The impact of coronary artery disease severity on late survival after combined aortic valve replacement and coronary artery bypass grafting – experience of a single cardiac surgery center

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Abstract

Introduction: The severity of coronary artery disease (CAD) may have an impact on the outcomes of patients (pts) after aortic valve replacement (AVR) and coronary artery bypass grafting (CABG).

Aim: The aim of the study was to analyze survival after simultaneous AVR and CABG with respect to CAD severity.

Material and methods: The study involved 143 consecutive pts (40 women and 103 men) with a mean age of 65.1 ± 7.7 years treated between 2006 and 2009. The indication for surgery was aortic stenosis accompanied by left main or three-vessel disease (group A; $n = 43$) and by single- or two-vessel disease (group B; $n = 100$). In-hospital and late mortality were analyzed. Post-discharge survival was estimated using the Kaplan-Meier method. Moreover, selected preoperative clinical and echocardiographic data as well as intraoperative variables were compared between the groups.

Results: In-hospital mortality was 4.7% in group A and 3.0% in group B (NS). The 12-month and 48-month survival probability rates were 0.88 ± 0.05 and 0.83 ± 0.06 in group A, and 0.97 ± 0.01 and 0.92 ± 0.03 in group B, respectively ($p < 0.05$). Patients in group A and B differed ($p < 0.05$) with respect to the preoperative prevalence of arterial hypertension (65.1% vs. 42.0%) and atrial fibrillation (18.6% vs. 6.0%) as well as with regard to the rate of complete revascularization (20.9% vs. 85.0%, group A and B, respectively).

Conclusions: Coronary artery disease severity impacts long-term survival after combined AVR and CABG. Patients with left main or three-vessel disease more often undergo incomplete surgical revascularization, and this fact may be one of the predictors of an unfavorable outcome.

Key words: coronary artery disease, aortic valve replacement, combined procedures, mortality, long-term outcomes.

Streszczenie

Wstęp: Zaawansowanie choroby wieńcowej może mieć wpływ na wyniki kliniczne leczenia chorych poddanych jednoczesnej wymianie zastawki aortalnej (*aortic valve replacement* – AVR) oraz pomostowaniu aortalno-wieńcowemu (*coronary artery bypass grafting* – CABG).

Cel: Analiza przeżycia chorych po jednoczesnych zabiegach AVR i CABG zależnie od zaawansowania choroby wieńcowej.

Materiał i metody: Badaniem objęto 143 kolejnych chorych (40 kobiet i 103 mężczyzn) w wieku 65,1 ± 7,7 roku leczonych w latach 2006–2009. Wskazaniem do operacji było zwężenie zastawki aortalnej ze współistniejącym zwężeniem pnia i chorobą trzech tętnic wieńcowych (grupa A; $n = 43$) lub chorobą jednej i dwóch tętnic wieńcowych (grupa B; $n = 100$). Analizowano zgony szpitalne i w obserwacji odległej. Przeżycie po wypisaniu ze szpitala oszacowywano z użyciem metody Kaplana-Meiera. Ponadto porównywano między grupami wybrane dane przed- (kliniczne i echokardiograficzne) oraz śródoperacyjne.

Wyniki: Śmiertelność szpitalna wyniosła 4,7% w grupie A oraz 3,0% w grupie B (NS). Prawdopodobieństwo przeżycia 12 i 48 miesięcy oszacowano odpowiednio na 0,88 ± 0,05 i 0,83 ± 0,06 w grupie A oraz 0,97 ± 0,01 i 0,92 ± 0,03 w grupie B ($p < 0,05$). Chorzy w grupie A i B różnili się między sobą ($p < 0,05$) pod względem częstości występowania nadciśnienia tętniczego (65,1% *vs* 42,0%) i migotania przedsionków (18,6% *vs* 6,0%) oraz wykonania pełnej rewaskularyzacji serca (20,9% *vs* 85,0%, odpowiednio w grupie A i B; $p < 0,001$).

Wnioski: Zaawansowanie choroby wieńcowej ma wpływ na przeżycie w obserwacji odległej u chorych poddanych jednoczesnym zabiegom AVR i CABG. U pacjentów z chorobą pnia i trzech tętnic wieńcowych częściej wykonuje się niepełną rewaskularyzację serca i ten fakt może być jednym z niekorzystnych czynników rokowniczych wyników odległych.

Słowa kluczowe: choroba wieńcowa, wymiana zastawki aortalnej, zabiegi łączone, śmiertelność, wyniki odległe.

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Introduction

Aortic stenosis (AS) and coronary artery disease (CAD) share risk factors (e.g., hypertension, hyperlipidemia, diabetes) and proposed pathophysiological mechanisms [1]. Individuals undergoing simultaneous operations for AS and CAD constitute a systematically growing group of patients; in some countries, their number has as much as doubled in recent years. It is generally accepted that the outcomes after combined procedures of aortic valve replacement (AVR) and coronary artery bypass grafting (CABG) are markedly worse than those after isolated AVR or isolated CABG [2, 3]. However, patients with AS and CAD usually have more independent risk factors for an unfavorable outcome, including age, impaired cardiac performance, or other comorbidities [4, 5]. Moreover, co-existing CAD may vary with respect to the number of involved vessels, location (proximal, medial, or distal segments), and lesion severity (i.e., degree of stenosis). It has been suggested that CAD severity (defined as the number of diseased vessels) has an impact on the late outcomes of simultaneous AVR and CABG procedures [6, 7].

Thus, the purpose of this study was to analyze patient survival after combined procedures of AVR and CABG with respect to CAD severity and to try to identify the possible reasons for the influence of CAD severity on late outcomes based on the experience of a single cardiac surgery center.

Material and methods

Patients

All consecutive patients who underwent simultaneous procedures of AVR for AS and CABG between January 2006 and December 2009 were enrolled in the study. Ultimately, the study encompassed 143 patients (40 females and 103 males) with a mean age of 65.1 ± 7.7 years (ranging from 43 to 79). The indication for surgery was AS accompanied by left main or three-vessel disease (group A; $n = 43$) and by one- or two-vessel disease (group B; $n = 100$). Selected preoperative data of the patients enrolled in this study are outlined in Table I.

Surgery

Patients were qualified for surgery on the basis of echocardiographic study (M + 2D + Doppler) and coronary angiography. The findings of the preoperative examinations performed in both patient groups are summarized in Table II.

All operations employed median sternotomy, extracorporeal circulation (ECC) with moderate hypothermia (28-29°C), and standard cannulation of the ascending aorta and right atrium. In all cases, cold cardioplegic solution according to the St Thomas Hospital formula was infused directly into the coronary ostia with an initial dose of 10 ml/kg, repeated every 20 minutes. Retrograde infusion of the cardioplegic solution was applied only in a few cases with critical left main stenosis and complete occlusion of the proximal segment of the right coronary artery. During the surgery, the performance of distal anastomoses of the saphenous veins and radial arteries was followed by aortic valve replacement and the subsequent implantation of the left internal thoracic artery (LITA) (usually to the left anterior descending artery – LAD). After the aortic clamp had been released, the proximal anastomoses on the partially side-clamped ascending aorta were performed.

The most crucial details regarding the operations are listed in Table III. A modified definition of complete revascularization by Synnergren *et al.* was applied in our study. In short, surgical revascularization was considered complete when all arterial territories (LAD, circumflex artery [Cx], and right coronary artery [RCA]) with significantly stenotic segments (i.e., more than 70% on preoperative angiography) were bypassed by at least 1 bypass graft. In the case of left main disease (stenosis of at least 50%), grafts had to be performed to both the LAD and Cx territories [8]. Completeness of revascularization was assessed retrospectively.

In-hospital mortality and long-term survival

In-hospital mortality, defined as death occurring within the first 30 postoperative days, was assessed irrespectively

Tab. I. Preoperative clinical data

Variable*	Group A ($n = 43$)	Group B ($n = 100$)	p
Age (years)	66.3 ± 8.0	64.5 ± 7.5	0.211 [NS]
Gender (M/F)	35 (81.4%)/8 (18.6%)	68 (68.0%)/32 (32.0%)	0.115 [NS]
BMI	30.6 ± 4.8	29.5 ± 3.9	0.330 [NS]
Obesity (BMI > 30)	20 (46.5%)	44 (44.0%)	0.925 [NS]
Arterial hypertension	28 (65.1%)	42 (42.0%)	0.019
Hyperlipidemia	29 (67.4%)	58 (58.0%)	0.382 [NS]
Diabetes	15 (34.9%)	32 (32.0%)	0.877 [NS]
Diabetes on insulin	8 (18.6%)	20 (20.0%)	0.152 [NS]
Previous MI	13 (30.2%)	19 (19.0%)	0.208 [NS]
PCI in history	4 (9.3%)	4 (4.0%)	0.385 [NS]
Atrial fibrillation**	8 (18.6%)	6 (6.0%)	0.023

*Categorical variables are presented as numbers (%) and continuous variables as mean ± standard deviation.
**At least one documented episode of atrial fibrillation.
BMI – body mass index, F – female, M – male, MI – myocardial infarction, n – number, NS – non-significant, PCI – percutaneous coronary intervention

Tab. II. Preoperative echocardiographic and angiographic data

Variable*	Group A (*n* = 43)	Group B (*n* = 100)	*p*
LVEDd (mm)	49.0 ± 8.5	47.3 ± 9.2	0.699 [NS]
LVPWd (mm)	14.4 ± 2.8	15.2 ± 3.2	0.204 [NS]
IVSd (mm)	16.0 ± 4.9	16.1 ± 3.0	0.892 [NS]
LA (mm)	42.6 ± 5.8	40.3 ± 7.0	0.092 [NS]
RV (mm)	30.1 ± 5.9	28.6 ± 4.8	0.227 [NS]
LVEF (%)	55.6 ± 17.6	58.8 ± 15.9	0.470 [NS]
LV dysfunction (LVEF 40% or less) (*n* [%])	10 (23.3%)	15 (15.0%)	0.341 [NS]
Regional abnormality in LV contractility (*n* [%])	18 (41.8%)	22 (22.0%)	0.026
Peak PG (mmHg)	64.4 ± 25.4	89.2 ± 27.9	< 0.001
Peak PG < 60 mmHg (*n* [%])	17 (39.5%)	18 (18.0%)	0.011
Peak PG < 60 mmHg and LVEF > 40% (*n* [%])	15 (34.9%)	1 (1.0%)	< 0.001
Single-vessel disease (*n* [%])	–	65 (65.0%)	N/A
Two-vessel disease (*n* [%])	–	35 (35.0%)	N/A
Three-vessel disease (*n* [%])	23 (53.5%)	–	N/A
Isolated LM disease (*n* [%])	8 (18.6%)	–	N/A
LM and RCA disease (*n* [%])	12 (27.9%)	–	N/A

*Categorical variables are presented as numbers (%) and continuous variables as mean ± standard deviation.
IVSd – interventricular septum diastolic thickness, LA – left atrial dimension, LM – left main, LV – left ventricular, LVEDd – left ventricular end-diastolic dimension, LVEF – left ventricular ejection fraction, LVPWd – left ventricular posterior wall diastolic thickness, RCA – right coronary artery, n – number, N/A – non applicable, NS – non-significant, PG – pressure gradient, RV – right ventricular dimension

Tab. III. Intraoperative data

Variable*	Group A (*n* = 43)	Group B (*n* = 100)	*p*
ECC time (min)	119.0 ± 23.9	113.4 ± 21.2	0.339 [NS]
ACC time (min)	89.7 ± 18.5	85.3 ± 19.0	0.352 [NS]
AVR + 1 graft	7 (18.6%)	79 (79.0%)	< 0.0001
AVR + 2 grafts	26 (60.6%)	21 (21.0%)	< 0.0001
AVR + 3 grafts	9 (20.9%)	–	N/A
Bioprostheses/mechanical valves	15 (34.9%)/28 (65.1%)	32 (32.0%)/68 (68.0%)	0.886 [NS]
Complete revascularization**	9 (20.9%)	85 (85.0%)	< 0.0001
Reasons for incomplete revascularization			
Diffuse disease	21	9	0.735 [NS]
Small arteries	12	5	0.832 [NS]
Difficult access	2	1	0.778 [NS]

*Categorical variables are presented as numbers (%) and continuous variables as mean ± standard deviation.
**Complete revascularization is defined in the text (see subsection Surgery).
ACC – aortic cross clamping, AVR – aortic valve replacement, ECC – extracorporeal circulation, n – number, N/A – non-applicable, NS – non-significant

of the actual location of the patients (our department, rehabilitation center, home).

The majority of our patients were referred to rehabilitation centers, routinely after 7-9 days after the operations. After the completion of postoperative rehabilitation, all patients were followed up at the outpatient clinic. If they were not supervised in the outpatient facilities, we tried to contact them or their families by phone at the end of the follow-up period. In the case of death, it was defined as cardiac- or non-cardiac-related.

Data management and statistical analysis

All continuous data were checked for normality with the Shapiro-Wilk *W* test. If the values were normally distributed, they were expressed as mean ± standard deviation and then compared (group A vs. group B) using Student's unpaired *t*-test. Nominal data were presented as numbers (*n*) and percentages (%) and were compared with the Yeats corrected χ^2 test. Differences with respect to ordinal variables (e.g., the number of diseased coronary arteries) were analyzed with the Kruskal-Wallis rank test. Post-discharge

survival was estimated using the Kaplan-Meier method, and survival probability curves for both groups were compared with the Gehan-Wilcoxon test. A *p* value < 0.05 was considered statistically significant. All statistical analyses were performed using Statistica 9.0 for Windows (StatSoft, Inc., Tulsa, OK, USA).

Results

Preoperative and intraoperative variables

There were several differences between group A and group B with respect to both preoperative and intraoperative variables. More patients in group A had been diagnosed with arterial hypertension and had suffered at least one episode of atrial fibrillation according to their preoperative medical history (Table I). Echocardiographic parameters assessing cardiac dimensions and left ventricular systolic performance (i.e., left ventricular ejection fraction [LVEF]) did not differ between the subsets of patients (Table II). However, the degree of aortic stenosis, expressed as peak systolic transvalvular pressure gradient, was less severe in group A than in group B patients, even when patients with impaired LV systolic function (LVEF < 40%) were taken into account. Fifteen cases in group A and only 1 in group B had a peak systolic transvalvular gradient below 60 mmHg and relatively well-preserved LV performance (LVEF above 40%) (*p* < 0.0001). Several significant differences were noted between the examined subgroups regarding the intraoperative variables; particularly, the rate of complete revascularization was significantly higher in group B than in group A (*p* < 0.0001) (Table III). The reasons for incomplete revascularization were, predominantly, diffuse CAD precluding appropriate anastomosis, narrow coronary arteries (less than 1 mm in diameter), and, rarely, coronary arteries inaccessible for grafting (intramuscular course, location in the atrioventricular groove).
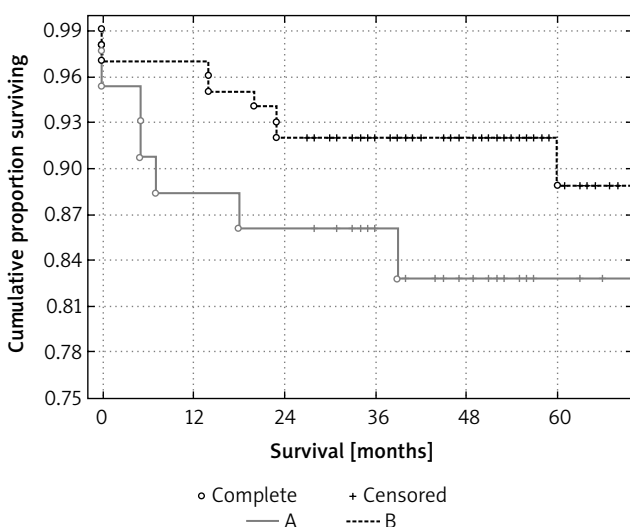
Fig. 1. Probability of patient survival assessed with the Kaplan-Meier curve. Statistical analysis (the Gehan-Wilcoxon test) revealed statistical significance (*p* < 0.05) with respect to long-term survival

In-hospital period

Five patients, including 2 in group A (mortality rate 4.7%) and 3 (3.0%) in group B, died during the early postoperative period (NS). Three of them died due to postoperative low cardiac output syndrome, and 2 died due to gastrointestinal complications.

Furthermore, the peak level of troponin I, detected usually 24 hours after the surgery, was significantly higher in group A than in group B (18.9 ± 7.6 vs. 10.2 ± 4.8 µg/l; *p* < 0.001). Notwithstanding, pre-discharge transthoracic echocardiography (M + 2D + Doppler) revealed additional postoperative disturbances in regional myocardial contractility (as compared to the preoperative assessment) in only 1 case in group A and 2 cases in group B (NS).

Late outcomes

During the post-discharge follow-up period, which lasted 45.5 ± 17.5 months (542.9 patient-years) and was completed by 98.6% of patients, 11 more individuals died (5 in group A and 6 in group B). Cardiac-related deaths were noted in 4 cases in group A (80%; due to myocardial infarction [*n* = 3] or progressive heart failure [*n* = 1]) and 3 in group B (50%; heart failure [*n* = 2] or acute coronary syndrome [*n* = 1]). Among them, only 1 group B patient received complete surgical revascularization.

The probability of 12-month, 24-month, and 48-month survival calculated using the Kaplan-Meier curves was, respectively, 0.88 ± 0.04, 0.86 ± 0.05, and 0.83 ± 0.06 in group A and 0.97 ± 0.01, 0.92 ± 0.03, and 0.92 ± 0.03 in group B (*p* < 0.05) (Fig. 1).

Discussion

In our study, we have confirmed the earlier reports that the severity of CAD had an impact on patient survival after combined CABG and AVR procedures. Nonetheless, early mortality was similar in both study groups and was comparable to the findings of previously published studies [9, 10]. The medical literature includes several reports confirming that the co-existence of both cardiac pathologies markedly increases early mortality in comparison to isolated AS or isolated CAD [11, 12]. Hemodynamically significant lesions in the coronary arteries may inhibit the effective perfusion of the usually hypertrophic myocardium with cardioplegic solution because of relatively high resistance to flow (high-resistance, low-flow perfusion areas) [13]. It is possible that the higher levels of troponin I in group A resulted from insufficient intraoperative myocardial protection even though the retrograde perfusion technique was additionally applied in the particular cases (diagnosed with left main critical stenosis and occlusion of the proximal segments of the right coronary arteries). However, control echocardiography performed on the day prior to discharge did not reveal significant differences in regional myocardial contractility disturbances.

The present study demonstrated that the post-discharge follow-up period played the most important role

in the difference in survival rates after combined AVR and CABG between the studied groups (A vs. B). Unfortunately, the relatively small number of patients enrolled in this study and the low mortality rate (only 16 subjects in both groups, including 8 group A patients) did not allow us to perform multivariate regression analysis in order to reveal the independent risk factors for the reduced survival rate in group A. Instead, we were only justified to compare selected perioperative variables between the studied groups of patients. Patients with more severe forms of CAD (group A) were more often diagnosed with arterial hypertension and were more likely to have suffered at least one episode of atrial fibrillation before surgery as compared to group B patients. These variables have been shown to have a significant adverse impact on the survival of patients undergoing AS surgery [14, 15]. Notwithstanding, the majority of our hypertensive patients had relatively well-controlled arterial blood pressure at the time of admission.

It is generally accepted that complete surgical revascularization should be a goal of CABG. However, there is no consensus on the clinical importance of complete revascularization in multivessel CAD. Some meta-analyses revealed that it might enable the achievement of better survival rates in comparison to incomplete revascularization, while the SYNTAX study did not support these findings [8, 16, 17]. This may be a result of some differences in the adopted definitions of complete revascularization. Some authors have taken into account all coronary arteries (Synnergren *et al*.), while others considered only those > 1 mm in diameter [8, 18]. In our analysis, the more strict definition was adopted, and this fact may explain the low rate of complete revascularization in group A. There is a paucity of data on the effects of incomplete surgical revascularization on long-term outcomes after simultaneous AVR and CABG procedures. In our study, group A patients with pre-existing multivessel CAD presented a reduced survival rate in the late postoperative period. The majority of post-discharge deaths in group A were cardiac-related, particularly in con sequence of acute coronary syndromes. None of the group A patients who died as a result of cardiac events during the follow-up had received complete surgical revascularization. It should be underscored once more that, in only one in every five group A patients, all the diseased coronary arteries were bypassed, predominantly due to diffuse atherosclerosis in the coronary arteries or the small diameters of the recipient vessels, especially in the Cx territory. Thus, the location of atherosclerotic plaques also appears to be of paramount importance for the late outcome. Isolated proximal lesions accompanied by peripheral segments of adequate diameter (i.e., > 1.5 mm) in the recipient coronary vessels usually enable healthy anastomosis and favorable long-term follow-up. It is likely that the reduced long-term survival in group A resulted from the more severe and more diffuse CAD, extending beyond the proximal segments of the coronary arteries, rather than from incomplete myocardial revascularization per se.

Conclusions

The study found that the severity of CAD has an impact on the long-term survival of patients undergoing combined AVR and CABG procedures. Patients with left main or three-vessel disease are more likely to undergo incomplete surgical revascularization, and this fact may be one of the predictors of an unfavorable outcome. However, incomplete revascularization is likely a result of more diffuse pre-existing CAD.

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Dislocure

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