10

Relationship Between Aortic Valve Replacement and Old Age

Jean-Michel Maillet[1] and Dominique Somme[2]
[1]Centre Cardiologique du Nord, Saint-Denis,
[2]Hopital Européen Georges Pompidou, Paris,
France

1. Introduction

Many factors can explain the most important increase of human life expectancy during the XX[th] century: better socioeconomic conditions, improved working conditions, development of preventive measures, less alcoholism, appearance of antibiotics, advances in medical practices, etc… At present, the fastest growing age group in western countries is people >80 years old; they will represent 9–10.5% of the population in those countries in 2050. Today, life expectancy at 80 years is, on average, 10 years for a woman and 7 years for a man in western countries (Health at a glance OECD indicators). This population is at high risk of cardiovascular disease (Assey, 1993). More specifically, aortic stenosis (AS) is the most frequent valvulopathy in adults ≥ 75 years old, being present in as many 4.6% (Nkomo et al., 2006). Progress made in anesthesia, surgery and intensive care explain why doctors, surgeons and cardiologists are less-and-less reluctant to propose aortic valve replacement (AVR) for older-and-older patients.

However, for this very specific population, many questions remain to be answered before such surgery can be undertaken:

- What is the spontaneous evolution of the disease?
- Is there a therapeutic option other than surgery?
- What are the postoperative results in terms of morbidity and mortality?
- Will surgical treatment relieve the symptoms and improve the quality of life (QOL) at intermediate and long term?
- What are the complications and constraints associated with the prosthesis?
- Are those results universal?
- Will my patient become frail or disabled after surgery?

2. Rationale for proposing surgical AVR for the elderly

2.1 Natural history of severe AS

Above all, the natural history of severe aortic stenosis (SAS) has a dismal prognosis. Once symptoms appear, life expectancy is 5 years for angina, 3 years for dyspnea or syncope and 2 years for cardiac failure (Chizner et al., 1980; Ross and Braunwald, 1968). Even though those results were obtained from old studies conducted during the 1960s and 1970s (Chizner et al., 1980; Horstkotte & Loogen, 1988; Ross & Braunwald, 1968), concerned young patients

(20 and 60 years old) and included small numbers of patients (15–55), more recent publications continue to emphasize the very poor natural history of SAS (Schueler et al., 2010; Varadarajan et al., 2006).

2.2 Failure of medical treatment

The introduction of medical treatments, such as beta-blockers, statins and angiotensin-converting–enzyme inhibitors, has not specifically modified SAS prognosis (Schueler et al., 2010). Recently, Schueler et al. prospectively compared the prognoses of medically treated elderly SAS patients (mean age: 86 years) at high surgical risk to age- and sex-matched patients with non-severe AS; at 2 years, 41.8% and 59.8%, respectively, were survivors. Independent factors associated with death of SAS patients were Society Thoracic Surgeons predicted risk of mortality (STS-PROM) score (Shroyer et al., 2003), pulmonary arterial pressure >30 mm Hg, creatinine and diabetes (Schueler et al., 2010). Scharwz et al. (1982) compared the prognoses of 135 SAS patients treated surgically with AVR versus 19 denied surgery: at 3 years, 87% of the surgical group were alive vs 21% of medically treated group ($p<0.001$). Varadarajan et al. (2006) showed that conservatively treated SAS patients had poorer outcomes, with respective 1-, 5- and 10-year survival rates of 62%, 32% and 18%.

2.3 Failure of balloon aortic valvuloplasty

Although balloon aortic valvuloplasty (BAV) acutely increases the aortic valve area and attenuates symptoms, neither change significantly improved prognosis, with high mortality and complication rates (NHLBI Balloon Valvuloplasty Registry participants, 1991). Moreover, its restenosis rate at 1 year was >80% (Eltchaninoff et al., 1995). Current indications for BAV are very limited, with valvuloplasty primarily considered a bridge to surgery or transvalvular aortic implantation (TAVI) in hemodynamically unstable patients (Vahanian and Otto, 2010).

Thus, for the time being, surgical AVR remains the treatment of choice for SAS. Notably, the international recommendations do not provide any specific guidelines concerning age (Bonow et al., 2006; Vahanian et al., 2007).

2.4 Age, aging and prognosis

Age is a known independent risk factor for in-hospital mortality after admission to the intensive care unit after cardiac surgery (Knaus et al., 1993; Roques & Nashef, 2003). However, although disease severity assessed with APACHE III can explain 80% of in-hospital deaths, age can explain only 13% (Knaus et al., 1993). The mechanism of excess death independent of elderly patients' disease severity has not yet been clearly elucidated. Setting aside the excess mortality linked to less intensive treatment of the elderly, it could be intrinsic, because of the greater vulnerability to disease, or extrinsic, attributable to a poorer response or even poorer tolerance of the therapeutic modalities used in intensive care. For both hypotheses, physiological particularities specific to the older patient are implicated. From a global perspective, Bouchon (1984) proposed a model in which morbidity of elderly patients resulted from 3 components (Figure 1).

Clinically detectable morbidity is usually the sum of organ aging, possible organic deterioration resulting from more-or-less quiescent chronic disease and deterioration appended by acute disease. We cannot detail here all those deteriorations organ-by-organ (Somme et al., 2009), but retain the broad lines that transcend organ specificities. First, the role of aging itself on organ decline is difficult to demonstrate. Indeed, a study on elderly individuals in very good health (old senior athletes) often had physiological cardiovascular system performances quite close to those of younger athletes but that is not the case for their osteoarticular system! Thus, the descriptions of so-called changes 'linked' to aging (i.e., frequent or typical of the old-old), be they histological or physiological performances, are the means of populations heterogeneous in terms of life style, exposures to personal or environmental risk factors and pathologies. When an attempt was made to show the same 'age-linked' changes exclusively in healthy aged or physically fit subjects, none was found (Somme et al., 2009). Hence, defining the slope of line 1 for individuals is difficult (Fig. 1), as it depends, organ by organ, on personal and environmental factors. Nevertheless, it could be useful to predict vulnerability, like an old person's response to treatment or knowing his/her level of physical activity, which is probably a better marker of physiological cardiovascular aging than chronological age. It is widely accepted that, for the young subject, cardiac function is the main parameter conditioning the maximal stress level, whereas for the elderly subject, it seems more often to be limited by respiratory function (Chan & Welsch, 1998). Finally, physiological aging can be represented as the functional state of adaptation mechanisms (or reserves) that are overwhelmed during stress or effort. These physiological particularities render the elderly more susceptible to acute diseases. This frailty should not limit access to intensive care for old patients, but should rather plead in favor of their adapted and early management.

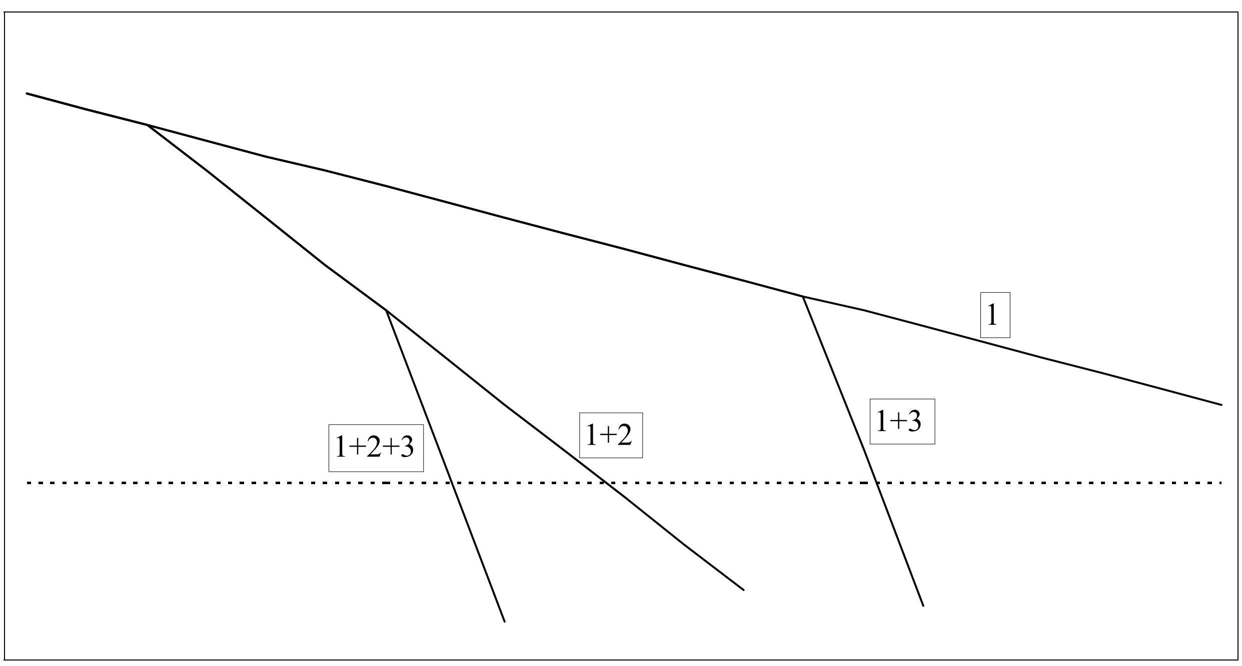


Fig. 1. Organ decline (regardless of the organ) due to aging is represented by slope 1. Two types of events are able to shift this organ under the threshold (dashed line) of organ insufficiency: a chronic (according to slope 2) or acute disease (the steepest slope 3). Adapted from 1+2+3: how to be effective in geriatrics? (Bouchon, 1984)

2.5 Threshold of old age

In practice, old age is defined 2 ways: that set by a chronological age and a dynamic approach taking into consideration the evolution of the health of the population.

The fixed chronological age definition (around 65–75 years for young-old; between 75–80 and 85–90 for the old-old, and >85–90 for the oldest-old) is the most extensively used in the medical literature. It has the advantages of enabling comparisons between published historical data and not encouraging interpretation. However, it does not account for the evolution of life expectancy at 60 years and, even less, its evolution without handicap(s). Indeed, life expectancy for a 60-year-old man in France increased from 15.4 to 21.7 years between 1950 and 2010. This prolongation obviously has an impact on the premonitory usefulness of aggressive therapies, like cardiac surgery after 60 years during that interval.
A dynamic definition of the old-age threshold can take those aspects into consideration. Several can be proposed but one seems readily accessible: survival at life expectancy at birth (Table 1). If we accept this definition, the percentage of 'aged' individuals (so defined) in France did not increase between 1950 (~11%) and 2010 (~9%), because life expectancy rose more quickly than the number of aged persons.

	1950	2010
Life expectancy at birth for males, years	63.4	78.1
Life expectancy at birth for females, years	69.2	84.8
Persons >65 years old in the population	11.4%	
Persons >75 years old in the population		9%

Table 1. 1950 to 2010: Evolution of life expectancy in France and the aged population

Age has always been identified as a major risk factor for mortality after cardiac surgery (Roques et al., 2003; Shroyer et al., 2003), but the mean age of operated patients is rising. Indeed, surgery on octogenarians is performed daily in western countries. Are there some limits for age and cardiac surgery? Florath et al. (2010) identified >84 years as an important independent risk factor for mortality 6 months after AVR for octogenarians. However, some publications indicated that surgeons seem less-and-less reluctant to operate on nonagenarians (Edwards et al., 2003; Praschker et al., 2006). During the 1980s, the age limit for cardiac surgery was progressively increased >80 years without drama considering outcomes (Edmunds et al., 1988). Should the story repeat itself for nonagenarians or even centenarians in the future?

2.6 Postoperative outcomes of surgical AVR for octogenarians

Surgical AVR results for octogenarians are acceptable and compare favorably with those of younger patients (Alexander et al., 2000; Thourani et al., 2008). Table 2 summarizes the early postoperative mortality (≤30 days) rate after AVR for octogenarians.
De facto, studies during the 1990s and 2000s included more patients than during 1980s. For example, in the UK, between 1996 and 2003, the rate of surgery performed on octogenarians increased 2-fold, from 4.1% to 9.8% (Stoica et al., 2006). For the studies with >200 patients, early in-hospital mortality (≤30 days) ranged from 6.6% to 10.1%. Very few studies included only patients with isolated AVR (Table 2). Most studies included AVR with and without coronary-artery bypass graft (CABG). Postoperative mortality rates were higher when CABG was combined with AVR compared to AVR alone.
However, the postoperative morbidity rate was very high for octogenarians after AVR (Melby et al., 2007; Thourani et al., 2008) and more than two-thirds of octogenarians will develop ≥1 postoperative complications (Collart et al., 2005; Kolh et al., 2007; Maillet et al.,

2009). Descriptions of the complications, their definitions, their characteristics and rates varied widely from one study to another. The most frequent complications are transfusion (48.8–81.4%), new onset supraventricular arrhythmia (31.2–45.2%), low cardiac output (16.7–35.7%), prolonged mechanical ventilation (≥24 hours) (22–26%), reoperation for bleeding (6–9%), permanent strokes (3–6%), acute renal failure (4.6–12%), infections (2.4–5.6%) and heart block requiring a pacemaker (2.3–5%) (Collart et al., 2005; Kohl et al., 2007; Maillet et al., 2009; Melby et al. 2007; Sundt et al., 2000; Thourani et al., 2008).

First Author	Year	N	Study period	I AVR	Mean age, yr	Overall operative mortality	Operative mortality I AVR	AVR+CABG
Edmunds	1988	50	1976–1987	66%	81	NR	30%	23.5%
Levinson	1989	64	1974–1987	50%	82	9.4%	3.2%	16.1%
Bashour	1990	24	1983–1986	50%	83	12.5%	8.3%	16.6%
Culliford	1991	71	1976–1988	50%	82	12.7	5.7%	19.4%
Freeman	1991	87	1982–1986	50%	82	15.7%	9.6%	17.9%
Olsson	1992	44	1981–1989	100%	82	14%	14%	
Elayda	1993	152	1975–1991	45%	83	17.5%	5.2%	27.7%
Tsai	1994	132	1982–1992	42%	83	4.5%	1.8%	6.6%
Asimakopoulos	1997	1100	1986–1995	100%	82	6.6%	6.6%	
Sundt	2000	133	1993–1998	33.1%	84	11%	NR	NR
Sjögren	2004	117	1990–1993	NR	82	3.4%	NR	NR
Collart	2005	215	1993–2003	74%	83	8.8%	NR	NR
Chiappini	2004	115	1992–2003	62.1%	82	8.5%	NR	NR
Langanay	2004	771	1978–2003	85.2%	83	10.1%	NR	NR
Langanay	2006	442	2000–2004	77.8%	83	7.5%	NR	NR
Stoica	2006	706	1996–2003	27.2%	83	9.8%	9.4%	9.7%
Melby	2007	245	1993–2005	57%	84	9%	10%	NR
Kolh	2007	220	1992–2004	76%	83	13%	9%	24%
Huber	2007	136	1999–2003	25%	82	4.4%	NR	NR
Thourani	2008	88	1996–2006	100%	83	5.7%	5.7%	
Leonteyv	2009	282	1995–2006	100%	82	9.2%	9.2%	
Maillet	2009	84	1998–2003	49%	84	16.7%	10.2%	25.7%
Florath	2010	493	1996–2006	51%	83	8.4%	7.6%	9.5%
Folkmann	2010	154	2005–2007	52%	83	7.8%	NR	NR

AVR = aortic valve replacement; I AVR = isolated AVR;
CABG = coronary artery bypass graft; NR = not reported.

Table 2. Postoperative mortality rates after AVR with/without CABG for octogenarians between 1976 and 2010

2.7 Intermediate-term AVR results

At intermediate term, all studies documented impressive symptom regression, with 73.2–92.5% of the survivors being in New York Heart Association (NYHA) classification I or II (Collart et al., 2005; Kolh et al., 2007; Maillet et al., 2009,). The mean NYHA classification of survivors fell from 3.1 to 1.7 ($p<0.001$) (Sundt et al., 2000). Lastly, 91% of survivors were angina-free (Kolh et al., 2007).

Concerning the intermediate-term prognosis, crude results were good (Table 3), particularly compared with the natural course of SAS (Schwarz et al., 1982). At 5 years, survival ranged from 52% (Florath et al., 2010) to 82% (Stoica et al., 2006) for populations whose mean age at surgery was 83 years. Some authors reported a 30% 10-year survival rate with a Kaplan–Meier median-survival estimate of 7.4 years (Thourani et al., 2008). Many studies also showed that, compared to an age- and sex-matched population, prognoses were comparable in different western countries: France (Maillet et al., 2009) and Sweden (Sjögren & Thulin, 2004). Stoica et al. (2006) found that the standardized mortality ratio (observed postAVR mortality/observed mortality for matched population) was 45.6% in favor of the surgical population in the UK, with 5-year survival rates of 82.1% for the surgical group versus 55.9% for a general population with the same age–sex distribution ($p<0.001$). The most common causes of late death were dominated by malignancy (20.5%), non-valve related cardiac failure (18.5%), valve-related stroke (18%) and pneumonia (11%) in a cohort of 1100 elderly patients included in the UK Heart Valve Registry. It must be kept in mind that one-third of the patients with malignancy died within 18 months after cardiac surgery. That observation emphasizes the improved preoperative cancer screening of elderly patients before AVR (Asimakopoulos et al., 1997).

First Author	Year	N	Study period	I AVR	Age at surgery	Survival at			
						1 year	3 years	5 years	8 years
Elayda	1993	171	1975–1991	45%	83	90.8%	84.2%	76%	
Tsai	1994	132	1982–1992	42%	83	82%		62%	
Asimakopoulos	1997	1100	1986–1995	100%	82	89%		69%	45.8%
Sundt	2000	133	1993–1998	33.1%	84	80%		55%	
Chiappini	2004	115	1992–2003	62.1%	82	86.4%		69.4%	
Sjögren	2004	117	1990–1993	NR	82	92.3%		65%	
Collart	2005	215	1993–2003	74%	83	84%		56%	
Stoica	2006	706	1996–2003	27.2%	83	83.7%		82.1%	
Huber	2007	136	1999–2003	25%	82	94%	94%	75%	
Kolh	2007	220	1992–2004	76%	83	85.5%	80.8%	73.2%	
Melby	2007	245	1993–2005	57%	84	82%	70%	56%	
Thourani	2008	88	1996–2006	100%	83	87%	68.2%	61%	
Leontyev	2009	282	1995–2006	100%	83	81%	71%	57%	
Florath	2010	493	1996–2006	51%	NR	82%		52%	30%

AVR = aortic valve replacement; I AVR = isolated AVR; NR = not reported.

Table 3. Intermediate-term AVR outcomes of octogenarians

2.8 Impact of AVR on QOL among octogenarians

Improving QOL is one of the most important aims of AVR especially for octogenarians. Authors of retrospective studies concluded that QOL was good after AVR at intermediate term but, in many studies, preoperative QOL had not been evaluated (Maillet et al., 2009; Sundt et al., 2000). Using the medical outcomes study Short Form-36 (SF-36), Sundt et al. (2000) showed that the QOL of a surgical population with a mean age of 84 years was comparable to that predicted for the general population >75 years old. Olsson et al. (1996), prospectively compared QOL evolution for 2 groups of patients referred for isolated AVR; 30 octogenarians vs 30 patients 65–75 years old. At 1-year postAVR, octogenarians, despite their more compromised preoperative status, had markedly regressed symptoms, and their physical abilities and general well-being were of a similar magnitude to those of the younger patients. Those improvements appeared as of 3 months. With mean follow-up of 8.3±1.9 years, Sjögren & Thulin (2004) found long-term postoperative QOL to be comparable to that of an age-matched population. In addition, Huber et al. (2007) showed that 97% of the survivors lived in their own homes. Finally, 81% had no or few self-perceived restrictions in their daily activities (Kohl et al., 2007), 93% felt much better after the operation and 81% of octogenarians had few disabilities in daily activities (Huber et al., 2007). Also, QOL was not affected by the constraints entailed by treatment(s) associated with the type of prosthesis. Indeed, after postoperative month 3, >90% who had received a bioprosthesis were in sinus rhythm and were taking only low-dose aspirin. Vicchio et al. (2008) compared the QOL of 62 octogenarians with bioprosthetic valves vs 98 with mechanical valves during a mean follow-up of 3.4 ± 2.8 years and found that the prosthesis type had no impact on their QOL.

2.9 Limitations of those studies

However, all those studies had some limitations. Indeed, all of them were retrospective except for Olsson et al. (1996). Only those by Asimakopoulos et al. (1997) and Stoica et al. (2007), representing UK registry results, were multicenter investigations. Very few studies specifically and exclusively evaluated the outcomes of isolated AVR for SAS (Asimakopoulos et al., 1997; Leonteyv et al., 2009; Thourani et al., 2008). Some studies mixed AVR with CABG or other operations, whereas others mixed AVR for SAS or severe aortic insufficiency (i.e., Stoica et al., 2006; Sundt et al., 2000). The sample sizes also varied widely from one study to another: ranging from 24 (Bashour et al., 1990) to 1100 patients (Asimakopoulos et al., 1997). Lastly, those studies retrospectively covered long periods, lasting 5 (Sundt et al., 2000) to 16 years (Elayda et al., 1993).

2.10 Decision-making

Those results must be interpreted carefully, keeping in mind that octogenarians with SAS referred to a surgeon are highly selected, as that decision-making is complex. Bouma et al. (1999) showed that only 59% of the patients who should have had an AVR according to international guidelines (Bonow et al., 2006) were actually offered surgical treatment. They were mainly symptomatic, >80 years old and had high transaortic valve gradients. On the other hand, Iung et al. (2005) observed that a decision not to operate was made for 33% of SAS patients. Multivariate analyses retained left ventricular ejection fraction and age (OR 1.84 for 80–85 year olds, OR = 3.38 for those ≥85 years) as being significantly and independently associated with the decision not to operate. Neurological dysfunction was the only comorbidity associated with that decision. During 2007, Freed et al. (2007) retrospectively studied the outcomes of SAS patients referred to their echocardiography laboratory. Among the 106 SAS patients, only 31% underwent surgery. The most common reasons symptomatic SAS patients did not undergo AVR were: their symptoms were thought to be unrelated to AS, too high surgical risk and/or patients refused (Freed et al., 2010).

3. Promises of a new approach: TAVI

In light of increasing life expectancy, the high incidence of AS in the elderly, the fact that many SAS patients are denied surgery, and because of improved endovascular technology, a new therapeutic approach using new devices is rapidly evolving, becoming widespread and would revolutionize AS treatment: TAVI.
After successful animal experimentation, Cribier et al. (2002) successfully performed the first human implantation of a balloon-expandable aortic valve prosthesis. Two TAVI devices are now under postmarketing surveillance in Europe: the balloon expandable Edwards SAPIEN™ prosthesis (Edwards Life-Sciences, CA) and the self-expandable CoreValve Revalving prosthesis™ (Medtronic Inc, MN). Two approaches are used: anterograde with transapical (TA) access or retrograde with transfemoral (TF) access. Two videos illustrating the TAVI procedures are available at www.NEJM.com.

3.1 Postoperative and short-term TAVI results

The first step in the development of these devices was to demonstrate a high rate of successful implantation that is improving with time, from 88% to >98% (Grube et al., 2007; Tamburino et al., 2011; Webb et al., 2009). At 30 days, outcome was good with 9–18% mortality (Zajarias & Cribier, 2009) for high-risk patients for whom surgery was denied (octogenarians, high Logistic EuroSCORE ≥20% (Roques & Nashef, 2003), STS-PROM ≥10% (Shroeyr et al., 2003) or specific surgical contraindication(s) (e.g. porcelain aorta, history of mediastinal radiotherapy). In all studies, the observed mortality was below those predicted by STS-PROM or Logistic EuroSCORE.
Surgery relieved symptoms with systematically lower NYHA classification and impressive decreases of the mean transvalvular gradient from 46 mm Hg preoperatively to 10 mm Hg thereafter, associated with increased aortic surface from 0.6 to 1.6 cm^2, respectively, for example, in the study by Webb et al. (2009). The NYHA classification and echocardiographically detected improvement of the mean gradient and aortic surface were sustained at 1 year (Tamburino et al., 2011; Webb at al., 2009). Survival at 1 year ranged from 73.8% (Webb et al., 2009) to 85% (Tamburino et al., 2011) and compared favorably with the spontaneous SAS evolution.
Prognosis at 1 year seems mostly related to comorbidities rather than cardiac status (Webb et al., 2009). In an Italian multicenter study, independent risk factors associated with late death were: prior stroke (hazard ratio (HR) 5.4; 95% confidence interval (CI) 1.47–20.39; p=0.01), prior acute pulmonary edema (HR 2.7; 95% CI, 1.1–6.7: p=0.03), chronic kidney disease (HR 2.5; 95% CI 1.0–6.4; p=0.048) and postprocedural paravalvular leak ≥2+ (HR 3.8; 95% CI 1.6–9.1: p=0.03) (Tamburino et al., 2011).
A landmark multicenter, prospective, randomized trial compared SAS patients, who surgeons considered unsuitable surgical candidates and were given standard treatment (including BAV) or TF transcatheter implantation of a balloon-expandable bovine pericardial valve (Leon et al., 2010). At 1 year, the death rate from any cause was 30.7% with TAVI and 50.7% with standard therapy (TAVI HR 0.55; 95% CI 0.4–0.74; p<0.001).
A principal concern of TAVI for octogenarians is its impact on QOL, for which data are scarce. At 3 months postTAVI, Krane et al. (2010) used SF-36, and found significantly improved QOL concerning the physical health summarized score, while the mental health summarized score remained unchanged. For a population ≥81 years, comparison of 6 months postTAVI to preoperative SF-36 data, Bekeredjian et al. (2010) obtained significantly

improved physical and mental component summary scores from 28.4±10 to 46.8±9.2 ($p<0.001$) and from 37.3±10.8 to 50.6±10.1 ($p<0.001$), respectively.

3.2 Specific TAVI-related complications

The results of all studies demonstrated that TAVI can be implanted safely, with intraprocedural mortality now a mean of 1% (Webb et al., 2009; Tamburino et al., 2011). Implantation failure is becoming rare, with the successful implantation rate ≥98% in the most recent studies (Bleiziffer et al., 2009; Tamburino et al., 2011). Changing the surgical approach during the intervention has also become very rare.

Coronary obstruction rarely complicates valve implantation (<1%). Valve positioning is challenging, particularly when the distance between the annulus and the coronary artery is short, as the native valve may be pushed against the coronary ostium (Lefèvre et al., 2011).

Some complications seem to be related to the access route used. With TF access, major vascular complications occur in 6.8–11.7% of the cases (Bleiziffer et al., 2009; Webb et al., 2009). However, technological advances have permitted sheath-size reduction from 24F to 18F, thereby allowing a percutaneous procedure with locoregional anesthesia and fewer vascular injuries. Improved screening, case selection and experience should surely lower the vascular injury rate further.

Second, 10% of the patients suffer clinical strokes (Grube et al. 2007). In a recent diffusion-weighted, magnetic resonance imaging study on TAVI patients, the risk of diffuse cerebral embolism was 72.7%, with patients frequently having multiple new but clinically silent brain lesions. Although cerebral embolism was extremely common in the TF-TAVI cohort, the clinical stroke rate was 3.6% (Ghanem et al., 2010). It was suggested that TA-TAVI might be associated with fewer cerebral embolic events. However, results are controversial and further studies with larger cohorts are needed. Two mechanisms are involved: aortic atheroemboli and valvular calcific emboli. The elderly are at particularly high risk for perioperative neurological events because of advanced cerebral ischemic disease present preoperatively (Wang et al., 2010).

For both accesses, annulus measurement is challenging. Indeed, no gold standard currently exists for aortic annular measurement but transesophageal echocardiography provides accurate data to guide valve sizing before implantation (Messika-Zeitoun et al., 2010). Paravalvular aortic regurgitation is common after TAVI but remains stable at late follow-up (Webb et al., 2009). In the PARTNER study, moderate-or-severe perivalvular leakage was present in 11.8% of the patients at 30 days and 10.5% at 1 year (Leon et al., 2010). However, postprocedural paravalvular aortic regurgitation ≥2+ (HR 3.79) mainly affected later outcomes between 30 days and 1 year (Tamburino et al., 2011).

Conduction abnormalities are frequent after TAVI (Roten et al., 2010). The occurrence of atrioventricular block requiring pacemaker insertion at 30 days seems lower with the Edwards SAPIEN™ (<5%) (Lefèvre et al., 2011) than the CoreValve™ (up to 30%) (Jilaihawi et al., 2009). One possible explanation could be that the CoreValve™ was designed to be seated lower than the SAPIEN™ valve and might compress the underlying conduction system. However, based on a cohort of 67 patients (41 received CoreValve™ and 26 SAPIEN™), Roten et al. showed that the sole independent risk factor for complete atrioventricular block after TAVI was preexisting right bundle branch block (Roten et al., 2010). Because prosthesis sizing is a critical issue, to avoid perivalvular leakage and valve migration, “over sizing” of TAVI might have increased the risk of atrioventricular block (Bleiziffer et al., 2009). Further investigations are mandatory.

The results of some studies showed that the postoperative and short-term outcomes were worse for patients treated with TA than TF access, because the former were more severely ill and had more severe comorbidities. The Logistic EuroSCORE predicted risk was significantly higher for TA than TF, respectively: 35% vs 25% (p=0.01), as did STS-PROM 10.3% vs 8.7% (Webb et al., 2009). In-hospital mortality was 8% for the TF group vs 27% for TA group, with respective 1-year survival rates of 74±11% vs 60±13% (Al-attar et al., 2009). At 1 year, the European PARTNER study results were comparable (Lefèvre et al., 2011).

3.3 Risk assessment and patient selection

TAVI development has highlighted the complexity of risk assessment and patient selection. At present, TAVI is indicated only for SAS patients ineligible for conventional AVR, but the definition of "ineligible" remains vague. TAVI was initially designed to treat old-old patients, mean age 81–86 years (Bleiziffer et al., 2009; Tamburino et al., 2011), with high Logistic EuroSCORE predicted risk ≥20%, mean range 22–29% (Grube et al., 2007; Webb et al., 2009) or STS-PROM score ≥10%, mean range 16–23% (Al-attar et al., 2009; Bleiziffer et al., 2009) or with contraindication(s) for surgery.

Logistic EuroSCORE and STS-PROM scores are increasingly being used to estimate operative mortality based on cardiac and extracardiac factors. The STS-PROM score appears to be more reliable than the EuroSCORE for predicting outcomes of high-risk AVR patients. However, STS-PROM tends to underestimate mortality (Dewey et al., 2007). A meta-analysis showed EuroSCORE to have low discrimination ability for valve surgery and it slightly over predicted risk (Parolari et al., 2010), particularly for octogenarians referred for AVR (Leontyev et al., 2009). Both scores share the same limitations: predictive ability is limited for high-risk patients, who represented only a small proportion of the population used to derive them. They do not take into account the surgical results in a given institution, relationship between volume and mortality, and the impact of progress concerning surgical techniques, cardiopulmonary bypass, anesthesia and intensive care. The scores also fail to evaluate fully the high-risk patient because they do not integrate a very important element: clinical judgment. Indeed, many factors that negatively influence prognosis are not considered: cirrhosis, impact of body mass index, chest irradiation, chest deformation, multivalve surgery, porcelain aorta, previous CABG and vascular tortuosity for TAVI. It is estimated that neither the Logistic EuroSCORE nor STS-PROM would have classed approximately one-quarter of the patients at high risk and yet they were refused surgery because of such factors (Webb et al., 2009).

For the specific SAS octogenarian population, it seems that the development of a new specific scoring classification is necessary (Florath et al., 2010), especially one including demographic variables, such as nutritional status, disability, dementia and frailty.

3.4 Unanswered questions concerning TAVI

TAVI is not suitable for all patients ineligible for conventional AVR and patients referred for TAVI are also highly selected. In a cohort of 469 SAS patients referred for participation in a TAVI trial, 362 (77.1%) patients did not meet the inclusion/exclusion criteria. The main exclusion criteria were low STS-PROM score <10% (72 patients), peripheral vascular or aorta disease (58 patients), aortic valve area >0.8 cm² (54 patients), significant coronary artery disease (43 patients) and renal failure (25 patients). Among those 362 patients, 75 (20.7%) had 2 exclusion criteria and 26 (7.1%) had 3 exclusion criteria. Eighty-eight patients underwent surgery and 274 were treated medically, 177 of whom had BAV. At 2 years, the mortality rate was significantly lower for the surgical group vs the medically treated group, respectively, 28.1% vs 53.4% ($p<0.001$) (Ben-Dor et al., 2010). Another TAVI limitation is also the high incidence of severe coronary artery disease among elderly SAS patients that also influences prognosis and requires specific treatment.

Long-term durability of TAVI must now be demonstrated. TAVI provides acceptable hemodynamic results up to 3 years (Webb et al., 2009). At present, outcomes reflect comorbidities rather than cardiac status (Tamburino et al., 2011). Patient selection is a major concern for long-term durability evaluation of TAVI. Future studies should include patients with expected life expectancy unrelated to cardiac disease >5 years. At 2 years, survival was 60.9% in the study by Webb et al. (2009); what will the sample size be at 5 years?

With the learning curve, technological improvement and better patient selection, TAVI-related morbidity should decline, particularly concerning vascular injuries, strokes, pacemaker implantation and perivalvular leakage.

The next step for TAVI for SAS management should be its direct comparison with surgery for high-risk patients without contraindication(s) for surgery, and then for intermediate- and low-risk patients. Historical comparisons, case–control studies, propensity-score matching (Johansson et al., 2011) or comparison with spontaneous evolution are not able to answer these questions adequately. Multicenter, randomized–controlled trials should answer them (prognosis, durability, specific morbidity, etc…) in few years, thereby allowing the widespread development of this very promising technique.

4. Frailty and geriatric evaluation of octogenarians for SAS management

4.1 Frailty

To evaluate better an individual's situation on which the final therapeutic decision generally depends, the concepts of frailty or vulnerability are the themes of several international gerontology publications. We highlight that, at present, no consensual definition of frailty exists (Bergman et al., 2007; Karunananthan et al., 2009). However, the various authors agree that frailty is a state of susceptibility to aggression, which explains that, for a given health event, despite the same management and apparently sufficiently similar health status, the individuals will have very different outcomes. Thus, frailty is always defined as a function of the event that serves as the judgement criterion: falls, loss of autonomy, institutionalization, death… It is also defined by the time at which it is assessed. Therefore, an effective definition over the long term (Province et al., 1995) might not be operative to distinguish individuals in terms of consequences of hospitalization (Gill et al., 2004).

Regardless of the definition retained, the authors defined a certain number of common characteristics (Rockwood, 2005): frailty is a continuous state that is not simply present or absent; it is not the consequence of single organ involvement; the clinical manifestations are multiple. It can be recognized clinically, with that identification being considered the threshold of entry into frailty, the occurrence of the negative event marking the end of frailty in relationship to this factor (institutionalization or handicap, for example). The definitions of frailty are multiple (Ferrucci et al., 2004), but the most used are those that refer to the diminished physiological reserves, with a core event being the development of sarcopenia. This type of definition has shown its efficacy to predict the loss of autonomy, institutionalization or death in a cohort of patients with cardiovascular diseases but not initially handicapped and followed for 1 year (Fried et al., 2004). Its effect can be associated

with those of a disability and comorbidity, even though none of these 3 dimensions is superimposable or sufficient alone to explain the outcome (Fried et al., 2004).
According to those authors' definition (Fried et al., 2004), at least 3 criteria among the following must be satisfied to be qualified as 'fragile': diminished gripping force of the dominant hand, the feeling of fatigue/exhaustion, slower walking speed and non-intentional weight loss. Each of the elements is evaluated according to precise criteria. Such a definition could prove useful to study the long-term outcome of patients after cardiac surgery. In addition, this type of definition conceptually excludes the cognitive, sociofamilial and psychological dimensions of frailty (Fried et al., 2004). To take those dimensions into account, 2 types of solutions are proposed: an inventory of the situations at risk that can be extremely complex and overall clinical judgment, whose pertinence concerning loss of autonomy and death were recently validated (Jones et al., 2005).

4.2 Frailty and cardiac surgery

The concept of frailty and its clinical use in surgery in general and, more specifically, cardiac surgery, has recently appeared in the literature. Two recent studies (Afilalo et al., 2010; Lee et al., 2010) documented that frailty increased the risk of complications after cardiac surgery independently of age and included information from standard prognostic scores. Pertinently, those 2 studies are complementary.
Indeed, Afilalo et al. (2010) defined frailty as requiring assistance to accomplish at least one essential life activity, a diagnosis known of dementia or limited mobility. Although their definition can be debated on a conceptual level, because it mixes disability and fragility, it has the advantage of being clinically operational. The existence of a frailty phenotype, as defined, was independently associated with mortality (OR 1.8 [95% CI 1.1–3.0]), institutionalization and discharge from that facility (OR 6.3 [95% CI 4.2–9.4]) and intermediate-term survival (OR 1.5 [95% CI 1.1–2.2]).
Lee et al. (2010) defined frailty more precisely and more sensitively: walking speed tested as a mean time needed to go 5 m during 3 consecutive tries (limited to 6 seconds). Their definition is directly in line with the conceptual frailty–sarcopenia model. In their study, the risk of postoperative morbidity–mortality was multiplied by 3.05 [95% CI 1.23–7.64] for frail patients, even after adjustment for the STS-PROM score. In addition, frailty defined in this way doubled the risk of institutionalization or a prolonged stay there. Finally, in a manner not entirely clear, the risks linked to frailty are greater for women than men.
The results of those studies confirmed the findings of others concerning non-cardiac surgery, i.e., that such a definition of frailty is associated with "geriatric syndromes" (Robinson et al., 2009), sarcopenia (Makary et al., 2010) or a more holistic score-based definition (Dasgupta et al., 2009). In all those cases, the frailty phenotype was independently associated with age and other known prognostic factors of higher risk of morbidity and/or mortality.
Only authors of rare studies have envisaged frailty's appearance as a surgical consequence. Researchers of a single center study supported that hypothesis and strongly recommended that the appearance of that phenotype should be considered in future outcome investigations because this fragility is linked even more strongly to QOL than self-reported overall assessments of "health status" (Maillet et al., 2009).
We would also like to underscore the areas of uncertainty that persist today and that represent as many research projects. Afilalo et al.'s (2010) and Lee et al.'s (2010) examinations of potential relationships between a frailty phenotype and outcomes after cardiac surgery

were based on large majorities of patients (>60%) who underwent simple coronary artery bypass surgery. Even though the type of intervention was entered into the model, the phenotype's effect on valve-surgery complications (and even more so for the newer interventional techniques) warrants further clarification. The models currently used in cardiac surgery are mainly based on the frailty–sarcopenia concept. The contributions of other frailty dimensions to explaining outcome (biological, psychological, environmental and social) are also worthy of more detailed exploration. Finally, the available studies focused on subjects who were certainly old (>70 years), but the usefulness of the scores and the thresholds applied undoubtedly need to be adapted for the oldest–old (>85–90 years).

4.3 Contribution of geriatric evaluation to AVR decision-making

All of the above underscore the complexity of decision-making and follow-up of the oldest-old when AVR becomes necessary, and support an interdisciplinary approach bringing together cardiologists, surgeons, geriatricians, anesthesiologists and intensivists. However, convincing data on the impact of a geriatric approach in this setting are still lacking. The geriatrician is most probably in an ideal position, in terms of professional competence, to detect frailty, but the impact of this identification on the decisions to be made and, even more so, on the outcomes are not yet documented. As we have seen, it is also likely that the consequences of cardiac surgery, beyond its cardiovascular impact, are multidimensional (Maillet et al., 2009). It seems highly probable that an overall approach, like that proposed by geriatricians in another context (Rydwik et al., 2008), would contribute to improving the outcomes of individuals, not only in functional terms but also nutritional, psychological, social and even cognitive aspects.

4.4 Adapted rehabilitation

Rehabilitation after cardiac surgery is not less effective in the elderly than young patients (Macchi et al., 2007; Pasquali et al., 2001) and improves the outcome, even though information on the oldest-old are scarce (Pasquali et al., 2001). Indeed, it seems, for the aged patient, that rehabilitation after cardiac surgery should not be postponed and should be prolonged (Macchi et al., 2009). This is especially true for women >80 years who achieve a gain in functional autonomy 1 year after the intervention (Barnett & Halpin, 2003). Some authors recommend particular preoperative precautions, notably respiratory. The preoperative identification of frail patients could also be a pertinent way to select patients likely to benefit the most from specific programs, e.g., early mobilization in the intensive care unit (Needham, 2008). Multidimensional rehabilitation programs also achieved favorable results (Eder et al., 2010; Mazza et al., 2007; Opasich et al., 2010), which, in addition, proved their safety and efficacy in terms of rehabilitation, nursing needs, mobility capability, muscle force, equilibrium and, last but certainly no least, duration of stay.

5. Conclusion

Surgical AVR for SAS in octogenarians is the treatment of choice and is performed daily, with good intermediate-term results, despite high postoperative morbidity. In the very near future, TAVI should profoundly modify the treatment strategy for SAS. Despite all the improvements since the beginning of cardiac surgery, much progress remains to be achieved in all the steps: improving patient selection, more accurately stratifying the risks, choosing the best treatment, limiting morbidity regardless of the technique used, and proposing a personalized and adapted rehabilitation program. New scoring systems, including specific markers for elderly patients (disability, frailty, etc…), should be developed. A multidisciplinary approach, including surgeons and cardiologists, along with geriatricians, intensivists and rehabilitation specialists, would contribute to achieving all those improvements. The scarcity of scientific literature on the link between age (and particularly old-old age >85 years), outcomes and the frailty-syndrome subset opens vast avenues for future research.

6. References

Afilalo, J., Eisenberg, M.J., Morin, J.F., Bergman, H., Monette, J., Noiseux, N., Perrault, L.P., Alexander, K.P., Langlois, Y., Dendukuri, N., Chamoun, P., Kasparian, G., Robichaud, S., Gharacholou, S.M., & Boivin, J.F. (2010). Gait speed as an incremental predictor of mortality and major morbidity in elderly patients undergoing cardiac surgery. *J Am Coll Cardiol*, 56, 1668–1676, ISSN 0735-1097

Al-Attar, N., Himbert, D., Descoutures, F., Iung, B., Raffoul, R., Messika-Zeitoun, D., Brochet, E., Francis, F., Ibrahim, H., Vahanian, A., & Nataf, P. (2009). Transcatheter aortic valve implantation: selection strategy is crucial for outcome. *Ann Thorac Surg*, 87, 1557–1563, ISSN 0003-4975

Alexander, K., Anstrom, K.J., Muhlbaier, L.H., Grosswald, R.D., Smith, P.K., Jones, R.H., & Peterson, E.D. (2000). Outcomes of cardiac surgery in patients ≥ 80 years: results from the national cardiovascular network. *J Am Coll Cardiol*, 35, 731–738, ISSN 0735-1097

Asimakopoulos, G., Edwards, M.B., & Taylor, K.M. (1997). Aortic valve replacement in patients 80 years of age and older: survival and cause of death based on 1100 cases: collective results from the UK Heart Valve Registry. *Circulation*, 96, 3403–3408, ISSN 0009-7322

Assey, M.E. (1993) Heart disease in the elderly. *Heart Dis Stroke*, 2, 330–334, ISSN 1058–2819

Barnett, S.D., & Halpin, L.S. (2003). Functional status improvement in the elderly following coronary artery bypass graft. *J Nurs Care Qual*, 18, 281–287, ISSN 1057-3631

Bashour, T.T., Hanna, E.S., Myler, R.K., Mason, D.T., Ryan, C,. Feeney, J., Iskikian, J., Wald, S.H., Antonin, C., Sr., & Malabed, L.L. (1990). Cardiac surgery in patients over the age of 80 years. *Clin Cardiol*, 13, 267–270, ISSN 0160-9289

Bekeredjian, R., Krumsdorf, U., Chorianopoulos, E., Kallenbach, K., Karck, M., Katus, H.A., & Rottbauer, W. (2010). Usefulness of percutaneous aortic valve implantation to improve quality of life in patients > 80 years of age. *Am J Cardiol*, 106, 1777–1781, ISSN 0002-9149

Ben-Dor, I., Pichard, A., Gonzalez, M.A., Weissman, G., Li, Y., Goldstein, S.A., Okubagzi, P., Syed, A.I., Maluenda, G., Collins, S.D., Delhaye, C., Wakabayashi, K., Gaglia, M.A., Torguson, R., Xue, Z., Satler, L.F., Suddath, W.O., Kent, K.M., Lindsay J., & Waskman R. (2010). Correlates and causes of death in patients with severe symptomatic aortic stenosis who are not eligible to participate in a clinical trial of transcatheter aortic valve implantation. *Circulation*, 122 (Suppl 1), S37–S42, ISSN 0009-7322

Bergman, H., Ferrucci, L., Guralnik, J., Hogan, D.B., Hummel, S., Karunananthan, S., & Wolfson, C. (2007). Frailty: an emerging research and clinical paradigm – issues and controversies. *J Gerontol A Biol Sci Med Sci*, 62, 731–737, ISSN 1079-506

Bleiziffer, S., Ruge, H., Mazzitelli, D., Schreiber, C., Hutter, A., Laborde, J.C., Bauernschmitt, R., & Lange, R. (2009). Results of percutaneous and transapical transcatheter aortic valve implantation performed by a surgical team. *Eur J Cardiothorac Surg*, 35, 615–621, ISSN 1010-7940

Bonow, R.O., Carabello, B.A., Chatterjee, K., de Leon, A.C., Faxon, D.P., Freed, M.D., Gaasch, W.H., Lytle, B.W., Nishimura, R.A., O'Gara, P.T., O'Rourke, R.A., Otto, C., Shah, P.M., Shanewise, J.S., Smith, S.C., Jacobs, A.K., Adams, C.D., Anderson, J.L., Antman, E.M., Faxon, D.P., Fuster, V., Halperin, J.L., Hiratzka, L.F., Hunt, S.A., Lytle, B.W., Nishimura, R., Page, R.L., & Riegel, B. (2006). ACC/AHA 2006 practice guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Task Force on Practice Guidelines (Writing Committee to revise the 1998 guidelines for the management of patients with valvular heart disease). *J Am Coll Cardiol*, 48, e1–e148, ISSN 0735-1097

Bouchon, J.P. (1984). 1 + 2 + 3. Comment être efficace en Gériatrie. *Rev Prat*, 34, 888–892, ISSN 0035–2640

Bouma, B.J., van der Brink, R.B.A., van der Meulen, J.H.P., Chereix, E.C., Hamer, H.P.M., Dekker, E., Lie, K.I., & Tijssen, J.G.P. (1999). To operate or not on elderly patients with aortic stenosis: the decision and its consequences. *Heart*, 82, 143–148, ISSN 1355-6037

Chan, E.D., & Welsh, C.H. (1998). Geriatrics respiratory medicine. *Chest*, 114, 1704–1733, ISSN 0012-8703

Chiappini, B., Camurri, N., Loforte, A., Di Marco, L., Di Bartolomeo, R., & Marinelli, G. (2004). Outcome after aortic valve replacement in octogenarians. *Ann Thorac Surg*, 78, 85–89, ISSN 0003-4975

Chizner, M.A., Pearle, D.L., & deLeon, A.C. (1980). The natural history of aortic stenosis in adults. *Am Heart J*, 99, 419–424, ISSN 0002-8703

Collart, F., Feier, H., Kerbaul, F., Mouly-Bandini, A., Riberi, A., Mesana, T.G., & Metras, D. (2005). Valvular surgery in octogenarians: operative risks factors, evaluation of EuroSCORE and long term results. *Eur J Cardiothorac Surg*, 27, 276–280, ISSN 1010-7940

Cribier, A., Eltchaninoff, H., Bash, A., Borenstein, N., Tron, C., Bauer, F., Derumeaux, G., Anselme, F., Laborde, F., & Leon, M.B. (2002). Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human, case description. *Circulation*, 106, 3006–3008, ISSN 0009-7322

Culliford, A.T., Galloway, A.C., Colvin, S.B., Grossi, E.A., Baumann, G., Esposito, R., Ribakove, G.H., & Spencer, F.C. (1991). Aortic valve replacement for aortic stenosis in persons aged 80 years and over. *Am J Cardiol*, 67, 1256–1260, ISSN 0002-9149

Dasgupta, M., Rolfson, D.B., Stolee, P., Borrie, M.J., & Speechley, M. (2009). Frailty is associated with postoperative complications in older patients with medical problems. *Arch Gerontol Geriatr*, 48, 78–83, ISSN 0167-4943

Dewey, T.M., Brown, D., Ryan, W.H., Herbert, M.A., Prince, S.L., & Mack, M.J. (2007). Reliability of risk algorithms in predicting early and late operative outcomes. *J Thorac Cardiovasc Surg*, 135, 180–187, ISSN 0022-5223

Eder, B., Hofmann, P., von Duvillard, S.P., Brandt, D., Schmid, J.P., Pokan, R., & Wonisch, M. (2010). Early 4-week cardiac rehabilitation exercise training in elderly patients after heart surgery. *J Cardiopulm Rehabil Prev*, 30, 85–92, ISSN 1932-7501

Edmunds, L.H., Jr., Stephenson, L.W., Edie, R.N., & Ratcliffe, M.B. (1988). Open-heart surgery in octogenarians. *N Engl J Med*, 319, 131–136, ISSN 0028-8614

Edwards, M.B, Taylor, M.P., & Taylor, K.M. (2003). Outcomes in nonagenarians after heart valve replacement operation. *Ann Thorac Surg*, 75, 830–834, ISSN 0003-4975

Elayda, M.A., Reul, R.M., Alonzo, D.M., Gillette, N., Reul, G.J., Jr., & Cooley, D.A. (1993) Aortic valve replacement in patients 80 years and older. Operative risks and long term results. *Circulation*, 88, II11–II16, ISSN 0009-7322

Eltchaninoff, H., Cribier, A., Tron, C., Anselme, F., Koning, R., Soyer, R., & Letac, B. (1995). Balloon aortic valve valvuloplasty in elderly patients at high risk for surgery, or inoperable: an alternative to valve replacement? *Eur Heart J*, 16, 1079–1084, ISSN 0195-668X

Ferrucci, L., Guralnik, J.M., Studenski, S., Fried, L.P., Cutler, G.B., Jr., & Watson, J.D. (2004). Designing randomized controlled trials aimed at preventing or delaying functional decline and disability in frail, older persons: a consensus report. *J Am Geriatr Soc*, 52, 625–634, ISSN 0002-8614

Florath, I., Albert, A., Boening, A., Ennker, I.C., & Ennker, J. (2010). Aortic valve replacement in octogenarians: identification of high-risk patients. *Eur J Cardiothorac Surg*, 37, 1304–1310, ISSN 1010-7940

Folkmann, S., Gorlitzer, M., Weiss, G., Harrer, M., Thalmann, M., Poslussny, P., & Grabenwoger, M. (2010). Quality of life in ocotogenarians one year after aortic valve replacement with or without coronary artery bypass surgery. *Interact Cardiovasc Thorac Surg*, 11, 750–753, ISSN 1569-9293

Freed, B.H., Sugeng, L., Furlong, K., Mor-Avi, V., Raman, J., Jeevanandam, V., & Lang, R.M. (2010). Reasons for nonadherence to guidelines for aortic valve replacement in patients with severe aortic stenosis and potential solutions. *Am J Cardiol*, 105, 1339–1342, ISSN 0002-9149

Freeman, W.K., Schaff, H.V., Orszulak, T.A., & Tajik, A.J. (1991). Cardiac surgery in the octogenarian: outcome and clinical follow-up. *J Am Coll Cardiol*, 18, 29–35, ISSN 0735-1097

Fried, L.P., Ferrucci, L., Darer, J., Williamson, J.D., & Anderson, G. (2004). Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci*, 59, 255–263, ISSN 1079-5006

Ghanem, A., Muller, A., Nähle, C.P., Kocurek, J., Werner, N., Hammerstingl, C., Schild, H.H., Schwab, J.O., Mellert, F., Fimmers, R., Nickenig, G., & Thomas, D. (2010). Risk and fate of cerebral embolism after transfemoral aortic valve implantation. *J Am Coll Cardiol*, 55, 427–432, ISSN 0735-1097

Gill, T.M., Allore, H.G., Holford, T.R., & Guo, Z. (2004). Hospitalization, restricted activity and the development of disability among older persons. *JAMA,* 292, 2115–2124, ISSN 0098-7484

Grube, E., Schuler, G., Buellesfeld, L., Gerckens, U., Linke, A., Wenaweser, P., Sauren, B., Mohr, F.W., Walther, T., Zickmann, B., Iversen, S., Felderhoff, T., Cartier, R., & Bonan, R. (2007). Percutaneous aortic valve replacement for severe aortic stenosis in high-risk patients using the second- and the current third-generation self-expanding CoreValve prosthesis. *J Am Coll Cardiol*, 50, 69–76, ISSN 0735-1097

Health at a glance OECD indicators. www.sourceoecd.org/socialissues/9789264061538

Horstkotte, D., & Loogen, F. (1988). The natural history of aortic valve replacement. *Eur Heart J*, 9 (Suppl E), 57–64, ISSN 0195-668X

Huber, C.H., Goeber, V., Berdat, P., Carrel, T., & Eckstein, F. (2007). Benefits of cardiac surgery in octogenarians – a postoperative quality of life assessment. *Eur J Cardiothorac Surg,* 31, 1099–1105, ISSN 1010-7940

Iung, B., Cachier, A., Baron, G., Messika-Zeitoun, D., Delahaye, F., Tornos, P., Gohlke-Bärwolf, C., Boersma, E., Ravaud, P., & Vahanian, A. (2005). Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgery? *Eur Heart J*, 26, 2714–2720, ISSN 0195-668X

Jilaihawi, H., Chin, D., Vasa-Nicotera, M., Jeilan, M., Spyt, T., Ng, G.A., Bence, J., Logtens, E., & Kovac, J. (2009). Predictors for permanent pacemaker requiring after transcatheter aortic valve implantation with the CoreValve bioprosthesis. *Am Heart J,* 157, 860–866, ISSN 0002-8703

Johansson, M., Nozohoor, S., Kimblad, P.O., Harnek, J., Olivecrona, G.K., & Sjögren, J. (2011). Transapical versus transfemoral aortic valve implantation: a comparison of survival and safety. *Ann Thorac Surg,* 91, 57–63, ISSN 0003-4975

Jones, D., Song, X., Mitnitski, A., & Rockwood, K. (2005). Evaluation of a frailty index based on a comprehensive geriatric assessment in a population based study of elderly Canadians. *Aging Clin Exp Res*, 17, 465–471, ISSN 1594-0667

Karunananthan, S., Wolfson, C., Bergman, H., Beland, F., & Hogan, D.B. (2009). A multidisciplinary systematic literature review on frailty: overview of the methodology used by the Canadian Initiative on Frailty and Aging. *BMC Med Res Methodol*, 12, 68, ISSN 1471-2288

Knaus, W.A., Wagner, D.P., Zimmerman, J.E., & Draper, E.A. (1993). Variations in mortality and length of stay in intensive care units. *Ann Intern Med*, 118, 753–761, ISSN 0003-4819

Kolh, P., Kerzmann, A., Honore, C., Comte, L., & Limet, R. (2007). Aortic valve surgery in octogenarians: predictive factors of operative and long-term results. *Eur J Cardiothorac Surg*, 31, 600–606, ISSN 1010-7940

Krane, M., Deutsch, M.A., Bleizziffer, S., Schneider, L., Ruge, H., Mazzitelli, D., Schreiber, C., Brockmann, G., Voss, B., Bauernschmitt, R. & Lange, R. (2010). Quality of life among patients undergoing transcatheter aortic valve implantation. *Am Heart J*, 160, 451–457, ISSN 0002-8703

Langanay, T., De Latour, B., Ligier, K., Derieux, T., Agnino, A., Verhoye, J.P., Corbineau, J., & Leguerrier, A. (2004). Surgery for aortic stenosis in octogenarians: influence of coronary disease and other comorbidities on hospital mortality. *J Heart Valve Dis,* 13, 545–552, ISSN 0966-8519

Langanay, T., Verhoye, J.P., Ocampo, G., Vola, M., Tauran, A., De La Tour, B., Derieux, T., Ingels, A., Corbineau, H., & Leguerrier, A. (2006). Current hospital mortality of aortic valve replacement in octogenarians. *J Heart Valve Dis*, 15, 630–637, ISSN 0966-8519

Lee, D.H., Buth, K.J., Martin, B.J., Yip, A.M., & Hirsch, G.M. (2010). Frail patients are at increased risk for mortality and prolonged institutional care after cardiac surgery. *Circulation*, 121, 973–978, ISSN 0009-7322

Lefèvre, T., Kappetein, A.P., Wolner, E., Nataf, P., Thomas, M., Schächinger, V., De Bruyne, B., Eltchaninoff, H., Thielmann, M., Himbert, D., Romano, M., Serruys, P., & Wilmmer-Greinecker, G., on behalf PARTNER EU Investigator Group. (2011). One year follow-up of the multi-centre European PARTNER transcatheter heart valve study. *Eur Heart J,* 32, 148–157, 0195-668X

Leon, M.B., Smith, C.R., Miller, M.M., Moses J.W., Svensson, L.G., Tuzcu, E.M., Webb, J.G., Fontana, G.P., Makkar, R.R., Brown, D.L., Block, P.C., Guyton, R.A., Pichard, A.D., Bavaria, J.E., Herrmann, H.C., Douglas, P.S., Peterson, J.L., Akins, J.J., Anderson, W.N., Wang, D., & Pocock, S., for the PARTNER Trial investigators. (2010). Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*, 363, 1597–1607, ISSN 0028-8614

Leonteyv, S., Walther, T., Borger, M.A., Lehmann, S., Funkat, A.K., Kempfert, J., Falk, V., & Morh, F.W. (2009). Aortic valve replacement in octogenarians: utility of risk stratification with EuroSCORE. *Ann Thorac Surg*, 87, 1440–1445, ISSN 0003-4975

Levinson, J.R., Akins, C.W., Buckley, M.J., Newell, J.B., Palacios, I.F., Blosk, P.C., & Fifer, M.A. (1989). Octogenarians with aortic stenosis. Outcome after aortic valve replacement. *Circulation*, 80, 49–56, ISSN 0009-7322

Macchi, C., Fattirolli, F., Lova, R.M., Conti, A.A., Luisi, M.L., Intini, R., Zipoli, R., Burgisser, C., Guarducci, L., Masotti, G., & Gensini, G.F. (2007). Early and late rehabilitation and physical training in elderly patients after cardiac surgery. *Am J Phys Med Rehabil*, 86, 826–834, ISSN 0894-9115

Macchi, C., Polcaro, P., Cecchi, F., Zipoli, R., Sofi, F., Romanelli, A., Pepi, L., Sibilo, M., Lipoma, M., Petrelli, M., & Molino-Lova, R. (2009). One-year adherance to exercise in elderly patients receiving postacute inpatient rehabilitation after cardiac surgery. *Am J Phys Med Rehabil*, 88, 727–734, ISSN 0894-9115

Makary, M.A., Segev, D.L., Pronovost, P.J., Syin, D., Bandeed-Roche, K., Patel, P., Takenaga, R., Dervgan, L., Holzmueller, C.G., Tian, J., & Fried, L.P. (2010). Frailty as a predictor of surgical outcomes in older patients. *J Am Coll Surg*, 210, 901–908, ISSN S1072-7515

Maillet, J.M., Somme, D., Hennel, E., Lessana, A., Saint-Jean, O., & Brodaty, D. (2009). Frailty after aortic valve replacement in octogenarians. *Arch Gerontol Geriatr*, 48, 391–396, ISSN 0167-4943

Mazza, A., Camera, F., Maestri, A., Longoni, F., Patrignani, A., Gualco, A., Opasich, C., & Cobeli, F. (2007). Elderly patient-centered rehabilitation after cardiac surgery. *Monaldi Arch Chest Dis*, 68, 36–43, ISSN 1112–0643

Melby, S.J., Zierer, A., Kaiser, S.P., Guthrie, T.J., Keune, J.D., Schuessler, R.B., Pasque, M.K., Lawton, J.S., Moazami, N., Moon, M.R., & Damiano, R.J., Jr. (2007). Aortic valve replacement in octogenarians: risk factors for early and late mortality. *Ann Thorac Surg*, 83, 1651–1657, ISSN 0003-4975

Messika-Zeitoun, D., Serfaty, J.M., Brochet, E., Ducrocq, D., Lepage, L., Detaint, D., Hyafil, F., Himbert, D., Pasi, N., Laissy, J.P., Iung, B., & Vahanian, A. (2010). Multimodal assessment of the aortic annulus diameter: implications for transcatheter aortic valve implantation. *J Am Coll Cardiol*, 55, 186–194, ISSN 0735-1097

Needham, D.M. (2008). Mobilizing patients in the intensive care unit: neuromuscular weakness and physical function. *JAMA*, 300, 1685–1690, ISSN 0098-7484

NHLBI Balloon Valvuloplasty Registry participants. (1991). Percutaneous balloon aortic valvuloplasty: acute and 30-day follow-up results from the NHLBI Balloon Valvuloplasty Registry. *Circulation*, 84, 2383–2397. ISSN 0009-7322

Nkomo, V., Gardin, J.M., Skelton, T.N., Gottdiener, J.S., Scott, C.G., & Enriquez-Sarano, E. (2006). Burden of valvular heart diseases: a population-based study. *Lancet*. 368, 1005–1011, ISSN 0140-6736

Olsson, M., Granstrom, L., Lindblom, D., Rosenqvist, M., & Ryden, L. (1992). Aortic valve replacement in octogenarians with aortic stenosis: a case study. *J Am Coll Cardiol*, 20, 1512–1516, ISSN 0735-1097

Olsson, M., Janfjall, H., Orth-Gomer, K., Unden, A., & Rosenqvist, M. (1996). Quality of life in octogenarians after valve replacement due to aortic stenosis. *Eur Heart J*, 17, 583–589, 0195-668X

Opasich, C., Patrignani, A., Mazza, A., Gualco, A., Cobelli, F., & Pinna, G.D. (2010). An elderly-centered, personalized, physiotherapy program early after cardiac surgery. *Eur J Cardiovasc Prev Rehabil,* 17, 582–587, ISSN S1741-8267

Parolari, A., Pesce, L.L., Trezzi, M., Cavallotti, L., Kassem, S., Loardi, C., Pacini, D., Tremoli, E., & Alamanni, F. (2010). EuroSCORE performance in valve surgery: a meta-analysis. *Ann Thorac Surg*, 89, 787–793, ISSN 0003-4975

Pasquali, S.K., Alexander, K.P., & Peterson, E.D. (2001). Cardiac rehabilitation in the elderly. *Am Heart J*, 142, 748–755, ISSN 0002-8703

Praschker, B.G.L., Leprince, P., Bonnet, N., Rama, A., Bors, V., Liévre, L., Pavie, A., & Gandjbakch, I. (2006). Cardiac surgery in nonagenarians: hospital mortality and long-term follow-up. *Interact Cardiovasc Thorac Surg*, 5, 696–700, ISSN 1569-9293

Province, M.A., Hadley, E.C., Hornbrook, M.C., Lipsitz, L.A., Miller, J.P., Mulrow, C.D., Ory, M.G., Sattin, R.W., Tinetti, M.E., & Wolf, S.L. (1995). The effects of exercise on falls in elderly patients. A preplanned meta-analysis of the FICSIT trials. Frailty and Injuries: Cooperative Studies of Intervention Techniques. *JAMA*, 273, 1341–1347, ISSN 0098-7484

Robinson, T.N., Eiseman, B., Wallace, J.L., Church S.D., McFann, K.K., Pfister, S.M., Sharp, T.J., & Moss, M. (2009). Redefining geriatric preoperative assessment using frailty, disability and co-morbidity. *Ann Surg*, 250, 449–455, ISSN 0003-4932

Rockwood, K. (2005). Frailty and its definition: a worthy challenge. *J Am Geriatr Soc*, 53, 1069–1070, ISSN 0002-8614

Roques, F., Michel, P., Goldstone, A.R., Nashef, S. (2003). The Logistic EuroSCORE. *Eur Heart J*, 24, 881–882, ISSN 0195-668X

Ross, J., & Braunwald, E. (1968). Aortic stenosis. *Circulation,* 38(Suppl I), I61–I67, ISSN 0009-7322

Roten, L., Wenaweser, P., Delacretaz, E., Hellige, G., Stortecky, S., Tanner, H., Pilgrim, T., Kadner, A., Eberle, B., Zwahlen, M., Carrel, T., Meier, B., & Windecker, S. (2010). Incidence and predictors of atrioventricular conduction impairment after transaortic valve implantation. *Am J Cardiol*, 106, 1473–1480, ISSN 0002-9149

Rydwik, E., Lammes, E., Frändin, K., & Akner, G. (2008). Effects of a physical and nutritional intervention program for a frail elderly people over age 75. A randomized controlled pilot treatment trial. *Aging Clin Exp Res*, 20, 159–170, ISSN 1594-0667

Scharwz, F., Baumann, P., Manthey, J., Hoffmann, M., Schuler, G., Mehmel, H.C., Schmitz, W., & Kübler, W. (1982). The effect of aortic valve replacement on survival. *Circulation*, 66, 1105–1110, ISSN 0009-7322

Shroyer, A.L., Coombs, L.P., Peterson, E., Eiken, M.C., DeLong, E.R., Chen, A., Ferguson, T.B., Grover, F.L., & Edwards, F; Society of Thoracic Surgeons. (2003). The Society of Thoracic Surgeons: 30-day operative mortality and morbidity risk models. *Ann Thorac Surg*, 75, 1856–1865, ISSN 0003-4975

Schueler, R., Hammersting, C., Sinning, J.M., Nickenig, G., & Omran, H. (2010). Prognosis of octogenarians with severe aortic valve stenosis at high risk for cardiovascular surgery. *Heart*, 96, 1831–1836, ISSN 1355-6037

Sjögren, J., & Thulin, L.I. (2004). Quality of life in the very old elderly after cardiac surgery: a comparison of SF-36 between long term survivors and an age-matched population. *Gerontology*, 50, 407–410, ISSN 0304-324X

Somme, D., Maillet, J.M., & Fagon, J.Y. (2009). Particularités physiologiques du sujet âgé, In: *Réanimation Médicale* sous l'égide du Collége National des Enseignants de Réanimation Médicale, pp. 218–225, Masson, Paris, ISBN 978-2-294-08855-1

Stoica, S.C., Cafferty, F., Kitcat, J., Baskett, R.J.F., Goddard, M., Sharples, L.D., Wells, F.C., & Nashef, S.A.M. (2006). Octogenarians undergoing cardiac surgery outlive their peers: a case for early referral. *Heart*, 92, 503–506, ISSN 1355-6037

Sundt, T.M., Bailey, M.S., Moon, M.R., Mendeloff, E.N., Huddleston, C.B., Pasque, M.K., Barner, H., & Gay, Jr, W.C. (2000). Quality of life after aortic valve replacement at the age of > 80 years. *Circulation*, 102 (Suppl III), III70–III74, ISSN 0009-7322

Tamburino, C., Capodanno, D., Ramondo, A., Petronio, A.S., Ettori, F., Santoro, G., Klugmann, S., Bedogni, F., Maisano, F., Marzocchi, A., Poli, A., Antoniucci, D., Napodano, M., De Carlo, M., Fiorina, C., & Ussia, G.P. (2011). Incidence and predictors of early and late mortality after transcatheter aortic valve implantation in 663 patients with severe aortic stenosis. *Circulation*, 123, 299–308, ISSN 0009-7322

Thourani, V.H., Myung, R., Kilgo, P., Thompson, K., Puskas J.D., Lattouf, O.M., Cooper, W.A., Vega, J.D., Chen, E.P., & Guyton, R.A. (2008). Long-term outcome after isolated aortic valve replacement in octogenarians: a modern perspective. *Ann Thorac Surg*, 86, 1458–1465, ISSN 0003-4975

Tsai, T.P., Chaux, A., Matloff, J.M., Gray, R.J., DeRobertis, M.A., & Khan, S.S. (1994). Ten-year experience of cardiac surgery in patients aged 80 years and over. *Ann Thorac Surg*, 58, 445–450, ISSN 0003-4975

Vahanian,A. & Otto, C.M.(2010). Risk stratification of patients with aortic stenosis. Eur Heart J, 31, 416–423, ISSN 0195-668X

Vahanian, A., Baumgartner, H., Bax, J., Butchard, E., Dion, R., Filippatos, G., Flachskampf, F., Hall, R., Iung, B., Kasprzak, J., Nataf, P., Tornos, P., Torracca, L., & Wenink, A. (2007). Guidelines on the management of valvular heart disease. The Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology. *Eur Heart J*, 28, 230–268, ISSN 0195-668X

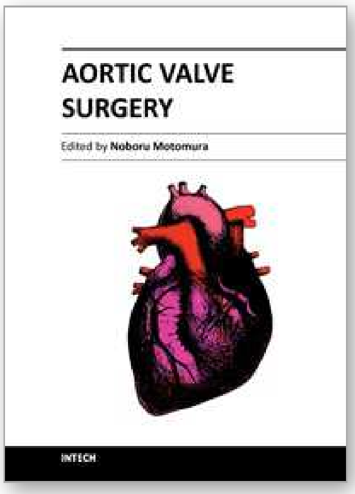
Varadarajan, P., Kapoor, N., Bansal, R.C., & Pai, R.G. (2006). Clinical profile and natural history of 453 non surgically managed patients with severe aortic stenosis. *Ann Thorac Surg*, 82, 2111–2115, ISSN 0003-4975

Vicchio, M., Della Corte, A., De Santo, L.S., De Feo, M., Caianiello, G., Scardone, M., & Cotrufo, M. (2008). Tissue versus mechanical prostheses: quality of life in octogenarians. *Ann Thorac Surg*, 85, 1290–1295, ISSN 0003-4975

Wang, P., Acker, M.A., Bilello, M., Melhem, E.R., Stambrook, E., Ratcliffe, S.J., & Floyd, T.F.; DENOVO (determining neurologic outcomes from valve operations) investigators. (2010). Sex, ageing and preexisting cerebral ischemic disease in patients with aortic stenosis. *Ann Thorac Surg*, 90, 1230–1235, ISSN 0003-4975

Webb, J.G., Altwegg, L., Boone, R.H., Cheung, A., Ye, J., Lichtenstien, S., Lee, M., Masson, J.B., Thompson, C., Moss, R., Carere, R., Munt, B., Nietlispach, F., & Humphries, K. (2009). Transcatheter aortic valve implantation. Impact on clinical and valve-related outcomes. *Circulation*, 119, 3009–3016, ISSN 0009-7322

Zajarias, A. & Cribier, A.G. (2009). Outcomes and safety of percutaneous aortic valve replacement. *J Am Coll Cardiol*, 53, 1829–1836, ISSN 0735-1097



Aortic Valve Surgery
Edited by Prof. Noboru Motomura

ISBN 978-953-307-600-3
Hard cover, 246 pages
Publisher InTech
Published online 22, December, 2011
Published in print edition December, 2011

The aortic valve is located at the center of the heart. It is the core of cardiac anatomy and aortic valve surgery has led the field of cardiac surgery. This book describes all aspects of aortic valve surgery and it will help clarify daily questions regarding the clinical practice in aortic valve surgery, as well as induce inspiration and new insights into this field.

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

Jean-Michel Maillet and Dominique Somme (2011). Relationship Between Aortic Valve Replacement and Old Age, Aortic Valve Surgery, Prof. Noboru Motomura (Ed.), ISBN: 978-953-307-600-3, InTech, Available from: http://www.intechopen.com/books/aortic-valve-surgery/relationship-between-aortic-valve-replacement-and-old-age

INTECH
open science | open minds

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