Scientific Research Publishing

World Journal of Cardiovascular Surgery, 2019, 9, 143-154
https://www.scirp.org/journal/wjcs
ISSN Online: 2164-3210
ISSN Print: 2164-3202

Does Additional Coronary Artery Bypass Grafting Increase Hospital Mortality of Patients Requiring Valve Surgery?

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How to cite this paper: Benyoussef, H., Makani, S., Benzha, M.Y., Haoudar, A., Kantri, A., Hamidi, C.E.K., Scadi, S., El Ouradi, A., Sabry, M. and Houssa, M.A. (2019) Does Additional Coronary Artery Bypass Grafting Increase Hospital Mortality of Patients Requiring Valve Surgery? *World Journal of Cardiovascular Surgery*, **9**, 143-154.
https://doi.org/10.4236/wjcs.2019.910016

Received: August 23, 2019
Accepted: September 27, 2019
Published: September 30, 2019

Abstract

Background: The aim of this study was to evaluate the impact of additional coronary revascularization on the early results in patients submitted to valve surgery. **Patients and Methods:** A retrospective review of the cardiac surgical database between January 2000 and December 2018 was performed. A total of 1667 patients were included and divided into two groups: Group A isolated valve surgery (IVS n = 1608) and Group B with valve surgery combined to coronary artery bypass grafting (VS + CABG n = 59). Demographic, operative data and postoperative outcomes were compared between groups. **Results:** Patients with combined procedure were older than patients who underwent isolated valvular surgery (64.9 ± 9.2 years vs 44.4 ± 13.1 years; p = 0.0001) and there was a higher proportion of diabetics (40.7% vs 6.6%; p = 0.0001). The 30 days mortality rate in the combined procedure group was 18.6% versus 6.2% in isolated valve surgery (p = 0.001). Also post-operative complications were more frequent than for patients who underwent IVS. Additionally we noted a high prevalence of coronary artery risk factors in patients with combined procedures. **Conclusion:** Surgical mortality and morbidity of coexisting coronary and heart valve disease were substantially higher than IVS. More efforts in medical management may reduce the incidence of adverse outcomes.

Keywords

Valvular Disease, Coronary Artery Disease, Coronary Artery Bypass Grafting

1. Introduction

In developing countries, rheumatic heart disease prevails as the main cause of valvular heart disease (VHD) [1]. Over the last decade, patients undergoing heart valve surgeries are more likely to be at higher surgical risk [2] [3] compared to previous data. The most common factor influencing outcomes after heart valve surgery is coronary artery disease (CAD) [4] [5]. Isolated valvular surgery seems to have a negative impact on the operative mortality when coronary artery stenosis was neglected [6]. Conversely, a significant reduction in mortality is seen in such patients who undergo concomitant coronary revascularization procedures [7] [8]. In some previous reports, combined procedure was associated with elevated short- and long-term mortality [9]. More recently, improvement in surgical techniques, myocardial protection and post-operative care could explain better short-term outcomes. The purpose of the present study is to analyze the influence of coronary artery bypass grafting (CABG) on hospital mortality and morbidity in patients undergoing heart valve surgery in our institutions.

2. Patients and Methods

A retrospective review of the cardiac surgical data base from two institutions between January 2000 and December 2018 was performed to evaluate and compare the immediate outcome for patients undergoing isolated heart valve surgery (IVS) compared to patients undergoing a combined procedure including heart valve surgery and coronary artery bypass grafting (VS + CABG). During the study period, all consecutive patients with a valvular heart disease undergoing heart valve surgery were included. A total of 1667 patients were included and divided into two groups: Group A isolated heart valve surgery (IVS, n = 1608) and Group B with heart valve surgery and coronary artery bypass grafting (VS + CABG, n = 59). Although these two groups are expected to be very different in terms of cardiovascular risk, morbidity and mortality, we found very useful to make the comparison. Valve dysfunction and pathology was investigated by echocardiography and color Doppler while coronary artery disease (CAD) was defined as more than 50% stenosis of at least one major epicardial coronary artery [10]. Anesthetic, surgery and per operative management were practiced per divisional protocols. All surgical procedures were performed by cardiac surgeons of our medical centers. All procedures were performed through a median sternotomy with cardiopulmonary bypass (CPB) and under mild systemic hypothermia (32˚C - 34˚C). Myocardial protection was achieved with cold blood cardioplegia.

For patients undergoing combined surgery, distal anastomoses were performed

before valve surgery. Proximal vein graft anastomoses were performed after valve surgery and aortic cross clamp was removed. Both bioprostheses and bi-leaflet mechanical heart valve were used for heart valve replacement. Heart valve repair was performed using a rigid ring. CABG was performed using the left internal mammary artery (LIMA), right internal mammary artery (RIMA) and/or venous grafting. To conclude the surgical indication, patients were discussed in a multidisciplinary heart team meeting.

3. Definitions

30 days mortality was defined as death within 30 days of operation. Major cardio vascular events included: post operative acute myocardial infarction (AMl), stroke, cardiac death. Operative morbidity was defined as all postoperative complications: acute renal failure (ARF), stroke, prolonged ventilation, AMI, wound infection, re exploration for bleeding, Low cardiac output syndrome (LOS) causing longer Intensive Care Unit (lCU) stay, Multiple Organ Dysfunction Syndrome (MODS).

The local ethical committees of each participating institution approved aims and methods of this study.

Statistical analysis: Database management and statistical analysis were performed using SPSS version 19.0 (SPSS, lnc. Chicago, USA).

All continuous variables were expressed as mean ± SD. For asymetric variables, the median with the range interquartile were displayed. Normal and ordinal variables were expressed as effectif and percentages. For nominal variables, the chi-square tester Fisher's exact test were used to compare the groups. Continuous variables were analyzed using student's t test for normal distributions and Mann-Whitney's test for non-normal distributions. P value < 0.05 was considered to be statistically significant. Missing data were handled by multiple imputations, extreme outliers were kept during post-test analysis and there was no need to indeterminate results management.

4. Results

A total of 1667 adult consecutive patients who underwent heart valve surgery were included in the study. Among them 59 patients (3.5%) underwent combined procedure: valvular surgery + coronary artery bypass graft surgery (VS + CABG). Demographic and preoperative characteristics of the two groups are shown in Table 1.

Aortic Valve Replacement was more common in the VS + CABG goup 74.5% versus 51.6% in the Isolated Valve Surgery group while Aortic and Mitral Valve Replacement was less common 6.7% versus 24.7% in the IVS group (see Table 2).

Analysis shows a significant difference in gender ($p = 0.0001$). Patients with combined procedure were older than patients who underwent isolated valvular surgery (64.9 ± 9.2 years vs 44.4 ± 13.1 years; $p = 0.0001$) and there was a higher proportion of diabetics (40.7% vs 6.6%; $p = 0.0001$).

Table 1. Pre-operative patient characteristics.

Variable	Isolated Valve Surgery (IVS)	Valve Surgery + CABG (VS + CABG)	p-value
	n = 1608	n = 59	
Age (years)	44.4 ± 13.1	64.9 ± 9.2	<0.001
Gender F/M	48%/52%	19%/81%	<0.001
Diabetes mellitus	6.6% (n = 107)	40.7% (n = 24)	<0.001
Arterial hypertension	9.2% (n = 148)	35.6% (n = 21)	<0.001
Dyslipidemia	6.4% (n = 103)	30.5% (n = 18)	<0.001
Tabacco use	25.0% (n = 402)	49.1% (n = 29)	<0.001
Chronic obstructive pulmonary disease	4.2% (n = 69)	6.7% (n = 4)	NS
Renal failure	5.1% (n = 83)	5.0% (n = 3)	NS
Stroke	5.2% (n = 84)	1.6% (n = 1)	NS
Euroscore	2.49 ± 2.6	5.64 ± 2.6	<0.001
Logistic euroscore	3.34 ± 6.0	6.1 ± 5.9	0.001
Cardiovascular risk factors	0.60 ± 0.83	1.73 ± 1.11	<0.001
BMI (Kg/m^2)	24.2 ± 4.7	25.9 ± 2.7	0.004
CCSIII	0.7% (n = 10)	5.2% (n = 3)	0.013
Dyspnea NYHA III-IV	59.7% (n = 960)	38.9% (n = 23)	0.002
Cardiac heart failure	9.8% (n = 158)	3.4% (n = 2)	NS
Sinus rhythm	57.4% (n = 923)	88.1% (n = 52)	<0.001
Atrial fibrillation	42.6% (n = 685)	11.9% (n = 7)	<0.001
Cardio thoracic index	0.57 ± 0.07	0.55 ± 0.06	0.028
Echocardiographic findings:			
Left atrium diameter (mm)	53.1 ± 11.2	43,5 ± 6.9	<0.001
ESLVD (mm)	38.8 ± 10.3	39.4 ± 9.3	0.69
EDLVD (mm)	56.8 ± 11.5	57.7 ± 10.2	0.57
LVEF (%)	58.0 ± 11.2	52.8 ± 13.7	0.001
Low left ventricle ejection fraction (<40%)	9.5% (n = 154)	30.5% (n = 18)	<0.001
PASP (mmHg)	50.8 ± 18.8	45.1 ± 17.0	0.11
Pre-operative blood tests			
Hemoglobine (g/dl)	13.3 ± 1.9	13.6 ± 1.3	0.24
Uree (g/l)	0.41 ± 0.24	0.44 ± 0.16	0.30
Creatinine (mg/l)	10.0 ± 5.5	10.7 ± 3.3	0.36
Platelets count ($\times 10^3/mm^3$)	225.1 ± 69.3	199.1 ± 55.2	0.008

Table 2. Valve surgery procedures between groups.

Variable	Isolated Valve Surgery (IVS)	Valve Surgery + CABG (VS + CABG)
	n = 1608	n = 59
Mitral Valve Replacement	53.4% (n = 859)	23.7% (n = 14)
Aortic Valve Replacement	51.6% (n = 831)	74.5% (n = 44)
Aortic and Mitral Valve Replacement	24.7% (n = 398)	6.7% (n = 4)
Mitral Valve Repair	2.9% (n = 48)	8.4% (n = 5)
Tricuspid Valve Repair	23.7% (n = 382)	0% (n = 0)

The VS + CABG group had worse cardiac risk profiles, with significantly more diabetes mellitus ($p = 0.0001$), arterial hypertension (35.6% vs 9.2%; $p < 0.001$), dyslipidemia (30.5% vs 6.4%; $p < 0.001$), smoking (49.1% vs 25%; $p < 0.001$).

The mean number of cardiovascular risk factors was 1.73 ± 1.11 (VS + CABG) versus 0.60 ± 0.83 (IVS) ($p = 0.0001$). At the time of surgery, VS + CABG group had a worse clinical status with high NYHA class (NYHA functional class III-IV; 59.7% vs 38.9% ($p = 0.002$)). No significant differences were noted between groups in regard to previous stroke, chronic pulmonary obstructive disease (CPOD) and renal dysfunction.

A significant difference was found between the groups in terms of left ventricular ejection fraction (LVEF) 52.8% ± 13.7% (VS + CABG) vs 58.0% ± 11.2% (IVS) ($p = 0.001$). Patients with combined procedure had a higher proportion of left ventricular dysfunction (LVEF < 40%) 30.5% (VS + CABG) vs 9.5% (IVS) ($p = 0.0001$). The distribution of coronary artery disease in combined procedure group was: left main coronary stenosis (10.1%), left anterior descending artery LAD (77.9%), circumflex artery stenosis (30.5%), right coronary artery stenosis (20.3%). The prevalence of coronary artery disease (CAD) was higher in patients with aortic stenosis (AS) when compared to mitral valve disease. (AS + CAD = 39 cases). Aortic regurgitation + CAD = 1 case, mitral regurgitation + CAD = 6 cases, mitral + aortic disease + CAD = 5 cases. Coronary revascularization was performed in combined surgical procedure with a mean of 1.66 ± 0.76 (range = 1 - 4) distal grafts per patient.

Operative and post operative data were listed in Table 3 and Table 4. In VS + CABG group, CPB time, aortic cross clamp time, mechanical respiratory support time, and ICU stay were longer when compared to patients who underwent IVS.

The 30 days mortality rate in the combined procedure group was 18.6% versus 6.2% in isolated valve surgery ($p = 0.001$). The relative risk of overall 30 days mortality increases by 3 times between VS + CABG and IVS group. The main cause of early death was low cardiac output syndrome (LOS).

The main post operative complications included LOS, Acute Renal Failure, Myocardial Infarction, infection, re-exploration for bleeding and Multiple Organ Dysfunction Syndrome. All of these complications were more frequent in the VS

+ CABG group. This group also required Red Blood Cells transfusion more than IVS group ($p < 0.001$).

Table 3. Operative data.

Variable	Isolated Valve Surgery (IVS)	Valve Surgery + CABG (VS + CABG)	p-value
	n = 1608	n = 59	
Urgent Surgery	3.6% (n = 59)	1.6% (n = 1)	NS
Pre-operative Intra Aortic Balloon Pump Use	2.1% (n = 35)	17.2% (n = 10)	<0.001
CPB Time (minutes)	99.3 ± 41.8	161.4 ± 51.1	<0.001
Long CPB Time	27.4% (n = 434)	75.4% (n = 43)	<0.001
Aortic Cross Clamp Time (minutes)	69.7 ± 33.0	117.0 ± 39.0	<0.001
Operative Room Time (minutes)	194.6 ± 57.5	297.7 ± 76.6	<0.001
Inotropic and/or Adrenergic Support	12.1% (n = 195)	31.0% (n = 18)	<0.001

Table 4. Results and outcomes:

Variable	Isolated Valve Surgery (IVS)	Valve Surgery + CABG (VS + CABG)	p-value
	n = 1608	n = 59	
Artificial Ventilation (hours)	8 (5 - 17)	15 (6.5 - 32.5)	<0.001
Artificial Ventilation > 48 h	6.2% (n = 100)	25.8% (n = 15)	<0.001
ICU Time (hours)	24 (44 - 48)	48 (46.5 - 106)	<0.001
In-hospital Stay (days)	12.3 ± 11.1	17.4 ± 17.0	0.004
Low Cardiac Output Syndrome (in ICU)	8.8% (n = 143)	29.3% (n = 17)	<0.001
Hemoglobine (g/dl at H20)	11.0 ± 1.5	11.0 ± 1.1	NS
Bleeding (ml at H20 mean)	394	693	<0.001
Blood Transfusion	28.3% (n = 450)	61.4% (n = 35)	<0.001
Platelet count ($\times 10^3/mm^3$ at H20)	149.1 ± 55.3	133.8 ± 61	0.06
Fibrinogene (H 20)	4.1 ± 3.7	3.7 ± 0.9	NS
Re-Exploration for Bleeding or Tamponnade (Surgery)	3.0% (n = 49)	10.3% (n = 6)	0.011
Infection	5.2% (n = 84)	18.9% (n = 11)	<0.001
Acute Renal Failure	6.5% (n = 104)	18.9% (n = 11)	0.002
Digestive Complications	1.3% (n = 21)	1.7% (n = 1)	NS
Significant Bleeding	5.5% (n = 89)	17.2% (n = 10)	0.002
Myocardial Infarction	0.9% (n = 15)	17.2% (n = 10)	<0.001
Stroke	1.0% (n = 16)	0.0% (n = 0)	NS
Multi Organ Dysfunction SYNDROM	4.4% (n = 70)	17.2% (n = 10)	<0.001
Death within 30 Days	6.2% (n = 100)	18.6% (n = 11)	0.001

5. Discussion

The principal findings of this study are that combined surgery had a higher hospital mortality rate and more post operative complications than isolated valve surgery. Indeed, undergoing CABG procedure increases 3 times the overall 30 days mortality when compared to IVS group. This is not only related to the CABG procedure itself but also to more risk factors (age, Diabetes, Hypertension, higher Euroscore, high CVS risk factors, poor LVEF (40%)) and higher cardiopulmonary bypass and aortic cross clamp time.

The worse immediate results of combined procedure (VS + CABG) were associated with the effect of pre existing co morbidities.

This study compares IVS group and VS + CABG group in 1667 consecutive patients so that means the real heart valve surgery practice in our institutions. Although these two groups are very different in terms of cardiovascular risk, morbidity and mortality, we have compared them for many reasons: 1) to measure how important is the impact of cardiovascular risk factors between groups; 2) to evaluate the mortality in the combined group and assess prognosis for such patients in our daily surgical practice; 3) to compare the overall 30 days mortality between groups (to our knowledge no such comparisons have been done previously); 4) to define the relative risk of mortality for CABG in patients undergoing heart valve surgery; 5) to contribute to a very limited literature in developing countries in this topic.

Patients with VS + CABG were older and more symptomatic, and had more coronary risk factors than patients with isolated valve surgery. Some previous reports observed similar characteristics in patients candidates for combined surgery [11] [12] [13]. Patients with severe left ventricular dysfunction found to have worse early outcomes. Our results noted that more proportion of patients with valvular disease and CAD had impaired LV function compared to those with isolated valve disease, and it is well known that it contribute to early mortality [14].

In the present study, patients with valvular heart disease and coexisting coronary artery disease undergoing Heart Valve Surgery and Coronary Artery Bypass Grafting had substantially higher 30 days mortality than those having valve surgery procedure alone (18.6% vs 6.2%, $p = 0.001$). This result was consistent with some previous reports [15] [16]. As the most valvular heart disease was aortic stenosis (AS) in our series, the increase in mortality could be related to subendocardial ischemia related to coronary artery disease with left ventricular hypertrophy; it is also known that hypertrophied heart is more susceptible to inflammatory response and ischemia-reperfusion injury during cardiopulmonary bypass [17]. Left ventricle hypertrophy and its effects were certainly increased by the Arterial Hypertension history among the VS + CABG group (35.6% versus 9.2% in the IVS group). The increased mortality observed could also be related to the prevalence of diabetes mellitus in the VS + CABG (40.7% versus 6.6% in the IVS group) as it is well known that this cardiovascular risk factor can in-

crease mortality 2 to 4 times and may be more in patients with severe atherosclerotic coronary artery disease. Gunay *et al.* [18] reported an overall operative mortality of concomitant AS + CABG as 10% with aortic stenosis having a higher mortality 11.2% than aortic regurgitation 5%. However, the early surgical results have been improving during the last decade as result of improvement of surgical technique, better understanding of myocardial protection, and postoperative management [19]. Sakakura *et al.* [20] found no significant difference in 30-day mortality between Group A (Aortic Valve Replacement for aortic stenosis) and Group AC (Aortic Valve Replacement for aortic stenosis associated to CABG): 1.5% vs. 0.8%, p = 1.000.

The present study demonstrates that patients undergoing this major surgical procedure experienced also adverse postoperative events. This is particularly true in previous Vasques *et al.* [21] reports concerning patients of 80 years and older undergoing Aortic Valve Replacement and CABG.

The classic incidence of CAD in patients' candidates for valvular surgery varies widely from 37% to 20% [22]. In previous reports, the overall prevalence of CAD in patients undergoing valve replacement has been shown to vary widely from 9% to 41% [22] [23]. In western countries, the majority of those patients are elderly, have degenerative valve disease and multiple coronary risk factors. Aortic valve stenosis is the most frequent valve disease requiring intervention in the advanced age, and coronary artery disease affects 40% to 60% of them [24] [25], however, in developing countries heart valve disease is rheumatic and the prevalence of concomitant CAD is lower [26]. In the present study, the prevalence of CAD in patients submitted to valve surgery was 3.5% which is much consistent with reports published by other developing countries [27].

Oliveira [28] observed that presence of more than one coronary lesion, determined risk of hospital death 4.99 times higher than in patients without this association. In our study, 66.1% of patients had more than one coronary artery disease lesion. The Fractional Flow Reverve (FFR)-Guided revascularization in patients with aortic stenosis in patients treated with CABG impacts the management with less venous grafts and anastomoses without increasing adverse event rates up to 5 years [29]. More recently, Shah *et al.* [30] suggested that the validity of FFR to guide surgical treatment in concomitant valvular disease is controversial and was "downgrading" coronary lesions. These findings could be related to left ventricular hypertrophy, and elevated left ventricle end-diastolic pressure (LVEDP) leading to increased microvascular resistance.

The prevalence of CAD according to valvular dysfunctions was reported by Emren [31]: mitral stenosis (26.4%), mitral regurgitation (41.9%), aortic stenosis (57.7%) and aortic regurgitation (44.4%). As it is known the incidence of CAD is more common in patients with aortic stenosis as compared to other groups 66.1% in the VS + CABG group in our series. This phenomenon most likely reflects similar pathogenic mechanisms related to calcify aortic stenosis and atherosclerotic coronary artery disease [32]. Age related calcification of the aortic

valve is the most common cause of AS in adult population [33]. Therefore, there is a growing consensus that degenerative calcifies AS shares common pathophysiological features and metabolic pathways with atherosclerosis that can be targeted of disease [34] [35].

6. Study Limitation

The findings from this study suffer from the limitations due to its retrospective design. Also, the results showed comparable hospital mortality morbidity with some previous reports, but the comparison of the results in terms of risk factors for mortality seems to be difficult because of small sample and heterogeneous valve pathology.

7. Conclusion

We conclude that coexistent coronary artery has a negative influence on the early results in patients submitted to combined surgery. Early mortality in VS + CABG group is very high, and three times higher than IVS group. It is related to the risk factors, the coronary artery disease, the heart valve disease (and its consequences), the CABG procedure and the perioperative management. Indeed more careful patient management contributes to improve results and reduce hospital mortality.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Tarasoutchi, F., Montera, M.W., Grinberg, M., Barbosa, M.R., Pineiro, D.J., Sanchez, C.R., *et al.* (2011) Brazilian Valve Disease Directive-SBC 2011/Inter-American Valve Disease Directive—SIAC 2011. Diretriz Brasileira de Valvopatias SBC 2011/Diretriz lnteramericana de Valvopatias-SIAC 2011. *Arquivos Brasileiros de Cardiologia*, **97**, 1-67. https://doi.org/10.1590/S0066-782X2011002000001

[2] Folkmann, S., Gorlitzer, M., Weiss, G., Harrer, M., Thalmann, M., Poslussny, P., *et al.* (2010) Quality of Life in Octogenarians One Year after Aortic Valve Replacement with or without Coronary Artery Bypass Surgery. *Interactive CardioVascular and Thoracic Surgery*, **11**, 750-753. https://doi.org/10.1510/icvts.2010.240085

[3] Thourani, V.H., Weintraub, W.S., Craver, J.M., Jones, E.L., Mahoney, E.M. and Guyton, R.A. (2000) Ten-Year Trends in Heart Valve Replacement Operations. *The Annals of Thoracic Surgery*, **70**, 448-455. https://doi.org/10.1016/S0003-4975(00)01443-0

[4] Davarpasand, T., Hosseinsabet, A. and Jalali, A. (2015) Concomitant Coronary Artery Bypass Graft and Aortic and Mitral Valve Replacement for Rheumatic Heart Disease: Short- and Mid-Term Outcomes. *Interactive CardioVascular and Thoracic Surgery*, **21**, 322–328. https://doi.org/10.1093/icvts/ivv132

[5] De Waard, G.A., Jansen, E.K., De Mulder, M., Vonk, A.B. and Umans, V.A. (2012) Long-Term Outcomes of Isolated Aortic Valve Replacement and Concomitant AVR

and Coronary Artery Bypass Grafting. *Netherlands Heart Journal*, **20**, 110-117. https://doi.org/10.1007/s12471-011-0238-6

[6] Roberts, W.C., Roberts, C.C., Vowels, T.J., *et al.* (2012) Effect of Coronary Bypass and Valve Structure on Outcome in Isolated Valve Replacement for Aortic Stenosis. *American Journal of Cardiology*, **109**, 1334-1340. https://doi.org/10.1016/j.amjcard.2011.12.028

[7] Mullany, C.J., Elveback, L.R., Frye, R.L., Pluth, J.R., Edwards, W.D., Orszulak, T.A., *et al.* (1987) Coronary Artery Disease and Its Management: Influence on Survival in Patients Undergoing Aortic Valve Replacement. *Journal of the American College of Cardiology*, **10**, 66-72. https://doi.org/10.1016/S0735-1097(87)80161-4

[8] Florath, L., Albert, A., Hassanein, W., Arnrich, B., Rosendahl, U., Ennker, L.C., *et al.* (2006) Current Determinants of 30 Days and 3 Month Mortality in over 2000 Aortic Valve Replacements, Impact of Routine Laboratory Parameters. *European Journal of Cardio-Thoracic Surgery*, **30**, 716-721. https://doi.org/10.1016/j.ejcts.2006.08.009

[9] Kaul, K.T., Al Khadimi, R., Sharif, H. and Ramsdale, D.R. (1989) Results of Combined Valve Replacement and Myocardial Revascularization. Relation to Method of Myocardial Protection. *The Journal of Cardiovascular Surgery*, **30**, 322-327.

[10] Fihn, S.D., Blankenship, J.C., Alexander, K.P., *et al.* (2014) ACC/AHA/AATS/PCNA/SCAI/STS Focused Update of the Guideline for the Diagnosis and Management of Patients with Stable Ischemic Heart Disease: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *Journal of the American College of Cardiology*, **64**, 1929-1949. https://doi.org/10.1016/j.jacc.2014.07.017

[11] Kobayashi, K.J., Williams, J.A., Nwakanna, L.U., *et al.* (2009) EuroSCORE Predict Short and Mid Term Mortality in Combined Aortic Valve Replacement and Coronary Artery Bypass Patients. *Journal of Cardiac Surgery*, **24**, 637-643. https://doi.org/10.1111/j.1540-8191.2009.00906.x

[12] Taylor Jr., H.A., Clark, B.L., Garrison, R.J., *et al.* (2005) Relation of Aortic Valve Sclerosis to Risk of Coronary Heart Disease in African-Americans. *American Journal of Cardiology*, **95**, 401-404. https://doi.org/10.1016/j.amjcard.2004.09.043

[13] Li, Z., Anderson, I., Amsterdam, E.A., Young, J.N., Parker, J. and Armstrong, E.J. (2013) Effect of Coronary Artery Disease Extent on Contemporary Outcomes of Combined Aortic Valve Replacement and Coronary Artery Bypass Graft Surgery. *The Annals of Thoracic Surgery*, **96**, 2075-2082. https://doi.org/10.1016/j.athoracsur.2013.07.035

[14] Yelazquez, R.J., Lee, K.L., Deja, M.A., *et al.* (2011) Coronary Artery Bypass Surgery in Patients with Left Ventricular Dysfunction. *The New England Journal of Medicinec*, **364**, 1607-1616. https://doi.org/10.1056/NEJMoa1100356

[15] DiSesa, C.J., Cohn, L.H., Collins Jr., J.J., Koster Jr., J.K. and VanDevanter, S. (1982) Determinants of Operative Survival Following Combined Mitral Valve Replacement and Coronary Revascularization. *The Annals of Thoracic Surgery*, **34**, 482-489. https://doi.org/10.1016/S0003-4975(10)62992-X

[16] He, G.W., Hughes, C.F., McCaughan, B., Thomson, D.S., Leckie, B.D., Yang, C.Q., *et al.* (1991) Mitral Valve Replacement Combined with Coronary Artery Operation: Determinants of Early and Late Results. *The Annals of Thoracic Surgery*, **51**, 916-923. https://doi.org/10.1016/0003-4975(91)91005-G

[17] Suleiman, M.S., Hancock, M., Shukla, R., Rajakaruna, C. and Angelini, G.D. (2011) Cardioplegic Strategy to Protect the Hypertrophic Heart during Cardiac Surgery. *Perfusion*, **26**, 48-56. https://doi.org/10.1177/0267659111420607

[18] Gunay, R., Sensoz, Y., Kayacioglul, I., Tuygun, A.K., Balci, A.Y., Kisa, U., *et al.* (2009) ls the Aortic Valve Pathology Type Different for Early and Late Mortality in Concomitant Aortic Valve Replacement and Coronary Artery Bypass Surgery? *Interactive CardioVascular and Thoracic Surgery*, **9**, 630-634. https://doi.org/10.1510/icvts.2009.206078

[19] Biancari, F., Martin, M., Bordin, G., Vettore, E., Vinco, G., Anttila, V., Airaksinen, J. and Vasques, F. (2014) Basic Data from 176 Studies on the Immediate Outcome after Aortic Valve Replacement with or without Coronary Artery Bypass Surgery. *Journal of Cardiothoracic and Vascular Anesthesia*, **28**, 1251-1256. https://doi.org/10.1053/j.jvca.2013.07.020

[20] Sakakura, R., Asai, T., Suzuki, T., Kinoshita, T., Enomoto, M., Kondo, Y. and Shiraishi, S. (2019) Outcomes after Aortic Valve Replacement for Aortic Valve Stenosis, with or without Concomitant Coronary Artery Bypass Grafting. *General Thoracic and Cardiovascular Surgery*, **67**, 510-517. https://doi.org/10.1007/s11748-018-1053-4

[21] Vasques, F., Lucenteforte, E., Paone, R., Mugelli, A. and Biancari, F. (2012) Outcome of Patients Aged ≥80 Years Undergoing Combined Aortic Valve Replacement and Coronary Artery Bypass Grafting: A Systematic Review and Meta-Analysis of 40 Studies. *American Heart Journal*, **164**, 410-418. https://doi.org/10.1016/j.ahj.2012.06.019

[22] Lacy, J., Goodin, R., McMartin, D., Masden, R. and Flowers, N. (1970) Coronary Atherosclerosis in Valvular Heart Disease. *The Annals of Thoracic Surgery*, **23**, 429-435. https://doi.org/10.1016/S0003-4975(10)64162-8

[23] Sonmez, K., Gencbay, M., Akcay, A., *et al.* (2002) Prevalence and Predictors of Significant Coronary Artery Disease in Turkish Patients Who Undergo Heart Valve Surgery. *The Journal of Heart Valve Disease*, **11**, 431-437.

[24] Nogo, D.T.M., Sverdlov, A.L., Willoughby, S.R., *et al.* (2009) Determinants of Occurrence of Aortic Sclerosis in an Aging Population. *JACC*: *Cardiovascular Imaging*, **2**, 919-927. https://doi.org/10.1016/j.jcmg.2009.03.016

[25] Perez, S., Thielhelm, T.P. and Cohen, M.G. (2018) To Revascularize or Not before Transcatheter Aortic Valve Implantation? *Journal of Thoracic Disease*, **10**, S3578-S3587. https://doi.org/10.21037/jtd.2018.09.85

[26] Jose, V.J., Gupata, S.N., Joseph, G., *et al.* (2004) Prevalence of Coronary Artery Disease in Patients with Rheumatic Heart Disease in the Current Era. *Indian Heart Journal*, **56**, 129-131.

[27] Kruczan, D.D., Silva, N.A., Pereira, B.B., Romao, V.A., Correa Filho, W.B. and Morales, F.E. (2008) Coronary Artery Disease in Patients with Rheumatic and Non rheumatic Valvular Heart Disease Treated at A Public Hospital in Rio de Janeiro. *Arquivos Brasileiros de Cardiologia*, **90**, 197-203. https://doi.org/10.1590/S0066-782X2008000300010

[28] Junior, O., de Lima, J., *et al.* (2009) Does the Coronary Disease Increase the Hospital Mortality in Patients with Aortic Stenosis Undergoing Valve Replacement? *Revista Brasileira de Cirurgia Cardiovascular*, **24**, 453-462.

[29] Di Gioia, G., Pellicano, M., Toth, G.G., Casselman, F., Adjedj, J., Van Praet, F., Ferrara, A., Stockman, B., Degrieck, I., Bartunek, J., Trimarco, B., Wijns, W., De Bruyne, B. and Barbato, E. (2016) Fractional Flow Reserve-Guided Revascularize-

tion in Patients with Aortic Stenosis. *American Journal of Cardiology*, **117**, 1511-1515. https://doi.org/10.1016/j.amjcard.2016.02.023

[30] Shah, T., Geleris, J.D., Zhong, M., Swaminathan, R.V., Kim, L.K. and Feldman, D.N. (2017) Fractional Flow Reserve to Guide Surgical Coronary Revascularization. *Journal of Thoracic Disease*, **9**, S317-S326. https://doi.org/10.21037/jtd.2017.03.55

[31] Emren, Z.Y., Emren, S.V., Kiliçaslan, B., Solmaz, H., Susam, I., Sayın, A., *et al.* (2014) Evaluation of the Prevalence of Coronary Artery Disease in Patients with Valvular Heart Disease. *Journal of Cardiothoracic Surgery*, **9**, 153. https://doi.org/10.1186/s13019-014-0153-1

[32] Jian, B., Narula, N., Li, Q.Y., Mohler, E.R. and Levy, R.J. (2003) Progression of Aortic Valve Stenosis: TGF-β1 Is Present in Calcified Aortic Valve Cusps and Promotes Aortic Valve Interstitial Cell Calcification via Apoptosis. *The Annals of Thoracic Surgery*, **75**, 457-465. https://doi.org/10.1016/S0003-4975(02)04312-6

[33] Rajamannan, N.M., Gersh, B. and Bonow, R.O. (2003) Calcific Aortic Stenosis: From Bench to the Bedside-Emerging Clinical and Cellular Concepts. *Heart*, **89,** 801-805. https://doi.org/10.1136/heart.89.7.801

[34] Olsen, M.H., Wachtell, K., Bella, J.N., Gerdts, E., Palmieri, V., Niemien, M.S., Smith, G., lbsen, H. and Devereux, R.B. (2005) LIFE Substudy. Aortic Valve Sclerosis Relates to Cardiovascular Events in Patients with Hypertension (a LIFE Substudy). *American Journal of Cardiology*, **95**, 132-136. https://doi.org/10.1016/j.amjcard.2004.08.080

[35] Rajamannan, N.M. and Otto, C.M. (2004) Targeted Therapy to Prevent Progression of Calcific Aortic Stenosis. *Circulation*, **110**, 1180-1182. https://doi.org/10.1161/01.CIR.0000140722.85490.EA