was applied. Thirty minutes after the initiation of the thrombolytic therapy, the patient's chest pain improved, and fifteen minutes later resolution of ST segment changes on ECG was observed (Figure 1B). Thrombolytic therapy was considered to have been successful. The patient remained hemodynamically stable with aspirin, clopidogrel, metoprolol, ramipril, atorvastatin and heparine treatment, and on the next day she was referred to the catheterization laboratory. Coronary angiography revealed the anomalous origin of the coronary arteries, with the left (LAD) and right (RCA) coronary arteries originating from the right sinus of Valsalva, and the circumflex artery (CX) originating from the left sinus of Valsalva. LAD was thought to

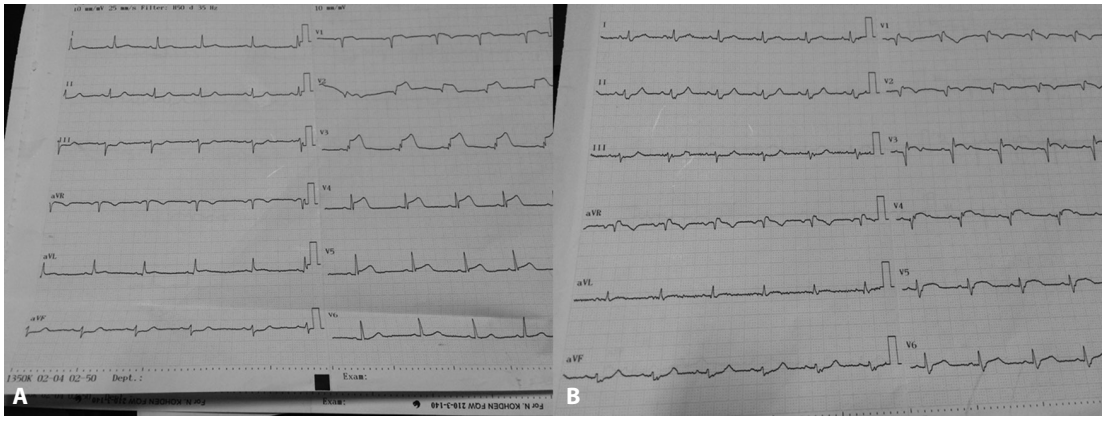

Figure 1 A: ECG of the patient on admission showing ST segment elevation in V1-4 with Pardee curves and depression in reciprocal leads. B: ECG of the patient showing succesful thyrombolytic treatment.

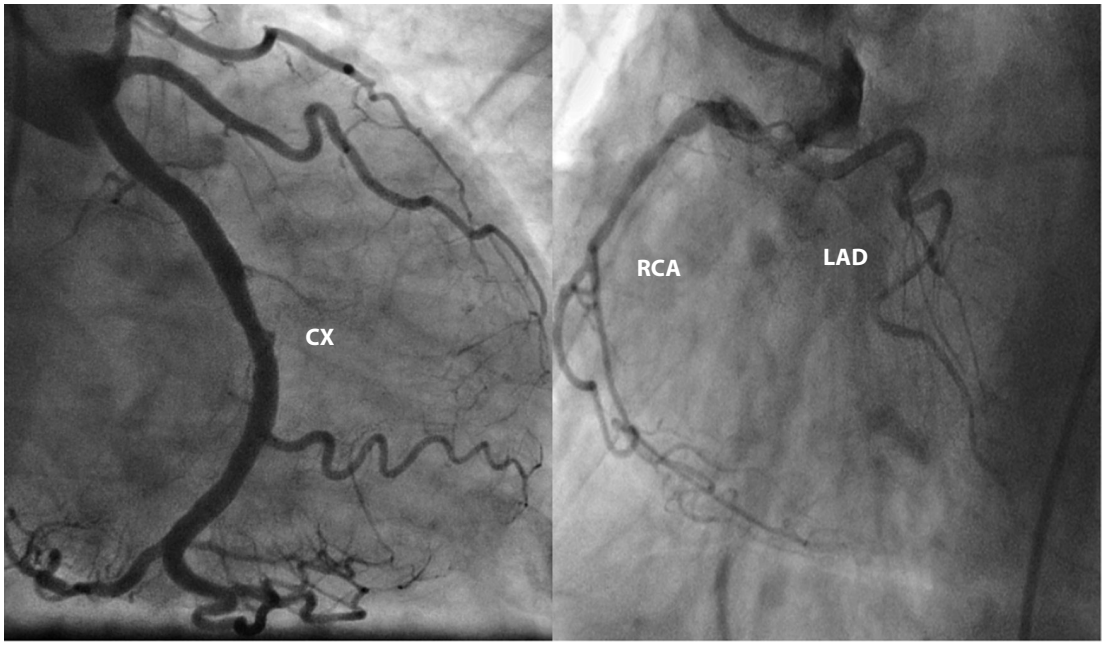

Figure 2 Coronary angiography showing the circumflex artery (CX) originating from the left sinus of valsalva and right (RCA) and left (LAD) coronary arteries originating from the right sinus of valsalva. There is plaque in all the coronary arteries, which are free of hemodynamically significant stenoses.

be the culprit vessel causing anterior wall STEMI which was free of any significant obstruction after successful thrombolysis and it was decided to be followed up with medical treatment. There was plaque in all of the coronary arteries, which were free of hemodynamically significant stenoses (Figure 2).

The patient remained under observation in the cardiology service after the coronary angiography. Follow-up ECG showed normal sinus rhythm with the invertion of T waves in V 1-4. The follow-up echocardiogram was consistent with the bed side echocardiography performed in the coronary intensive care unit, demonstrating ccTGA. Moreover, there were no findings of complications such as ventricular septal defect or aneurysm of the morphological right ventricle. Follow-up laboratory tests also revealed a peak in the cardiac enzymes (troponin I >25 ng/ml, creatine kinase-MB: 108.3 U/l). The patient's condition continued to be asymptomatic and stable, and she was discharged home after 3 days.

Discussion

To our knowledge, there are no published data regarding a ccTGA patient with STEMI successfully treated with thrombolytic therapy. There is also no record of a coronary artery anomaly showing the circumflex artery originating from the left sinus of Valsalva and the right and left coronary arteries originating from the right sinus of Valsalva in this patient group.

Cardiovascular diseases are the main cause of death all around the world, and their cause is the occlusion of the blood vessels with a blood clot or thrombus. Restoring the blood flow immediately can save organ functions and lives (4, 5). Although thrombolytic therapy has been used for years for this reason, its adequacy and reliability have been inadequate because of the side effects and failure of the therapy. Consequently, catheter guided endovascular procedures, such as percutaneous coronary intervention (PCI), have been the preferred treatment

modality for clinicians instead of thrombolysis. Although endovascular procedures are more successful and safer than thrombolysis, there are some limitations of this treatment modality. Some of them are the technical difficulties and cost, they are time-consuming and cannot be used in cases of insufficient access (4). Although primary PCI is not contraindicated in congenital heart defect patients presenting with STEMI, and it is recommended therapy according to the guidelines, we preferred thrombolytic therapy instead of endovascular procedures because we believed thrombolysis to be the more appropriate treatment in this patient. Additionally, our patient did not have any contraindications for thrombolytic therapy, such as known bleeding disorders, history of ischaemic stroke, intracranial haemorrhage, gastrointestinal bleeding, trauma or injury, and she was admitted to hospital in three hours after the chest pain started which increases the possibility of successful reperfusion with thrombolytic therapy. Although we could have preferred primary PCI as the first line therapy in this patient, we chose thrombolytic therapy due to the suspicion of a coronary artery anomaly which could cause time to be wasted, technical difficulties and complications during PCI. Thus, after successful reperfusion with thrombolytic regimen, we proved the presence of a coronary artery anomaly in the catheterization laboratory. Haemodynamically non-significant stenoses were observed incidentally during the coronary angiography, for which the patient did not need further processing, such as angioplasty or stenting procedure.

The main goal of therapy in acute myocardial infarction is to ensure the blood flow to the myocardial cells as soon as possible, and thrombolytic therapy is one of the treatment strategies (5). However, in the literature there is no report supporting the use of thrombolytic agents in the presence of a suspected coronary artery anomaly, and there are very little data on the combination of ccTGA patients and acute coronary syndromes. Lampropoulos et al. described a case of an acute coronary syndrome and a ccTGA patient, in whom they performed coronary angiography. The angiogram of the patient showed haemodynamically non-significant stenoses, and they suspected that the cardiac enzyme increase was secondary to microvascular ischemia or hypertrophy (6). Gungor et al. described a case of a patient with a history of coronary artery disease who complained of unstable anginal chest pain and cardiac enzyme elevation. They planned an early invasive procedure on the patient because of the acute coronary syndrome and diagnosed ccTGA during and after the coronary angiography (7). In our case, the ccTGA patient was complaining of chest pain and she had ST segment elevation on ECG, which needed emergency reperfusion treatment, so we treated the patient successfully with thrombolytic treatment. We selected thrombolytic treatment due to the possibility of a coronary artery anomaly and, to the best of our knowledge, this is the first ccTGA patient presenting with STEMI, successfully treated with thrombolytic treatment in the literature. In this case, we also demonstrated the circumflex artery originating from the left sinus of Valsalva and the right and left coronary arteries originating from the right sinus of Valsalva, which is a coronary artery anomaly not previously mentioned in this patient group.

Conclusion

A coronary artery anomaly may be observed in ccTGA patients and in the case of the need for emergency reperfusion, thrombolytic treatment can be an alternative treatment modality in this patient group.

What is already known on this topic

Congenitally corrected transposition of the great arteries is a rare cardiac anomaly which is characterized by atrioventricular and ventriculoarterial discordance. Acute coronary syndomes are described very rarely in patients with congenitally corrected transposition of the great arteries. Treatment of myocardial infarction with thrombolytic therapy is an alternative strategy in selected patients, instead of primary percutaneous coronary intervention.

What this article adds

This is the first case report describing a patient with congenitally corrected transposition of the great arteries and ST segment elevation myocardial infarction who was treated with thombolytic therapy. This is the first case report describing a patient with congenitally corrected transposition of the great arteries and coronary artery anomaly in which the left and right coronary arteries originate from the right sinus of Valsalva and the circumflex artery originates from the left sinus of the valsalva. In patients suspected of having a coronary artery anomaly who need emergency reperfusion treatment, thrombolytic treatment can be a good choice.

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

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

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Case report

Acta Medica Academica 2016;45(2):163-168
DOI: 10.5644/ama2006-124.173

Accessory coracobrachialis muscle with two bellies and abnormal insertion - case report

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Received: 1 June 2016
Accepted: 26 October 2016

Key words: Coracobrachialis muscle ▪ Variation ▪ Clinical applications.

Objective. In the current study a brief review is presented of the coracobrachialis muscle's morphological variability, action, embryological development and clinical significance. **Case report**. We report a case of a left-sided coracobrachialis muscle consisting of two bellies. The deep belly inserts into the usual site in the middle area of the antero-medial aspect of the left humerus, whereas the superficial belly inserts through a muscular slip into the brachial fascia and the medial intermuscular septum, forming a musculo-aponeurotic tunnel in the middle region of the left arm, for the passage of the median nerve, brachial artery and veins, medial antebrachial cutaneous nerve and ulnar nerve. **Conclusion**. Awareness of such a muscle variant should be kept in mind by physicians and surgeons during interpretation of neural and vascular disorders of the upper limb, since such a variant may potentially lead to entrapment neuropathy and/or vascular compression, predisposing to neurovascular disorders, as well as during preparation of that muscle in cases of utilizing it as a graft in reconstruction of defects.

Introduction

The coracobrachialis muscle (CBM) is a widely known muscle of the anterior compartment of the arm that has received little attention from anatomists and clinicians, due to its minor importance for the forward flexion of the arm. However, the CBM has recently received greater surgical significance since it is utilized as a graft in reconstructive surgery after mastectomy, in the treatment of defects of the axillary and infraclavicular area (1), or in therapy for long standing facial palsy (2). Apart from the CBM's usual insertion site into the median portion of the antero-medial aspect of the humerus, the muscle may also insert into variable anatomical sites, such as the surgical neck of the humerus (3), the tendon of the latissimus dorsi (4), the medial head of the triceps (5), the brachial fascia (6), the medial epicondyle of the humerus or the antebrachial fascia (7).

However, the presence of a variant CBM type, as the finding of the current study, where its superficial portion participates in the formation of a musculo-aponeurotic tunnel including median, ulnar nerves, as well the brachial vessels, has not been detected so frequently. This type of CBM muscular slip could under circumstances such as hypertrophy, hematoma or strong CBM contraction under resistance, predispose to

median and/or ulnar neuropathy, as well as to vascular disorders.

In the current study a brief review of the CBM's morphological variability, action, embryological development and clinical significance is presented.

Case report

During routine educational dissection an abnormal CBM was detected in an adult male cadaver, aged 78 years old, on the left side. In particular, after meticulous preparation and

Figure 1 An accessory coracobrachialis muscle on the anterior aspect of the left arm is shown, composed of a superficial head (SH) and deep head (DH). The SH terminates into a muscular slip (asterisk) that inserts into the brachial fascia (BF). The musculo-aponeurotic channel formed in that way contains the nerves and vessels of the medial bicipital groove of the arm (1: brachial artery, 2: median nerve, 3: medial antebrachial cutaneous nerve, DM: deltoid muscle).

dissection of the skin and the underlying fascia of the left arm region, we came across a bicipital CBM, consisting of a superficial and a deep belly originating together from the tip of the coracoid process. The deep belly terminated via a musculo-aponeurotic tendon into its usual insertion site, that is the middle area of the antero-medial aspect of the left humerus. The superficial belly terminated through a muscular slip into the brachial fascia and the medial intermuscular septum. The latter muscular slip formed a musculo-aponeurotic channel in the middle region of the left arm for the passage of the median nerve, brachial artery and veins, the medial antebrachial cutaneous nerve and the ulnar nerve (Figure 1). It should be noted that the CMB on the right side did not display any morphological variations. The cadaver was fixed by formalin and alcohol solution. The cause of death was unrelated to the current study, whereas no other variations, pathological conditions or evidence of previous surgical procedures were present in the arm. The morphology and topographic relationship of the current variant were recorded with repeated photographs.

Discussion

As is widely known, the CBM originates from the apex of the coracoid process, along with the tendon of the short head of the biceps, and by muscular fibers from the proximal part of that tendon. The CBM terminates in an impression, midway across the medial border of the humeral shaft (8). However, the CBM's origin and its insertion display great variability. As regards the CBM's insertion, which is the case in the current study, it may be located in various anatomical sites, from the shoulder joint capsule to the medial epicondyle, the olecranon process or the antebrachial fascia (7, 9, 10).

As long ago as in 1867, John Wood described three portions of the CBM. The upper or short portion is the smallest, originating from the coracoid process and inserted into the shoulder joint capsule. This portion was termed by Wood the "coracobrachialis superior or brevis or rotator humeri". The lower or long portion is inserted into the internal condyloid ridge, the internal intermuscular septum or the trochlea, and was termed by Wood the "coracobrachialis longus". The middle portion of the muscle is the largest and is inserted into the middle of the inner surface of the humerus. This portion of the CBM was termed the "coracobrachialis proprius or medius" by Wood (9). Wood considered that the middle portion is usually found in human subjects (9), however other authors speculated that the middle and lower portions are fused, trapping the musculocutaneous nerve between them (4, 6). However, there are instances (3.5-6.5%) in which the CBM is not traversed by the musculocutaneous nerve (4). Mori observed in 6% of cases that the course of the musculocutaneous nerve is on the ventral surface of the CBM (11).

Apart from Wood's classification system of the CBM's morphology and attachment sites, in 1964 Mori mentioned the existence of the CBM's separation into superficial and deep layers. In particular, in 16% of cases the CBM's belly was completely separated, whereas in 8% it was incompletely separated into a superficial and a deep layer (11). In our case, the CBM displays two muscular heads, one superficial and one deep. The deep head is inserted into the medial aspect of the humerus as usual, whereas the superficial head terminates through a muscular slip into an aponeurotic lamina, which blends into the brachial fascia and the medial intermuscular septum. The latter head of the CBM creates a fibro-muscular tunnel for the passage of the vessels and nerves of the medial bicipital groove of the arm. This variant resembles that mentioned by Ray et al. where two CBM bellies were displayed,

with the superficial one inserted into the brachial fascia (6). Our case differs from this in that the deep CBM head is musculo-aponeurotic, whereas the deep belly in Ray et al. was totally muscular. Furthermore, the current finding resembles the abnormal muscle observed by Paraskevas et al. that originated from the CBM and the tendon of the long head of the biceps brachii, and inserted into the medial intermuscular septum and the brachial fascia, forming a musculo-aponeurotic channel for the passage of the nerves and vessels of the arm (12). We suggest that our abnormal muscle consists of a superficial layer of the CBM corresponding to the CBM's lower portion.

Some cases of additional CBM heads have been reported in the relevant literature. Chouke noted an accessory CBM head arising from the conoid ligament of the clavicle, blending with the main CBM and inserting into the medial intermuscular septum (13). Previously, Wood noticed an accessory head inserted into the internal condyloid ridge of the humerus, as well as additional head inserted into the fibrous capsule of the shoulder joint (9). Gupta et al. observed an additional CBM head, which originated from an abnormal site on the coracoid process and inserted via a long thin aponeurotic tendon into the CBM's usual insertion site (14). An accessory CBM was noted by Kopuz et al., inserted into the antebrachial fascia and the medial epicondyle of the humerus (7).

Other unusual sites of CBM insertion are the tendon of the latissimus dorsi (minor coracobrachial muscle of Cruveilhier), the skin and fascia of the axilla, the tendon of the subscapular muscle (4, 15), the surgical neck of the humerus, the intertubercular sulcus (3), the medial head of the triceps (5), the tendon of the teres major (9), and the olecranon process (10). As regards the embryological explanation of such varieties, it should be emphasized that the upper limbs' muscles are derived from the lateral mesoderm. In order for a certain muscle to be formed, muscle primordia are fused. Some muscle primordia disappear through cell death. The persistence of some cells between the CBM and the biceps brachialis muscle may result in an accessory CBM belly (1, 14). Alternatively, someone could hypothesize that during the CBM's embryological development, a combination occurs of the CBM's tangential splitting into two heads and migration of the CBM's superficial head into more distal and medial region (16). As regards the CBM's action, the muscle flexes the arm forward and medially, especially from a position of brachial extension (8). The CBM, according to Wood, resembles the triceps adductor femoris. In particular, the short upper portion of the muscle corresponds to the adductor brevis, the middle portion to the adductor longus and the long lower portion of the CBM to the adductor magnus. In accordance with Wood's suggestions, the CBM's middle and lower portions act as the adductor and elevator of the upper arm. In addition, the lower portion will render the brachial fascia tense. The short upper portion of the CBM acts as an external rotator of the humerus. Moreover, in cases of the CBM's insertion into the shoulder joint capsule, Wood considered that this portion draws the capsule forward, preventing it being rucked up into folds, or pinched in extreme adduction (9). Ilayperuma et al. considered that the CBM acts as an enhancing muscle for the tendon of the short head of the biceps brachii, since it takes its origin from both sides of that tendon. These authors claimed that CBM provides the optimum position for the aforementioned tendon, to exert the proper action of the muscle on the glenohumeral joint (17).

As regards the potential functional significance of our finding, we consider that the additional superficial CBM head could potentially induce symptoms of median or ulnar neuropathy in instances of its hyper-

trophy or traumatic injury. Gessini et al. mentioned that the hypertrophic coracobrachialis longus muscle may be an etiological factor for potential entrapment of the median nerve and/or vascular disturbances, due to compression of the brachial artery (18). Ray et al. rightly asserted that, due to the fact that it is difficult to distinguish median or ulnar neuropathy in the upper arm from that in the lower arm, these types of CBM variation should be kept in mind (6). Furthermore, awareness of the CBM's variations should be highlighted for surgeons in that field, since that muscle may be utilized as a guide for the location of the axillary artery, as a vascularized graft for treatment of long standing facial palsy (2), for post-mastectomy reconstruction, and in defects of the axillary and infraclavicular regions (1).

Conclusion

A profound understanding of this muscular variation is indispensable for physicians and surgeons in that field for interpretation of sensory, motor and vascular disturbances of the upper limb, as well during preparation of the CBM to be utilized as a free or vascularized graft for reconstruction of defects of adjacent areas, or for long standing facial palsy.

What is already known on this topic

The origin of the coracobrachialis muscle (CBM) as well as its insertion display great variability. As regards CBM's insertion, which is the case in the current study, it may be located in various anatomical sites, from the shoulder joint capsule to the medial epicondyle, the olecranon process or the antebrachial fascia. Specifically, this muscle may insert into variable anatomical sites, such as the surgical neck of the humerus, the tendon of the latissimus dorsi, the medial head of the triceps, the brachial fascia, the medial epicondyle of the humerus, or the antebrachial fascia.

What this study adds

Some cases of additional CBM heads have been reported in the relevant literature. However, the presence of a bicipital CBM with abnormal insertion of its superficial head, as in the current study, where its superficial portion participates in the formation of a musculo-aponeurotic tunnel including the median, ulnar and medial antebrachial cutaneous nerves, as well the brachial vessels, is not so commonly detected. As regards the potential functional significance of our finding, we consider that the additional superficial CBM head could potentially induce symptoms of median or ulnar or medial antebrachial cutaneous neuropathy, or vascular disorders in instances of its hypertrophy, hematoma or strong CBM contraction under resistance.

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

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

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Acta Medica Academica 2016;45(2):169-170
DOI: 10.5644/ama2006-124.174

Twiddler's syndrome

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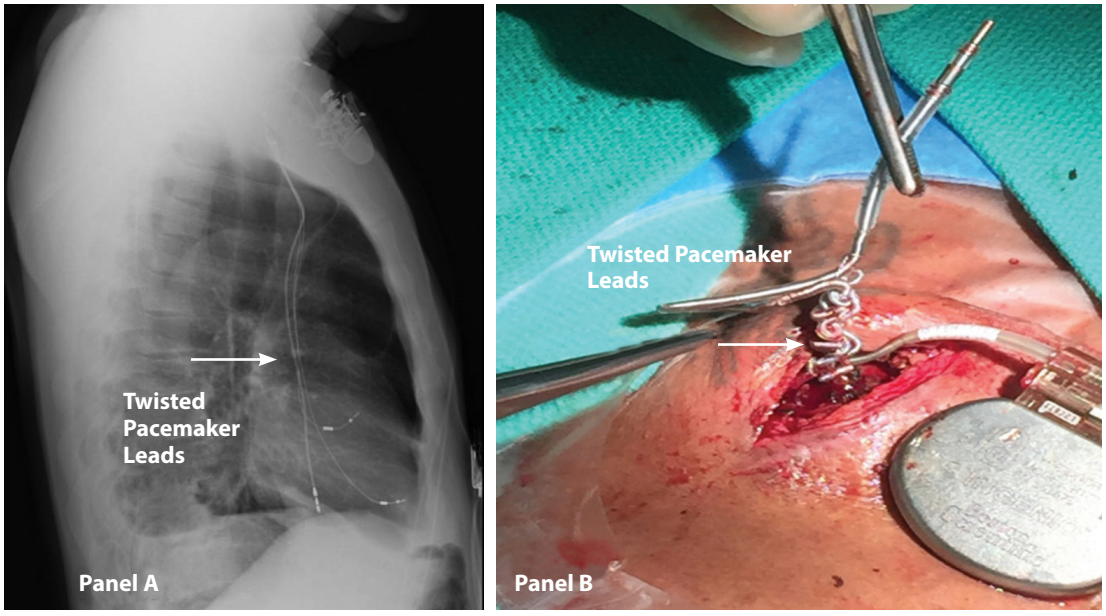

Twisted pacemaker leads or Twiddler's syndrome, are a rare cause of pacemaker malfunction. This condition typically results from the rotation of the device in its pocket, causing lead dislodgment (1). At risk individuals are usually obese, female, elderly, suffer from psychiatric disorders, or have a small size implanted device relative to the pocket size (2, 3). A 60 year old male with hypertension, Chronic Obstructive Pulmonary Disease, and Sick Sinus Syndrome presented to our emergency department with a complaint of chest pain which the patient described as an intermittent "firing/shock in my chest". Patient had a dual chamber pacemaker implanted in 2014, with new lead implantation two months previously due to the fracture of the right ventricular lead. Interrogation of the pacemaker revealed that the new lead was not sensing. Chest x-ray showed dislodged ventricular lead in the right atrium (Panel A). The generator with severely twisted leads (Panel B) along with all the leads were extracted. New pacemaker

leads were inserted on the right side using the right subclavian vein access and attached to the new generator. The patient is currently asymptomatic with regularly scheduled check up for the pacemaker.

Key words: Twiddler's syndrome ▪ Sick sinus syndrome ▪ Pacemaker ▪ Pacing leads ▪ Lead dislodgement.

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

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

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Received: 28 September 2016
Accepted: 25 November 2016

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Historical article

Acta Medica Academica 2016;45(2):171-174
DOI: 10.5644/ama2006-124.175

Postal censorship of Bosnian public health institutions during the Second World War: The Independent State of Croatia versus Dr. Stanko Sielski

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Received: 6 August 2016
Accepted: 9 September 2016

Key words: Postal censorship ▪ Stanko Sielski ▪ History of medicine.

This study aims to present evidence of censorship during World War II by the Independent State of Croatia of one of its public health officials, Dr. Stanko Sielski who was a physician trained in epidemiology and public health. During World War II, he directed the Institute for Combating Endemic Syphilis in the Bosnian town Banja Luka. The staff under his direction consisted solely of Jewish physicians. We analyzed two groups of envelopes either sent by or to Dr. Stanko Sielski during the War and found evidence of censorship only in communications with a Jewish physician dated towards the end of the War. Dr. Stanko Sielski would be posthumously recognized for his efforts to shield his Jewish colleagues. **Conclusion.** The newly available, but still limited data, which we present indicates efforts to censor Dr. Stanko Sielski's postal communications towards the War's end. The censors targeted specifically Dr. Stanko Sielski's correspondences with the Jewish physicians he was protecting. This material highlights the many challenges his public health service experienced during the time of armed conflict.

Introduction

The Independent State of Croatia (ISC) was founded on April 10th, 1941, after the invasion of Yugoslavia by the Axis powers and dissolved after the military defeat of Germany in May 1945. It consisted of most of modern-day Croatia and Bosnia and Herzegovina (BH), together with some parts of modern-day Serbia (1). The modern public health infrastructure developed in BH during the Austro-Hungarian occupation in the later part of the 19th century (2) and continued after the first World War. By the outbreak of World War II in 1941, the ISC had established the Institute for Combating Endemic Syphilis (ICES) in the Bosnian town Banja Luka. At that time, all of the physicians working there were Jewish. The ICES was founded in order to eradicate the disease in rural Bosnian villages (3). Dr. Stanko Sielski, a talented and dynamic BH native physician and important ethnographer, served as the head of the ICES from 1941 to 1944 (4). Dr. Stanko Sielski was born and educated in BH, and spent his entire professional career there principally helping the impoverished and sickly rural populations whose misfortunes were compounded by both World Wars (4). Recent and ongoing scholarship has characterized another population assisted by Dr. Stanko Sielski; Jewish physicians practicing in BH (4). Both the Allies and the

Axis practiced the censorship of mail during the Second World War. Civil, military and prisoner populations were all monitored to various degrees (5). Censorship of public health institutes throughout Europe at that time is less certain.

This study presents evidence that the ISC censored the communications of Dr. Stanko Sielski, the director of a State public health institute. The timing of the censorship and the persons it is directed against suggest the ISC had begun to suspect the institute of subversion.

The description of State censorship of Dr. Stanko Sielski's communications

Were the authorities of the ISC suspicious of Dr. Stanko Sielski's motives to shield Jewish doctors from the Holocaust? We would like to present a small piece of evidence which can help to address this question. Currently, there are at least two collections of Dr. Stanko Sielski's envelopes existent from the period of the Second Word War. One group (six envelopes, all addressed to Dr. Stanko Sielski) (6) contains one envelope that bears the postal censor's ("CENZURA", Croatian) mark (Figure 1). The others in this group were not marked (Figure 2).

The second group of ten envelopes is archived in the Section of History of Medicine in the Croatian Academy of Sciences and Arts in Zagreb; the collection includes seven letters that Dr. Stanko Sielski sent to Dr. Vladimir Ćepulić, the head of the Croatian Medical Association, and three in return (7). No letter from the Zagreb collection bares the mark of censorship.

The censored letter was postmarked 1944, which is later than any of the other letters Dr. Stanko Sielski received. Furthermore, the censored letter was sent from Dr. Emil Reich (Figure 1 inset lower right-hand corner), a Jewish physician who worked under Dr. Stanko Sielski at the Institute (8). While this cannot be considered proof, it does indicate that the State had become suspicious of Dr. Stanko Sielski, specifically in his communications with the Jewish doctors

Figure 1 Letter (cover) addressed to Dr. Stanko Sielski with "Censura 117" stamp postmarked 1944. Inset lower right hand corner: Reverse of envelope showing Dr. Emil Reich, Vrapče, Zagreb.

Figure 2 Composite image of 4 uncensored letters addressed to Dr. Stanko Sielski with dates ranging from 1942 (upper left), 1943 (upper right), 1943 (bottom right) and 1943 (bottom left).

whom he directed. Unfortunately, we lack the envelopes contents but speculate that it may have been related to Dr. Emil Reich's recent hospitalization (9).

The censor's suspicion about Dr. Stanko Sielski most likely was related to his efforts to help his Jewish colleagues. Due to Dr. Husref Tahirović's (an author) advocacy, Dr. Stanko Sielski's efforts were recognized posthumously by the State of Israel who awarded him the Righteous Among Nations. This award is given to non-Jewish peoples whose efforts contributed to saving Jewish lives. Dr. Stanko Sielski is one of only a few physicians to receive the honor (10).

Conclusion

Dr. Stanko Sielski was a dynamic Bosnian doctor whose interest in rural public health put him in a unique, but dangerous situation during World War II. He not only fulfilled his duty in helping impoverished rural War stricken Bosnians, but he also used his position as Director of the Institute for Combating Endemic Syphilis to shield Jewish physicians working under him. From the envelope covers extant, we show that some of Dr. Stanko Sielski's correspondences with Jewish physicians were being monitored, and that this activity may have begun during the later War years. We hope this paper can add to the understanding of European public health institute censorship during World War II. More scholarship in this area is needed and more on the dynamic figure of Dr. Stanko Sielski is forthcoming.

What is already known on this topic

Civil and military institutions are targets of censorship during times of war. There is less known about censorship of public health institutions during times of armed conflict. Data on

postal censorship of European public health institutes during the Second World War are insufficient.

What this study adds

This paper adds to the understanding of European public health institute censorship during World War II. While the data is limited, it suggests that censorship of these institutes may have occurred later in the war, and as a result, certain institutes were used to shield Jewish physicians from the Holocaust.

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

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

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Acta Medica Academica 2016;45(2):175-177
DOI: 10.5644/ama2006-124.176

From process management towards dynamic capability

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Received: 27 July 2016; Accepted: 27 July 2016

Key words: Process management ▪ Quality management ▪ Improvement knowledge ▪ Exploitation and exploration ▪ Dynamic capability.

Healthcare organizations are facing a large number of challenges: more demanding customers, an aging population, new possibilities for cure and care that require new treatment regimens – sometimes making curing and caring much better, simpler and cheaper but sometimes driving costs. On a global scale, as well as within nations, there are wide variations in quality, safety and equity, and in many healthcare systems costs are increasing. The current digitalization and increased awareness of healthcare as a service activity with the emphasis on co-production is challenging for most healthcare systems. In addition, some countries may have specific problems due to, for example, prior histories of war and migration (1, 2). In short, there is a need for a systematic approach towards healthcare improvements.

These challenges have to be met, not only in, for example, primary and secondary care institutions, but also in the education of young, up and coming healthcare professionals. To support them in their preparation for a future working life in an increasingly changing work environment, there is a need for improvements and renewal of educational systems. As emphasised by Batalden and Davidoff (3): We need quality improvement defined as "*the combined and unceasing efforts of everyone—healthcare professionals, patients and their families, researchers, payers, planners and educators—to make the changes that will lead to better patient outcomes (health), better system performance (care) and better professional development (learning).*" Support from educational institutions is crucial.

The challenges for the education system are accentuated by the new possibilities created by digitalized educational materials, and internet availability that creates new challenges and opportunities difficult to foresee. MOOCs (Massive Open Online Courses) and flipped classrooms are just two new possibilities that will probably change education a great deal. Problem based learning, that has been with us for some time, might be powerfully revived with increased possibilities for simulation of realistic situations and "gamification". Attention has to be re-directed from teaching towards learning – how do we create (or rather sustain) a habit of learning in our young ones, to be sustained throughout their life-long learning.

To improve efficiency, process management (4) has been suggested (see also for example (5)). By critically investigating and mapping how activities are performed in or-

der to achieve the desired results, it is possible to find possibilities for improvement, i.e. unnecessary activities, inadequate activities and activities that are missing. An ambitious effort to this end is described in (4). The process approach is seen as an important principle of quality management. However, the quality management approach requires a concerted application of a set of interacting principles, of which the process approach is just one. Other principles are: customer focus, fact based decisions, continual improvement, and engagement of people (6, 7). Thus, the process approach is not enough. In (4) the business processes were mapped and improvements suggested. However, the most important, the most difficult, and the most challenging parts of the improvement process are still to be realised: that of turning the possibilities for improvement into real changes: "*…actual improvements based on implementation of the analysis of the weak points depended on the readiness of the school management to enforce these changes…*" (4). To overcome resistance to change, it is important not only to convince management but also those affected by the change. As noted above, people involvement is an important principle of quality management. Thus, it is important to involve and commit people from the early stages of an improvement endeavour. For the success of the approach taken in (4), this aspect is crucial.

For successful improvement of healthcare, it is important to gain an understanding of some important areas of knowledge, as first discussed by Batalden and Stoltz (8) based on what Deming (9) called "profound knowledge". One enhanced interpretation of the domains of improvement knowledge is (2): Understanding variations (not only handling and reduction of variations, but also the positive side of variations, as for example experimentation, exploration and evolution); Psychology and social sciences (the importance of understanding intrinsic motivation and positive psychology, people's often irrational behavior, as discussed by David Kahneman (10), and our dependence on social structures); Knowledge theory, i.e. how knowledge is created (for example: learning cycles as originating from pragmatic philosophy manifested in the PDSA-cycle); and understanding of systems and their dynamics and complexity. Currently, improvement knowledge, sometimes also under the heading "Improvement science", is strongly emphasised in the healthcare improvement discourse, (3, 2) and references cited there. A special section of *Journal of Teacher Education 2015, 66:5*, is dedicated to improvement science in education.

In a rapidly changing technology environment, it is not always enough to find the incremental types of improvements indicated above – more radical changes are needed. This creates a dilemma – the organization needs to be both good at working with the current processes and their improvement (exploitation) but also good at exploring new possibilities that may create radically different solutions to the way work is performed (exploration). In a thorough survey of research on process management, Brenner and Tuchman (11) came to the conclusion that process management, even if beneficial in some situations, could be a barrier to exploration, i.e. to finding new technological solutions necessary for meeting future challenges.

The ability to handle exploitation of the current work processes and their improvement, and concurrently to explore radically new ways of working is called "dynamic capability", see for example (12). For healthcare to meet the definition of quality improvement, as described above (3), such a dynamic capability will be essential. The work performed in (4) may be considered a very first step on such a journey.

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

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Invited commentary

Acta Medica Academica 2016;45(2):178-179
DOI: 10.5644/ama2006-124.177

Benefits of the EduPlan/EX software platform in managing teaching processes

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Received: 29 July 2016; Accepted: 30 July 2016

Key words: Management of teaching processes ▪ Medical school ▪ EduPlan/EX software.

In their paper entitled *Management of teaching processes using Share point platform: A case study from the University of Split School of Medicine* Sapunar, Grković, Lukšić and Marušić draw our attention to the development of a software tool which provides a systematic solution to the problem of budget allocation to medical schools in Croatia and, in general, a reliable aid in managing teaching processes (1).

As reported by the authors, according to the experience with the Medical School in Split, the EduPlan/EX software successfully deals with systematic determining the teaching load which is the main element for new employments in Croatian academic community. This makes the teaching load one of the main factors in determining budget allocation. Taking into consideration the fact that currently there are no clear budget allocation principles and that the documents, which serve as a basis for determining the schools´ budgets, are rather scarce (1), one easily becomes aware of the importance of having a software platform that encompasses all information relevant for automatic generation of teaching loads. However, determination of the teaching load is not the only benefit of the EduPlan/EX software platform. Let´s have a closer look at other advantages of this application.

The system involves the scheduling functionality aimed at creating precise timetable several months before the start of the academic year. Not only does this functionality allow planning and scheduling of teaching and extracurricular activities, but it also provides online access to timetable (of all teaching/space allocation modalities) and allows avoiding conflict in classroom booking. As the planning includes entry of all elements of the teaching based on one teaching hour as the core unit comprising course, topic, time, teaching room, teacher, type of the teaching and the student group, the platform offers real time availability information for all teaching locations. This then allows resource sharing and the efficient management of teaching resources. The planning and scheduling functionality also removed the initial discrepancies between the syllabi of several subjects and their plans for the current academic year, as well as the

discrepancies between the teaching plans and data entered in the program. This again allowed further synchronizing all the relevant data to the satisfactory level. EduPlan/EX software also allows identifying departments with high teaching load of external experts and distributing that teaching load to employed faculty, which results in reducing the costs of contract teachers.

It is exactly the aspect of external teachers that additionally illustrates the usability and efficiency of this Share point platform. It provides automatic generation of payment contracts for numerous external experts, which considerably reduces exhausting administrative work of several School´s offices. Not to mention that such a reduction of administrative work has been, of course, achieved with respect to all the faculty members. The system allows automatic processing of all the relevant data related to the faculty members´ teaching workload, with numerous variations of their contracts, their academic status, planned and completed teaching hours. Due to its functionality related to generation of the reports on planned and delivered teaching activities, the platform provides an easily operated IT framework for conducting analyses which could result in information necessary for making adjustments, corrections and improvements in the teaching process.

Finally, EduPlan/EX software keeps track of the changes in the planned teaching activities that occur due to the engagement of different teachers. These changes, which seem to be relatively frequent and difficult to manage on time, present an area within which the authors announce further improvements of the currently used version of the program.

Having in mind the above stated benefits of the EduPlan/EX software one can hardly be surprised by the fact that this program was proclaimed a business solution with highest business value at the Windays 2012 conference. The University of Split School of Medicine project team and its partners managed to develop a software tool that presents a valuable contribution to solving administrative problems of the medical schools in Croatia and is an example of successful implementation of IT technology in medical school management (2). Due to its reliance on omnipresent IT technology as well as to its applicability to different types of higher education institutions, we find their software solution highly relevant for the management of teaching processes not only in Croatia, but in a much wider educational context (3).

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

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Acta Medica Academica 2016;45(2):180-181
DOI: 10.5644/ama2006-124.178

Information retention among attendees at a traditional poster presentation session

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Received: 8 June 2016; Accepted: 15 August 2016

Key words: Medical education ▪ Retention ▪ Conferences.

Dear Editor,

Medical poster presentations provide an interactive opportunity to share work at conferences with limited podium space (1). There is scarce data evaluating how effectively medical poster presentations facilitate attendees' retention of medical knowledge (2). We performed an IRB exempt pilot study to investigate how well attendees retained information presented in medical posters.

Four poster presenters at the 2013 Society of Teachers of Family Medicine (STFM) Annual Spring Conference were invited to participate in our study. Each presenter identified the central theme and the top two "take home points" for their poster. Conference attendees were invited to participate; those who consented were given a map showing the location of the four posters and asked to view them in the manner they normally view posters.

Three and ninety days after the conference, participants were sent an electronic survey asking about basic demographic information, participants' engagement with the posters, and information retention. We expected learners to retain at least 30% of information conveyed via a medical poster, based on the National Training Laboratory Institute for Applied Behavioral Science's "Learning Pyramid" (3).

Twenty-six attendees responded at both 3 and 90 days with a mean retention of 14.9% and 11.3% respectively. The most common reason reported for attending the poster presentation session was "to learn new information." Information retention was associated with interaction with poster presenters for only 1 of the 4 posters. No associations between gender, age, primary reason for attending the poster presentation session, current position or history of having presented posters in the past and information retention were found. The decline was higher in males and in those further removed from their residency.

Although there are many potential benefits of poster presentations at conferences,

our study demonstrates that in their current format information retention may not be one of them. Future studies might compare retention between randomly selected posters (like this study) and posters the attendees self-select. Future studies might also evaluate the impact of changing traditional poster presentations to higher engagement modalities, as learner engagement is correlated with increased information retention (4). Specific changes could be to upgrade posters to digital interactive media, flipping the poster session by emailing the posters to attendees in advance of the conference and having poster presenters host round table discussion with interested attendees, or by using moderated poster sessions. These modalities might significantly improve retention without losing the other benefits of poster presentations.

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

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

Funding: Intramural Grant from the Uniformed Services University of the Health Sciences.

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by Nerma Tanović

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More than six authors:

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ISSN 1840-1848