ARTYKUŁ ORYGINALNY / ORIGINAL ARTICLE

Assessment of cardiovascular risk in patients undergoing total joint alloplasty: the CRASH-JOINT study

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Abstract

Background: Risk assessment is of particular importance for patients undergoing surgical interventions. Orthopaedic procedures, especially total joint alloplasty, are major procedures associated with high perioperative risk, as well as one of the highest rates of complications.

Aim: The aim of the present study was to establish the prevalence of classical and non-classical cardiovascular risk factors in patients undergoing total hip or knee alloplasty.

Methods: The CRASH-JOINT (Cardiovascular Risk Assessment ScHeme in JOINT alloplasty) was a prospective, epidemiological study performed in consecutive patients scheduled for total joint (hip or knee) replacement surgery. Patients enrolled into the study were screened for cardiovascular risk factors and had ambulatory blood pressure performed for the diagnosis of hypertension.

Results: The present study enrolled 98 patients. During initial screening eight patients were disqualified from the study and the surgery, in the majority due to the cardiac causes. Sixty-five patients had a hip joint replacement and 25 had knee joint replacement (mean age 63.7 ± 12.2 years, 62.2% female). Fifty (55.6%) patients were diagnosed with arterial hypertension in the past, ten (11.1%) patients had diabetes mellitus, two (2.2%) had a history of myocardial infarction, and family history of cardiovascular disease was present in 24 (26.7%) cases. Mean body mass index (BMI) was 28.0 ± 5.1 kg/m² and 39 (43.3%) patients were overweight, while 28 (31.1%) were obese. Patients undergoing hip replacement were significantly younger (61.8 \pm 12.6 vs. $68.5 \pm$ 10.0 years; p = 0.02), were more often current smokers (24.6% vs. 4.0%; p = 0.03), had significantly lower BMI (26.8 \pm 4.5 vs. 31.2 \pm 5.3 kg/m²; p < 0.0001), and were less often obese (18.5% vs. 64.0%; p < 0.0001). There were no significant differences between patients scheduled for primary surgery and reoperation.

Conclusions: The study showed that classical cardiovascular risk factors in patients undergoing total hip or knee alloplasty have a higher prevalent than in the general population, which can potentially contribute to the higher risk of development of perioperative complications.

Key words: orthopaedics, hip replacement, knee replacement, cardiovascular risk

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INTRODUCTION

Assessment of cardiovascular (CV) risk is a critical issue with population impact. Newest estimations show that 40% of deaths in men and almost 50% in women in Europe are caused by CV disease [1]. The majority of those diseases could be avoided or better treated thanks to proper and

early screening. Therefore, screening and CV risk assessment schemes are widely used and recommended for everyday clinical practice [2].

Risk assessment is of particular importance for patients undergoing surgical interventions, because of the dangers associated with undiagnosed cardiac conditions during opera-

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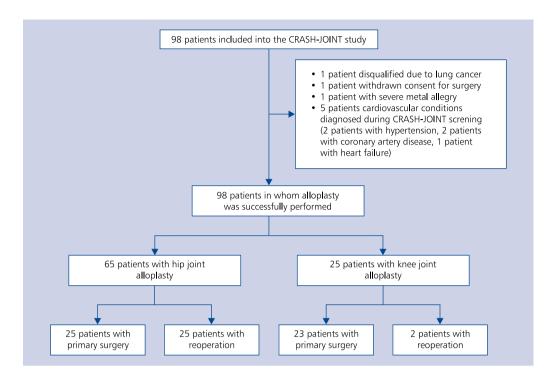


Figure 1. CRASH-JOINT study flow chart

tion, and the additional risk associated with the procedure itself [3]. Cardiac disease is a potential source of complications during every surgery, and the risk of perioperative complications depends on the condition of the patient and the awareness of the doctors performing the procedure. Particular risk may be associated with orthopaedic surgery [4]. Orthopaedic procedures, especially total joint alloplasty, are major operations related to perioperative risk, as well as one of the highest rates of thromboembolic complications, and orthopaedic patients are usually at elevated CV risk [5, 6]. Therefore, in these patients, early assessment and screening are of particular importance. The aim of the present study was to establish the prevalence of classical and non-classical CV risk factors in patients undergoing total hip or knee alloplasty.

METHODS

The CRASH-JOINT (Cardiovascular Risk Assessment ScHeme in JOINT alloplasty) was a prospective, epidemiological study performed in consecutive Polish patients scheduled for total joint (hip or knee) replacement surgery in a tertiary University Hospital. The CRASH-JOINT study is an epidemiological project focused on establishing the prevalence of CV risk factors in patients undergoing total hip or knee alloplasty. The study project is aimed at finding the factors associated with the procedure effectiveness and, in the long-term, patients' prognosis.

The study was performed with respect to the Declaration of Helsinki, and approval from the Ethics Committee by the Medical University of Warsaw was obtained before the begin-

ning of the study. Written, informed consent was obtained from every study participant before the study enrolment.

Study population

Into the study, we enrolled patients who were hospitalised for an elective operation of total hip or knee replacement surgery. All patients were screened for CV risk factors before the surgery and had their medical records re-evaluated after the procedure. Exclusion criteria were: age < 18 or \ge 75 years, disqualification from the operation, the absence of written informed consent, or contraindications for any of the study protocol examinations.

Diagnosis of cardiovascular risk factors

All patients were interviewed, screened, and had their medical records checked for prior diagnosis of CV risk factors, including arterial hypertension, diabetes mellitus, heart failure, previous stroke and myocardial infarction, chronic kidney disease, etc. Diagnosis of the condition was made according to the current guidelines. For example, diagnosis of arterial hypertension was made when office blood pressure (BP) was equal or exceeded the values of 140 mm Hg for systolic blood pressure (SBP) and/or 90 mm Hg for diastolic blood pressure (DBP), and/or the patient had eligible medical records proving the previous diagnosis, and/or the patient was currently taking medications used for hypertension treatment. All patients had a resting electrocardiogram performed and were examined by a qualified physician. Diagnosis of non-classical risk factors was made

using dedicated risk assessment schemes: the Epworth Sleepiness Scale for the diagnosis of excessive daytime sleepiness, consistent with high risk of sleep-disordered breathing, and the Beck Depression Inventory used for diagnosing depression.

ABPM

All study participants were screened for arterial hypertension using ambulatory blood pressure monitoring (ABPM). Patients had ABPM performed before the procedure after a night's rest. The study was performed and scored by a qualified physician before the surgery procedure. Diagnosis of arterial hypertension was made when any of the mean 24-h, awake or asleep BP values exceeded the threshold for normal values used for ABPM scoring. The number of required measurements, measure techniques, and settings were in agreement with the current guidelines for arterial hypertension diagnosis and management of the European Society of Cardiology and European Society of Hypertension [7, 8]. All studies were performed using the BR-102 plus (Schiller AG, Baar, Switzerland), which is a device validated and approved for ABPM studies [9].

Statistical analysis

Statistical analysis was performed using the SPSS v 21.0 (SPSS Inc., Chicago, IL, USA). Continuous data are presented as mean \pm standard deviation and were compared using the Mann-Whitney test or Student's t-test. Categorical variables were analysed using either the χ^2 or Fisher's exact test. A p value of less than 0.05 was considered statistically significant, and the confidence intervals were 95%.

RESULTS

The present study enrolled 98 patients who met the inclusion criteria and were screened for CV risk factors in the CRASH-JOINT study. During the hospitalisation eight patients were disqualified from the surgery (one patient due to newly diagnosed lung cancer, one patient withdrew consent for the surgery, one patient was diagnosed with an allergy to the metal used in the joint prosthesis, and five patients had CV contraindications for surgery newly diagnosed during the CRASH-JOINT screening [two patients had poorly controlled hypertension, two patients had coronary artery disease, and one patient had heart failure]). Therefore, the final analysis covered 90 patients, in whom total joint replacement surgery was performed. Sixty-five patients had hip joint replacement and 25 had knee joint replacement. In 68 (75.6%) cases it was a primary procedure (45 cases in the hip group and 23 cases in the knee group), while 22 patients had reoperation performed (Fig. 1).

When we analysed the baseline characteristics of the study population we found that the mean age of the study group was 63.7 ± 12.2 years, and the majority of patients were female (62.2%). Classical and non-classical CV risk factors were observed in the study group: 50 (55.6%)

Table 1. Baseline characteristics of the study population

Parameter	Value (% or	
	mean ± SD)	
Male sex	34 (37.8%)	
Age [years]	63.7 ± 12.2	
Previously diagnosed arterial hypertension	50 (55.6%)	
Prior myocardial infarction	2 (2.2%)	
Prior stroke or TIA	5 (5.6%)	
Heart failure	4 (4.4%)	
Diabetes mellitus	10 (11.1%)	
Chronic kidney disease	3 (3.3%)	
Asthma or COPD	8 (8.9%)	
Family history of CVD	24 (26.7%)	
Smoking	17 (18.9%)	
Weight [kg]	77.5 ± 15.4	
Height [cm]	166.3 ± 9.1	
BMI [kg/m²]	28.0 ± 5.1	
Normal BMI	23 (25.6%)	
Overweight	39 (43.3%)	
Obesity	28 (31.1%)	
Neck circumference [cm]	37.3 ± 3.6	
Waist [cm]	97.0 ± 13.8	
Hips [cm]	101.9 ± 11.8	
WHR	0.95 ± 0.1	
Abdominal obesity	72 (80.0%)	
Daytime sleepiness	8 (8.9%)	
Depression	28 (31.1%)	
ABPM results:		
Arterial hypertension in ABPM	41 (45.6%)	
24-h SBP [mm Hg]	123.4 ± 12.6	
24-h DBP [mm Hg]	71.6 ± 7.5	
Awake SBP [mm Hg]	124.6 ± 12.6	
Awake DBP [mm Hg]	73.5 ± 8.0	
Sleep SBP [mm Hg]	119.8 ± 14.9	
Sleep DBP [mm Hg]	66.5 ± 8.4	

Data are presented as number (%) or mean ± standard deviation (SD); ABPM — ambulatory blood pressure monitoring; BMI — body mass index; COPD — chronic obstructive pulmonary disease; CVD — cardio-vascular disease; DBP — diastolic blood pressure; SBP — systolic blood pressure; TIA — transient ischaemic attack; WHT — waist/hip ratio

patients were diagnosed with arterial hypertension in the past, 10 (11.1%) patients had diabetes mellitus, two (2.2%) had history of myocardial infarction, five (5.6%) had history of stroke or transient ischaemic attack, and family history of CV disease was present in 24 (26.7%) cases. As for the non-classical CV risk factors, eight (8.9%) patients reported excessive daytime sleepiness and 28 (31.1%) reported symp-

Table 2. Differences between patients undergoing hip and knee alloplasty

Parameter	Hip alloplasty group	Knee alloplasty group	р
	(n = 65)	(n = 25)	
Male sex	28 (43.1%)	7 (28.0%)	0.33
Age [years]	61.8 ± 12.6	68.5 ± 10.0	0.02
Previously diagnosed arterial hypertension	34 (52.3%)	16 (64.0%)	0.34
Prior myocardial infarction	2 (3.1%)	0 (0.0%)	1.00
Prior stroke or TIA	3 (4.6%)	2 (8.0%)	0.62
Heart failure	2 (3.1%)	2 (8.0%)	0.31
Diabetes mellitus	6 (9.2%)	4 (16.0%)	0.46
Chronic kidney disease	3 (4.6%)	0 (0.0%)	0.56
Asthma or COPD	3 (4.6%)	5 (20.0%)	0.04
Family history of CVD	14 (21.5%)	10 (40.0%)	0.11
Smoking	16 (24.6%)	1 (4.0%)	0.03
Weight [kg]	74.2 ± 14.1	86.2 ± 15.5	0.001
Height [cm]	166.3 ± 9.4	166.2 ± 8.2	0.97
BMI [kg/m²]	26.8 ± 4.5	31.2 ± 5.3	< 0.0001
Normal BMI	20 (30.8%)	3 (12.0%)	0.10
Overweight	33 (50.8%)	6 (24.0%)	0.03
Obesity	12 (18.5%)	16 (64.0%)	< 0.0001
Neck circumference [cm]	36.9 ± 3.4	38.3 ± 3.9	0.19
Waist [cm]	95.0 ± 13.3	102.1 ± 14.0	0.05
Hips [cm]	100.0 ± 10.2	107.0 ± 14.1	0.01
WHR	0.95 ± 0.1	0.96 ± 0.1	0.73
Abdominal obesity	49 (75.4%)	23 (92.0%)	0.14
Daytime sleepiness	4 (6.2%)	4 (16.0%)	0.21
Depression	19 (29.2%)	9 (36.0%)	0.62
ABPM results:			
Arterial hypertension in ABPM	29 (44.6%)	12 (48.0%)	0.82
24-h SBP [mm Hg]	122.2 ± 11.5	126.7 ± 14.9	0.17
24-h DBP [mm Hg]	71.3 ± 7.9	72.3 ± 6.3	0.61
Awake SBP [mm Hg]	123.4 ± 12.3	128.2 ± 13.3	0.14
Awake DBP [mm Hg]	73.5 ± 8.4	73.7 ± 7.0	0.70
Sleep SBP [mm Hg]	118.2 ± 13.3	124.4 ± 18.4	0.13
Sleep DBP [mm Hg]	66.0 ± 8.8	67.9 ± 7.1	0.36

Data are presented as number (%) or mean ± standard deviation; Bold indicates statistically significant values; ABPM — ambulatory blood pressure monitoring; BMI — body mass index; COPD — chronic obstructive pulmonary disease; CVD — cardiovascular disease; DBP — diastolic blood pressure; SBP — systolic blood pressure; TIA — transient ischaemic attack; WHT — waist/hip ratio

toms consistent with depressive disorders. Mean body mass index (BMI) was 28.0 ± 5.1 kg/m², and 39 (43.3%) patients were overweight while 28 (31.1%) were obese. According to the waist circumference, abdominal obesity was diagnosed in 72 (80.0%) patients (Table 1).

When we divided patients according to the type of the procedure (hip or knee replacement), we saw several differences between the groups. First of all, patients undergoing hip replacement were significantly younger (61.8 \pm 12.6 vs. 68.5 \pm 10.0 years; p = 0.02) than those in whom total knee alloplasty was performed. Moreover, patients scheduled for hip replacement were more often current smokers (24.6% vs. 4.0%; p = 0.03). Several differences were also noticed regarding anthropometric features. Patients with hip alloplasty had significantly lower BMI (26.8 \pm 4.5 vs. 31.2 \pm 5.3 kg/m²; p < 0.0001), were less often obese (18.5% vs. 64.0%; p < 0.0001), and had lower waist (95.0 \pm 13.3 vs. 102.1 \pm 14.0 cm; p = 0.05) and hip

Table 3. Differences between patients undergoing primary alloplasty or reoperation

Parameter	Primary alloplasty group	Reoperation group (n = 22)	р
	(n = 68)		
Male sex	24 (35.3%)	10 (45.5%)	0.27
Age [years]	63.5 ± 12.6	64.2 ± 11.3	0.87
Previously diagnosed arterial hypertension	37 (54.4%)	13 (59.1%)	0.50
Prior myocardial infarction	2 (2.9%)	0 (0.0%)	0.57
Prior stroke or TIA	4 (5.9%)	1 (4.5%)	0.65
Heart failure	3 (4.4%)	1 (4.5%)	0.68
Diabetes mellitus	7 (10.3%)	3 (13.6%)	0.46
Chronic kidney disease	2 (2.9%)	1 (4.5%)	0.57
Asthma or COPD	7 (10.3%)	1 (4.5%)	0.37
Family history of CVD	21 (30.9%)	3 (13.6%)	0.09
Smoking	12 (17.6%)	5 (22.7%)	0.40
Weight [kg]	77.9 ± 14.7	76.4 ± 17.5	0.52
Height [cm]	166.2 ± 9.3	166.7 ± 8.6	0.71
BMI [kg/m²]	28.2 ± 4.9	27.4 ± 5.7	0.38
Normal BMI	16 (23.5%)	7 (31.8%)	0.31
Overweight	30 (44.1%)	9 (40.9%)	0.50
Obesity	22 (32.4%)	6 (27.3%)	0.44
Neck circumference [cm]	37.2 ± 3.5	37.6 ± 3.9	0.78
Waist [cm]	97.2 ± 13.6	96.4 ± 14.7	0.58
Hips [cm]	102.5 ± 12.2	100.3 ± 10.3	0.30
WHR	0.95 ± 0.8	0.96 ± 0.1	0.89
Abdominal obesity	54 (79.4%)	18 (81.8%)	0.54
Daytime sleepiness	6 (8.8%)	2 (9.1%)	0.63
Depression	24 (35.3%)	4 (18.2%)	0.09
ABPM results:			
Arterial hypertension in ABPM	29 (42.6%)	12 (54.5%)	0.23
24-h SBP [mm Hg]	124.5 ± 13.1	120.4 ± 10.6	0.26
24-h DBP [mm Hg]	71.5 ± 7.1	71.7 ± 8.5	1.00
Awake SBP [mm Hg]	125.2 ± 13.0	123.0 ± 11.7	0.50
Awake DBP [mm Hg]	73.2 ± 7.5	74.4 ± 9.3	0.73
Sleep SBP [mm Hg]	121.2 ± 15.9	116.1 ± 11.4	0.41
Sleep DBP [mm Hg]	66.5 ± 8.6	66.5 ± 8.1	0.87

Data are presented as number (%) or mean ± standard deviation; ABPM — ambulatory blood pressure monitoring; BMI — body mass index; COPD — chronic obstructive pulmonary disease; CVD — cardiovascular disease; DBP — diastolic blood pressure; SBP — systolic blood pressure; TIA — transient ischaemic attack; WHT — waist/hip ratio

 $(100.0 \pm 10.2 \text{ vs. } 107.0 \pm 14.1 \text{ cm}; p = 0.01)$ circumference, than those with knee replacement surgery (Table 2).

We also compared patients with primary alloplasty surgery and those undergoing reoperation. No significant differences regarding CV risk factors were found between the groups. Interestingly, the prevalence of depression was much higher in the primary-surgery group (35.3% vs. 18.2%), but the findings were on the edge of statistical significance (p = 0.09).

ABPM results

When we analysed ABPM results, we saw that abnormal BP values consistent with the diagnosis of hypertension in ABPM were found in 45.6% of patients. Mean 24-h SBP was 123.4 \pm 12.6 mm Hg and mean 24-h DBP was 71.6 \pm 7.5 mm Hg. Mean awake SBP was 124.6 \pm 12.6 mm Hg, and mean awake DBP was 73.5 \pm 8.0 mm Hg, while asleep values were 119.8 \pm 14.9 mm Hg and 66.5 \pm 8.4 mm Hg, respectively, for SBP and DBP.

The results were also analysed separately for patients with hip and knee replacement as well as primary and reoperation groups, but no statistically significant differences were found. The results are presented in Tables 2 and 3.

DISCUSSION

The occurrence of cardiac complications after surgery depends on the risk factors of the patient, the type of operation, and the circumstances of its execution [10]. Surgical factors that influence cardiac risk are associated with invasiveness, the type and the length of operation, as well as changes in deep body temperature, blood loss, and shifts in fluid [11]. Each operation triggers a stress response. This response is initiated by tissue damage, developed with the participation of neuroendocrine factors, and may cause an imbalance between the activity of the sympathetic and parasympathetic. During the operation, the myocardial oxygen consumption increases. The operation also causes changes in the balance between prothrombotic factors and fibrinolytic factors, potentially leading to increased thrombogenicity in coronary arteries. The severity of such changes is proportional to the extent and duration of the intervention. These factors, together with the position of the patient, changes in body temperature, the type of anaesthesia, and bleeding may contribute to the formation of haemodynamic instability leading to myocardial infarction and heart failure. Patient-related factors are usually more important than the kind of operation, but the procedure type also cannot be ignored. In the case of orthopaedic surgery, the perioperative risk is significantly increased [10]. Effective strategies for reducing the risk of cardiac complications in the perioperative period should include assessment of cardiac risk factors, carried out by interviews before surgery. There is no doubt that the intensity of preoperative cardiac evaluation must be tailored to the patient's clinical condition and the urgency of the operation.

In most clinical situations, it is possible to use a more comprehensive, systematic approach to the evaluation of cardiac risk, initially based on the clinical characteristics of the patient and the type of operation, and then supplemented with resting electrocardiogram, laboratory tests, and other non-invasive studies. In the last 30 years, there have been some risk indicators based on multivariate analysis of observational data, which express the relationship between clinical characteristics and perioperative mortality and morbidity from cardiac causes or perioperative complications [12]. The popular schemes were developed by Goldman et al. [13], Detsky et al. [14], and Lee et al. [15].

The CRASH-JOINT study revealed the relatively high prevalence of both classical as well as non-classical CV risk factors in patients undergoing total hip or knee replacement and showed that those factors are more common than in the general population. As was shown by the pre-screening phase, a large percentage of the study group required immediate care

from a cardiologist, and over 8% of patients were disqualified from the surgery mainly due to CV disease. After selection of patients burdened with increased CV risk, we were able to introduce specialist care and therefore improve their prognosis. Multi-specialist care is associated in most cases with better control of the risk factors, which improves the overall health and prognosis of the patients, and also allows the best methods of risk stratification and treatment to be determined, thereby optimising the current procedures. The introduction of complex CV evaluation before orthopaedic surgeries could be useful in facilitating patient care in general practice. Primary prevention of diseases of the CV system is one of the most important elements of patient care. Early diagnosis and implementation of treatment, including lifestyle modification and drug therapy, helps to avoid adverse CV events and prolong the life of patients, consequently minimising the risk of the operation [3]. The CRASH-JOINT screening protocol proved to be efficient and easy to introduce into general practice.

Additional findings from CRASH-JOINT showed some differences between patients undergoing knee and hip replacement, particularly regarding anthropometric features. Patients with knee replacement were shown to have higher BMI, were more likely to be obese, had higher hip and waist circumference, and were younger. These observed differences may be in part associated with higher load put on the knee joint, which leads to deformation and injuries in younger age.

CONCLUSIONS

In conclusion, the CRASH-JOINT study showed that classical and non-classical CV risk factors in patients undergoing total hip or knee alloplasty are more prevalent than in the general population, which can potentially contribute to the increased risk of development of perioperative complications.

Conflict of interest: none declared

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Ocena ryzyka sercowo-naczyniowego u pacjentów poddawanych alloplastyce stawów: badanie CRASH-JOINT

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Streszczenie

Wstęp: Ocena ryzyka ma szczególne znaczenie u pacjentów poddawanych interwencjom chirurgicznym. Zabiegi ortopedyczne, w szczególności całkowita alloplastyka stawów, są operacjami związanymi z wysokim ryzykiem okołooperacyjnym, jak również jednym z najwyższych odsetków powikłań.

Cel: Celem niniejszej pracy było określenie częstości występowania klasycznych i nieklasycznych czynników ryzyka sercowo-naczyniowego u pacjentów poddawanych całkowitej alloplastyce stawu biodrowego lub kolanowego.

Metody: CRASH-JOINT (*Cardiovascular Risk Assessment ScHeme in JOINT alloplasty*) było prospektywnym badaniem epidemiologicznym przeprowadzonym u pacjentów poddawanych operacji całkowitej alloplastyki stawu biodrowego lub kolanowego. Chorzy włączeni do projektu byli badani pod kątem klasycznych i nieklasycznych czynników ryzyka sercowo-naczyniowego i przeprowadzono u nich całodobowe pomiary wartości ciśnienia tętniczego.

Wyniki: Do badania włączono 98 osób. Podczas wstępnej ewaluacji 8 pacjentów zostało wykluczonych z badania i wyłączonych z zabiegu, w większości z powodu przyczyn sercowych. U 65 chorych przeprowadzono wymianę stawu biodrowego i 25 stawu kolanowego (średni wiek 63.7 ± 12.2 roku, 62.2% kobiet). Wśród klasycznych czynników ryzyka zwracało uwagę 50 (55,6%) osób z rozpoznaniem nadciśnienia tętniczego w przeszłości, 10 (11,1%) pacjentów miało cukrzycę, 2 (2,2%) wystąpił zawał serca w przeszłości, a u 24 (26,7%) w wywiadzie rodzinnym zanotowano choroby sercowo-naczyniowe. Średni wskaźnik masy ciała (BMI) wynosił 28.0 ± 5.1 kg/m², nadwagę zaobserwowano u 39 (43,3%) pacjentów, a u 28 (31,1%) — otyłość. Pacjenci poddawani wymianie stawu biodrowego byli istotnie młodsi (61,8 \pm 12,6 vs. 68.5 ± 10.0 lat; p = 0,02), byli częściej palaczami tytoniu (24,6% vs. 4,0%; p = 0,03), mieli istotnie niższe BMI (26,8 \pm 4,5 vs. 31,2 \pm 5,3 kg/m², p < 0,0001) i rzadziej byli otyli (18,5% vs. 64,0%, p < 0,0001). Nie stwierdzono istotnych różnic między pacjentami zakwalifikowanymi do operacji pierwotnej i ponownej reoperacji.

Wnioski: Badanie wykazało, że czynniki ryzyka sercowo-naczyniowego u osób poddawanych całkowitej alloplastyce stawu biodrowego lub kolanowego są obecne częściej niż w populacji ogólnej, co może potencjalnie przyczynić się do podwyższonego ryzyka rozwoju powikłań okołooperacyjnych.

Słowa kluczowe: ortopedia, alloplastyka stawu biodrowego, alloplastyka stawu kolanowego, ryzyko sercowo-naczyniowe Kardiol Pol 2017; 75, 3: 213–220

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