ORIGINAL ARTICLE

UDC: 616.728.3-089:657.478
https://doi.org/10.2298/VSP161105033P

Analysis of inpatient costs in patients with knee osteoarthritis treated by implantation of total condylar knee endoprosthesis

Analiza troškova bolničkog lečenja obolelih od gonartroze implantacijom totalkondilarne endoproteze kolena

Ana Pejčić*, Aleksandar Radunović†, Maja Vulović‡

University of Kragujevac, *Faculty of Medical Sciences, Kragujevac, Serbia; Military Medical Academy, †Clinic for Orthopedic Surgery and Traumatology, Belgrade, Serbia; University of Kragujevac, Faculty of Medical Sciences, ‡Department of Anatomy and Forensic Medicine, Kragujevac, Serbia

Abstract

Background/Aim. Total knee replacement is an elective and high cost surgical procedure which is performed more frequently as a result of increasing prevalence of knee osteoarthritis. The aim of this study was to provide insight into the value and structure of inpatient costs associated with total knee replacement in Serbia. **Methods.** This study was conducted as an in-depth, bottom-up, retrospective, case series analysis of services consumption patterns and costs associated with inpatient treatment of patients with knee osteoarthritis by implantation of primary total condylar knee endoprosthesis from perspective of the national Republic Health Insurance Fund. We obtained data on 97 patients treated with primary unilateral or bilateral total knee replacement in 2014 at the Clinic for Orthopaedic Surgery and Traumatology of the Military Medical Academy in Belgrade, a tertiary health care university hospital. **Results.** Mean age of entire study sample was 67.89 years. Majority of patients (60 patients; 61.9%) had unilateral implantation of total condylar knee endoprosthesis. Bilateral implantation was performed in 37 (38.1%) patients. Mean total inpatient cost per patient for both unilateral and bilateral implantation of total condylar knee endoprosthesis was EUR 2,709.1, ranging from EUR 1,685.2 to EUR 5,356.6. Mean total inpatient cost per patient was EUR 2,093.8 for unilateral implantation and EUR 3,706.8 for bilateral implantation. Two major cost drivers were surgery specific material and surgery. Cost of implants was the highest single cost driver in all observed groups of patients. **Conclusion.** Our findings imply that inpatient costs associated with implantation of primary total condylar knee endoprosthesis are substantial. It seems that the most important cost drivers are surgery and surgery specific material, with implants being the highest single cost driver. Further research should be focused on analyzing factors that influence these costs in order to develop effective strategies which could contribute to substantial savings in the future.

Key words:
arthroplasty, replacement, knee; inpatients; costs and cost analyses; cost control; knee prosthesis; serbia.

Apstrakt

Uvod/Cilj. Totalna artroplastika kolena je elektivna i skupa procedura koja se u današnje vreme sprovodi sve češće kao posledica rastuće prevalencije gonartroze. Cilj ovog rada bio je analiza vrednosti i strukture bolničkih troškova lečenja obolelih od gonartroze implantacijom totalkondilarne endoproteze kolena. **Metode.** Ova studija je sprovedena kao opservaciona retrospektivna studija troškova zasnovana na pristupu „od dna prema vrhu“. Istraživanu populaciju činilo je 97 bolesnika sa gonartrozom kojima je tokom 2014. godine urađena primarna unilateralna ili bilateralna implantacija totalkondilarne endoproteze kolena na Klinici za ortopedsku hirurgiju i traumatologiju Vojnomedicinske akademije u Beogradu. Bolnički troškovi su izračunati iz perspektive Republičkog fonda za zdravstveno osiguranje, na osnovu analize baze podataka nastale na osnovu anonimizirane fakturisane medicinske dokumentacije na otpustu. **Rezultati.** Prosečna starost ispitanika bila je 67,89 godina. Većini bolesnika (njih 60, tj. 61,9%) je izvršena unilateralna implantacija totalkondilarne endoproteze kolena. Bilateralna implantacija je izvedena kod 37 bolesnika (38,1%). Prosečan ukupni bolnički trošak po bolesniku za zajedno posmatrane unilateralnu i bilateralnu implantaciju iznosio je 2.709,1 € (opseg: 1.685,2–5.356,6 €). Prosečan ukupni bolnički trošak po bolesniku iznosio je 2.093,8 € za unilateralnu implantaciju, dok je za bilateralnu implantaciju iznosio 3.706,8 €. Dve kategorije sa najvećim troškovima bili su troškovi materijala korišćenog tokom operacije i troškovi same operacije. Troškovi endoproteze

Correspondence to: Aleksandar Radunović, Military Medical Academy, Clinic for Orthopedic Surgery and Traumatology, Crnotravska 17, 11 000 Belgrade, Serbia. E-mail: aradunovic@yahoo.com

bili su pojedinačno najveći u odnosu na ostale podkategorije troškova. **Zaključak.** Rezultati ove studije ukazuju na to da su bolnički troškovi implantacije primarne totalkondilarne endoproteze kolena značajni i da najveće kategorije troškova čine upravo troškovi same operacije i materijala korišćenog tokom operacije, pri čemu su pojedinačno najveći troškovi endoproteze. Buduća istraživanja bi mogla biti usmerena na analizu faktora koji utiču na ove troškove, kako bi se razvile efikasne strategije za uštedu u budućnosti.

Ključne reči:
artroplastika kolena; hospitalizacija; cene i analize cena; cene, kontrola; koleno, proteza; srbija.

Introduction

Assessment of economic implications of orthopaedic surgeries is gaining more attention as musculoskeletal disorders demanding such procedures are on the rise [1]. Total knee replacement (also referred to as total knee arthroplasty) is an elective, expensive, but cost-effective surgical procedure which is being performed more frequently as a result of increasing prevalence of knee osteoarthritis (gonarthrosis) [2–7]. Osteoarthritis is a degenerative disease of cartilage and surrounding tissue associated with joint pain, stiffness and limitation of movement which affects about 10% of persons over the age of 60 years [8–11]. Knee replacement involving implantation of total condylar endoprosthesis is indicated when conservative treatment can not reduce knee joint pain and dysfunction and is associated with a substantial improvement in quality of life and pain relief in patients with knee osteoarthritis [5, 6, 12]. This procedure involves altering the articular surfaces in a way that enables replacement of total damaged knee joint with a prosthetic implant [4, 5]. Total condylar knee endoprosthesis resurfaces all three compartments of the knee (lateral, medial, and patellofemoral) [13].

The mean utilization rate of knee replacement in Organisation for Economic Co-operation and Development (OECD) countries was 150 procedures per 100,000 people in 2011 [14]. The number of performed total knee replacements has been increasing worldwide as rise in the prevalence of osteoarthritis follows the pace of acceleration of global population ageing and rising trends of obesity [12, 15–24]. The recently published Global Burden of Disease, Injuries and Risk Factors Study noted that disability-adjusted-life-years (DALYs) attributable to high body mass index (BMI) increased the most among the top five risk factors from 1990 to 2015 [22]. The demand for primary total knee replacements is projected to grow to 3.48 million procedures annually in the United States by 2030 [20]. However, accessibility to this procedure is inconsistent across the world and is affected by high cost and limited number of skilled personnel who can perform it [25]. Patients seeking care in publicly-funded institutions frequently spend weeks or months on the waiting list for provision of this surgery unless they are able to pay for private care [26]. For example, the mean length of time spent on waiting for this procedure within the Veterans Affairs Connecticut Healthcare System in the United States can be as long as two years [27]. These all have negative impact on patients as they experience great pain and suffer functional limitations while they await surgery [4].

The costs associated with total knee replacement are becoming increasing concern worldwide because they put a significant financial burden on most healthcare systems [12, 28]. This procedure was associated with one of the most noticeable increase for inpatient costs among all payer types in the United States [29]. Aggregate inpatient costs of total knee replacement reached United States dolar (USD) 9.2 billion in 2007, and they grew by 27.5% between 2004 and 2007 [30]. Previous studies reported that cost of implants, hospital room and operating room segment of care may account over 75% of inpatient costs [31–34]. However, the cost of implants is usually the highest and it can even reach up to 87% of overall inpatient cost [6, 29, 35]. The inpatient costs associated with total knee replacement varies across different regions. Costs reported in European studies vary from EUR 4,103 in public hospitals in Portugal [36] to EUR 15,358 in Italy [37]. A report published in the United States in 2015 noted substantial variation of hospital charges for knee replacement procedures ranging from USD 11,317 in Alabama to USD 69,654 in New York [38]. Such variations in cost of care are one of the main reasons for increasing number of patients from developed countries who travel to hospitals in emerging market countries like Taiwan, Thailand, India and Singapore where cost of this procedure can be 8 to 10 times less expensive than in the United States due to low labor and maintenance cost [39–42].

Nearly 20,000 patients were on the waiting lists for knee and hip replacement in Serbia in 2014 with reported increase of 20% compared to previous year [43]. Average length of time that patients spent waiting for these procedure was 311 days in 2014, which was 25 days less than was reported in 2013 [43]. It is likely to expect that demand for these procedures will continue to rise in Serbia with continuing population ageing [44]. The core fund in Serbia in charge for most inpatient care expenditures is Republic Health Insurance Fund which is a non-profit state owned institution subject to budget shortages [44–46]. Consequently, there is a need to assess major inpatient cost drivers in order to make more efficient health policy programs. Since health expenditures related to total knee replacement are substantial, it is crucial to understand cost of care provided across various settings in order to provide baseline data for pharmacoeconomic analyses in the future.

So far, there is a substantial knowledge gap on actual inpatient cost of total knee replacement in Serbia. Therefore, the aim of this study was to provide insight into the value and structure of inpatient costs associated with total knee replacement by implantation of total condylar knee endoprosthesis in Serbia.

Methods

Study design and patient selection

This study was conducted as an in-depth, bottom-up, retrospective, case series analysis of services consumption patterns and costs associated with inpatient treatment of patients with knee osteoarthritis by implantation of primary total condylar knee endoprosthesis from the perspective of the third party payer, i.e., from the national Republic Health Insurance Fund. Indirect cost and out-of-pocket patient's expenditure, as well as costs in settings other than inpatient, remained out of scope of this study. We obtained data on patients who were treated with primary unilateral or bilateral total knee replacement in 2014 at the Clinic for Orthopaedic Surgery and Traumatology of the Military Medical Academy in Belgrade, a tertiary health care university hospital. The source of data was an anonymised database consisting of electronic hospital discharge invoices. In total, 97 complete patient files were analysed. Data on age, gender and length of hospitalisation were also collected.

Structure and pricing of the used recourses

The official Republic Health Insurance Fund pricelist was applied at the time of the service provision. Average middle exchange rate for Euro (EUR) given by the National Bank of Serbia for 2014 was used to convert costs originally reported in the national currency Serbian Dinar (RSD): EUR 1 = RSD 117.2478 [47].

For the present study, total inpatient costs associated with the implantation of primary total condylar knee endoprosthesis were collected. Costs were separated into the following categories: general surgery related medical care (hospital admission day and consumables, rehabilitation services, and all other services such as social care, transport, counseling, epidemiological measures), surgery (surgical intervention and anesthesia), imaging diagnostics [classical imaging diagnostics – Roentgen, contrasts, films and consumables intended for imaging diagnostics services provision, computed tomography (CT) and ultrasound imaging diagnostics], surgery specific materials (implants, dressing material, consumables for surgical intervention and other consumables such as gloves, braunilas, tubes), laboratory analysis (general biochemistry and hematology, coagulation status analysis, microbiology related lab), medicines (parenteral and enteral nutritive solutions and systems, blood and its derivatives – transfusions, antibiotics, antimicotics, antiviral and antiprotozoal drugs, analgesics, thromboprophylactic medicines and all other drugs).

Statistical analysis

Categorical variables were presented as frequencies of certain categories, while continuous variables were summarized as mean and standard deviation, as well as median and minimum and maximum values. Patients were divided into two groups based on the type of implantation: unilateral (implantation performed on only one knee) and bilateral (implantation performed on both knees). The differences in continuous variables were assessed by Mann Whitney U test because data were not normally distributed. The χ^2 test was used to assess differences in categorical variables. The differences were considered significant if probability of null hypothesis was less than 0.05. Costs are presented as mean and median cost per patient including standard deviation, minimum and maximum values. All mean and median cost values refer only to those patients that have actually used a particular service, as some services were used by few patients. Share of cost of certain category in total inpatient cost was calculated and presented graphically. Statistical analyses were performed using Microsoft Office Excel 2007® and IBM SPSS® Statistics for Windows, Version 20.0 (IBM Corp, Armonk, NY, USA).

Results

Study sample consisted of 97 patients. Baseline characteristics of study sample are shown in Table 1. Mean age of entire study sample was 67.89 years, ranging from 41 to 83 years. There were 40 (41.2%) female patients and 57 (58.8%) male patients. Majority of patients (60, 61.9% patients) had unilateral implantation of total condylar knee endoprosthesis. Bilateral implantation was performed in 37 (38.1%) patients. There was no statistical difference in the mean age and mean duration of hospitalisation of patients who had unilateral implantation compared to patients who had bilateral implantation. However, fewer women had bilateral implantation compared to men.

Results of descriptive statistical analysis of cost domains are presented in Table 2.

Table 1

Baseline characteristics of study sample

Variable	Unilateral implantation (n = 60)	Bilateral implantation (n = 37)	Test value and significance of null hypothesis (*p*)	All patients (n = 97)
Age (years)	67.90 ± 8.77 [70 (41–83)]	67.86 ± 6.92 [67 (50–82)]	U = 1049.0; *p* = 0.650	67.89 ± 8.08 [69 (41–83)]
Gender				
female	30 (50.0)	10 (27.0)	χ^2 = 4.082; *p* = 0.043*	40 (41.2)
male	30 (50.0)	27 (73.0)		57 (58.8)
Mean duration of hospitalization (days)	8.05 ± 3.14 [7.5 (2–21)]	9.05 ± 4.99 [7 (2–26)]	U = 1051.0; *p* = 0.658	8.43 ± 3.95 [7 (2–26)]

Results are presented as mean ± SD [median (minimum-maximum)], or n (%); *significant difference.

Table 2

Cost domains of inpatient treatment of patients with knee osteoarthritis by implantation of total condylar knee endoprosthesis

Domain	Mean cost per patient ± standard deviation [Median cost per patient (minimum–maximum)][#] (EUR)		
	Unilateral implantation (n = 60)	Bilateral implantation (n = 37)	All patients (n = 97)
General Surgery Related Care	137.6 ± 65.2 [119.3 (39.5–350.6)]	157.8 ± 87.0 [145.0 (36.8–418.1)]	145.3 ± 74,5 [131.3 (36.8–418.1)]
hospital admission day and consumables	120.4 ± 56.3 [105.4 (26.4–329.0)]	135.4 ± 87.2 [118.6 (26.4–418.1)]	126.2 ± 69.7 [105.4 (26.4–418.1)]
rehabilitation services	27.3 ± 20.9 [21.1 (6.0–95.7)]	35.7 ± 19.7 [32.9 (5.8–83.7)]	30.5 ± 20.7 [25.7 (5.8–95.7)]
all other services (social care, transport, counseling, epidemiological measures...)	21.8 ± 10.3 [21.8 (14.5–29.1)]	N/A ± N/A [39.6 (39.6–39.6)]	27.7 ± 12.6 [29.1 (14.5–39.6)]
Surgery	356.5 ± 39.2 [378.5 (270.3–431.3)]	525.3 ± 44.6 [544.7 (419.2–634.9)]	420.9 ± 92.1 [391.0 (270.3–634.9)]
surgical interventions	216.1 ± 0.0 [216.1 (216.1–216.1)]	379.9 ± 0.0 [379.9 (379.9–379.9)]	278.6 ± 80.0 [216.1 (216.1–379.8)]
anesthesia	140.4 ± 39.2 [162.4 (54.1–215.2)]	145.4 ± 44.6 [164.8 (39.3–255.1)]	142.3 ± 41.2 [162.9 (39.3–255.1)]
Imaging Diagnostics	11.0 ± 9.6 [8.3 (5.5–68.7)]	16.9 ± 7.7 [16.5 (10.9–58.0)]	13.3 ± 9.3 [10.3 (5.5–68.7)]
classical imaging diagnostics – röntgen	9.4 ± 3.1 [8.3 (5.5–29.4)]	15.1 ± 2.1 [15.7 (10.9–18.6)]	11.6 ± 4.0 [10.3 (5.5–29.4)]
contrasts, films and consumables intended for imaging diagnostics services provision	N/A ± N/A [2.8 (2.8–2.8)]	N/A ± N/A [2.8 (2.8–2.8)]	2.8 ± N/A [2.8 (2.8–2.8)]
ct imaging diagnostics	N/A	N/A ± N/A [44.3 (44.3–44.3)]	N/A ± N/A [44.3 (44.3–44.3)]
ultrasound imaging diagnostics	48.5 ± 12.9 [48.5 (39.4–57.7)]	N/A ± N/A [18.6 (18.6–18.6)]	38.5 ± 19.5 [39.4 (18.6–57.7)]
Surgery specific materials	1,461.7 ± 232.0 [1,409.9 (1,084.0–2,683.9)]	2,808.1 ± 397.8 [2,795.1 (1,444.6–4,406.7)]	1,975.2 ± 724.3 [1,465.8 (1,084.0–4,406.7)]
implants	1,273.7 ± 223.8 [1.223.8 (917.0–2,473.4)]	2,525.7 ± 383.3 [2,468.9 (1,224.7–4,049.3)]	1,751.2 ± 677.9 [1,270.5 (917.0–4,049.3)]
dressing material	75.7 ± 31.7 [73.2 (37.0–293.9)]	119.6 ± 22.5 [120.6 (62.2–153.6)]	92.5 ± 35.6 [80.3 (37.0–293.9)]
consumables for surgical intervention (sutures, staplers, drains, antiseptics, etc.)	74.1 ± 50.7 [64.3 (53.4–451.4)]	121.6 ± 30.1 [128.6 (38.3–145.8)]	92.2 ± 49.6 [73.1 (38.3–451.4)]
other consumables (gloves, braunilas, tubes, etc.)	38.2 ± 17.1 [30.3 (5.8–73.3)]	41.1 ± 15.6 [37.5 (7.4–67.4)]	39.3 ± 16.5 [34.1 (5.8–73.3)]
Laboratory Analysis	20.5 ± 11.3 [17.8 (3.9–48.7)]	26.6 ± 19.9 [23.7 (2.6–94.4)]	22.8 ± 15.3 [19.8 (2.6–94.4)]
general biochemistry and hemathology	19.7 ± 11.0 [17.4 (3.9–48.7)]	25.7 ± 17.5 [23.7 (2.6–80.5)]	21.9 ± 14.0 [19.3 (2.6–80.5)]
coagulation status analysis	6.1 ± 5.9 [2.8 (1.8–14.0)]	N/A ± N/A [29.3 (29.3–29.3)]	9.4 ± 10.3 [3.7 (1.8–29.3)]
microbiology related lab	N/A ± N/A [7.0 (7.0–.7.0)]	N/A ± N/A [1.3 (1.3–1.3)]	4.2 ± 4.0 [4.2 (1.3–7.0)]
Medicines	108.4 ± 45.1 [97.2 (41.1–223.7)]	172.9 ± 64.0 [162.6 (63.1–351.0)]	133.2 ± 61.6 [120.3 (41.1–351.0)]
parenteral and enteral nutritive solutions and systems	16.3 ± 10.2 [14.7 (4.6–76.1)]	20.9 ± 18.1 [17.3 (2.7–119.8)]	18.1 ± 13.9 [15.6 (2.7–119.8)]
blood and its derivatives – transfusions	40.4 ± 25.6 [33.1(15.8–124.7)]	66.9 ± 31.8 [57.2 (19.5–160.2)]	54.5 ± 31.7 [52.3 (15.8–160.2)]
antibiotics, antimicotics, antiviral and antiprotozoal drugs	20.5 ± 9.9 [21.0 (4.3–47.8)]	24.3 ± 15.5 [21.7 (4.5–71.5)]	22.0 ± 12.4 [21.5 (4.3–71.5)]
analgesics	7.1 ± 11.1 [3.0 (0.6–59.7)]	9.1 ± 12.6 [3.5 (0.6–50.2)]	7.9 ± 11.7 [3.33 (0.6–59.7)]
thromboprophilactic medicines	42.7 ± 21.9 [36.0 (9.5–113.7)]	57.4 ± 27.2 [52.2 (1.7–124.2)]	48.3 ± 25.0 [42.9 (1.7–124.2)]
all other drugs	3.2 ± 2.9 [2.6 (0.3–13.2)]	4.1 ± 4.2 [3.2 (0.3–19.0)]	3.6 ± 3.4 [3.0 (0.3–19.0)]
Total inpatient cost	2,093.8 ± 253.0 [2,029.6 (1,685.2–3,358.2)]	3,706.8 ± 439.9 [3,669.2 (2,195.3–5,356.6)]	2,709.1 ± 855.7 [2,195,3 (1,685.2–5,356.6)]

#All values refer only to those patients that have actually used a particular service; N/A = not available; n = number; EUR = Euro.

Mean total inpatient cost per patient for both unilateral and bilateral implantation of total condylar knee endoprosthesis was EUR 2,709.1, ranging from EUR 1,685.2 to EUR 5,356.6. Mean total inpatient cost per patient was EUR 2,093.8 (range: 1,685.2–3,358.2) for unilateral implantation and EUR 3,706.8 (range: 2,195.3–5,356.6) for bilateral implantation.

Structure and percentage ratio of mean costs per patient are shown in Figure 1. Two major cost drivers were surgery specific material and surgery. Cost of implants was the highest single cost driver in all observed groups of patients (Table 2, Figure 2). The cost associated with imaging diagnostic services was the lowest (Table 2, Figure 1).

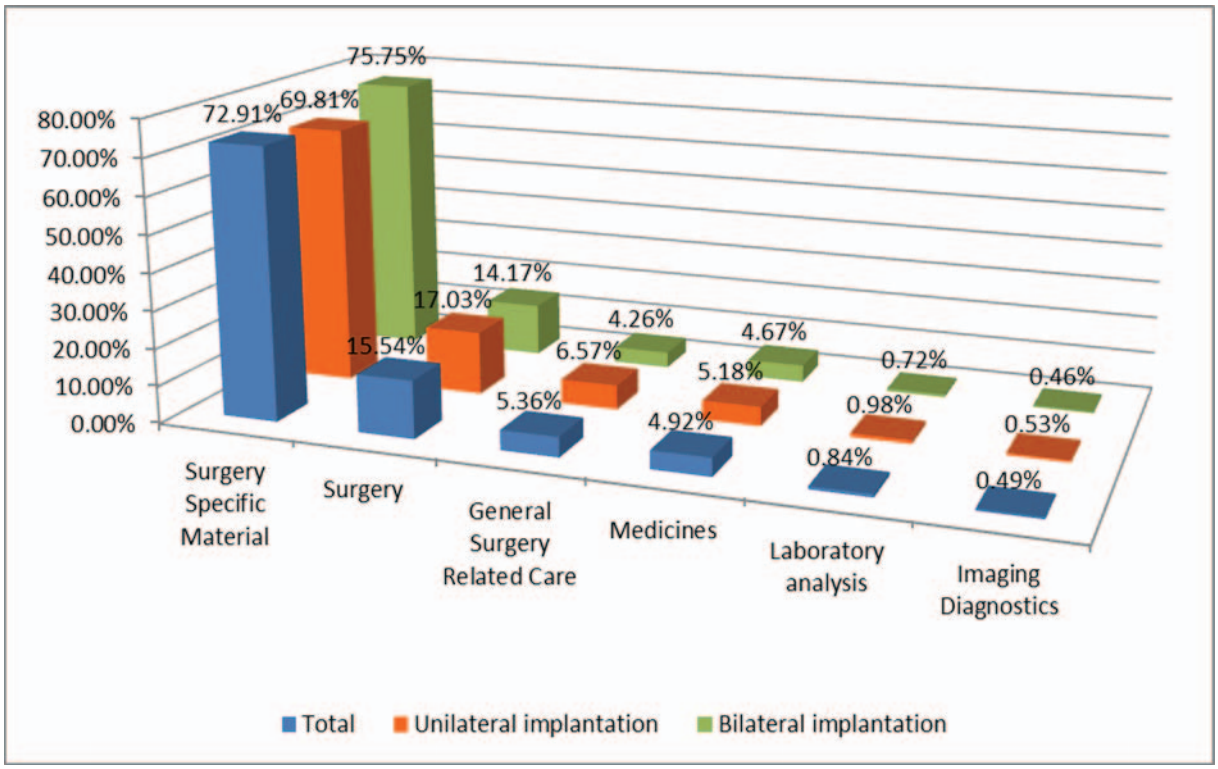

Fig. 1 – Structure and percentage ratio of mean costs per patient.

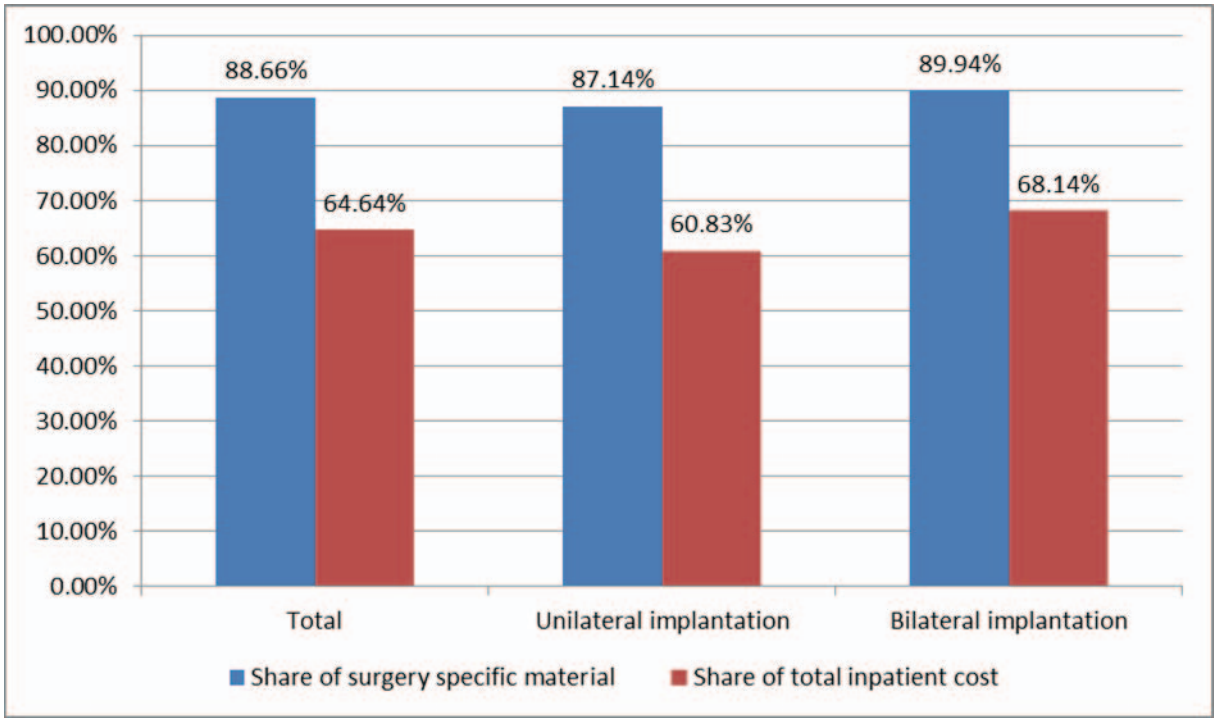

Fig. 2 – Share of implant cost in cost of surgery specific material and total inpatient cost.

Discussion

The value of previously reported mean inpatient cost of primary total knee replacement differs widely from country to country. When comparing results of different studies, it should be kept in mind that methods, data sources (e.g., hospital accounting system, reimbursement rates and charges, etc.) and categorization of costs may vary significantly. Mean total inpatient cost of total knee replacement estimated in our study is comparable with the mean inpatient cost in public (EUR 4,103) and private (EUR 5,226) hospitals in Portugal [36]. Studies conducted in Spain [48], France [49], Italy [37, 50] and United Kingdom [7] reported somewhat higher values. In France, mean hospital cost was EUR 7,404 [49]. In Spain, mean total inpatient cost was EUR 7,645 [48]. In Italy, mean hospital cost per knee and hip replacement procedure was EUR 6,952, whereas the mean cost of the surgical procedure was EUR 3,798, while that of the inpatient care was EUR 2,924 [50]. Another Italian study reported that average cost per patient (including hospital, rehabilitation and complication cost) was EUR 15,358 [37]. In the United Kingdom, on average each admission costs British Pound (GBP) 6,363 according to the analysis of patient level data and services valued at 2007–2008 prices from the Knee Arthroplasty Trial [7]. In China, the total cost for unilateral procedure was USD 8,173.25, whereas for bilateral procedure it was USD 14,257.64 in 2010 [51]. In Taiwan, mean total medical cost for unilateral procedure was USD 3,919 [52], whereas median cost of simultaneous bilateral procedure was USD 6,994.4 [53]. Early studies conducted in the United States reported that mean total inpatient cost for unilateral total knee replacement was USD 10,081 [54] during 1991–1994, USD 12,561 during 1991–1992 [55] and USD 15,673 during 2000–2008 [56]. These costs can be even higher if patients have concomitant diagnosis of depression and anxiety [57] or venous thromboembolism and bleeding [58]. In a cohort of Australian patients, mean inpatient cost of knee replacement in the first 30 days postoperatively was Australian dolar (AUD) 21,006 for a period 2011–2012 [19]. Estimated mean inpatient cost can range from Canadian dolar (CAD) 12,500 [59] to CAD 14,758 [60] in Canada. Higher reported costs in other countries may be attributed to the differences in the local healthcare systems, clinical, coding, administrative and costing practices in individual countries as well as patient demographics and surgeon practices.

As costs related to total knee replacement are substantial, it is important to develop strategies for their control and reduction. Orthopaedic surgeons should be the first and the most important patient advocates who will carefully evaluate hospital cost saving programs and ensure their enactment do not compromise treatment outcomes [6]. Several reports have highlighted that safe cost reduction can be achieved through the knee implant standardization process to reduce variation in implant selection and implementation of the clinical pathway programs which coordinate and standardize the activities of the physicians, nurses and other staff involved in providing care to the patients [6, 32, 61–64]. One study reported that substantial cost savings can be achieved when one versus two packets of bone cement is used in combination with a hand mixing technique with no difference in clinical outcomes [28]. There are also proposals to increase number of total knee replacements in an outpatient setting [65]. However, it is more complicated to monitor recovery process as patients do not stay overnight under supervision and there is a lack of high quality evidence that directly compares outcomes of outpatient and inpatient orthopaedic procedures [65]. It has also been shown that shortening of waiting times for surgery is cost-effective and may also be cost saving [66].

Growing body of literature has shown that the cost of implants contribute significantly to total cost of joint replacement procedures [6, 29, 51, 67]. Large share of implant costs (64.64%) in total inpatient cost is an important finding of our study that confirms previous observations. Robinson et al. [35] reported that share of implant cost can vary from 13% to as high as 87% of total inpatient cost. Some other studies reported lower share. For example Portuguese study reported 28%–33% [36] and the US study 29%–40% [54]. Mean implant cost in our study was EUR 1,751.2, which again is similar to the cost reported in Portuguese study (EUR 1,259 – EUR 1,447) [36] and Italian study (EUR 1,850) [50]. Fixed implant cost associated with total knee replacement was CAD 3,060 in Canada [59]. An early US study reported that the average implant cost was USD 3,963 for unilateral procedure and USD 7,428 for bilateral procedure [54]. Variation in share and value of implant cost may be attributable to the patient characteristics and hospital characteristics as well as different categorization of other costs [35]. In addition, factors that may have influence on final cost of the implants are costs of design, research, development and manufacture as well as the cost of support staff such as industry representatives [68].

The average prices of hip and knee implants have increased more than 100% over the past decade, although it would be expected to decrease with the increasing number of procedures if orthopaedic implant device companies followed conventional economies-of-scale principles [35, 67]. Proposed strategies for restraining implant cost are volume-discounted vendor contracts, single-price contracts, unilateral price caps, implant standardization programs as well as surgeons cost awareness discussions [6, 31, 32, 64, 69]. Access to information on the prices of devices should be available to orthopaedic surgeons, and there should also be incentives for their participation in cost reductions programs [70]. It has also been shown that innovative implants used for total knee replacement should decrease failure of this procedure by 50%–55%, or more, compared to standard implants to be broadly cost-effective [71]. In addition, the patents on many widely used implants have recently expired and introduction of generic implants has the potential for major cost savings [68]. Companies that put generic implant replicas on the market have been established, but formal independent systems which should evaluate their absolute equivalence are yet to be founded [68]. The new generic implants are similar to the originals by a process of reverse engineering and their equivalence has been assessed in terms of geometry, but the monitoring and their independent evaluation to verify biomechanical compatibility is essential in order to prove that they are as good and safe as the originals [68].

Our findings should be interpreted in light of some potential limitations. Our analysis was restricted to the direct medical costs of procedure in inpatient setting. We did not take into account out-of-pocket patient's expenditure, indirect costs and costs associated with post-discharge period in outpatient setting when rehabilitation and complication costs may be considerable. In addition, hospital discharge invoices to Republic Health Insurance Fund may be partly unreliable in some cases as data entering is usually left to nurses or clerks who may not have sufficient comprehension of this process which can lead to incorrect data entry. Certain fraction of invoices is even disputed by the Republic Health Insurance Fund. For example, in the first half of 2016, the Republic Health Insurance Fund through the control of regularity of invoicing and demands for drug reimbursement noted that the amount of incorrect claims had a value of RSD 8,256,642.95 (about EUR 67,072) [72]. In 2016, estimated expenditure of the Republic Health Insurance Fund on health care was RSD 204.3 billion (about EUR 1.66 billion) [73]. The pattern of services and materials acknowledged by the Republic Health Insurance Fund in some cases may also lead to the differences between what was invoiced and what patients really consumed, so our findings might have underestimated the true cost of some consumed services and materials. Another limitation is rather modest sample size. However as included patients represent entire population of knee osteoarthritis patients, who were treated over a period of entire year in one of the largest university hospitals in Serbia, they certainly provide valuable insight into the value and structure of inpatient cost of total knee replacement in this region.

Conclusion

Our findings imply that inpatient costs associated with implantation of total condylar knee endoprosthesis are substantial. It seems that the most important cost drivers are surgery and surgery specific material, with implants being the highest single cost driver. Further research should be focused on analyzing factors that influence these costs in order to develop effective strategies which could contribute to substantial savings in the future.

Acknowledgements

Ana Pejčić is awarded with the Scholarship of the Ministry of Education, Science and Technological Development of the Republic of Serbia for PhD students. Publication of results was not contingent to Ministry's censorship or approval.

REFERENCES

1. *Brauer CA, Rosen AB, Olchanski NV, Neumann PJ.* Cost-utility analyses in orthopaedic surgery. J Bone Joint Surg Am 2005; 87(6): 1253–9.
2. *Ceyhan E, Gursoy S, Akkaya M, Ugurlu M, Koksal I, Bozkurt M.* Toward the Turkish National Registry System: A Prevalence Study of Total Knee Arthroplasty in Turkey. J Arthroplasty 2016; 31(9): 1878–84.
3. *Losina E, Walensky RP, Kessler CL, Emrani PS, Reichmann WM, Wright EA*, et al. Cost-effectiveness of total knee arthroplasty in the United States: patient risk and hospital volume. Arch Intern Med 2009; 169(12): 1113–21; discussion 1121–2.
4. *Lizaur-Utrilla A, Martinez-Mendez D, Miralles-Muñoz FA, Marco-Gomez L, Lopez-Prats FA.* Negative impact of waiting time for primary total knee arthroplasty on satisfaction and patient-reported outcome. Int Orthop 2016; 40(11): 2303–7.
5. *Kocic M, Stankovic A, Zlatanovic D, Ciric T, Karalajic S, Dimitrijevic I,* et al. Functional improvement up to six months after total knee arthroplasty: measured by knee range of motion and self-reported questionnaire. Acta Medica Medianae 2015; 54(4): 52–8.
6. *Healy WL, Iorio R, Ko J, Appleby D, Lemos DW.* Impact of cost reduction programs on short-term patient outcome and hospital cost of total knee arthroplasty. J Bone Joint Surg Am 2002; 84-A(3): 348–53.
7. *Dakin H, Gray A, Fitzpatrick R, Maclennan G, Murray D;* KAT Trial Group. Rationing of total knee replacement: a cost-effectiveness analysis on a large trial data set. BMJ Open 2012; 2(1): e000332.
8. *World Health Organization.* The burden of muskulosceletal conditions at the start of the new millennium. Geneva: World Health Organization; 2003. Available from: whqlib-doc.who.int/trs/WHO_TRS_919.pdf [accessed 2016 October 23].
9. *Johnson VL, Hunter DJ.* The epidemiology of osteoarthritis. Best Pract Res Clin Rheumatol 2014; 28(1): 5–15.
10. *Litwic A, Edwards MH, Dennison EM, Cooper C.* Epidemiology and burden of osteoarthritis. Br Med Bull 2013; 105: 185–99.
11. *Zhang Y, Jordan JM.* Epidemiology of osteoarthritis. Clin Geriatr Med 2010; 26(3): 355–69.
12. Carr AJ, Robertsson O, Graves S, Price AJ, Arden NK, Judge A, et al. Knee replacement. Lancet 2012; 379(9823): 1331–40.
13. *Insall J, Scott WN, Ranawat CS.* The total condylar knee prosthesis. A report of two hundred and twenty cases. J Bone Joint Surg Am 1979; 61(2): 173–80.
14. *Pabinger C, Lothaller H, Geissler A.* Utilization rates of knee-arthroplasty in OECD countries. Osteoarthritis Cartilage 2015; 23(10): 1664–73.
15. *Fransen M, Bridgett L, March L, Hoy D, Penserga E, Brooks P.* The epidemiology of osteoarthritis in Asia. Int J Rheum Dis 2011; 14(2): 113–21.
16. *Fisher ES, Bell JS, Tomek IM, Esty AR, Godman DC.* Trends and regional variation in hip, knee, and shoulder replacement: In: Dartmouth Atlas Surgery Report. Hanover, NH: The Dartmouth Institute for Health Policy and Clinical Practice; 2010.
17. *Jakovljevic M, Laaser U.* Population aging from 1950 to 2010 in seventeen transitional countries in the wider region of South Eastern Europe . SEEJPH 2015; doi: 10.12908/SEEJPH-2014-42.
18. *Loeser RF, Collins JA, Diekman BO.* Ageing and the pathogenesis of osteoarthritis. Nat Rev Rheumatol 2016; 12(7): 412–20.
19. *Peel TN, Cheng AC, Liew D, Buising KL, Lisik J, Carroll KA*, et al. Direct hospital cost determinants following hip and knee arthroplasty. Arthritis Care Res (Hoboken) 2015; 67(6): 782–90.
20. *Kurtz S, Ong K, Lau E, Mowat F, Halpern M.* Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am 2007; 89(4): 780–5.
21. *Jakovljevic M.* The aging of Europe. The unexplored potential. Farmeconomia. Health Econom Ther Pathways 2015; 16(4): 89–92.

22. GBD 2015 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016; 388(10053): 1659–724.
23. GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016; 388(10053): 1459–544.
24. GBD 2015 SDG Collaborators. Measuring the health-related Sustainable Development Goals in 188 countries: a baseline analysis from the Global Burden of Disease Study 2015. Lancet 2016; 388(10053): 1813–850.
25. *March L, Smith EU, Hoy DG, Cross MJ, Sanchez-Riera L, Blyth F,* et al. Burden of disability due to musculoskeletal (MSK) disorders. Best Pract Res Clin Rheumatol 2014; 28(3): 353–66.
26. *Gutacker N, Siciliani L, Cookson R.* Waiting time prioritisation: Evidence from England. Soc Sci Med 2016; 159: 140–51.
27. *Hussain T, Bell B, Brandt C, Nuzzo J, Erdos JJ.* Using VistA electronic medical record data extracts to calculate the waiting time for total knee arthroplasty. J Arthroplasty 2010; 25(2): 213–5.
28. *Maheshwari AV, Argawal M, Naziri Q, Pivec R, Mont MA, Rasquinha VJ.* Can cementing technique reduce the cost of a primary total knee arthroplasty? J Knee Surg 2015; 28(3): 183–90.
29. *Weiss AJ, Elixhauser A, Andrews RM.* Characteristics of Operating Room Procedures in U.S. Hospitals, 2011: Statistical Brief #170. 2014 Feb. Healthcare Cost and Utilization Project (HCUP) Statistical Briefs [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2006. Available from: http://www.ncbi.nlm.nih.gov/books/NBK195245/
30. *Stranges E, Russo CA, Friedman B.* Procedures with the Most Rapidly Increasing Hospital Costs, 2004–2007: Statistical Brief #82. 2009 Dec. Healthcare Cost and Utilization Project (HCUP) Statistical Briefs [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2006 Feb-. Available from: http://www.ncbi.nlm.nih.gov/books/NBK53597/
31. *Bosco JA, Alvarado CM, Slover JD, Iorio R, Hutzler LH.* Decreasing total joint implant costs and physician specific cost variation through negotiation. J Arthroplasty 2014; 29(4): 678–80.
32. *Healy WL, Rana AJ, Iorio R.* Hospital economics of primary total knee arthroplasty at a teaching hospital. Clin Orthop Relat Res 2011; 469(1): 87–94.
33. *DiGioia AM 3rd, Greenhouse PK, Giarrusso ML, Kress JM.* Determining the True Cost to Deliver Total Hip and Knee Arthroplasty Over the Full Cycle of Care: Preparing for Bundling and Reference-Based Pricing. J Arthroplasty 2016; 31(1): 1–6.
34. *Sculco TP.* The economics of new age arthroplasty: can we afford it? Orthopedics 2010; 33(9): 628.
35. *Robinson JC, Pozen A, Tseng S, Bozic KJ.* Variability in costs associated with total hip and knee replacement implants. J Bone Joint Surg Am 2012; 94(18): 1693–8.
36. *Ribiero MV.* The cost variations in total the cost variations in total hip and knee implant surgeries across and within two Portuguese Hospitals [thesis]. Porto: University of Porto; 2015.
37. *Piscitelli P, Iolascon G, Di Tanna G, Bizzi E, Chitano G, Argentiero A,* et al. Socioeconomic burden of total joint arthroplasty for symptomatic hip and knee osteoarthritis in the Italian population: a 5-year analysis based on hospitalization records. Arthritis Care Res (Hoboken) 2012; 64(9): 1320–7.
38. Blue Cross Blue Shield. A Study of Cost Variations for Knee and Hip Replacement Surgeries in the U.S. The Health of America Report, 2015. Available from: https://www.bcbs.com/about-us/...of.../study-cost-variations
39. *Piazolo M, Zanca N.* Medical tourism: A case study for the USA and India, Germany and Hungary. Acta Polytechnica 2011; 8: 27–38.
40. *Dawn SK, Pal S.* Medical Tourism in India: Issues, Opportunities and Designing Strategies for Growth and Development. Int J Multidiscip Res 2011; 1(3): 185–202.
41. *Khan M.* Medical tourism: outsourcing of healthcare. International CHRIE Conference-Refereed Track. 2010. Available from: http://scholarworks.umass.edu/refereed/CHRIE_2010/Friday/23. [accessed 2016 October 15].
42. *Haung CY, Wang SP, Chiang CW.* Cost feasibility of a prechecking medical tourism system for U.S. patients undertaking joint replacement surgery in Taiwan. Chang Gung Med J 2010; 33(6): 684–92.
43. *Institute of Public Healrth of Serbia "Dr Milan Jovanović Batut".* Report on improving the quality of work in health institutions of the Republic of Serbia in 2014. Belgrade; Institute of Public Healrth of Serbia "Dr Milan Jovanović Batut"; 2015.
44. *Stojkovic M, Milovanovic O.* Health spending follows pace of population aging: challenges lying ahead of the largest Western balkan market. Front Public Health 2015; 3: 58.
45. *Jakovljević M, Jovanović M, Lazić Z, Jakovljević V, Đukić A, Velicković R,* et al. Current efforts and proposals to reduce healthcare costs in Serbia. Serb J Exp Clin Res 2011; 12(4): 161–3.
46. *Jakovljevic MB.* Resource allocation strategies in Southeastern European health policy. Eur J Health Econ 2013; 14(2): 153–9.
47. *National Bank of Serbia.* Exchange rate lists for a specific period. Available from: https://www.nbs.rs/export/sites/default/internet/english/skripts/kl_period.html
48. Herrera-Espiñeira C, Escobar A, Navarro-Espigares JL, Castillo Jde D, García-Pérez L, Godoy-Montijano A. Total knee and hip prosthesis: variables associated with costs. Cir Cir 2013; 81(3): 207–13. (Spanish)
49. *Maravic M, Landais P.* Usefulness of a national hospital database to evaluate the burden of primary joint replacement for coxarthrosis and gonarthrosis in patients aged over 40 years. Osteoarthritis Cartilage 2006; 14(6): 612–5.
50. *Boniforti F.* Assessing hospital cost of joint arthroplasty. Joints 2016; 3(4): 186–90.
51. *Wang K.* Comparison of total knee replacement costs between 2005 and 2010. Osteoarthritis Cartilage 2015; 23: A202.
52. *Liao CY, Chan HT, Chao E, Yang CM, Lu TC.* Comparison of total hip and knee joint replacement in patients with rheumatoid arthritis and osteoarthritis: a nationwide, population-based study. Singapore Med J 2015; 56(1): 58–64.
53. *Lin AC, Chao E, Yang CM, Wen HC, Ma HL, Lu TC.* Costs of staged versus simultaneous bilateral total knee arthroplasty: a population-based study of the Taiwanese National Health Insurance Database. J Orthop Surg Res 2014; 9: 59.
54. *Reuben JD, Meyers SJ, Cox DD, Elliott M, Watson M, Shim SD.* Cost comparison between bilateral simultaneous, staged, and unilateral total joint arthroplasty. J Arthroplasty 1998; 13(2): 172–9.
55. *Meyers SJ, Reuben JD, Cox DD, Watson M.* Inpatient cost of primary total joint arthroplasty. J Arthroplasty 1996; 11(3): 281–5.
56. *Maradit Kremers H, Visscher SL, Moriarty JP, Reinalda MS, Kremers WK, Naessens JM,* et al. Determinants of direct medical costs in primary and revision total knee arthroplasty. Clin Orthop Relat Res 2013; 471(1): 206–14.
57. *Stundner O, Kirksey M, Chiu YL, Mazumdar M, Poultsides L, Gerner P,* et al. Demographics and perioperative outcome in patients with depression and anxiety undergoing total joint arthroplasty: a population-based study. Psychosomatics 2013; 54(2): 149–57.

58. *Vekeman F, LaMori JC, Laliberté F, Nutescu E, Duh MS, Bookhart BK*, et al. In-hospital risk of venous thromboembolism and bleeding and associated costs for patients undergoing total hip or knee arthroplasty. J Med Econ 2012; 15(4): 644–53.
59. *Younger AS, MacLean S, Daniels TR, Penner MJ, Wing KJ, Dunbar M,* et al. Initial hospital-related cost comparison of total ankle replacement and ankle fusion with hip and knee joint replacement. Foot Ankle Int 2015; 36(3): 253–7.
60. *Marshall DA, Wasylak T, Khong H, Parker RD, Faris PD, Frank C*. Measuring the value of total hip and knee arthroplasty: considering costs over the continuum of care. Clin Orthop Relat Res 2012; 470(4): 1065–72.
61. *Walter FL, Bass N, Bock G, Markel DC*. Success of clinical pathways for total joint arthroplasty in a community hospital. Clin Orthop Relat Res 2007; 457: 133–7.
62. *Kim S, Losina E, Solomon DH, Wright J, Katz JN*. Effectiveness of clinical pathways for total knee and total hip arthroplasty: literature review. J Arthroplasty 2003; 18(1): 69–74.
63. *Ho DM, Huo MH*. Are critical pathways and implant standardization programs effective in reducing costs in total knee replacement operations? J Am Coll Surg 2007; 205(1): 97–100.
64. *Zywiel MG, Ulrich SD, Suda AJ, Duncan JL, McGrath MS, Mont MA*. Incidence and cost of intraoperative waste of hip and knee arthroplasty implants. J Arthroplasty 2010; 25(4): 558–62.
65. *Crawford DC, Li CS, Sprague S, Bhandari M*. Clinical and Cost Implications of Inpatient Versus Outpatient Orthopedic Surgeries: A Systematic Review of the Published Literature. Orthop Rev (Pavia) 2015; 7(4): 6177.
66. *Mather RC 3rd, Hug KT, Orlando LA, Watters TS, Koenig L, Nunley RM*, et al. Economic evaluation of access to musculoskeletal care: the case of waiting for total knee arthroplasty. BMC Musculoskelet Disord 2014; 15: 22.
67. *Jain NB*. Joint replacement costs in the era of healthcare reform: commentary on an article by James C. Robinson, PhD, MPH, et al.: "Variability in costs associated with total hip and knee replacement implants". J Bone Joint Surg Am 2012; 94(18): e140(1–2).
68. *Atrey A, Heylen S, Gosling O, Porteous MJ, Haddad FS*. The manufacture of generic replicas of implants for arthroplasty of the hip and knee: is It regulated and will it save money? Bone Joint J 2016; 98-B(7): 892–900.
69. *Healy WL, Iorio R, Lemos MJ, Patch DA, Pfeifer BA, Smiley PM,* et al. Single Price/Case Price Purchasing in orthopaedic surgery: experience at the Lahey Clinic. J Bone Joint Surg Am 2000; 82(5): 607–12.
70. *Okike K, O'Toole RV, Pollak AN, Bishop JA, McAndrew CM, Mehta S,* et al. Survey finds few orthopedic surgeons know the costs of the devices they implant. Health Aff (Millwood) 2014; 33(1): 103–9.
71. *Suter LG, Paltiel AD, Rome BN, Solomon DH, Thornhill TS, Abrams SK*, et al. Placing a price on medical device innovation: the example of total knee arthroplasty. PLoS One 2013; 8(5): e62709.
72. *Republic Health Insurance Fund*. Report on conducted controls in healthcare institutions for 01.01.-30.06.2016. period. Available from: http://www.rfzo.rs/index.php/arhiva-vesti/906-izvrsene-kontrole-do-300616. [accessed 2017 February 1]. (Serbian)
73. *Republic Health Insurance Fund*. Decision on the change of financial plan of the Republic Health Insurance Fund for the year 2016. Available from: http://www.rfzo.rs/download/fin_plan/odluka%20%20izmenama%20FP%20RFZO%20za%202016.%20godinu.pdf. [accessed 2017 February 1]. (Serbian)

Received on November 05, 2016.
Revised on February 03, 2017.
Accepted on February 07, 2017.
Online First March, 2017.