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ARTERIAL STIFFNESS AND CENTRAL AORTAL PRESSURE AS SIGNIFICANT PREDICTORS OF COMPLICATIONS AFTER OFF-PUMP CORONARY ARTERY BYPASS GRAFTING

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ABSTRACT — Some studies have shown that an increase in arterial stiffness and central aortic pressure increase the risk of postoperative complications for off-pump coronary artery bypass grafting (off-pump CABG).
AIM: To determine the significance of arterial stiffness and central aortic pressure indicators for predicting acute kidney injury (AKI) and cardiac events in patients after off-pump CABG.
MATERIALS AND METHODS: An analysis of off-pump CABG outcomes was carried out in 196 patients (mean age 62.7 ± 5.3 years) without clinical signs of chronic kidney disease. The patients were divided into a test (n = 56) and control (n = 140) groups, depending on the presence or absence of AKI, acute coronary syndrome (ACS), or cardiac arrhythmias in the early postoperative period. Pulse wave velocity indicators (PWV) were processed on the carotid-femoral (cfPWV) and brachio-ankle (baPWV) segments, and the results of measuring central aortic pressure (CAP).
RESULTS: It has been proven that the incidence of AKI is significantly higher in patients with higher cfPWV (n <0.001), baPWV (n = 0.034) and systolic aortic pressure (SAP) (n = 0.013). ACS was more often observed in patients with higher SAP (n <0.001) and diastolic (DAP) (n = 0.005) aortic pressure, and cardiac arrhythmias in patients with higher SAP and office systolic pressure (n < 0.001). Based on the results of logistic regression analysis, it was determined (by regression coefficients — B) that an increase in cfPWV by 1 m/s increases the risk of AKI by 85.0%. An increase in SAP by one unit significantly increases the risk of ACS by 111.0% and cardiac arrhythmias by 58.0%. It was shown that the measurement of CAP has a greater diagnostic value than the office measurement of blood pressure.
CONCLUSION: Arterial stiffness is an independent predictor of AKI for off-pump CABG. A decrease in PWV value is accompanied by a decrease in the incidence of AKI. CAP indices have a more significant prognostic value with respect to the likelihood of cardiac events after an off-pump CABG than the data of measurement of blood pressure.

KEYWORDS — arterial stiffness, central aortic pressure, acute kidney injury, acute coronary syndrome, off-pump coronary artery bypass grafting.

INTRODUCTION

Coronary artery bypass grafting (CABG) applied for multivessel disease in patients with coronary heart disease, is still one of the most common methods of myocardial revascularization [1, 2]. However, it is known that this highly traumatic intervention is associated with a high risk of postoperative complications [3]. Their prediction is difficult in patients with comparable demographic indicators and comorbid backgrounds.

To exclude the risk of perioperative complications associated with cardiopulmonary bypass used for on-pump CABG, in patients with preserved cardiac reserve, it is recommended to perform CABG on the beating heart (off-pump CABG) [1, 3]. But even such tactics cannot completely eliminate the risk of life-threatening complications in the early postoperative period.

It is difficult to predict cardiac events (acute coronary syndrome (ACS) or arrhythmias (HR)) or acute kidney injury (AKI) based on the results of standard preoperative examination of patients with coronary artery disease (CHD). However, a number of studies have shown that this category of adverse effects was often associated with impaired organ perfusion in patients with increased central aortic pressure (CAP) and arterial stiffness (AF) [4, 5, 6]. And these indicators with a sufficient degree of reliability can be assessed by non-invasive methods and do not require significant labor costs [7, 8, 9].

In clinical practice, arterial stiffness is assessed in terms of pulse wave velocity (PWV) in elastic (carotid-femoral PWV (cfPWV)) and muscle segments (brachial-ankle PWV (baPWV)) of the arterial bed [10] It has been proven that the cfPWV index, the measurement of which is considered the *gold standard*, is an independent predictor of postoperative complications [8, 9, 10].

MATERIALS AND METHODS

In the period from January 2018 to December 2020 a prospective controlled study was conducted at the clinic of the Department of Anesthesia and Resuscitation (Volgograd Medical University, Russia).

The results of planned off-pump CABG for coronary artery disease in patients with multivessel coronary artery disease were analyzed. All patients gave informed consent for participating in the study and publishing the results under assurance of confidentiality. The study was approved by the Volgograd Regional Independent Ethics Committee (IRB 00005839 IORG 0004900 [ref: 109/2017/12/07]).

Inclusion criteria:

1. Patients over 18 years of age, of both sexes scheduled to off-pump CABG;
2. Presence of a valid study of CAP and arterial stiffness.

Exclusion criteria:

1. Patients who underwent on-pump CABG;
2. Placement of a shunt;
3. Patients with permanent atrial fibrillation (AF), chronic kidney disease (CKD) stages 3–5, obesity II–III degree and mental disorders.

A total of 237 patients who met the inclusion criteria were analyzed. 41 patients were excluded from the study, who had one or more signs that met the exclusion criteria: 11 patients were diagnosed with permanent AF, 9 with CKD stage 3 (glomerular filtration rate (GFR) less than 60 ml/min/1.73 m^2), in 26 — obesity of II–III degree (BMI ≥ 35.0 kg/m^2), in 5 — one shunt was imposed, in 2 patients due to clinical necessity (unstable hemodynamics) on-pump CABG was performed. Thus, the outcomes of surgical treatment in 196 patients were finally processed.

The primary endpoint was death, clinical signs of AKI, acute coronary syndrome (ACS) or arrhythmia (AF, paroxysmal ventricular tachycardia (PVT)).

All patients were divided into the main and control groups. The main group (n = 56) included patients in whom studied complications (AKI, ACS, or clinically significant arrhythmia (ARR)) were diagnosed in the early postoperative period. The control group (n = 140) included patients without these complications. The main group was subdivided into subgroups: AKI-subgroup (n = 28), ACS-subgroup (n = 12) and ARR-subgroup (n = 25). In 9 patients, the postoperative period was complicated by the development of AKI and persistent cardiac arrhythmias, which accounts for their inclusion both in the AKI-subgroup and the ARR-subgroup for a univariate analysis.

In all patients, a planned preoperative examination was performed including the assessment of anthropometric parameters, the data of standard laboratory (including lipid, carbohydrate and protein metabolism, biomarkers of myocardial damage) and instrumental studies (ECG, echocardiography, coronary angiography, ultrasonography of the carotid arteries, assessment of the function of external respiration, etc.).

In the morning, in a state of physical and mental rest, each patient underwent 3-fold (to ensure data validity) measurements of cfPWV and baPWV using the Vicorder system (Skidmore Industries, UK). The indicators of CAP (systolic aortic (SAP), diastolic aortic (DAP) and pulse aortic pressure (PAP)) were determined after daily monitoring of blood pressure.

During off-pump CABG, all patients received general anesthesia (total intravenous anesthesia + inhalation anesthesia + narcotic analgesics with or without thoracic epidural analgesia).

Acute kidney injury was established with an increase in blood plasma creatinine by 2 times or more from the initial values and a urine output level of less than 0.5 ml/kg/h for 12 hours or more (2–3 degree AKI according to KDIGO criteria [11]). When diagnosing acute coronary syndrome (ACS), we took into account the appearance or expansion of zones of hypokinesis (according to echocardiography), an increase in ischemic changes on an electrocardiogram, an increase in the level of serum markers of myocardial necrosis (troponin-T). Arrhythmia episodes were taken into account if they lasted 24 hours or more and required medical correction.

Statistical processing of the obtained results using Statistica 10 software (StatSoft Inc., USA), after checking for normal distribution by the Shapiro-Wilk test, was performed using parametric (Student's t-test for unrelated groups) with normal distribution and nonparametric tests (U-test Mann-Whitney, Fisher's exact test) when deviating from the normal distribution. To identify independent predictors of AKI and cardiac events, multiple regression analysis was used with the determination of β-regression coefficients (B). The difference between the compared groups of variables of more than 95% ($p < 0.05$) was considered a statistically significant difference.

RESULTS AND DISCUSSION

In total, more than 50 variables were analyzed in 196 patients enrolled in the study during the entire period of hospitalization. Clinical and demographic data are presented in Table 1. None of the patients had a history of CKD or a permanent form of cardiac arrhythmias, all were in a stable condition and underwent planned preoperative preparation.

As shown in Table 1, the majority of those operated were men (83.7% of men versus 16.3% of women) and the average age of patients exceeded 60 years (62.4 ± 5.4 years). There was a fairly significant number of patients with overweight (25.0–29.9 kg/m^2) and

Table 1. *Clinical and demographic parameters*

Parameters	Study groups		P
	Main group (n=56)	Control group (n = 140)	
Age (mean±SD)	61.6±5,7	62.9±4,8	0.093
Sex (F / M)	9/47	23/117	0.569
BMI (mean±SD)	28.3 (27.5-30.2)	28.1 (25.1-29.1)	0.189
GFR, ml / min / 1.73m^2 (mean±SD)	85.9±9.1	87.4±8.3	0.364
Operation duration (mean±SD)	280.1±69.6	265.0±66.7	0.125
General anesthesia:			
Without TEA, n (%)	46 (82.1)	109 (77.9)	0.323
With TEA, n (%)	10 (17.9)	31 (22.1)	
Comorbidities:			
Hypertension, n (%)	32 (57.1)	81 (57.9)	0.526
DM, n (%)	19 (33.9)	41 (29.3)	0.318
COPD, n (%)	6 (10.7)	13 (9.3)	0.472
CCI, n (%)	14 (25.0)	27 (19.3)	0.241

Note: *BMI — Body mass index; TEA — Thoracic epidural analgesia: GFR — Glomerular filtration rate; DM — Diabetes mellitus; COPD — Chronic obstructive pulmonary disease; CCI — Chronic cerebral ischemia; SD — Standard deviation.*

obesity of the 1st degree (30.0–34.9 kg/m^2) (68.9% and 16.8% of observations, respectively), which somewhat prolonged operative duration due to the difficulty of surgical entry. Average off-pump CABG for patients included in the study was estimated as 273.1 ± 65.3 minutes.

An unfavorable comorbid status was observed in 100% of patients. Arterial hypertension was diagnosed in 57.7% of patients, type 2 diabetes mellitus in 30.6%, chronic obstructive pulmonary disease in 9.7%, and chronic cerebral ischemia in 20.9% of patients. Comparison groups for the studied parameters were comparable (p> 0.05).

Comparative analysis of PWV, CAP and blood pressure (BP) in patients of the study subgroups is presented in Tables 2, 3 and 4. In patients in whom the early postoperative period was complicated by AKI (Table 2), in the preoperative period, there were higher indicators of arterial stiffness in elastic and muscle segments of the arterial bed, as indicated by significantly higher values of cfPWV and baPWV (13.4 (13.3: 14.0) versus 8.9 (7.6; 10.6) m/s (p < 0.001) and 15.1 (14.6; 15.9) versus 10.1 (9.2; 11.9) m/s (p = 0.034), respectively). Higher levels of CAP and BP were found in patients with AKI, but a statistically significant difference was found only in SAP (131 (128; 142) versus 119 (110; 123) mm Hg, p = 0.013).

Comparative analysis of the data obtained from patients with ACS and without it (Table 3) revealed that significant differences were revealed only in terms of CAP. In patients with ACS, the SAP and DAP values were significantly higher (132 (127; 142) versus 120 (118; 129) mm Hg (p < 0.001) and 88 (83; 93) versus 79 (76: 83) mm Hg (p = 0.005), respectively) than in patients without ACS. Arterial stiffness and blood pressure were comparable.

Clinically significant arrhythmias were found in patients who had higher rates of CAP in the preoperative period (Table 4). In patients of this category, significantly higher indicators of SAP were revealed (139 (134: 142) versus 119 (110; 123) mm Hg, p <0.001) than in patients without this postoperative complication. Indicators of arterial stiffness and blood pressure did not significantly affect the incidence of arrhythmia.

It is recognized by many researchers that the use of multivariate tests can lead to an increase in the risk of type I error, but they allow to perform the modeling process and reveal the power of each predictor in relation to an increase in the risk of an adverse event.

Table 5 shows the results of the logistic regression analysis of the identified predictors of AKI and cardiovascular events. The most significant predictor of AKI was pulse wave velocity (cfPWV), with an increase of 1 m/s; the risk of developing this complication increased by 85.0%. The CAP and BP data did not have a significant prognostic value for AKI.

When predicting cardiac events, it is advisable to focus on the indicators of CAP. Hence, an increase in SAP by 10 mm Hg significantly increase the risk of ACS by 111.0%, and the risk of developing clinically significant arrhythmias by 44.0% of cases.

Table 2. *Comparative analysis of the parameters of PWV, central aortic pressure and blood pressure in patients with and without acute kidney injury (AKI)*

Parameters	AKI Me(IQR), n=28	No AKI Me(IQR), n=168	P
cfPWV, m / s	13.4 (13.3: 14.0)	8.9 (7.6; 10.6)	<0.001*
baPWV, m / s	15.1 (14.6; 15.9)	10.1 (9.2; 11.9)	0.034*
SAP, mm Hg	131 (128; 142)	119 (110; 123)	0.013*
DAP, mm Hg	87 (84,5; 95)	79,5 (71; 82)	0.078
PAP, mm Hg	44 (36; 45)	39,5 (36; 40,5)	0.746
SBP, mm Hg	135 (122; 141)	128 (119; 136)	0.067
DBP, mm Hg	85 (74: 93)	79 (72; 84)	0.071
PBP, mm Hg	50 (45; 56)	49 (45; 54)	0.518

Note: **P<0.05, statistically significant; cfPWV — carotid-femoral PWV; baPWV — brachial-ankle PWV; SAP, DAP and PAP — systolic, diastolic and pulse aortic pressure, respectively; SBP, DBP and PBP — systolic, diastolic and pulse blood pressure, respectively.*

Table 3. *Comparative analysis of the parameters of PWV, central aortic pressure and blood pressure in patients with and without acute coronary syndrome (ACS)*

Parameters	ACS Me(IQR), n=12	No ACS Me(IQR), n=184	P
cfPWV, m / s	10.0 (9.4; 12.0)	9.7 (9.3; 11.5)	0.491
baPWV, m / s	12.1 (9.9; 12.9)	10.1 (9.4; 12.5)	0.207
SAP, mm Hg	132 (127; 142)	120 (118; 129)	<0.001*
DAP, mm Hg	88 (83; 93)	79 (76: 83)	0.005*
PAP, mm Hg	45 (38; 48)	41 (34; 43)	0.116
SBP, mm Hg	133 (132; 141)	129 (125; 140)	0.801
DBP, mm Hg	86 (83; 92)	78 (73: 88)	0.746
PBP, mm Hg	47 (45; 53)	51 (47: 54)	0.440

Table 4. *Comparative analysis of the parameters of PWV, central aortic pressure and blood pressure in patients with and without cardiac arrhythmias (ARR)*

Parameters	ARR Me(IQR), n=25	No ARR Me(IQR), n=171	P
cfPWV, m / s	10.6 (9.1; 12.6)	9.1 (7.9; 10.8)	0.198
baPWV, m / s	11.4 (10.2; 14.4)	10.2 (9.4; 12.2)	0.597
SAP, mm Hg	139 (134:142)	119 (110; 123)	<0.001*
DAP, mm Hg	88 (80; 91)	80 (71; 82)	0.305
PAP, mm Hg	48 (41; 59)	37 (36; 42)	<0.001*
SBP, mm Hg	132 (131; 139)	127 (116; 134)	0.112
DBP, mm Hg	80 (77; 84)	78 (70; 84)	0.142
PBP, mm Hg	52 (50; 58)	49 (45; 52)	0.251

AKI and adverse cardiac events are the most common complications of off-pump CABG that require preventive measures.

This is one of the few studies investigating the relationship between arterial stiffness and AKI and between CAP and cardiac events after planned off-pump CABG. However, there are a number of studies confirming the relationship between increased PWV and renal dysfunction [4, 8]. So, S.A. Greenwood et al (2019) proved in their work that an increase in PWV is an independent risk factor for AKI after CABG [4]. Despite this, there are studies that describe an insignificant correlation between arterial stiffness and AKI [12]. But our study is larger than the sample size of E.

Table 5. *Indicators of logistic regression analysis of predictors of acute kidney injury, acute coronary syndrome and cardiac arrhythmias*

Complication	Predictor	B	SE	Exp(B)	95% CI		P
AKI	cfPWV	0.107	0.021	0.846	0.396	0.916	<0.001*
	baPWV	0.042	0.012	0.092	-0.119	0.491	0.635
ACS	SAP	0.021	0.003	1.113	0.085	0.293	<0.001*
	DAP	0.009	0.008	0.353	0.300	-0.997	0.181
	PAP	0.090	0.006	0.153	0.160	0.184	0.004*
ARR	SAP	0.015	0.001	0.557	0.444	0.818	<0.001*
	DAP	0.006	0.002	0.167	-0.168	2.709	0.090
	PAP	0.006	0.003	0.079	-0.546	2.718	0.301

Note: *SE — standard error; Exp(B) — regression coefficient; CI — confidence interval.*

Kidher et al. (2014). We have demonstrated that an increase in the risk of AKI is observed with an increase of 1 m/s PWV both in the elastic and in the muscular segment of the arterial bed (by 66.0% and 31.0%, respectively), which may be associated with a violation perfusion and barotrauma of the renal glomeruli [13].

There are many studies devoted to determining the relationship between the indicators of CAP and the risk of AKI and cardiovascular complications [6, 8, 9, 14], but there are not enough works that would determine the significance of these indicators in the perioperative period. Some studies have identified a close direct correlation between CAP and AKI [15], but in our study we did not find such a relationship, possibly due to the small sample size.

It is known that CAP, like arterial stiffness, is an independent predictor of cardiovascular events [8, 15]. We have proved that the CAP indicators are superior to the results of traditional blood pressure measurements in terms of the accuracy of ACS prediction. The expediency of using indicators of CAP, and not blood pressure, is also proved by other authors in their works [10]. And only in relation to the risk of postoperative arrhythmias, the use of CAP and standard blood pressure did we show a comparable prognostic value.

In our work, like many other authors, we recommend using preoperative monitoring of arterial stiffness and CAP in patients who are planned to undergo off-pump CABG in order to predict the development of AKI and adverse cardiac events. Moreover, it does not require significant material or labor costs.

Some limitations must be recognized. Firstly, the results of this study are based on a relatively small sample and, secondly, the data were processed only in patients with a low risk of AKI or cardiac events, who had CABG without cardiopulmonary bypass. Therefore, for widespread introduction of the obtained results into clinical practice, it is necessary to confirm them in large multicenter studies.

CONCLUSION

Arterial stiffness is an independent predictor of AKI in off-pump CABG. A decrease in PWV indicators is accompanied by a decrease in the incidence of AKI. Indicators of CAP have a more significant prognostic value than data of blood pressure in relation to the likelihood of cardiac events after off-pump CABG.

Conflict of interests

The authors state that they have no conflicts of interests.

Contributors

MIT and AMS collected, analysed, and interpreted data and made the figures. ASP did the literature review and collected data. AVE and YuIV collected data and made the figures. MIT interpreted and analysed the data. MIT, ASP, AVE, YuIV and AMS prepared the manuscript for submission.

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