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The 30 Day Complication Rate After Aortic Valve Replacement with a Pericardial Valve in a Mainly Geriatric Population

Wilhelm Mistiaen

*Artesis University College Antwerp, Dept of Healthcare Sciences
and University of Antwerp, Faculty of Medicine, Antwerp
Belgium*

1. Introduction

The stenotic degenerative aortic valve disease is a slowly developing condition. This condition is the result of an active process. Recently, it has been discovered that programmed cell death plays a major role in this progression (1-4). Stenotic degenerative aortic valve disease obstructs the outflow of the left ventricle (LV) and causes a pressure overload, with all its undesirable consequences. Once the disease has become symptomatic, the prognosis without surgical replacement of the valve is dismal: the life expectancy is reduced to 2 or 3 years with occurrence of syncope, angina pectoris and certainly with dyspnea (5). Age, left ventricular dysfunction and neurologic condition played a major role in the denial for AVR (6). Medical treatment and balloon valvotomy (7) do not improve the prognosis. Aortic valve replacement (AVR) is the only way to prolong life and improve its quality. In spite of technical improvements, the procedure involves a major procedure, with all its complications. Moreover, one condition (the valve disease) is replaced by another (the prosthetic valve).

The possible hospital or 30 day complications which can occur after AVR include valve related, cardiac non-valve related and non-cardiac events. Identification of their predictors could lead to an improved referral pattern and, hence to an improved 30 day outcome, provided these predictors are liable to changes.

2. Methods

In one centre for cardiac surgery, 1000 patients who underwent AVR with Carpentier-Edwards cardiac valve, were studied in a retrospective way. The operations were performed between the end of 1986 and the end of 2006. In most patients with degenerative aortic valve disease, coronary artery disease was also present. Hence, patients who received concomitant CABG were also included. Their median age was 75 (71-77) years. The surgical technique remained largely unchanged and was performed through a median sternotomy. After opening the pericardium, the ascending aorta, the vena cava inferior and superior could be accessed for connection to the extracorporeal circulation. The pulmonary artery was ligated temporarily in a gentle way. A vent was placed through the left superior pulmonary vein in

order to decompress the left ventricle. Before the extracorporeal circulation was started, the patient was fully heparinized. The patient was cooled to 30° Celsius and the heart was stopped and topically cooled with sludge ice. Systemic blood pressure, central venous pressure and left atrial pressure were continuously monitored. The ascending aorta was opened and cold cardioplegia was instilled within the coronary arteries. In case of severe coronary artery disease, additional cardioplegia was instilled through the coronary sinus. This was repeated after 30 minutes. The calcified aortic valve was inspected and excised. The ring was decalcified if necessary. The interrupted sutures were placed as three separate series through the aortic annulus, and then through the prosthesis in the same order. The valve was lowered into the annulus and the sutures were tied and severed at the desired length. If necessary, the great saphenous vein was harvested by another team for concomitant CABG. The suturing of the bypass on the coronary arteries were performed during the same clamping. The aortotomy was closed with a double running suture and the proximal end of the bypasses were also connected. The internal mammary artery was not often used. The extracorporeal circulation was stopped stepwise and then disconnected. Temporary pacemaker wires were attached to the surface of the ventricles. After thorough hemostasis and placement of drains, the chest cavity was closed. The patient was transferred to the intensive care unit and kept under sedation for 24 hours. In 1996, the anesthesia changed into a “short-track” procedure: the sedation was shortened from one day to 6 hours and extubation was performed as soon as possible thereafter.

The changes in referral pattern were documented by comparison of age and co-morbid conditions in four periods of 5 years (1986-1991; 1992-1996; 1997-2001 and 2002-2006). A chi-square analysis was used as statistical analysis to show significant differences over time.

Twenty five preoperative and five peri-operative factors were screened in two steps. In a first step, the effect on hospital events was studied by an univariate chi-square or a Fisher-exact analysis. In a second step, the significant factors were entered in a multivariate logistic regression analysis in order to identify the predictors.

The results are presented for each risk factor (first column of the table), n/N (second column), p or probability (third column), OR (fourth column) and 95%CI (last column), where N is the number of patients at risk (i.e. having the risk factor) and n the number of these patients who suffered the complication; OR is the odds ratio and 95%CI is the 95% confidence interval.

These factors were defined or dichotomized if appropriate and numbers are given.

Octogenarians	186		
Male gender	530		
COPD (chronic obstructive pulmonary disease)	235	defined on protocol by pneumologist	
Impaired renal function	109	plasma creatinine over 1.3 mg%	
Previous carcinoma	104	proven by histologic examination and treated with curative intent	
Hypertension	654	blood pressure repeatedly over 140/90 mmHg in resting conditions	
Diabetes	149	treated by diet, peroral antidiabetics or insulin	
Coronary artery disease	631	documented on coronarography	
Myocardial infarction	151	documented by ECG, enzymes (during previous admission)	

Previous CABG	81	previous admission and operation protocol
Carotid artery disease	238	stenosis of 40% or more on Doppler-duplex
History of TIA/CVA (Transient ischemic attack / cerebrovascular accident)	40/68	by history and CT (computer tomography), during previous admission
Left ventricular dysfunction	247	decrease documented by segmental analysis of ventricular wall on echocardiography
LV ejection fraction<50%	155	calculated by data obtained at echocardiography
Atrial fibrillation	197	chronic or paroxysmal, documented by ECG
Ventricular arrhythmias	74	documented by Holter monitoring
Heart failure	216	at least one previous admission for pulmonary edema
NYHA (New York Heart Association) class IV	251	by anamnesis at admission for AVR
Need for digitalis	152	by anamnesis at admission for AVR
Conduction defect	270	documented by ECG: of any type and of any degree
First degree AV (atrioventricular) block	33	ibid
Previous PaceMaker implant	33	during previous admission
Previous endocarditis	17	documented by bacteriological analysis during previous admission
Need for urgent AVR	25	condition needing AVR at the same day in order for the patient to survive
Cross-clamping>75 min	460	sum of cross clamping time for valve implantation and for additional procedures
Valve size 19	27	sizes ranging from 19 to 27
Concomitant CABG	610	
Mitral ring	13	
Aortoplasty	61	enlargement of reduction of the ascending aorta
Carotid endarterectomy	22	

The adverse events under scrutiny were

- hospital mortality (n=37)
- valve related events
 - endocarditis, documented by clinical signs, echocardiography and blood samples (n=2)
 - thrombo-embolism, with neurological signs (n=25), documented on CT or ischemic events on other locations (n=2)
 - bleeding, evident if external or documented on cerebral CT (n=20)
 - ventricular arrhythmias, documented on ECG (n=37)
- cardiac events not related to the valve
 - congestive heart failure defined by the inability of the heart to maintain an adequate circulation without support of inotropics or assist device (n=36)
 - conduction defects (new or progression of an pre-existing defect), documented on ECG, of any type and of any degree (n=101)

- atrial fibrillation, new or recurrence of a previously paroxysmal atrial fibrillation, documented on ECG (n=381)
- non-cardiac events
 - acute renal function impairment, documented by an increase of plasma creatinine with 0.3 mg% (n=53)
 - pulmonary complications: clinical and radiological signs of atelectasis or respiratory infection or prolonged intubation (n=58).

3. Results

Between the end of 1986 and 1991, 80 patients received a Carpentier-Edwards valve in aortic position. This number was 216 between 1992 - 1996, 345 between 1997 - 2001 and 365 between 2002 and the end of 2006. In our series, the changes in the four 5-year periods showed a significant increase in time for

- patients over 80 (from 6,3% to 25,5%),
- diabetes: 6.5% to 22.7%;
- COPD: 6.5% to 36.4%;
- renal function impairment: 0.9% to 17.7%;
- carotid artery disease: 2.5% to 40.1%;
- preoperative period of congestive heart failure: 12,5% to 28.3%;
- previously performed CABG: 1.3% to 11.3%;

All increases were highly significant ($p < 0.001$). Only for the need of digitalis, a significant decrease was observed: from 39.7% to 9.4% ($p < 0.001$). These results show that patients referred for AVR became older and have more co-morbidity. The reduction of use of digitalis could be due to the introduction of ACE inhibitors, angiotensin receptor, renin and beta blocking agents.

The hospital results showed a completely different pattern. Only for non-cardiac complications, a significant increase ($p = 0.001$) has been found over time, from about 20% in the first two five-year periods to about 30% in the last two five-year periods. Mortality and major cardiovascular complications rates such as ventricular arrhythmias, bleeding, congestive heart failure and thromboembolism all remained well below 5% throughout these observation periods, without a noteworthy increase. Atrial fibrillation remained between 30 and 40%, without an increase over time.

Although patients referred for AVR became older and sicker, 30-day postoperative survival seemed not affected. Therefore, age and the presence of co-morbid conditions do not necessarily represent formal contra-indications for AVR. Nevertheless, an increase of non-cardiac postoperative complications with concomitant increase in length of stay and use of economic resources could be expected if older and sicker patients are operated upon.

Hospital or 30 day mortality

Significant preoperative factors for mortality in an univariate analysis were:

- P<0.001: need for urgent surgery, age over 80, decreased left ventricular function,
- P<0.01: renal function impairment, LVEF below 50%, previous AMI, previous heart failure, need for digitalis,
- P<0.05: diabetes, chronic or paroxysmal atrial fibrillation,

The other risk factors had no significant effect. NYHA functional class II had a protective effect ($p < 0.001$) for mortality.

Multivariate analysis showed following results

Factor	n/N	p	OR	95%CI
Urgent AVR	7/25	<0.001	9.0	2.8-28.7
Digitalis	12/152	0.002	3.5	1.6-7.7
Age > 80	17/186	0.005	3.1	1.4-6.6

Mortality in the hospital phase was the most important outcome. It varied between 1.5% (8) and 24% (9). These differences were due to large differences in patient characteristics such as age and co-morbid conditions. With a time span of almost 20 year between the first and the last publication, improvement in surgical techniques and peri-operative care could also be responsible for these differences in mortality.

In most series, the hospital mortality was below 10%. In series where the mortality was over 10%, several risk factors were usually present. Independent predictors for hospital mortality were identified and confirmed that specific co-morbid conditions increased the early postoperative risk.

Most of these factors could be related to the left ventricle and hence to the patient. An emergency need for AVR (i.e. to operate on the same day as the admission in order for the patient to survive) has been identified as the most important predictor, with a increase of mortality of 10 times (10). This has been confirmed in other series (11,12). This indicated to an exhaustion of all compensatory mechanisms to maintain an adequate circulation. A need for urgent AVR has also been identified as a predictor for early postoperative congestive heart failure, which is a highly lethal condition (13). A high preoperative functional class NYHA IV (14,15) and a low-flow low-gradient problem also could be related to a protracted burden, and hence a decreased left ventricular function. Coronary artery disease, previous and the need for concomitant CABG (9,11,12,15) as well as a previous myocardial infarction (10,11) and previous CABG (12) could add to a decrease in left ventricular function.

Valvular factors such as severity of valvular disease and the type and size of valve prosthesis implanted also had an effect (15,16). The effect of non-cardiac factors such as diabetes (15) and renal disease (11,12,17) was also observed. Remarkably, the effect of age over 80 (9,12,18,19), although important, was less compared to the effect of need for urgent surgery on mortality(10).

Thromboembolic events

TE events were one of the most important and devastating events after AVR, especially if permanent neurological deficit was present. One also has to keep in mind that many TE events go unnoticed. In one small series, MRI after cardiac surgery could document silent events in 6 of 34 patients, which is rather high (20). We found this clinically evident thromboembolism in 27 of 1000 patients. In 25 cases, this was neurological. An univariate analysis identified a decreased left ventricular function (p<0.01) as sole risk factor.

This risk factor was confirmed in a multivariate analysis, which showed an ejection fraction below 50% as an independent predictor (11/247 patients), with p=0.027, an odds ratio of 2.5 with a 95% confidence interval between 1.1-5.7.

Some studies reported on the predictors for thromboembolism after AVR on long-term and none reported on such events on short-term. The short-term thromboembolic events, however, have their importance since these are a predictor for future events (21). A preoperative CVA seemed to have a comparable significance (21-24) for long-term events.

A low ejection fraction also has been identified as predictor (24). Congestive heart failure and a dilated ventricle are known risk factors for thromboembolism. Damage to the ventricular wall as well as an abnormal flow of blood (and possible stasis) can promote intra-ventricular thrombosis and hence embolization. If the LVEF is below 30%, life-long anticoagulation is required (25).

Age also has been identified as an independent predictor (23-27). The age distribution of any given patient population should be made known to appreciate fully the effect of this factor. Age might be related, however to co-morbid conditions such as diabetes and atheromatosis of the aorta and the cerebral vessels (23,24).

Carotid artery disease could be a matter for debate. In some series (23,24), it was identified as a predictor for thromboembolism, in other series, this was not (21). A Doppler-duplex investigation is a reliable tool for the detection of lesions and is routinely performed in some institutions. It cannot, however, detect atheromatosis of the intracranial vessels.

A long ECC time (24) might indicate to coronary artery disease (28) and hence, to the need for an associated procedure, which mostly is a CABG. This could confirm atheromatous vessels as a possible source for thromboembolic events. These cannot be considered entirely as valve related. A “smoking gun”, however, is often not found. And CABG itself has never been identified as a predictor for thromboembolism.

AF could also be a matter for debate: it is certainly a risk factor for thromboembolic events. However, it is also an indication for anticoagulation, which might cloud the effect of AF. In some series, AF was identified as a predictor (28), in others not (21,24).

It is by no means certain that risk factors for long-term thromboembolic events could be used to predict the occurrence of such events on short term. The latter, however, have their prognostic significance. Moreover, all these predictors indicate that the sources of thromboembolic events are multiple. Hence thromboembolism cannot be considered as entirely valve related (21,29), but also as patient related.

To prevent thromboembolism after AVR with a biological prosthesis, anticoagulant medication is given for three months after implantation, after which it can be replaced by acetyl salicylic acid, with good results (21), unless anticoagulants are indicated for another reason. An RCT to support this strategy does not exist (25), but the general idea is that vitamin K antagonists protect against early thromboembolism while re-endothelialization of the stent and the sutures is not yet complete. For mechanical heart valves, a life-long anticoagulant treatment is necessary. The target level for INR is determined by the valve position (for aortic this is lower than for mitral) and by the type of mechanical heart valves. Older types such as cage ball devices are more thrombogenic and require deeper anticoagulation. A strict classification for thrombogenicity is not available. There are too many patient related factors involved (25).

Bleeding events

Univariate analysis revealed three factors with a significant effect. This was confirmed by a multivariate analysis. The use of vitamin K antagonists could not be included since almost all patients received this medication for three months after operation. The three predictors were:

Factor	n/N	p	OR	95%CI
Concomitant CABG	17/610	0.046	3.6	1.0-12.5
COPD	8/235	0.051	2.6	1.0-6.6
Aortoplasty	4/61	0.058	3.5	1.0-12.6

Bleeding events could be considered as the other side of the coin of anticoagulation with vitamin K antagonists. Effective protection against thromboembolism holds the risk for bleeding. A continuous balance should be made. The INR does not only depend on the dose of vitamin K antagonists, but also on the adsorption of vitamin K by the mucosa of the colon and on its processing by the liver. No other reports concerning predictors for early bleeding after valve replacement appeared. Current results indicated that early bleeding seems related to the procedure and is different compared to bleeding events at long term, which is probably more related to anticoagulation. Nevertheless, other factors such as age and increased cardiothoracic index were identified as predictors for bleeding during long-term follow-up (26). Fragility in elderly might be an important reason. In other series, no predictors or risk factors could be identified (30,31).

Prosthetic valve endocarditis

The number of patients with early prosthetic valve endocarditis was low, hence no risk factors or predictors (such as preoperative endocarditis) could be identified in our series. Literature data only described long-term events. The linearized rate for long-term prosthetic valve endocarditis was low and mostly under 1% per patient year (26,27,32-39). The most event free rates after 5 to 25 year were well over 90%. This was true for mechanical heart valves (35,40,41) as well as for the different stented (30,42) and stentless tissue valves (27,36,43) as for homografts (8). No risk factors could be identified, although a previous endocarditis could arouse some suspicion. Prosthetic valve endocarditis carried a high risk for mortality, especially if Staphylococcus aureus has been detected (44). These micro-organisms often lead to ring abscesses and prosthetic paravalvular leak. The occurrence of congestive heart failure with prosthetic valve endocarditis has been the main indication for re-operation (45).

Congestive heart failure

Univariate analysis identified following risk factors:

P<0.001: Need for urgent surgery, chronic or paroxysmal atrial fibrillation
P<0.01: Age over 80, decreased left ventricular function, previous infarction
P<0.05: COPD, LVEF below 50%, preoperative heart failure, need for digitalis

NYHA class II had a protective effect (p<0.001)

Multivariate analysis showed following results

Factor	n/N	p	OR	95%CI
Urgent AVR	7/25	<0.001	10.5	3.6-30.8
Atrial fibr.	16/197	0.001	3.5	1.7-7.4
EF<50%	10/155	0.055	2.1	1.0-4.4

In-hospital congestive heart failure after AVR is a highly lethal complication (13,46). Hospital heart failure occurred in 2.6% of the patients in an earlier series (13), with need for urgent AVR as the sole independent predictor. This pointed to an exhaustion of all compensatory mechanisms to maintain an adequate circulation and this observation should reason not to postpone AVR, once it has become symptomatic. In another study, the level of B-type natri-uretic peptide was also identified as a predictor (46). Apoptosis or programmed cell death of cardiomyocytes could be an important event in these patients (47). Atrial fibrillation could lead to a decreased ventricular filling and cardiac output since the atrial contraction is lost. In an earlier series, this was also the case in long-term heart failure (13).

Early congestive heart failure should be distinguished from long-term heart failure: the latter was diastolic in nature and has some other risk factors such as conduction defects and coronary artery disease. An impaired relaxation occurred since after regression of the muscle mass, this fibrosis persists for a longer time. This stiffened the LV wall (48). The LVEF remained often normal. Hence, this could be labeled as a “diastolic” form of CHF (13). Concurrent conduction defects thereby could lead to perfusion defects and wall motion abnormalities, even in absence of coronary artery disease (49). Biventricular pacing often could correct this condition (50,51). Coronary artery disease could lead to ischemic loss of myocardial contractility, adding to the left ventricular function. Concomitant CABG, however was not identified as a predictor for postoperative CHF (13).

A small valve size has not been identified as a predictor for long-term heart failure in a previous series (13), neither in the current series for short-term heart failure. Hence, in patients with a small aortic root, it seemed not necessary to enlarge the root or to implant a stentless valve, which requires a more demanding technique, provided the LVF is normal.

However, it becomes important in patients with a low ejection fraction. When, in such patients, a small valve size leads to an even moderate prosthesis-patient mismatch, this might result in heart failure and an increased mortality (52).

Atrial fibrillation

Atrial fibrillation and other non-sinusal rhythms occurs in 20% of the postoperative patients (32). In other series, this was 40% or more (53,54). The definition and the diagnostic method for AF have also an effect on its incidence (54,55). Postoperative AF has not been considered as innocent: it could lead to other complications and an increased stay in the hospital. With atrial fibrillation, there was a higher incidence of postoperative mortality (54) heart failure, renal function impairment, infection and neurologic events (53).

Univariate analysis showed following risk factors

- P<0.01: Previous PTCA
- P<0.05: LVEF below 50%

In a multivariate analysis, previous PTCA was the only independent predictor ($p=0.006$; odds ratio 2.7; 95% confidence interval 1.3-5.4)

The risk factors for postoperative AF in other series were a history of paroxysmal atrial fibrillation, a large left atrium, a prolonged P wave, heart failure, high age, low ejection fraction and left ventricular hypertrophy (55-57). The effect of age, however remained a matter for debate: atrial fibrillation did not occur more frequently in octogenarians after AVR (27).

It seems that postoperative atrial fibrillation was preventable, at least in part. Pacing could half the frequency of this event (53). Timely and adequate treatment could increase the speed of postoperative rehabilitation and reduce the stay within the hospital (55).

Conduction defects

An univariate analysis showed as risk factors:

- P<0.001: preoperative heart failure
- P<0.01: carotid artery disease, concomitant CABG
- P<0.05: NYHA functional class IV

An AV block grade 1 showed a trend. A large valve size (27 mm) had no effect.

A multivariate analysis showed following results:

Factor	n/N	p	OR	95%CI
Preoperative heart failure	32/215	0.001	3.0	1.7-5.4
Concomitant CABG	69/610	0.007	2.0	1.2-4.2
NYHA class IV	23/249	0.039	1.9	1.0-3.4
AV Block grade 1	7/37	0.078	2.4	1.0-5.7

Conduction defects such as complete atrio-ventricular block, and hence permanent pacemaker implantation, occurred in almost 10% of the patients who underwent AVR (58). The occurrence of all new conduction defects is reported to be 15% (59). Other reports state a lower incidence for permanent pacemaker implantation, since not all conduction defects need this treatment. Sometimes, a new conduction defects could be reversible (58). Development of a new conduction defects resulted to an increased need for monitoring and hence a longer hospital stay (60)

The main predictor for permanent pace maker implantation in other series were preoperative conduction defects (58,61-63). Other predictors were female gender, annular calcification, bicuspid aortic valve, hypertension, myocardial infarction, electrolyte imbalance and prolonged cross-clamping time (60,64,65). Aortic regurgitation might also play a role since this condition usually required implantation of larger valves (58).

Preoperative changes in the conduction system might be degenerative and due to older age, to ischemia and mechanical factors, due to an increased left ventricular pressure (58).

Some factors such as a calcified annulus could lead to trauma of the conduction system during surgery. The link with a congenitally bicuspid aortic valve is less clear. Hypertension could lead to calcification but also to increased septal left ventricular hypertrophy, which makes the conduction system more difficult to protect during cross-clamping (60). Other traumas of the conduction system could be due to impingement by the prosthetic valve or by suturing (58).

Development of a new conduction defects such as left bundle branch block in the postoperative period was a marker for future adverse events, such as sudden death (59), which illustrates the importance of these defects.

Non cardiac hospital complications

Pulmonary complications occurred in 58/1000 patients after AVR (66).

Univariate analysis showed following risk factors

P=0.001:	postoperative heart failure
P<0.01:	preoperative PM implantation
P<0.05:	COPD

Multivariate analysis identified following predictors:

Factor	n/N	p	OR	95%CI
Pacemaker implant	7/33	0.002	4.4	1.8 – 11.2
COPD	21/235	0.073	1.7	0.95 – 3.1
Heart failure	7/34	0.001	4.7	1.8 – 11.9

Respiratory complications after AVR are common (9,66,67) but few reports appeared concerning their predictors. Their rate depends largely on the criteria used (need for prolonged ventilation, respiratory failure, pulmonary infection).

The basic mechanisms of these complications involved a lack of deep inspiration due to postoperative pain, with a shallow breathing pattern, a prolonged recumbent positioning, a temporary diaphragmatic dysfunction and an impaired mucociliary clearance with a decrease in cough effectiveness, increases the risks associated with retained pulmonary secretions and bronchial obstruction (68). Atelectasis, infection and prolonged stay within the intensive care unit could be the result of such obstruction (69,70).

The use of an extracorporeal circulation during cardiac operations certainly has side effects on the respiratory system, due to inflammation (71,72). With greater hemodilution this effect could increase resulting pulmonary edema and pneumonia, especially when endothelial cells are injured (73). Pulmonary edema was also a hallmark of postoperative heart failure, which has been identified as a clear risk factor for postoperative pulmonary complications. Chronic obstructive pulmonary disease could worsen the production of mucus, thereby increasing the risk for atelectasis and infection. Early postoperative heart failure, and hence pulmonary edema increase the need for ventilator support and prolong the stay on ICU. This also could make the patient more vulnerable for postoperative pulmonary problems (66).

In 58 of 1000 patients, we observed renal function impairment after AVR (17). Renal and cardiovascular disease could be linked in two ways. On the one hand, renal function impairment, even if this modest, has been an established element in the risk profile for atheromatosis (74,75). On the other hand, renal function impairment could also be the result of atheromatosis and has certainly been observed after major cardiovascular surgery such as AVR. Postoperative decrease of the renal function has been considered a serious complication with an increased mortality rate.

The risk factors in an univariate analysis for this complication were

Preop. renal impairment	22/108	29/890	<0.001
Age > 80	22/186	31/814	<0.001
Preop. atrial fibrillation	22/197	29/803	<0.001
Preop. pulmonary oedema	22/216	31/781	0.001
Preop. conduction defect	24/270	28/721	0.002
Diabetes	15/149	37/851	0.006
Preop. myocardial infarction	15/151	36/849	0.006
Postop. heart failure	6/34	47/966	0.007
CCT >75 min. (complete procedure)	29/460	7/275	0.015
Previously performed CABG	9/81	42/916	0.018
concomitant CABG	39/610	14/390	0.031
LV ejection fraction<0.50	13/155	31/723	0.033
Previous TIA/CVA	10/108	41/892	0.035

A multivariate analysis revealed following predictors

Factor	p	OR	95%CI
Preop. renal impairment	<0.001	5.5	2.9 – 10.4
Preop. atrial fibrillation	0.010	2.3	1.2 – 4.2
Age > 80	0.014	2.2	1.2 – 4.1
Myocardial infarction	0.022	2.2	1.1 – 4.4

Age over 80 has been associated with an increase in atheromatosis and myocardial infarction is certainly a marker for it. If atheromatosis also affects the renal arteries, a postoperative decrease in renal function could be expected (17).

Endothelial dysfunction of patients with CAVS could be a link with renal function impairment. This could help explaining the observed association between preoperative AF and postoperative renal complications. There are, however, several confounding factors (76,77).

Other risk factors were hypertension, peripheral arterial disease, bypass time over 70 minutes, severe angina and non-elective surgery (67,78).

Three difficulties could arise by comparing different series. First, the definition of previous renal function impairment as well as of postoperative decrease in renal function varied between series. In one series, a level of 2.0 mg/dl was used (78), in another 1.4 mg/dl (17). This could account for differences in results. The second difficulty has been the estimation of renal function: plasma creatinine, as a routine clinical procedure is not sufficient as estimate for glomerular filtration rate. Hence, its results should be interpreted cautiously. The estimation of glomerular filtration rate requires a 24-h urine collection, which is liable to errors. Third, defining a worsening of renal function by an increase of plasma creatinine (79) also had its difficulties: in patients with a plasma creatinine between 1 and 2 mg and hence, a moderate degree in renal function impairment, an additional increase with 0.3% could mean a serious additional renal damage. In patients with higher initial plasma creatinine, such an increase does not mean necessarily a major change in renal function: the slope of the relation between glomerular filtration rate and plasma creatinine is much less compared to the area with low initial plasma creatinine.

The extracorporeal circulation could have a damaging effect on the glomeruli, especially if the kidney already has been injured. Mechanisms inflicting renal damage are non-pulsatile perfusion, renal hypoperfusion, hypothermia, and increased levels of circulating catecholamines, cytokines, enzymes, free radicals and free hemoglobin (80). Keeping the cross-clamp time as short as possible or installing a minimal ECC could be helpful (81,82).

In spite of increasing age and co-morbid conditions in patients referred for AVR, the increase in hospital complications seemed to be limited to non-cardiac complications, which have a lower fatality rate than cardiovascular complications (83). The occurrence of renal and pulmonary postoperative events should be taken into account, however, if one chooses to operate older and sicker patients with symptomatic aortic valve disease.

4. Discussion and conclusions

Postoperative mortality and valve related complications received much attention in most patients series. Recently, other cardiac complications such as heart failure, conduction defects and atrial fibrillation were also scrutinized. Univariate analysis as screening and subsequent multivariate analysis as identification of risk factors for each event could be helpful patient selection and, more importantly, improve postoperative results if these risk factors are liable for alteration.

Mortality and congestive heart failure, which was identified as the most lethal cardiac complication, were clearly patient related. One might expect a reduction in these events if patients are referred early, once aortic valve degeneration has become symptomatic. This could avoid the appearance of a major risk factor, i.e. the need for urgent valve replacement. This is the clear consequence of a protracted pressure overload on the left ventricle by the diseased aortic valve and the ultimate marker for advanced heart valve disease.

Thromboembolism and bleeding are typically considered as valve related events. The former, however, could also be related to patient factors, while the latter could also be

related to the procedure. Both events could have a significance as risk factor for long-term recurrence.

Occurrence of early postoperative conduction defects and of atrial fibrillation could also be considered as markers of advanced valvular heart disease, since some of their risk factors might be the result of protracted pressure overload on the left ventricle. Hence, these events could be seen as patient related.

Non-cardiac complications could clearly be related to co-morbid conditions. These, however are not always liable to alterations. Hence, the peri- and postoperative care should be tailored for each patient. It has also become obvious that age over 80 is not a formal contraindication for AVR. Nevertheless, elderly usually have considerable co-morbidity. The EUROscore, which was developed for CABG patients overestimates the risk for hospital mortality considerably. Low ejection fraction, chronic pulmonary obstructive disease and peripheral artery disease have been identified as predictors, although (84). Pulmonary function after median sternotomy is reduced in a substantial way, probably by several mechanisms such as chest wall restriction, decreased movement of the diaphragm and impairment of diffusion across the alveolar membrane (85).

It seemed worthwhile, therefore, to explore some alternative techniques in valve surgery which could reduce the postoperative risk. These could be 1) minimal surgical access, 2) minimal extracorporeal circulation and 3) transcatheter aortic valve implantation.

The first alternative, minimal surgical access by ministernotomy (85-88) and anterolateral minithoracotomy (89-91) could expose the surgical field adequately. Possible indications could be obesity, chronic obstructive pulmonary disease (86) and previous chest irradiation or CABG with patent left internal mammary artery (91).

Some advantages have been described such as an economic benefit, improved cosmetic result, decrease in postoperative morbidity, length of stay, pain, blood loss and transfusion (86-90,92). Cross clamping time had increased, however (88). Two randomized trials have appeared, which compared minimal and conventional AVR. The first one, was very small and included 20 patients for every group (88). The second one excluded patients with obesity and pulmonary disease (85), in spite of previously mentioned indications (86). Pain and blood loss were less, but there was no less need for transfusion. No other benefits such as a decrease in renal or pulmonary complications or differences in postoperative pulmonary functions could be documented (85,88,93). Results in high risk patients were considered as excellent in a recent review, but randomized controlled trials comparing minimal with conventional AVR are needed (94).

The second approach involves the changes in extracorporeal circulation devices. The use of an extracorporeal circulation during AVR has the risks of hemodilution and of an inflammatory response, which could be reduced by an minimal extracorporeal circulation or MECC. This MECC is a closed system with a centrifugal pump, an oxygenator without a venous and cardiectomy reservoir. The patient functions as the venous reservoir (95). This reduces the contact of blood with artificial surfaces and with air. The risk for hemolysis and the need for blood transfusions also decreases (96). With MECC, there is less increase in C-reactive protein, troponin I level, and better preservation of platelets and renal function. Stroke and cerebral injury were also less. The improved biocompatibility of MECC is of special advantage in high risk patients (age over 65, renal and pulmonary dysfunction). The use of a minimal ECC involves a learning curve, however (82).

More recently, TAVI or transcatheter aortic valve implantation, either through an artery or through the cardiac apex has been developed as third alternative. In patients deemed unfit

for conventional AVR, TAVI was compared to balloon valvotomy through a randomized controlled (PARTNER) trial. Mortality (30-day and one-year) from any cause and repeat hospitalization as well as occurrence of cardiac symptoms (higher NYHA functional class) were significantly reduced after TAVI. Major strokes, bleeding events and major vascular events occurred more often, however. Balloon valvotomy did not alter the course of aortic valve disease. Paravalvular leaks after TAVI were usually mild and did not worsen after one year. Postprocedural stroke was troublesome, but might be reduced by developing smaller delivering devices. These results cannot be extrapolated to patients in whom conventional AVR is an option (7). The trans-apical approach for TAVI is a feasible alternative in high risk elderly patients with symptomatic aortic valve disease and peripheral artery disease. There is no need for sternotomy or extracorporeal circulation. No post-procedural stroke was observed, probably due to the avoidance of an atheromatous aortic arch. Presence of preoperative respiratory dysfunction proved to be a risk. The procedural success rate was high. Compared to a control group of patients who underwent conventional AVR (by propensity score analysis), 30-day and one-year survival superior for trans-apical TAVI, but this difference was not significant (97).

To document the superiority of either of these minimal approaches, RCT on sufficiently large scale are needed. For ministernotomy and minithoracotomy, these are feasible, but still lacking. For TAVI, it is currently unethical for patients to subject patients to the still unknown long-term results of TAVI if these are deemed fit for conventional AVR. Conventional AVR still can be considered as the standard therapy for degenerative aortic valve disease, with very predictable results, even in the elderly and patients with co-morbid condition.

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This book considers mainly the current perioperative care, as well as progresses in new cardiac surgery technologies. Perioperative strategies and new technologies in the field of cardiac surgery will continue to contribute to improvements in postoperative outcomes and enable the cardiac surgical society to optimize surgical procedures. This book should prove to be a useful reference for trainees, senior surgeons and nurses in cardiac surgery, as well as anesthesiologists, perfusionists, and all the related health care workers who are involved in taking care of patients with heart disease which require surgical therapy. I hope these internationally cumulative and diligent efforts will provide patients undergoing cardiac surgery with meticulous perioperative care methods.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

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InTech Europe

University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

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