Low output syndrome following aortic valve replacement. Predictors and prognosis

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Abstract

Introduction: Low output syndrome (LOS) is a dangerous postoperative complication, which significantly worsens the prognosis; it is an essential risk factor of postoperative death. The aim of the study was to analyze the predictors of postoperative low cardiac output syndrome in patients subjected to aortic valve replacement due to aortic stenosis or regurgitation.

Material and methods: Three hundred (300) patients with significant isolated aortic valve defect due to either aortic stenosis (n=150) or regurgitation (n=150), who underwent isolated aortic valve replacement were included in the study. Low cardiac output syndrome (LOS) was defined as the need for high dosages of inotropic medication, and/or intra-aortic balloon pumping to sustain adequate hemodynamic status.

Results: Postoperative low cardiac output syndrome was developed in 86 patients (28.6%), including 39 patients with aortic stenosis (26.0%) and 47 patients with aortic regurgitation (31.3%). We selected the following independent predictors of postoperative LOS (odds ratio in parentheses): (1) aortic stenosis group – advanced age (4.7), end-systolic (5.5) and end-diastolic intraventricular septum thickness (4.2) before the surgery, LVEF ≤50% (5.4) and insignificant mitral regurgitation (4.1) in the early postoperative period; (2) aortic regurgitation group – obesity (4.8), left ventricular end-systolic (4.5) and end-diastolic diameters (6.4) in the preoperative period and left ventricular end-systolic (4.7) and end-diastolic diameters (6.1), and left ventricular ejection fraction ≤50% (7.2) in the early postoperative period.

Conclusions: The patients at high risk for the development of low cardiac output syndrome should be the focus of trials of new techniques of myocardial protection to effectively resuscitate the ischemic myocardium and optimization of preexisting heart failure symptoms.

Key words: aortic valve defect, aortic valve replacement, low output syndrome, predictors.

Introduction

Presently, as a result of essential development of invasive cardiology and methods of pharmacological treatments, cardiac surgeons have

increasingly encountered complications with operating on elderly patients in severe conditions with very advanced heart disease and many coexistent diseases. Thereby, complications such as postoperative atrial fibrillation, delirium, mild renal failure and respiratory disorders can been observed more often. Despite of intensive development of devices and techniques of cardiac surgery and experienced cardiac surgeons, we cannot observe significant decrease of postoperative complications and mortality. On contrary – operating patients with more and more sever conditions causes the increase of early and long-term mortality [1, 2].

Low output syndrome (LOS) is one of the most dangerous postoperative complications, which significantly worsens the postoperative hemodynamic patient's condition, increase duration of intensive care unit (ICU) and hospitalization stay, and significantly worsens the prognosis, being an essential risk factor of postoperative death. In order to decrease this risk authors have tried to select independent predictors of postoperative LOS. In the available literature the following impact factors are *inter alia* mentioned: preoperative renal failure, low left ventricular ejection fraction (<35%), advanced age (>70 years), extracorporeal circulation time, diseased duration (in case of valvular diseases), aortic cross clamping time, repeat surgery, and recent myocardial infarction (especially in case of surgical revascularization) [3-5].

The aim of the study was to analyze the predictors of postoperative low cardiac output syndrome in patients subjected to aortic valve replacement due to aortic stenosis or regurgitation.

Material and methods

Patients

Three hundred patients with significant isolated aortic valve defect due to either aortic stenosis (n=150) or regurgitation (n=150), who underwent aortic valve replacement between 1999 and 2004 in the Department of Cardiac Surgery, 1st Chair of Cardiology and Cardiac Surgery in Lodz, Poland, were included in the study. All the study subjects signed the informed consent form before inclusion in the study. The study has been approved by the local Ethics Committee.

The mean age of the patients was 61.5±5.4 years; there were 143 (47.67%) men and 157 (52.33%) women. The mean Body Surface Area (BSA) and Body Mass Index (BMI) were 1.87±0.21 and 26.75±3.42 respectively, and mean preoperative ejection fraction (EF) was 49.13±7.8%. There were the following concomitant diseases in this group of patients: arterial hypertension (n=195; 64.7%), diabetes mellitus (n=60; 20%), renal failure (n=11; 3.67%) and severe heart failures with LVEF ≤35% (n=51; 17%).

All patients with the following conditions were excluded from the study: aortic valve defect in the course of infective valve defect, aortic valve defect as a result of myocardial infarction complication, a history of myocardial infarction or cerebrovascular event, a history of previous cardiac surgery, subjection to one-step surgery of other valve replacement/plastics and/or surgical revascularization, surgery in emergency/urgent mode, a history of preoperative arrhythmias (e.g. atrial fibrillation/flutter, ventricular arrhythmias, receiving antiarrhythmic drugs), or other significant co-existent conditions (e.g. severe renal, pulmonary diseases, neoplasms).

Each patient qualified for the aortic valve replacement underwent coronary angiography (on average 33±7.7 hours before the surgery, with a range of 19-63 hours), and no significant changes in coronary arteries were found. For each patient included in the study, 2-mode and Doppler echocardiographic examinations were performed in the preoperative period (up to 48 hours before the operation), in the early postoperative period (between 4 and 21 days following surgery; on average after 9 days), and in long-term observation as a follow-up examination (between 18 and 24 months after the surgery; on average after 21 months). The following echocardiographic parameters were evaluated: left ventricular ejection fraction (LVEF), left ventricular end-systolic and end-diastolic diameters (LVESd and LVEDd), end-systolic and end-distolic intraventricular septum thickness (ESIVST and EDIVST), left atrium dimension (LAd), and mean and maximal transvalvular gradient for patients with aortic stenosis. All investigations were performed on Philips Hewlett Packard Sonos 2000 and ACUSON Sequoia Echo C256 ultrasounds systems. The detailed characteristics of included patients are showed in Table I.

Other heart valves were also evaluated during the echocardiographic examinations. We did not observe any indications for the replacement/plastics of mitral and/or tricuspid valves in the examinations. The frequencies of co-existence of other heart valve defects are presented in Table I.

Surgical intervention

Each patients included in the study was subjected to aortic valve replacement (AVR) in the conditions of extracorporeal circulation. Following the removal of the native valve, all patients were implanted with mechanical valves from St. Jude Medical (St. Paul, MN, USA). Valve sizes ranged from 19 to 31 mm. All patients subjected to AVR were operated on normothermia with the use of cold crystalloid cardioplegia.

Low cardiac output syndrome evaluation

Low cardiac output syndrome (LOS) was defined as the need for high dosages of inotropic medication,

Table I. Detailed characteristics of the 300 patients included in the study

	AS	AR	p-value
n	150	150	–
sex (M/F) n (%)	73 [48.7%]/77 [51.3%]	70 [46.7%]/80 [53.3%]	–
age (years)	63.33±9.85	59.61±10.37	**<0.05**
weight (kg)	74.17±13.98	72.42±11.81	NS
BMI (kg/m^2)	27.35±4.35	26.57±3,81	**=0.02**
BSA	1.89±0.19	1.86±0.11	**<0.05**
max. gradient	86.54±20.6	–	–
LVEF (cm)	49.42±10.47	48.99±9.47	NS
LVESd (cm)	3.48±0.73	4.27±0.85	**<0.001**
LVEDd (cm)	5.12±0.77	5.97±0.94	**<0.001**
ESIVST (cm)	1.8±0.2	1.65±0.17	**<0.005**
EDIVST (cm)	1.43±0,16	1.31±0.15	**<0.001**
LAd (cm)	4.2±0.58	4.42±0.66	**<0.05**
MR n (%)			
0 degree	58 (38.67%)	49 (32.67%)	NS
I degree	58 (38.67%)	60 (40.0%)	NS
I/II degree	21 (14.0%)	13 (8.67%)	**<0.02**
II degree	7 (4.67%)	26 (17.33%)	**<0.001**
II/III degree	6 (4.0%)	2 (1.33%)	NS
TR n (%)			
0 degree	28 (18.7%)	22 (14.7%)	NS
I degree	38 (25.33%)	27 (18.0%)	**<0.01**
I/II degree	57 (38.0%)	54 (36.0%)	NS
II degree	21 (14.0%)	40 (26.7%)	**<0.01**
II/III degree	6 (4.0%)	7 (4.67%)	NS
HA n (%)	94 (62.67%)	101 (67.33%)	NS
DM n (%)	29 (19.33%)	31 (20.67%)	NS
HF n (%)			
LVEF ≥50%	77	80	
LVEF (35-50%)	45	47	
LVEF ≤35%	28	23	NS
RF n (%)	5 (3.33%)	6 (4.0%)	NS

*(*BSA – body surface area; BMI – body mass index; LVEF – left ventricle ejection fraction; LVESd – left ventricular end systolic dimension; LVEDd – left ventricular end diastolic dimension; ESIVST – end-systolic intraventricular septum thickness; EDIVST – end-diastolic intraventricular septum thickness; Lad – left atrium dimension; MR – mitral regurgitation; TR – tricuspid regurgitation; HA – arterial hypertension; DM – diabetes mellitus; HF – heart failure; RF – renal failure)*

and/or intra-aortic balloon pumping to sustain adequate hemodynamic status.

Statistical analysis

Statistical analyses were performed with STATISTICA PL 7.0 (StatSoft, Poland) and SPSS 12.0 Software (SPSS Inc., Chicago, IL, USA). Normality was tested using Shapiro-Wilk's test. The association between potential risk factors and mortality rate was first evaluated by univariate analysis. For categorical variables, chi-square test was used. The diagnostic utility of continuous risk factors was estimated through the use of receiver-operating characteristic (ROC) curves. Results were expressed in terms of the area under the curve (AUC) with a 95% confidence interval (CI) for this area. Factors significant to at least $p<0.10$ were then analyzed using multivariate logistic regression (odds

ratio (OR), ±95% CI, p-value), which was used to identify the independent clinical predictors of postoperative AF [6, 7].

Results

Postoperative low cardiac output syndrome developed in 86 patients (28.6%), including 39 patients with aortic stenosis (26.0%) and 47 patients with aortic regurgitation (31.3%).

Table II. Pre- and early postoperative significant risk factors of low cardiac output syndrome following aortic valve replacement due to aortic stenosis

Predictor	p-value	Adjusted odds ratio	95% confidence interval
preoperative			
age ≥70 years*	<0.005	4.7	1.8-8.5
BMI ≥30 kg/m^2	<0.05	1.8	1.2-2.1
ESIVST ≥1.8 cm*	<0.001	5.5	2.2-14.1
EDIVST ≥1.4 cm*	<0.002	4.2	1.6-9.4
LAd	<0.02	1.6	1.9-3.8
MR	<0.05	1.9	1.5-3.3
TR	<0.05	1.5	1.2-1.9
HF	<0.02	1.7	1.4-3.7
early postoperative			
LVEF ≤50%*	<0.001	5.4	2.1-12.1
ESIVST ≥1.8 cm	<0.05	1.7	1.4-3.4
EDIVST ≥1.4 cm	<0.05	1.9	1.7-3.4
MR*	<0.002	4.1	2.1-11.2

**Independent risk factors*

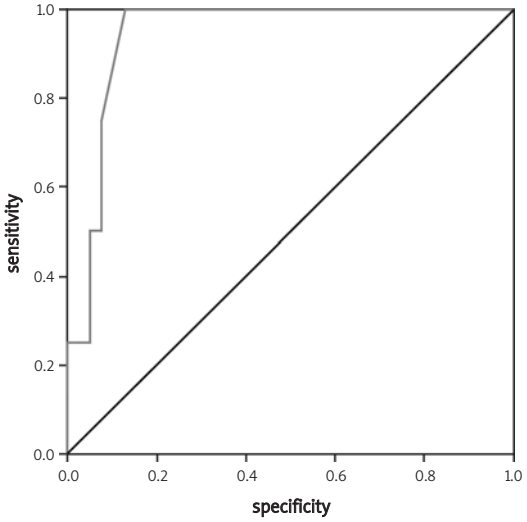

Figure 1. Low cardiac output syndrome in postoperative period significantly (p<0.001) differentiates patients from aortic stenosis group from the death point of view (AUC=0.942)

Patients with aortic stenosis

According to statistical analysis, factors significantly associated with LOS in patients subjected to aortic valve replacement due to aortic stenosis were: age ≥70 years (p<0.005), BMI ≥30 kg/m^2 (p<0.05), heart failure in the history (p<0.02), end-systolic (p<0.001) and end-diastolic intraventricular septum thickness (p<0.002) (respectively ESIVST ≥1.8 cm and EDIVST ≥1.4 cm), left atrium dimension ≥4.2 cm (p<0.02), insignificant mitral and tricuspid regurgitation (p<0.05 for both parameters) in the preoperative period, and LVEF ≤50% (p<0.001), ESIVST ≥1.8 cm (p<0.05), EDIVST ≥1.4 cm (p<0.05), and insignificant mitral regurgitation (p<0.002) in the early postoperative period.

Postoperative low cardiac output syndrome, in comparison with the conditions of the remaining 111 patients (74%) without postoperative LOS, was associated with: an increase in the length of ICU and hospital stay (respectively 3.41±3.33 vs. 2.46±2.11 days [p<0.001] and 13.99±7.12 vs. 10.91±4.61 days [p<0.001]); and early and long-term postoperative mortality (4 [10.3%] vs. 4 [3.6%] deaths (p<0.001) and 4 [11.4%] vs. 5 [4.7%] (p<0.001) in LOS (+) and LOS (–) groups respectively).

Multivariate logistic regression analysis identified 5 independent predictors of postoperative low cardiac output syndrome in patients with aortic stenosis subjected to AVR: advanced age (70 years and more), end-systolic and end-diastolic intraventricular septum thickness (≥1.8 cm and ≥1.4 cm respectively) before the surgery, and LVEF ≤50% and insignificant mitral regurgitation in the early postoperative period (Table II).

We showed that postoperative low output syndrome was an independent risk factor of postoperative death (OR=7.5; 95%CI 1.9-14.8; p<0.001) (Figure 1).

Patients with aortic regurgitation

According to statistical analysis, factors significantly associated with LOS in patients subjected to aortic valve replacement due to aortic regurgitation were: age ≥70 years (p<0.05), BMI ≥30 kg/m^2 (p<0.001), left ventricular ejection fraction ≤50% (p<0.02), left ventricular end-systolic and end-diastolic diameters (≥4.15 cm, p<0.005 and ≥5.9 cm, p<0.001 respectively), end-systolic and end-diastolic intraventricular septum thickness (ESIVST ≥1.6 cm, p<0.03 and EDIVST ≥1.35 cm, p<0.05 respectively), insignificant tricuspid regurgitation (p<0.05) in the preoperative period, heart failure in the history (p<0.02), and LVEF ≤50% (p<0.001), and LVESd and LVEDd (≥4.05 cm, p<0.005 and ≥5.65 cm, p<0.002 respectively) in the early postoperative period.

Postoperative low cardiac output syndrome, in comparison with the conditions of the remaining

103 patients (68.7%) without postoperative LOS, was associated with: an increase in the length of ICU and hospital stay (respectively 3.41±3.33 vs. 2.46±2.11 days (p<0.001) and 13.99±7.12 vs. 10.91±4.61 days (p<0.001)); and early and long-term postoperative mortality (4 [10.3%] vs. 4 [3.6%] deaths (p<0.001) and 4 [11.4%] vs. 5 [4.7%] (p<0.001) in LOS (+) and LOS (–) groups respectively).

Multivariate logistic regression analysis identified six independent predictors of postoperative LOS in patients with aortic regurgitation subjected to AVR: BMI ≥30 kg/m^2, left ventricular end-systolic and end-diastolic diameters in the pre- and early postoperative periods and left ventricular ejection fraction ≤50% in the early postoperative period (Table III).

On the basis of statistical analysis we observed that postoperative low output syndrome was an independent risk factor of postoperative death in patients subjected to AVR due to aortic regurgitation (OR=8.1; 95%CI 2.3-15.1; p<0.001) (Figure 2).

Discussion

Low cardiac output syndrome is a common complication following cardiac surgery, significantly increasing the length of ICU and hospital stay and, more importantly, the risk of death. We observed that advanced age, high BMI, low left ventricular ejection fraction before and following surgery, changes of hemodynamic parameters and co-existence of other, insignificant valve defects significantly increased the risk of postoperative low output syndrome.

There are only few available studies presenting the predictors of LOS in patients subjected to cardiac surgery. In the Sato et al. study, the authors examined 145 cases including 76 patients who underwent MVR (*Mitral Valve Replacement*), 42 AVR and 27 DVR (*Double Valve Replacement*). On the basis of statistical analysis they selected *inter alia* the following predictors of postoperative LOS: (1) MVR group: technical trouble, extracorporeal circulation time (ECCT), change of myocardial preservation methods, diseased duration, aortic cross clamping time; (2) AVR group: left ventricular myocardial mass index (LVMMI), ECCT, cardiac failure, NYHA (*New York Heart Association*) class, and in (3) DVR group: LVEDP (*Left Ventricular End Diastolic Pressure*), LVMMI, NYHA class, left ventricular diastolic eccentricity ratio, and ECCT. They also observed that preoperative ergometer exercise study during cardiac catheterization was useful in prediction of postoperative outcomes, especially in the MVR group [3].

In another study by Rao et al., the authors aimed to identify patients at risk for the development of low cardiac output syndrome after coronary artery bypass. LOS was defined as the need for postoperative intraaortic balloon pump or inotropic support for longer than 30 minutes in the intensive care unit to maintain the systolic blood pressure greater than 90 mm Hg and the cardiac index greater than 2.2 l/min per square meter. They included 4558 consecutive patients who underwent isolated coronary artery bypass grafting. The overall prevalence of low cardiac output syndrome was 9.1% (n=412). The operative mortality rate was

Table III. Pre- and early postoperative significant risk factors of low cardiac output syndrome following aortic valve replacement due to aortic regurgitation

Predictor	p-value	Adjusted odds ratio	95% confidence interval
preoperative			
age ≥70 years	<0.05	1.9	1.8-3.3
BMI ≥30 kg/m^2*	<0.001	4.8	2.3-5.1
LVEF ≤50%	<0.02	1.8	1.9-3.3
LVESd ≥4.15 cm*	<0.005	4.5	2.2-9.4
LVEDd ≥5.90 cm*	<0.001	6.4	1.9-11.9
ESIVST ≥1.6 cm	<0.03	1.5	1.6-2.8
EDIVST ≥1.35 cm	<0.05	1.6	1.7-4.1
TR	<0.05	1.5	1.4-2.9
HF	<0.02	1.7	1.6-3.5
early postoperative			
LVEF ≤50%*	<0.001	7.2	2.2-21.2
LVESd ≥4.15 cm*	<0.005	4.7	1.9-10.2
LVEDd ≥5.90 cm*	<0.002	6.1	1.8-9.9

**Independent risk factors*

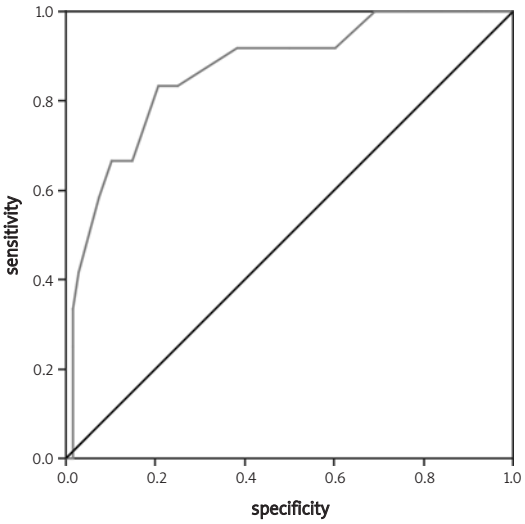

Figure 2. Low cardiac output syndrome in postoperative period significantly (p<0.001) differentiates patients from aortic regurgitation group from the death point of view (AUC=0.868)

higher in patients in whom low cardiac output syndrome developed than in those in whom it did not develop (16.9% vs 0.9%, p<0.001). Stepwise logistic regression analyses identified nine independent predictors of low output syndrome: left ventricular ejection fraction less than 20%, repeat operation, emergency operation, female gender, diabetes, age older than 70 years, left main coronary artery stenosis, recent myocardial infarction and triple-vessel disease. They concluded that patients at high risk for the development of low cardiac output syndrome should be the focus of trials of new techniques of myocardial protection to resuscitate the ischemic myocardium [5].

In the Maganti et al. study, the authors analyzed the predictors of low cardiac output syndrome in patients underwent isolated aortic valve surgery. They included 2255 patients who underwent aortic valve surgery with no other concomitant cardiac surgery. The overall prevalence of LOS was 3.9%. The independent predictors of LOS were: renal failure, earlier year of operation, left ventricular ejection fraction <40%, shock, female gender, and increasing age. Overall mortality was 2.9% and it was higher in patients who experienced LOS (38% vs 1.5%; p<0.001). They noticed that the independent predictors of mortality were: preoperative renal failure, urgency of surgery, previous stroke, congestive heart failure, previous cardiac surgery, hypertension, and small aortic valve size. Authors concluded that the novel strategies to preserve renal function, optimization of preexisting heart failure symptoms, and avoidance of prosthesis-patient mismatch may reduce the incidence of low cardiac output syndrome and lead to improved results after aortic valve surgery [4, 8, 9].

Our study partially confirmed the results above. We also observed that advanced age, low LVEF, heart failure in the history, and such hemodynamic parameters like left ventricular end-systolic and end-diastolic diameters are significant predictors of postoperative low cardiac output syndrome. However, we also found some new interesting factors that essentially influenced postoperative LOS occurrence, such as: obesity (high BMI), some hemodynamic parameters both from pre- and early postoperative period and co-existence of insignificant mitral and tricuspid regurgitation. We hope that it might help to create a score of the most important predictors of LOS in order to protect the high risk patients in the best known way [10].

Conclusions

Low cardiac output syndrome is a quite common complication following cardiac surgery, significantly increasing the length of ICU and hospital stay and the risk of death. On the basis of statistical analysis, we selected the following independent predictors of postoperative LOS (odds ratio in parentheses): (1) aortic stenosis group – advanced age (4.7), end-systolic (5.5) and end-diastolic intraventricular septum thickness (4.2) before the surgery, LVEF ≤50% (5.4) and insignificant mitral regurgitation (4.1) in the early postoperative period; (2) aortic regurgitation group – obesity (4.8), left ventricular end-systolic (4.5) and end-diastolic diameters (6.4) in the preoperative period and left ventricular end-systolic (4.7) and end-diastolic diameters (6.1), and left ventricular ejection fraction ≤50% (7.2) in the early postoperative period. Further studies should be performed to confirm these results.

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