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How Does the Referral Pattern for Aortic Valve Replacement Evolves over Time and How does this Affect Short-Term Outcome

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ABSTRACT

Introduction: The referral pattern for aortic valve replacement has changed during the last decades: the patients' age as well as their co morbidity increased. An ongoing change could, if it still occurs, have an effect on the short-term postoperative outcome.

Methods: Twenty-six preoperative and 5 operative factors as well as 13 postoperative events are analyzed for their occurrence in four 7-year periods, from 1987 to 2014. A chi-square analysis for categorical variables was used.

Results: The number of valve replacement has increased drastically over time. Patients, referred for aortic valve replacement are becoming older, with increasing co-morbid conditions, cardiovascular as well as non-cardiac. Even a malignancy in the patient's history is becoming more common. The need for urgent surgery is also becoming important. Concomitant procedures on the ascending aorta and on the mitral valve are also increasing. Coronary artery bypass graft, as most common concomitant procedure is not. Some major postoperative events such as congestive heart failure, acute renal injury and pneumonia also have increased. Other, potentially fatal events remain uncommon throughout the entire time span. These events include endocarditis, thromboembolism, major bleeding, and myocardial infarction. Nevertheless, mortality did not increase significantly.

Conclusion: There is a clear parallelism between on the one hand a rise in age, in preoperative non-cardiac comorbid conditions, severity of heart disease and on the other hand, a rise in postoperative complication rate. This affects cardiovascular as well non-cardiac systems. Prior results indicate that factors such as need for urgent surgery, congestive heart failure, chronic renal or pulmonary disease but also age have a clear effect on postoperative outcome. Although some rise of mortality can be observed, this increase was not significant. Remarkably, while the age and comorbidity of patients referred for aortic valve replacement are increasing, literature data also show that indications for the transcatheter valve implantation are expanding to younger patients with less co morbid conditions.

Key words: Aortic valve replacements; Co-morbid conditions; Postoperative complications

Abbreviations: AMI: Acute Myocardial Infarction; ARI: Acute Renal Injury; ASA: Acetyl Salicylic Acid; AF: Atrial Fibrillation; AVR: Aortic Valve Replacement; BMI: Body Mass Index; CABG: Coronary Artery Bypass Graft; CAD: Coronary Artery Disease; CHF: Congestive Heart Failure; CKD: Chronic Kidney Disease; COPD: Chronic Obstructive Pulmonary Disease; CVA: Cerebrovascular Accident; LCOS: Low Cardiac Output Syndrome; LF-LG: Low-Flow Low-Gradient; LVEF: Left Ventricular Ejection Fraction; LVF: Left Ventricular Function; NYHA: New York Heart Association; PAD: Peripheral Artery Disease; PAHT: Pulmonary Arterial Hypertension; PCI: Percutaneous Coronary Intervention; PM: Pace Maker; TAVI: Transcatheter Aortic Valve Implantation; TE: Thromboembolic; TVG: Trans Valvular Gradient; VKA: Vitamin K Antagonist

INTRODUCTION

Degenerative aortic valve disease is the third most common cardiovascular disease, after hypertension and Coronary Artery Disease (CAD) [1]. This condition can remain asymptomatic, but when symptoms such as dyspnea, angina or syncope appear, the prognosis becomes dismal [2,3]. Especially signs of left sided heart failure are ominous. Moreover, it can be difficult to distinguish valvular symptoms from those of other origin such as from Chronic Obstructive Pulmonary Disease (COPD), from Congestive Heart Failure (CHF) due to ischemic cardiomyopathy of from “just getting old”. However, it is in such patients that this distinction is important, because it has already been shown that there is a tendency to refer older and sicker patients for Aortic Valve Replacement (AVR). This was evident long before the breakthrough of Transcatheter Aortic Valve Implantation (TAVI): between 1978 and 1986, the proportion of patients aged over 70 years increased from 11% to 54% [4]. A more recent report which appeared in 2003, was derived from a nationwide US-Canada database. It showed that of 662,033 patients who underwent cardiac surgery, 59,576 were between 80 and 89 years, 1,092 were between 90 and 99 years and 5 patients were 100 or more years. In the group of patients over 90 years, 424 received a valve (aortic or mitral), with or without Coronary Artery Bypass Graft (CABG). Co-morbid conditions were clearly present [5] and showed remarkable similarity with the first two periods from our prior results [6], except that CHF and need or urgent surgery was lower in our group, while the mean Left Ventricular Ejection Fraction (LVEF) was higher. Our prior report also indicated that comorbid conditions were also becoming more common [6]. This rise in referral for AVR of older and sicker patients is in contrast with another report which states that AVR is denied in 33% of the patients. The reasons for this denial were older age and decreased Left Ventricular Function (LVF). Except for neurological dysfunction, comorbidity according the Charlson index was not a reason [7]. In any case, surgical AVR has proven its benefit over medical management in elderly patients. This benefit was more pronounced in patients under 80, with more severe aortic valve stenosis and with cardiac comorbidity [8]. Even in a small series of patients with advanced cancer, AVR proved to be useful [9]. In our previous published series, we could also demonstrate the effect of age and preoperative co-morbidity on outcomes such as mortality, thromboembolism (TE), low cardiac output syndrome (LCOS), Acute Renal Injury (ARI) and pulmonary complications [10-14]. Implantation of a Carpentier-Edwards valve has advantages, since this device has no sutures. The following questions arise in this respect

- Is the referral practice is still changing,
- To which extent are the future patients becoming older,
- To which extent is the comorbidity rising,
- What is its effect on short-term outcome
- What is the benefit of surgical AVR compared to medical treatment
- What will the share of surgical AVR be in an ever developing TAVI?

The aim of this report is to facilitate clinical decision making in the individual elderly patient with a stenotic aortic valve and a high degree of comorbidity.

PATIENTS AND METHODS

From the start of 1987 to the end of 2014, patient files were retrospectively studied. Those patients who received a biological valve in aortic position were considered for inclusion. Exclusion criteria were mechanical valves in any position, prior implantation of a biological valve in mitral or tricuspid position, concomitant mitral or tricuspid replacement. Surgery was performed in a general teaching hospital. In 2045 patients, a biological valve, mostly a Carpentier-Edwards pericardial was implanted. Valve replacement was performed through median sternotomy. If technically feasible, a so-called hemisternotomy was performed. After installation of the extracorporeal circulation, cold crystalline cardioplegia was instilled until the heart stopped and topical cooling was applied. After opening the aorta, the valve leaflets were excised and the biological prosthesis valve was implanted, using interrupted sutures (unless it was a Percival device). CABG was performed in presence of CAD. This was done during the same clamp as for the valve or by intermittent cross-clamping, according the discretion of the surgeon. If necessary, mitral valve repair, tricuspid valve repair, aortoplasty, replacement of the ascending aorta, myectomy according to Morrow or Maze-ablation were performed. These associated procedures were no reason for exclusion. After decanulation, left atrial pressure leads, pacemaker (PM) leads and drainage were installed. The patient was transferred to an intensive care unit. The patients were transferred to the ward within one day if no complications occurred or later, when complications had resolved. The stay in the ward was mostly 6 to 8 days. Twenty-six preoperative, 5 operative and 13 postoperative factors were analyzed for their occurrence in four 7-year periods, from January 1987 – December 1993, January 1994 – December 2000, January 2001 – December 2007 and January 2008 – December 2014. The data were collected by studying patient files. Factors were dichotomized in "present" or "absent". Statistical analysis was performed by a chi-square analysis. The definitions of factors are provided in table 1.

Table 1: Definitions of preoperative and operative factors and of postoperative complications.

Factor/complication	Definition
Diabetes:	diagnosed by a physician and treated with diet, oral medication or insulin
Malignancy:	any cancer or hematologic malignancy documented by histology,except basocellular carcinoma; mostly treated by curative intent or under control, as in chronic lymphatic leukemia
COPD:	forced expiratory volume at 1 second less than 80% of the predicted value
CKD:	plasma creatinine over 1.30 mg% or glomerular filtration rate below 60ml/min
CVA:	any sudden neurologic event that does not resolve within 24 hours (mostly documented on CT scan)
TIA:	any sudden neurologic event that resolves within 30 minutes (for which in most cases a CT was taken)
Hypertension:	blood pressure over 140/90 mmHg, repeatedly taken at rest
Carotid artery dis:	documented on duplex/Doppler with a stenosis of at least 50% or with severe calcification
AMI:	both STEMI and non-STEMI, documented on ECG and confirmed by blood analysis (cardiac troponin); this applies also to postoperative AMI
LV hypertrophy:	documented on echocardiography with wall thickness (septal and posterior) over 11 mm.
CHF:	documented by the referring cardiologist; if postoperative; called low cardiac output syndrome, documented by pulmonary edema or by continuous hemodynamic monitoring
Coronary artery dis:	a stenosis of at least 50%, in at least one coronary vessel, documented on coronary angiography
Conduction defect:	any degree at atrio-ventricular level or any bundle branch block; if postoperative: any new event or any progression
Atrial fibrillation:	documented on ECG, either as paroxysmal or chronic; if postoperative: any new or recurring AF
PVB:	documented on ECG, as a non-sustained short run, or as multifocal especially at exercise
Endocarditis:	suspected on clinical grounds and proven by blood culture and echocardiography (this applies to both pre and postoperative)
Regurgitation:	graded on echocardiography and indicated as dominant with grade 3/4 or 4/4
Use of digitalis:	recorded by anamnesis
Urgent AVR:	aortic valve replacement needed at the same day to save the patient's life
Aortoplasty:	any procedure on the ascending aorta during AVR (except root replacement): widening, narrowing or replacement of the ascending root.
Mitral valve repair:	annuloplasty, quadrangular resection of a leaflet, any procedure on the chorda
Thromboembolism:	any focal neurological event which is not due to bleeding or any embolism into other arteries (peripheral, visceral)
Bleeding:	any serious bleeding: digestive, urinary, soft tissues, cerebral (documented on CT)
Ventricular arrh:	frequent or multifocal PVB, ventricular tachycardia and fibrillation documented on ECG
Acute renal failure:	increase of postoperative plasma creatinine level by at least 0.30mg%
Pulmonary complic:	clinical and radiological signs of atelectasis or of pneumonia
Pleura complication:	need for prolonged aspiration or pleural effusion requiring needle aspiration
No complication:	absence of any of the pervious complications, without increased LOS

AF: atrial fibrillation; AMI: acute myocardial infarction; Arrh: arrhythmia; AVR: aortic valve replacement; CHF: congestive heart failure; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; complic: complication; CT: computer tomographic; CVA: cerebrovascular accident; dis: disease; ECG: electrocardiogram; LOS: length of stay; LV: left ventricle; PVB: premature ventricular beat; STEMI: ST-elevated myocardial infarction.

RESULTS

Table 2 shows the increase in number of patients as well as changes in preoperative factors. There were 2045 patients. Of these, 1254 patients received also CABG. The mean age of the patients increased from 72.3+/-5.0 years to 76.1+/-6.6 years. This is paralleled by a significant rise in referral of the elderly (over 80 years) and the very elderly patients (over 85 years). A clear rise of non-cardiac comorbid factors over time can be observed. Some, such as diabetes, COPD, Chronic Kidney Disease (CKD) and malignancy double or even triple in this 28 year time span. There is also a significant increase in cardiovascular comorbidity, such as presence of carotid artery disease, prior myocardial infarction (AMI), CHF, prior CABG or Percutaneous Coronary Intervention (PCI), left main stem disease, atrial fibrillation (AF, paroxysmal as well as chronic), premature ventricular beats, and last but not least need for urgent AVR. Some factors such as male gender, hypertension, and left ventricular hypertrophy showed no clear pattern or remained constant throughout. Aortic valve conditions which were mainly regurgitation and especially need for digitalis decreased considerably.

Table 2: changes of preoperative factors over time.

Preoperative factor	Period 1	Period 2	Period 3	Period 4	p
Number of patients	147	427	588	883	
Age over 80	8/147(5.4)	72/427(16.9)	152/588(26.0)	286/883(32.14)	<0.001
Age over 85	0/147(0.0)	13/427(3.0)	27/588(4.6)	84/883(9.5)	<0.001
Diabetes	14/147(9.5)	45/427(10.5)	125/584(21.4)	224/883(25.4)	<0.001
COPD	12/147 (8.2)	71/417 (17.7)	202/557 (36.3)	233/874 (25.5)	<0.001
CKD	2/147 (1.4)	30/425 (7.1)	111/582 (19.1)	130/878 (14.8)	<0.001
Hypertension	124/147 (84.4)	259/422 (61.4)	391/582 (67.2)	641/872 (73.5)	<0.001
CHF	17/147 (11.6)	78/424 (18.4)	154/582 (26.5)	236/879 (26.8)	<0.001
Carot.art. disease	2/147 (1.4)	75/422 (17.8)	213/573 (37.2)	177/874 (20.3)	<0.001
PCI	1/147 (0.7)	16/426 (3.8)	42/579 (7.3)	134/871 (14.4)	<0.001
Main stem disease	5/147 (3.4)	26/427 (6.1)	54/588 (9.2)	115/883 (13.0)	<0.001
Regurgitation	28/127 (22.0)	53/368 (14.4)	50/572 (8.7)	97/856 (11.3)	<0.001
Use of digitalis	39/117 (33.3)	69/377 (18.3)	48/567 (8.5)	29/861 (3.4)	<0.001
Need urgent AVR	0/147 (0.0)	16/427 (3.7)	20/582 (3.4)	54/864 (6.3)	=0.002
Atrial fibrillation	20/147 (13.6)	79/426 (18.5)	140/582 (241.1)	217/868 (25.0)	=0.002
Male gender	86/147 (58.5)	233/427 (54.6)	298/588 (50.7)	527/883 (59.7)	=0.003
malignancy	11/147 (7.5)	53/426 (12.4)	56/571 (9.8)	133/862 (15.4)	=0.003

PVB	14/147 (9.5)	29/427 (6.8)	57/576 (9.9)	114/868 (13.1)	=0.005
CABG	0/147 (0.0)	23/427 (5.4)	31/578 (5.4)	39/883 (4.4)	=0.034
AMI	15/147 (10.2)	56/426 (13.1)	106/583 (18.2)	144/877 (16.4)	=0.037
CAD	83/147 (56.5)	287/427 (67.2)	360/578 (62.3)	563/869 (64.8)	=0.089
CVA/TIA	10/147 (6.8)	44/427 (10.4)	77/584 (12.2)	111/876 (12.7)	=0.107
Conduction defect	42/147 (28.6)	107/427 (25.1)	170/571 (29.8)	273/863 (31.6)	=0.111
AVR	6/146 (4.1)	9/427 (2.1)	8/575 (1.4)	13/873 (1.5)	=0.127
LVEF<50%	21/131 (16.0)	(79/404 19.6)	101/467 (21.6)	105/428 (24.5)	=0.134
PM implant	3/147 (2.0)	14/426 (3.3)	31/573 (5.4)	37/869 (4.3)	=0.199
LV hypertrophy	93/101 (92.1)	305/332 (91.9)	420/473 (88.8)	654/739 (88.8)	=0.292
Endocarditis	2/147 (1.4)	8/427 (1.9)	7/583 (1.2)	16/878 (1.8)	=0.777

AMI: myocardial infarction; AVR: aortic valve replacement; CABG: coronary artery bypass graft; CHF: congestive heart failure; CAD; coronary artery disease; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; LVEF: left ventricular ejection fraction; PCI: percutaneous coronary intervention; PM: pacemaker; PVB: premature ventricular beat;

Table 3 shows the changes in operative factors. The need for CABG (overall 61.3%) did not change significantly throughout the 28 y time-span. There was an increasing need for procedures on the ascending aorta and even more on the mitral valve. The use of size 19 bioprosthesis decreased, but this was already low from the start.

Table 3: changes of operative factors over time.

Operative factor	Period1	Period 2	Period 3	Period 4	p
Diameter 19	5/147 (3.4)	22/427 (5.2)	14/588 (2.4)	12/876 (1.4)	<0.001
MVR	4/147 (2.7)	9/427 (2.1)	6/584 (1.0)	51/866 (5.9)	<0.001
Aortoplasty	8/147 (5.4)	21/427 (4.9)	45/583 (7.7)	77/868 (8.9)	=0.059
CABG	83/147 (56.5)	271/427 (63.5)	351/588 (59/7)	549/883 (62.2)	=0.069
Carotid surgery	0/147 (0.0)	9/427 (2.1)	17/583 (2.9)	20/868 (2.3)	=0.207

CABG: coronary artery bypass graft; MVR: mitral valve repair.

Table 4 shows the changes in postoperative factors. The number of patients without postoperative complications had decreased significantly. The non-cardiac complications had also increased considerably, while some other complications did not alter. The most lethal cardiac complication, CHF, also increased significantly. Mortality, however, remained largely unchanged. Some events such as endocarditis, TE, severe bleeding, ventricular arrhythmias and AMI were uncommon throughout the entire time span of 28 year, which might explain in some cases the lack of significant changes.

Table 4: changes of postoperative factors over time.

Postop factor	Period 1	Period 2	Period 3	Period 4	p
No complications	64/147 (43.5)	140/427 (32.8)	216/588 (36.7)	228/883 (25.8)	<0.001
ARF	6/147 (4.1)	23/427 (5.4)	53/581 (9.1)	184/862 (21.1)	<0.001
Pulmonary complications	9/147 (6.1)	28/427 (6.6)	36/584 (6.2)	140/872 (16.1)	<0.001
Pleura complications	2/147 (1.4)	15/427 (3.5)	54/585 (9.3)	136/870 (15.6)	<0.001
Bleeding	3/147 (2.0)	6/420 (1.4)	19/585 (3.2)	55/873 (6.3)	<0.001
CD	11/147 (7.5)	34/421 (8.1)	75/584 (12.8)	175/872 (20.0)	<0.001
CHF	3/147 (2.0)	17/421 (4.0)	26/585 (4.4)	64/871 (7.3)	=0.007
AF	48/147 (32.6)	160/421 (38.0)	210/586 (35.8)	364/873 (41.6)	=0.053
Mortality	7/147 (4.8)	14/427 (3.3)	24/588 (4.1)	49/883 (5.5)	=0.261
VA	2/147 (1.4)	19/418 (4.5)	23/585 (3.9)	28//873 (3.2)	=0.283
Endocarditis	1/147 (0.6)	1/419 (0.2)	0/584 (0.0)	3/873 (0.3)	=0.408
TE	4/147 (2.7)	10/420 (2.4)	20/585(3.4)	23/873 (2.6)	=0.758
AMI	0.147 (0.0)	3/427 (0.7)	3/584 (0.5)	6/873 (0.7)	=0.762

AF: atrial fibrillation; AMI: myocardial infarction; ARF: acute renal failure; CD: conduction defect; CHF: congestive heart failure; TE: thromboembolic event; VA: ventricular arrhythmia.

DISCUSSION

This patient series started with the implant of a Carpentier-Edward pericardial valve from early 1987 on. This device has been chosen because it has no sutures, and hence, no tears are to be expected. According to the ACC/AHA guidelines [15], biological valve prostheses are implanted mostly in patients older than 65 years old. A minority of our patients received this valve, not for age considerations, but for a decreased life expectancy for non-cardiac reasons. Including only biological valves, therefore gives an adequate reflection of elderly patients with symptomatic degenerative aortic valve disease. During a time span of 28 years, age, comorbidity and severity of heart disease increased significantly in patients referred for AVR. Parallel to this, there was a rise in complication rate, especially for renal, pleural and pulmonary causes, although there was also a rise in bleeding, conduction defects and LCOS. This is in contrast to our previous finding, where no significant increase in cardiovascular complications was observed [6]. Nevertheless, there was no significant change in mortality, in previous or in the current series. This confirms an old report, which states that "… associated arterial and extra-cardiac pathology does not significantly increase the mortality" [16]. Older age could also be found in a report from the same era, where the oldest patients were well over 80 [17]. The postoperative events under scrutiny are mortality, TE, LCOS, pulmonary complications and ARI.

Since aortic valve stenosis poses a continuous overload on the left ventricle, it seems worthwhile to examine the effect of changes in LVF on postoperative mortality. Mortality during hospital stay or within the first 30 days after operation is the most dramatic complication. In our prior results we found a mortality of just under 4%. Four predictors have been identified, 1) need for urgent surgery (9 - 10 times increased risk), 2) age over 80 (3.1 - 4.5 times increased risk), 3) need for digitalis (3.1 - 3.8 times increased risk) and 4) AMI (3.1 times increased risk). Other significant factors in a univariate analysis were prior period of CHF, decreased LVF, CKD, AF and diabetes. New York Heart Association (NYHA) functional class II had a protective effect [10,18]. Of these factors, need for urgent surgery, need for digitalis, prior AMI, prior CHF, NYHA functional class and decreased LVF or LVEF below 50% can directly or indirectly be related to the left ventricle. This part of the heart suffers directly from the pressure overload in aortic valve stenosis. Hence, LVF plays a pivotal role. Other useful factors related to the LVF could be the presence of Pulmonary Arterial Hypertension (PAHT), and lowering of the Transvalvular Gradient (TVG). The latter could serve as indicator for a low-flow / low-gradient (LF-LG) state. Of the predictors identified in our series, only need for digitalis decreased significantly. Hence, its importance has almost disappeared over time. The other three predictors, age over 80, need for urgent AVR and prior AMI had increased significantly in this time span. Their role as predictor has become more important. The same is true for prior the risk factors CHF, CKD and AF. Age, preoperative CKD [19] preoperative CHF [20] and recent AMI [21] were confirmed as predictors for hospital mortality in other series [19]. Patients with preoperative CHF had also a higher degree of comorbidity [20]. Other series risk factors such as BMI above 30 or below 20, prior CABG [21] or preoperative PAHT and its degree [22] were also identified. The role of prior CABG is debatable, however. An isolated AVR in octogenarians who had underwent prior CABG proved to be safe: postoperative mortality did not increase, compared to patients who had a first-time cardiac operation through sternotomy [23]. In one population of patients with aortic valve a decreased LVF was considered as an acceptable risk for AVR [19]. The LF-LG condition might also reflect the LVF. This condition could pose some difficulties in the diagnosis of aortic valve stenosis and the decision making for AVR [7]. As long as TVG is high, this after load can be held responsible for possible reduction in LVEF. Relief of that gradient by AVR should lead to postoperative improvement of LVF. When, in presence of severe aortic stenosis, the TVG is relatively small, this postoperative improvement will be limited, because the myocardium has been affected severely by the overload. This translates in a decreased survival after AVR. Nevertheless, this operation has far better results compared to medical treatment. It seems therefore necessary to stratify the LF-LG patients according 1) severity of stenosis (which might sometimes be overestimated) 2) contractile reserve with at least 20-25% increase in cardiac output, 3) presence of viable myocardial tissue in presence of CAD and 4) other comorbid conditions [3]. Low LVEF (35% or lower) and low mean TVG (30 mmHg or lower) in presence of small aortic valve area (1.0 cm^2 or lower) have been identified as risk factors for mortality. Higher Euro SCORE, multi-vessel CAD, concomitant CABG, and small size prosthesis were also risk factors for mortality [24,25]. Absence of contractile reserve was a strong predictor poor prognosis. Surgery in a more recent era had a protective effect [26]. Even in this subset of patients, AVR shows better results compared to medical treatment [25,26].

Thromboembolism during hospital stay can also have a devastating effect on patients if these leads to an irreversible neurological deficit. In our previous series, there were few events, with a rate of about 2.5%, of which the majority were neurologic in nature. LVEF below 50% was an independent predictor (2.5 times). There was also a trend for postoperative TE in patients with CKD [11,18]. However, even these few hospital events have a significance: these were identified as predictor for long-term TE events. Other risk factors for postoperative stroke were PAD, a history of cerebrovascular disease, diabetes and stroke [19].

There is a debate, however, concerning the anticoagulant or antithrombotic protocol after implantation of a bioprosthetic valve in aortic position. The main advantage of biological valve is the absence of need for vitamin K antagonists (VKA) on long-term [27], provided there is a low risk for TE [28]. The risk for TE events within the first three months is about 1% and can be considered as rare [29]. It seems that the differences in protocol has also its importance: up to 6 months, preoperative CVA and peripheral vascular disease were strong predictors of postoperative TE, major bleeding event or both, in patients treated with VKA, though not in patients treated with ASA. Anyway, elderly patients taking ASA and VKA together results in lower postoperative TE rates, compared to ASA or VKA alone. This, however is at the expense of a higher bleeding rate [29]. Moreover, patients who benefit from anticoagulation are more likely to be female, with severe preoperative symptoms, and small prostheses. Patients in sinus rhythm and otherwise low risk do not seem to benefit from early anticoagulation [30]. An isolated AVR in octogenarians who had underwent prior CABG proved to be safe: bypass time was longer but cross-clamp time did not change and postoperative stroke did not increase, compared to first-time sternotomy [23]. Summarized, one can state that there is only an “expert opinion pointing to similar use and advantage of acetylsalicylic acid (ASA) compared to VKA” [31].

A complication with high fatality rate is LCOS and occurred in 2.6% of our previous series, [6,12,18]. Need for urgent surgery was the most dominant predictor, followed by AF and LVEF below 50%. High NYHA class, CKD, prior AMI, need for digitalis, prior CHF and age over 80 also had an effect but only in a univariate analysis. Administration of digitalis has become uncommon: for heart failure, use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and renin blockers have become available as more efficient means: these agents effectively reduce symptoms and prolong life. Contemporary models can predict persistent or recurrent CHF on (long-term) after AVR: mean TVG, body surface area and preoperative functional NYHA class were predictors [32]. Hemodynamic parameters can return to normal after AVR, even in patients with reduced cardiac index and PAHT [33]. PAHT and its degree was associated with postoperative LCOS [22].

Pulmonary complications occurred in about 6% of our series. This was comparable with the results in trials focusing on minimally invasive AVR or on partial sternotomy [34,35]. These complications were defined as prolonged mechanical ventilation, respiratory failure requiring mechanical or non-invasive positive pressure ventilation, pneumonia and atelectasis requiring intervention. Atelectasis was the most frequent pulmonary complication. A change of postoperative ventilation regimen towards fast-track had no effect on the rate of pulmonary complications. Four predictors were identified. The two preoperative predictors were COPD and prior pacemaker implant. The two postoperative predictors were postoperative CHF and bleeding. No operative predictors could be identified [13]. In most patients who developed a fatal pulmonary complication, another complication was also involved [6]. In contrast to CABG, an extracorporeal circulation is always required in AVR. This can induce a systemic inflammation as well as an imbalance in the redox status of the patient [36]. Hemodilution with increase of the oncotic gradient, extravasation and injury of endothelial cells also might play a role [37]. TAVI through the arterial route seems to reduce the number pulmonary complications per patient significantly compared to apical access or the surgical replacement. The ventilation time and post-procedural / postoperative length of stay was also reduced [38].

For ARI, which occurred in about 5% of the patients, preoperative predictors were CKD, preoperative AF, age over 80 and prior AMI [14]. Especially in octogenarians, CKD – which was present in 16.3% of the cases – has been identified as risk factor [39]. Other predictors were body mass index and need for transfusion of red blood cells during operation. In only 1/25 of the cases, dialysis is needed [40]. The use of an extracorporeal circulation, which is always needed to perform AVR, could be held responsible in part. Free hemoglobin, free radicals and cytokines can damage glomeruli and tubuli. This is even more important in patients with PAD, CKD, diabetes or hypertension [19,41]. Postoperative ARI has a significance: it increases the risk for stroke [42], functional impairment, increased length of stay and increased mortality [39,40]. In our prior series [6], ARI was never alone responsible for fatality. At least one more complication was involved. One important note has to be made: ARI after cardiac surgery with an extracorporeal circulation occurs between about 3% and 43% pf the patients [40]. This depends largely on the definition of ARI. This can also be held responsible for a wide variation in predictors. For TAVI, a similar observation can be made. Factors identified as independent predictors of ARI were: CKD, high Euro SCORE, diabetes mellitus, hypertension, COPD, anemia, PAD, CHF, surgical priority, cardiopulmonary bypass time, reoperation, use of intra-aortic balloon pump, need for re-exploration, blood transfusion, postoperative thrombocytopenia, postoperative leukocytosis as well as demographic variables such as age and female gender [40]. A prior CABG in octogenarians who underwent isolated AVR was not identified as predictor for ARI [23], PAHT and its degree, however, was [22].

From the current results, it can be concluded that complications after AVR are inevitable, certainly with an ageing population and an increasing comorbidity. For every type of complication risk factors can be identified. These can be roughly divided into modifiable and non-modifiable factors. Non-modifiable factors include age and non-cardiac co-morbidities such as CKD, COPD, current or prior cancer and diabetes. Most neurological conditions such as dementia and Parkinsonism are also non-modifiable. Current and previous results indicate that age and most comorbid conditions are no contra-indication for AVR. Potentially modifiable factors include preoperative reduction of LVEF, periods of CHF, LF-LG condition and need for urgent AVR.

Development of these conditions could be prevented by timely operation, preferably at the onset of symptoms. However, even when these conditions have developed, most patients still have benefit from AVR, since medical treatment produces far worse results.

The introduction of TAVI altered the treatment of aortic valve disease drastically. Developments between 2008 and 2014 show a shift from AVR to TAVI in elderly patients: there was a small decline in isolate surgical AVR and surgical AVR with CABG; the TAVI showed a steep rise. Hence, the sum of all procedures increased drastically. TAVI has increased 20-fold and its volume has become larger than the number of isolated surgical AVR. While mortality of AVR remains the same (as in our population), the in-hospital mortality of TAVI decreased from 10.4% to 4.2%. Neurologic events were also comparable in spite of higher age and comorbidity in TAVI patients. Conversion to surgery became rare (0.6%). It seems that TAVI will go the same way as PCI [43]. Remarkably, while the surgical population increased in age and comorbidity, there is a trend to expand the indication for TAVI to younger patients with less comorbidity. Especially the introduction of TAVI on the patient population undergoing surgical AVR in the same institution showed some interesting effects. The mean age of patients referred for AVR did not alter significantly, but there was a significant decrease in prior CHF, CAD, hypertension, obesity and LVEF below 50%. There was also a trend towards lower logistic EuroSCORE I, preoperative COPD and increase of the very old (85 years or more). However, mortality and postoperative complication rate did not alter significantly [44]. As in our series, there was an increase in number of surgical AVR after the introduction of TAVI. Explanations could be 1) the increasing number of patients with aortic valve stenosis, 2) presence of the possibility of TAVI could increase referrals to tertiary centers, and 3) the favorable results in the surgical arm of trials, even in octogenarians. In contrast to the current series, these results show some decrease in comorbidity reflected in the logistic EuroSCORE. Nevertheless, TAVI has become the first-line treatment for inoperable patients with severe aortic valve stenosis. It is superior to surgical AVR in high-risk patients. With newer devices, complications have reduced further. Although, at the time, no randomized controlled trials exist, registries seem to suggest treatment of low-risk patients is already occurring [45]. Treatment of "off-label" (LVEF<20%, anatomical considerations, severe mitral regurgitation, pure aortic regurgitation, degenerated bioprosthesis and a higher EuroSCORE) has become a reality, but these high risk patients show a higher 30-day and 1-year mortality, except for those with degenerated bioprosthesis. For those patients, the valve-in-valve procedure shows promising results. In this respect TAVI could serve as alternative for redo-surgery. Patients with very low LVEF do very poor at 30-day and at 1-year [46]. For these reasons, the view of the cardiologists [47] should be balanced by the view of the cardiac surgeon [48]. There is a growing indication for TAVI, while results compared to AVR are superior in terms of short and mid-term survival as well as for functionality. Each approach has its own problems, however. Surgical AVR was associated with a higher risk for blood transfusion, whereas TAVI showed a significantly increased rate of vascular damage, permanent atrioventricular block and residual aortic valve regurgitation [49,50]. The techniques and methods for patient selection have been refined. Expansion to patients with intermediate surgical risk seems to be promising in terms of survival and occurrence of major cardiovascular events [51-54]. However, it still remains to be seen if the outcome of TAVI in lower risk groups be the same as for surgical AVR [48]. Risk scores have not been validated for TAVI and vital information (such as vascular anatomy, prior CABG, prior radiotherapy of the chest) is not included. Risk scores do not replace sound judgement of multidisciplinary teams [55]. Paraprosthetic leak which is graded more than mild is reported in all series and is an independent predictor of mortality at short and mid-term [56]. The need for a PM implantation is probably not so relevant in elderly, but the effect of a PM on hemodynamics [57] might be more important in younger patients. The durability of the implant seems promising in elderly [58] probably because high risk patients do not live long enough because of age or comorbid conditions. However, for younger patients with lower risk this is not true. Moreover some damage due to the effect of crimping and mounting on a delivery system has been demonstrated [59]. Last but not least, will TAVI go the way of PCI: in complex CAD, PCI showed more long-term adverse cardiovascular events compared to CABG [60]. The use of Perceval suture less valve and the TAVI valve-in-valve technique seem also to have a place in the armamentarium.

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