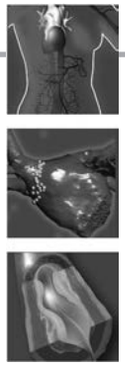

Comparing outcomes between surgical aortic valve replacement and transcatheter aortic valve implantation

Transcatheter aortic valve implantation (TAVI) has been introduced for the treatment of high-risk patients with symptomatic aortic stenosis. Surgical aortic valve replacement (SAVR) provides the therapeutic armamentarium for all complex valvular pathologies and is the established gold standard. TAVI has initially been restricted to non-operable patients. The extension of this treatment modality to less complex patient populations warrants a thorough comparison of safety and efficacy vis-à-vis SAVR. Perioperative mortality of SAVR for high-risk subpopulations such as octogenarians, patients with impaired LV function or previous sternotomy ranges from 5 to 19%. Peri-interventional mortality rates for TAVI amount to 6–23%. Reported stroke rates average 2–5% with both treatment modalities. While TAVI does not require cardiopulmonary bypass or general anesthesia, the spectrum of peri-interventional complications is extended to vascular access site complications as well as atrioventricular conductance disturbances. Results from randomized trials are necessary to prove safety and efficacy of TAVI compared with SAVR.

KEYWORDS: aortic stenosis ■ endovascular ■ surgical aortic valve replacement ■ transcatheter aortic valve implantation

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The prevalence of valvular heart disease increases substantially as the population ages and is associated with impaired survival (Figure 1) [1]. The natural course of symptomatic aortic stenosis portends a poor life expectancy once symptoms of angina, syncope or heart failure ensue (Figure 2) [2]. More recent data indicate an impaired prognosis even in asymptomatic patients [3,4]. Aortic valve replacement using surgical techniques has been shown to effectively alleviate symptoms and improve survival and represents one of the most frequently performed cardiac surgical procedures (Figure 3). However, up to a third of patients are said not to undergo surgery [5,6] due to advanced age, comorbidities and depressed left ventricular function, recent myocardial infarction or severe concomitant coronary artery disease [5].

Valvular heart surgery has been introduced into clinical practice in the early 1960s shortly after the establishment of cardiopulmonary bypass. Within only one decade, two categories of heart valves were established – mechanical and biological valve prostheses. The caged ball valve design applied in the first mechanical valve prostheses [7,8] was soon replaced by a tilting disc design (St Jude Medical) [9] still used in contemporary practice. The advent of biological homografts [10,11] and allografts soon advanced the field to biological heart valves made of porcine or bovine pericardium [12], which were complemented by stentless bioprostheses (Toronto SPV, St Jude Medical) in the 1990s. Despite continuous efforts to advance heart valve technology, mechanical prostheses retain a substantial risk of thromboembolism and anticoagulation-related bleeding, while structural deterioration remains the principal concern of biological valves. Technical refinements of valvular design went in parallel with efforts to elaborate minimally invasive surgical approaches. Following demonstration of the feasibility of transcatheter implantation of heart valves in aortic and pulmonary position in experimental models [13,14], Cribier performed the first transcatheter aortic valve implantation in man in 2002 [15], whereas Bonhoeffer reported the first transcatheter pulmonary valve implantation also in 2002 [16]. The antegrade approach of transcatheter aortic valve implantation via femoral vein access, transseptal puncture, passage of the left atrium and mitral valve was soon replaced by the retrograde approach via the femoral artery [17,18] and complemented by an antegrade surgical approach via direct transapical access [17,19].

Surgical aortic valve replacement (SAVR) is the current gold standard in the treatment of severe, symptomatic aortic stenosis owing to its proven safety and efficacy record over several decades in large patient populations with a wide spectrum of aortic disease. Conversely, transcatheter aortic valve implantation (TAVI) was only recently introduced into clinical practice and currently undergoes evaluation of safety

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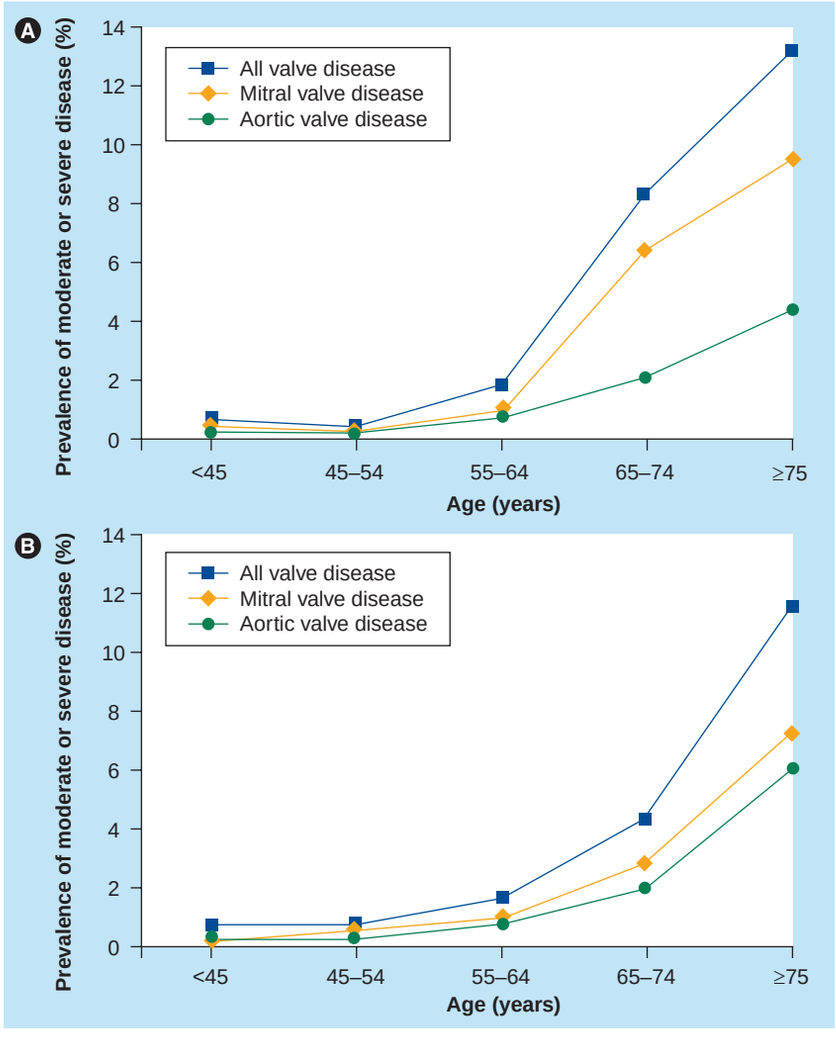


Figure 1. Prevalence of valvular heart disease by age. (A) Frequency in population-based studies and **(B)** in the Olmsted County community. Adapted with permission from [72].

and efficacy compared with SAVR as well as medical treatment in high-risk patients with severe aortic stenosis. Transcatheter valve-in-valve treatment of degenerated bioprosthetic valves has also been reported in selected cases and appears to be an attractive treatment alternative to repeat SAVR [20]. TAVI is currently not used for treatment of primary aortic regurgitation as well as concomitant pathology of the ascending aorta.

Transcatheter aortic valve implantation has been introduced as an alternative treatment for valvular aortic stenosis particularly in the subset of patients deemed at increased risk of SAVR. Consequently, patients assigned to this novel treatment strategy were primarily recruited from the patient population previously considered inappropriate candidates for open heart surgery. Both excitement and controversy surround this new treatment option as it provides a less invasive strategy appealing to both patients and physicians, while it has to prove safety and efficacy during short- and long-term follow-up vis-à-vis the established gold standard of SAVR.

Surgical aortic valve replacement

Aortic valve replacement through a standard median sternotomy or via minimally invasive approaches through a limited sternotomy or lateral thoracotomy shares the common necessity of cardiopulmonary bypass and mechanical ventilation. Surgical access facilitates concomitant interventions and hence provides treatment for the entire spectrum of valvular heart disease. Thus, aortic regurgitation due to dilatation or dissection of the ascending aorta can be managed in a similar way as well as concomitant mitral valve pathology or surgical revascularization of coronary arteries. Young patients with a long life-expectancy qualify for mechanical valve prostheses with prolonged durability and a lower risk of valve-related reinterventions. Conversely, patients aged 65 years and older frequently undergo implantation of bioprosthetic heart valves as event-free survival is similar to mechanical prostheses, and the risk of bleeding and thromboembolic complications substantially lowered. Compared with current transcatheter strategies, not only is SAVR the current gold-standard treatment for severe aortic stenosis, but TAVI also provides the therapeutic armamentarium for all complex cardiac pathologies (beyond isolated aortic stenosis).

■ Patient population

Valvular aortic stenosis is the most common pathology leading to SAVR worldwide. SAVR has been shown superior to a conservative treatment strategy in symptomatic [21] patients and recent data suggest the same for asymptomatic [3,4] individuals. Given the dismal prognosis of the natural course of symptomatic aortic stenosis, SAVR represents the treatment of choice ever since its introduction and is widely applied across different patient populations. Notwithstanding, SAVR requiring cardiopulmonary bypass, an open sternotomy and general anesthesia is associated with perioperative complications such as death and stroke as well as prolonged ventilation and hospitalization time particularly in high-risk and frail patients. In addition, porcelain aorta, exposure to radiation therapy and previous cardiac operations such as coronary artery bypass surgery are associated with an increased risk of adverse events.

■ Safety of SAVR

Perioperative mortality of isolated SAVR in the overall population averages 3%, whereas the mortality for combined SAVR and coronary artery bypass grafting (CABG) amounts to 5% [101]. Perioperative outcome of high-risk subpopulations is predominantly derived from retrospective analyses. Published data of SAVR in high-risk populations can be categorized into those focusing on elderly patients aged 80 years or older (Table 1) [22–36], patients with reduced left ventricular ejection fraction (Table 2) [37–45], patients with increased risk according to EuroSCORE [36,46], or patients with previous sternotomy (Table 3) [47,48]. Concomitant coronary artery bypass grafting has been associated with an incremental risk in some but not all of these studies [25,35,41].

■ Safety of SAVR in octogenarians

Perioperative mortality in patients 80 years of age or older has been reported in the range from 4.3 [25] to 19% (Table 1) [25]. Several studies consistently identified urgent surgery [27,30,33,36], pre- [35] and post-operative [29] renal failure as independent predictors of increased mortality. Moreover, reduced left ventricular ejection fraction, severe congestive heart failure (NYHA functional class IV) [27,30], and pulmonary hypertension have been shown to increase in-hospital mortality [36]. Most reports also indicate an increased risk of procedural mortality with SAVR and concomitant CABG.

Likosky *et al.* observed a procedural stroke risk of 2.1% in patients aged 80–84 years and of 4.6% in patients older than 85 years of age [35]. These findings correspond well with previous reports of octogenarians undergoing SAVR.

The diagnosis of peri-interventional myocardial infarction following SAVR is difficult and usually requires either new Q waves or the elevation of creatinine kinase-MB in association with persistent ST segment changes [24,29,30,32,34]. Six studies reported on the incidence of periprocedural myocardial infarction with a low frequency ranging from 0 to 4% (Table 1) [24,29,30,32,34,49].

■ Safety of SAVR in patients with impaired left ventricular function

The impact of impaired left ventricular function on clinical outcome after SAVR has been addressed in several studies with perioperative mortality ranging from 5 [31] to 18% [37] (Table 2). A multicenter study of 217 patients (71 ± 8 years) with low-flow/low-gradient aortic stenosis (left ventricular ejection fraction [LVEF] ≤35% and mean gradient ≤30 mmHg) reported a perioperative mortality of 16% in the overall population. However, the investigators noted a decrease in mortality from 20% in the decade 1990–1999 to more recently 10% in the period from 2000 to 2005 [39].

In a retrospective analysis of 76 patients with LVEF less than or equal to 30%, the incidence of perioperative stroke amounted to 5% in the isolated SAVR cohort and to 8% in the SAVR cohort with concomitant CABG [47]. Multivariate analysis identified low-flow/low-gradient aortic stenosis as an independent predictor of postoperative stroke in this study. Sharony *et al.* reported a perioperative stroke rate of 5.8% in their cohort of 260 patients with an LVEF less than or equal to 40% [43]. The overall stroke rate was 2.8-fold higher than the risk that was observed in the group with normal left ventricular function. Multivariate analysis identified peripheral vascular disease, previous history of cerebrovascular disease and diabetes as independent predictors of stroke [43].

The occurrence of perioperative myocardial infarction has not been addressed in patients with impaired LVEF undergoing SAVR.

■ Safety of SAVR in patients with previous cardiac surgery or increased EuroSCORE

Several reports have focused on the perioperative risk of SAVR after previous sternotomy (Table 3). Perioperative rates of death range from 4.6 to 8.4% [47,48,50,51] and of stroke from 1.2 to 5.2% [48,50,51].

One study investigated the outcome of redo-SAVR in a cohort of 71 octogenarians that was compared with a control group matched for age,

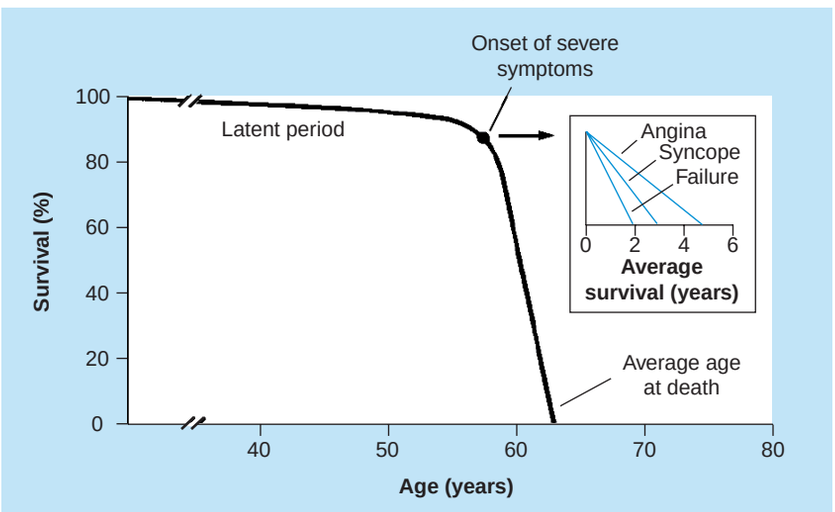
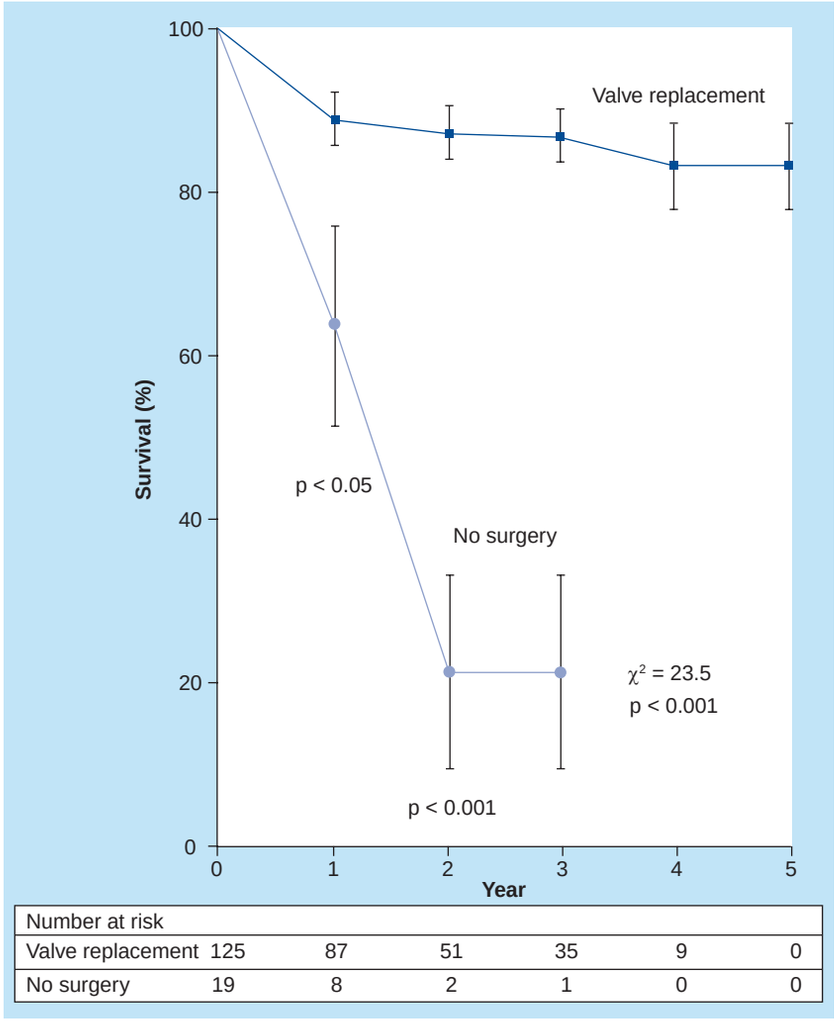


Figure 2. Natural history of aortic stenosis.
Adapted from [2].



Number at risk						
Valve replacement	125	87	51	35	9	0
No surgery	19	8	2	1	0	0

Figure 3. Effect of surgical aortic valve replacement on survival.
Adapted with permission from [21].

sex and year of aortic valve replacement. The study cohort underwent concomitant CABG in 20% and mitral valve replacement in 6% of patients. Mortality within 30 days amounted to 15.5% but did not differ significantly between the study cohort and the controls [52]. These findings are conflicting with data from Langanay and colleagues who identified redo-SAVR as independent predictor of in-hospital mortality [27].

Grossi *et al.* prospectively collected results of 731 high-risk patients as defined by a linear EuroSCORE greater than 7% undergoing isolated SAVR. While mean linear and logistic EuroSCORE predicted a 30-day mortality of 9.7 and 17.2%, respectively, in this population, actual in-hospital mortality amounted to 5.7 and 3.4% of patients suffered from stroke [46]. Another study evaluated outcome of octogenarians undergoing isolated SAVR at a single institution with a particular focus on risk stratification by EuroSCORE [36]. Patients were categorized into low-risk (log EuroSCORE ≤10%), moderate-risk (log EuroSCORE >10 to <20%) and high-risk groups (log EuroSCORE ≥20%). In-hospital mortality was 7.5% in the low-risk group (n = 107), 12.6% in the moderate-risk group (n = 103) and 12.5% in the high-risk group (n = 72).

■ Efficacy of SAVR

Surgical aortic valve replacement looks back to a long tradition of heart valve surgery using various prostheses and different surgical approaches and data on long-term survival after SAVR in octogenarians is available. The largest published cohort of octogenarians observed actuarial survival rates after 1, 3, 5 and 8 years of 89, 79, 69 and 46%, respectively [22]. Actuarial survival analysis of 345 octogenarians undergoing SAVR with a follow-up of 40 ± 33 months showed that 61% of patients at 5 years and 21% of patients at 10 years were alive [33]. Melby *et al.* observed an actuarial survival rate of 82% at 1 year, 70% at 3 years and 56% at 5 years during a mean follow-up of 4.2 ± 3.3 years [29], whereas Kolh *et al.* reported a 5-year survival rate of 73 ± 7% (mean follow-up 58.2 months) in 220 consecutive octogenarians undergoing SAVR [21]. Similar findings were reported by Unic *et al.* (actuarial survival rate at 1 year and 5 years of 92 ± 1% and 66 ± 5%) [25] and Filsoufi *et al.* (1-year survival: 90.3 ± 2.1%; 5-year survival: 63.8 ± 4.8%; mean follow-up 3.6 ± 2.5 years) [32]. Urgent procedures were independently associated with late mortality in two studies [30,36]. Moreover, previous stroke [36], prior myocardial infarction [30], postoperative stroke [29] and congestive heart failure [34] resulted in adverse long-term outcome.

Transcatheter aortic valve implantation

Transcatheter techniques for aortic valve implantation circumvent the need for cardiopulmonary bypass and general anesthesia. Currently, two valve types have received CE approval and each has been implanted in more than 10,000 patients worldwide. The Edwards-SAPIEN prosthesis consists of a balloon-expandable, stainless steel stent with a valve made of bovine pericardium, which currently can accommodate an aortic valve annulus of 18–25 mm (23 and 26 mm prosthesis). The 23-mm Edwards-SAPIEN prosthesis can be delivered through a 22-Fr transfemoral sheath, whereas the 26-mm valve requires a 24-Fr sheath. The Edwards-SAPIEN prosthesis can also be delivered through a

Table 1. Perioperative outcome of surgical aortic valve replacement in octogenarians (≥80 years).

Study	Patient (n)	Age (years)	EuroSCORE add/log	Concomitant CABG (n/%)	Perioperative outcome (30 day/in-hospital)			Ref.
					Mortality (n/%)	*Myocardial infarction (n/%)*	*Stroke (n/%)*	
Asimakopoulos (1997)	1100	82 ± 2			73 (6.6%)			[22]
Gilbert (1999)	103	83 ± 3		25 (24%)	19 (19%)		17 (17%)	[23]
Alexander (2000)	345	83 ± 2		345 (100%)	10.1%	3.0%	4.9%	[49]
Chiappini (2004)	115	82 ± 2		44 (38%)	10 (8.5%)	4 (3.8%)	1 (0.8%)	[24]
Unic (2005)	242	83 ± 3		148 (61%)	AVR: 4 (4.3%) AVR + CABG: 12 (8.2%)			[25]
Langanay (2006)	442	83 ± 2		86 (19%), 5 MV (1%), 7 aorta (2%)	33 (7.5%)			[27]
Melby (2007)	245	84 ± 3		140 (57%)	22 (9%) AVR: 10% AVR + CABG: 6% Emergent intervention: 16%	3 (1%)	8 (3%)	[29]
Kolh (2007)	220	83		58 (26%)	22 (10%)	10 (4%)	4 (2%)	[30]
Bose (2007)	68	83 ± 3	8.6 ± 1.2/ 12.0 ± 5.9	31 (46%)	13%		1 (1%)	[31]
Gulbins (2008)	236	83 ± 3	10.2 ± 1.9/ 19.4 ± 10.8%	215 (91%), 21 MV (9%)	22 (9.3%)		6/236 (2.5%)	[28]
Filsoufi (2008)	231	83 ± 3	23 ± 16% (log)	110 (48%)	12 (5.2%)	2 (0.9%)	9 (3.9%)	[32]
De Vincentiis (2008)	345	82 ± 2		150 (43%), 39 MV (11%)	26 (7.5%)			[33]
Thourani (2008)	88	83 ± 2		0%	5 (5.7%)	0 (0%)	3 (3.4%)	[34]
Likosky (2009)	1390			59%	AVR: 6.7% (80–84); 11.7% (≥85) AVR + CABG: (80–84) 9.4%; 8.5% (≥85)		AVR: 2.1% (80–84); 4.6% (≥85) AVR + CABG: 4.2% (80–84); 1.4% (≥85)	[35]
Leontyev (2009)	282	83 ± 3	16.2 ± 11.9 (log)	0%	30 (10.6%)		4 (1.4%)	[36]

add: Additive; AVR: Aortic valve replacement; CABG: Coronary artery bypass grafting; log: Logistic; MV: Mitral valve.

Table 2. Perioperative outcome of surgical aortic valve replacement in patients with impaired left ventricular ejection fraction.

Study	Patient (n)	Age (years)	Patient characteristics	EuroSCORE add/log	Concomitant CABG (n/%)	Perioperative outcome (30 day/in-hospital)			Ref.
						Mortality (n/%)	*Myocardial infarction (n/%)*	*Stroke (n/%)*	
Connolly (1997)	154	73 ± 10	LVEF ≤35%		78 (51%)	14 (9%)			[38]
Powell (2000)	55	73 ± 9	LVEF ≤30%			10 (18%)			[37]
Pereira (2002)	68	70 ± 9	LVEF ≤35%, mean gradient ≤30 mmHg			3 (8%)			[44]
Tarantini (2003)	52	69 ± 12	LVEF ≤35%		16 (31%)	4 (8%)			[42]
Sharony (2003)	260	73 ± 10	LVEF ≤40%		59%	25 (9.6%)		15 (5.8%)	[43]
Quere (2006)	66	68 ± 9	LVEF ≤40%, mean gradient ≤40 mmHg			6% with contractile reserve, 33% with no contractile reserve			
Levy (2008)	217	71 ± 8	LVEF ≤35%, mean gradient ≤30 mmHg	8.9 ± 2.7 (add)	74 (34%)	34 (16%)			[39]
Clavel (2008)	44	67 ± 10	LVEF ≤40%, gradient ≤30 mmHg		30 (68%)	18%			[40]
Pai (2008)	58	72 ± 12	LVEF ≤35%		59% (14% MV)	9%			[45]
Chikwe (2009)	76	71	LVEF ≤30%	10.5%	36 (47%)	AVR: 2 (5%) AVR + CABG: 3 (8%)		AVR: 1 (3%) AVR + CABG: 3 (8%)	[41]

add: Additive; AVR: Aortic valve replacement; CABG: Coronary artery bypass grafting; log: Logistic; LVEF: Left ventricular ejection fraction.

transapical sheath (27 Fr). The Medtronic CoreValve revalving system consists of a three-level self-expanding nitinol stent, which houses a valve made of porcine pericardium. The valve comes in two sizes (26 and 29 mm) and can accommodate an aortic valve annulus from 19 to 27 mm. Both, the 26- and 29-mm Medtronic CoreValve prostheses are delivered through an 18-Fr sheath, which allows access via the femoral or subclavian artery.

■ Patient selection

While SAVR slowly progressed from low- to high-risk patient populations, the opposite phenomenon is observed with TAVI, which was initially restricted to non-operable or high-risk patients and is slowly being extended to less complex patient populations. Moreover, certain anatomical features in terms of aortic valve dimension and peripheral access have to be fulfilled precluding eligibility of all patients for this treatment modality. Notwithstanding, technical refinement and growing experience have already led to an expansion from high-risk to lower-risk patients.

■ Safety of TAVI

Clinical studies investigating TAVI have been performed mostly in high-risk populations (Table 4) as attested by a mean age of more than 80 years and a surgical risk assessment by means of the logistic EuroSCORE greater than 20%. Data from the initial feasibility studies by Cribier *et al.* documented successful (antegrade transseptal or retrograde) transcatheter valve implantation in 27 out of 33 patients (82%) and showed a 30-day mortality of 22% (six patients) in those with successful implantation [53]. Subsequent studies reported separate results for the transfemoral and transapical access. Webb *et al.* published his initial experience with the retrograde transfemoral approach using the balloon expandable Edwards-SAPIEN prosthesis [54], whereas Grube *et al.* investigated outcomes with the self-expandable Medtronic CoreValve prosthesis delivered by the transfemoral route [55]. Procedural success was achieved in 86 and 74% in these early series including 50 and 86 patients, respectively, which increased to rates well above 95% in more recent, larger series [56–59]. The importance of a learning curve and operator experience was also demonstrated by improved outcomes in 30-day mortality with increased levels of experience. Thus, mortality at 30 days amounted to 12% in the first 50 patients undergoing TAVI by Webb [54], which decreased to 8% in a later cohort [57].

Table 3. Perioperative outcome of surgical aortic valve replacement in patients with previous sternotomy, Redo-SAVR or high EuroSCORE.

Study	Patient (n)	Age (years)	Patient characteristics	EuroSCORE add/log	Concomitant CABG (n/%)	Perioperative outcome (30 day/in-hospital)			Ref.
						Mortality (n/%)	*Myocardial infarction (n/%)*	*Stroke (n/%)*	
Potter (2005)	162	64 ± 15	Redo-AVR		41 (25.3%)	8 (4.9%)	0	2 (1.2%)	[51]
Eitz (2006)	71	80–84 (90.2%); ≥85 (9.8%)	≥80 years and cardiac reoperation of AV		CABG: 14 (19.7%) MVR: 4 (5.6%)	11 (15.5%)			[52]
Davierwala (2006)	216	59 ± 14	Redo-SAVR			4.6%	0.9%	4.6%	[50]
Grossi (2008)	731	>80 (44%)	EuroSCORE >7	9.7/17.2%	0%	57 (7.8%)			[46]
Khaladj (2009)	130	60–84 (75%)	Previous sternotomy	12 ± 3/ 32 ± 21%	0%	2 (5%)			[47]
LaPar (2010)	191	67 ± 13	Previous sternotomy		58 (30.4%) MV: 22 (11.5%) Aortic root: 9 (4.7%); tricuspid valve: 5 (2.6%)	16 (8.4%)		10 (5.2%)	[48]

add: Additive; AV: Aortic valve; AVR: AV replacement; CABG: Coronary artery bypass grafting; log: Logistic; LVEF: Left ventricular ejection fraction; MV: Mitral valve; MVR: MV replacement; SAVR: Surgical aortic valve replacement.

Table 4. Perioperative outcome of transcatheter aortic valve implantation.

Study	Patient (n)	Age (years)	Patient characteristics	EuroSCORE add/log	Perioperative outcome (30 day/in-hospital)			Ref.
					Mortality (n/%)	*Myocardial infarction (n/%)*	*Stroke (n/%)*	
Cribier (2006)	27	80 ± 7	High risk for conventional surgery	Add 12 ± 2	6 (22%)	0	1 (3.7%)	[53]
Webb (2007)	50	82 ± 7	High risk for conventional surgery	Log 28%	6 (12%)	1 (2%)	2 (4%)	[54]
Grube (2007)	86	82 ± 6	≥80 years + EuroSCORE ≥20 or ≥75 years + EuroSCORE ≥15	Log 21.7 ± 12.6%	10 (12%)	1 (1%)	9 (10%)	[55]
Grube (2008)	136	82 ± 7	≥80 years + EuroSCORE ≥20 or ≥75 years + EuroSCORE ≥15 or ≥65 years + severe comorbidities	Log 23.1 ± 15.0%	17 (12.5%)	3 (2.2%)	6 (4.4%)	[58]
Piazza (2008)	646	81 ± 7	≥75 years + EuroSCORE ≥15 or ≥65 years + severe comorbidities	Log 23.1 ± 13.8%	52 (8.0%)	4 (0.6%)	12 (1.9%)	[56]
Webb (2009)	168	84	High risk for conventional surgery	Log 28.6%	19 (11.3%)		1 (0.6%)	[57]
Himbert (2009)	75	82 ± 8	EuroSCORE ≥20% or STS ≥10%	Log 26 ± 13%	8 (10%)		3 (4%)	[64]
Ye (2009)	26	80 ± 9	High risk for conventional surgery	Log 37 ± 20%	6 (23%)	1 (4%)	1 (4%)	[73]
Osten (2009)	46	80 ± 7	High risk for conventional surgery	Log 25.3%	3 (6.5%)			[74]
Thielmann (2009)	39	81 ± 5	EuroSCORE >30%, STS >15%	14.2 ± 3.6/ 44.2 ± 12.6%	17.9%			[75]
PARTNER EU	61 TF 69 TA	82 ± 5 81 ± 6	Log EuroSCORE >20% and/or STS ≥10 or severe comorbidities	Log 25.7 ± 11.5% Log 33.8 ± 14.7%	5 (8.1%) 13 (18.8%)	1 (1.6%) 3 (4.3%)	2 (3.2%) 2 (2.9%)	[60]
SOURCE Registry	463 TF 575 TA	81.7 80.7		Log 25.7% Log 29.2%	29 (6.3%) 59 (10.3%)		11 (2.4%) 16 (2.6%)	[59]

add: Additive; log: Logistic; STS: Society of Thoracic Surgeons; TA: Transapical; TF: Transfemoral.

Similarly, 30-day mortality amounted to 12% [54,55] in the initial CoreValve experience reported by Grube, which subsequently decreased to 8% in the larger cohort reported by Piazza and colleagues [56]. Similar rates of 30-day mortality using the transfemoral approach have been reported in abstract form in the PARTNER EU [60] (8.1%) and the SOURCE registry [59] (6.3%) investigating the Edwards SAPIEN prosthesis.

Transcatheter aortic valve implantation by the transapical route has been typically performed in higher risk patients as indicated by an increased logistic EuroSCORE [57] compared with the transfemoral approach. Transapical implantation of the Edwards SAPIEN prosthesis was associated with a 30-day mortality of 18.2% in a series of 55 patients [57], 18.8% in 69 patients included in the PARTNER EU transapical study [51], and 10.3% in 575 patients included into the SOURCE transapical registry [59].

The risk of periprocedural stroke using the transfemoral approach appears similar with both devices and has been reported in the range of 0.6–10%. Of note, the stroke risk has been consistently lower in more recent reports (range 0.6–4%) possibly related to more careful technique, peri-interventional anticoagulation and postprocedural anti-thrombotic therapy. Although it has been suggested that the transapical approach may be associated with a lower risk of stroke, data from the PARTNER EU [60] and SOURCE registry [59] indicate a similar rate of stroke independent of the access route.

The risk of peri-interventional myocardial infarction is low and ranges from 0 to 4.3% of patients. Occlusion of the ostium of the left or right coronary artery has been rarely reported but is largely confined to the balloon-expandable Edwards SAPIEN prosthesis in case of proximity of the valve frame to the coronary ostia or due to displacement of components of the native calcified leaflets following valve insertion. As following SAVR, some patients require a permanent pacemaker after TAVI owing to disturbance of atrioventricular conduction with high-degree AV block. The need for a permanent pacemaker in patients treated with an Edwards SAPIEN prosthesis has been reported in the range of 4.4% [57] to 7.3% [59] akin to the one observed after SAVR (3–8.5% [61–63]). Conversely, patients undergoing TAVI with the Medtronic CoreValve Revalving system have been consistently reported to have a higher rate of permanent pacemaker implantation ranging from 9.3 to 33.3% [56,58]. Vascular access site complications are a frequent and potentially life-threatening complication of TAVI. Major

vascular injury was documented in 8.0% of patients with a transfemoral access and 3.5% of patients with a transapical approach in the study by Webb and colleagues using the Edwards Sapien prosthesis [57]. Himbert *et al.* found a vascular complication rate of 11% in 51 transfemoral and 24 transapical patients (12 and 8%, respectively) also using the Edwards Sapien prosthesis [64]. Perforation or damage to vessels, myocardium or valvular structures were observed in 15.0, 9.1, 19.7 and 17.9% in the REVIVE, REVIVAL and PARTNER EU trial for transfemoral access with the Edwards Sapien valve, respectively [59]. By contrast, the Expanded Evaluation Registry of the third-generation CoreValve Revalving System documented vascular access site dissection or tear in only 12 out of 646 patients (1.9%) [56]. Definitions of vascular complications vary across different reports and may contribute to differences in incidence and outcome. The Rotterdam group observed that the incidence of vascular complications ranged from as low as 4% to as high as 13% when applying different definitions to 99 consecutive patients following CoreValve implantation [65]. The transapical approach was associated with access complications in 9–20% in the REVIVAL TA, PARTNER EU and TRAVERCE TA studies [59]. The SOURCE registry reported an incidence of major vascular complications of 10.6% after transfemoral and 2.4% after transapical implantation of the Edwards Sapien valve [59]. Whereas access site complications were associated with adverse outcome in the transapical cohort of the SOURCE registry, transfemoral access was no longer a predictor of mortality, which was attributed to a learning curve in complication management. Three recent studies addressed vascular complications following TAVI. In a cohort of 45 consecutive patients from France, four patients (8.5%) suffered vascular complications necessitating vascular surgery; no significant differences between the Medtronic CoreValve and Edwards-SAPIEN prostheses were observed [66]. A somewhat higher vascular access complication rate was documented in 54 patients undergoing transfemoral implantation of the Edwards-SAPIEN prosthesis. Five patients (9.3%) with vascular rupture required surgical repair, whereas four patients (7.4%) with arterial dissection were managed with endovascular stents. However, no differences in hospital mortality or length of stay were observed in patients with and without vascular complications [67].

Transcatheter aortic valve implantation is associated with a higher incidence of postoperative aortic regurgitation compared with conventional stented or stentless aortic valve replacement (moderate AR in 8 vs 0 vs 0%, respectively, p<0.0001) [68]. In 74 patients undergoing TAVI using the balloon expandable device paravalvular aortic regurgitation grade 2/4 or more was observed in 21% [69]. The clinical significance of these findings is still under debate.

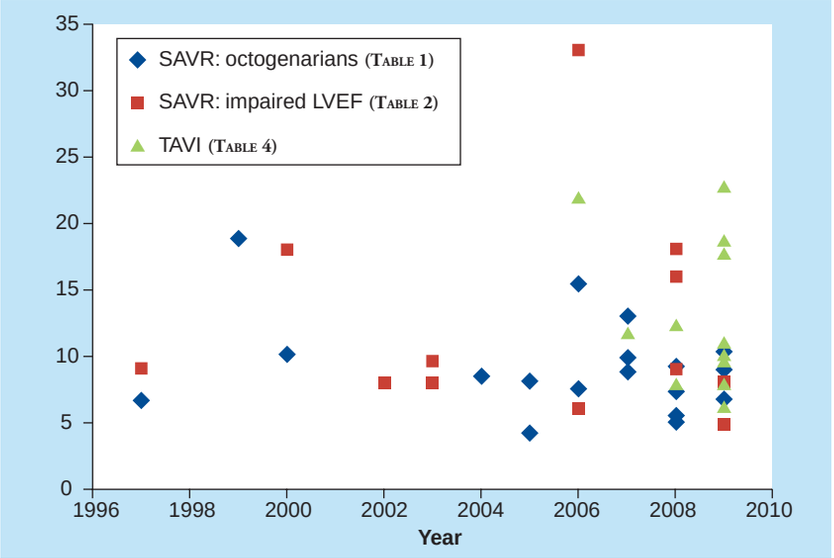


Figure 4. Perioperative mortality of surgical aortic valve replacement and transcatheter aortic valve implantation in high-risk patients.
Individual studies with references as listed in Tables 1, 2 & 4.

■ Efficacy of TAVI

Transcatheter aortic valve implantation is still in the early stages of clinical investigation. Although promising midterm results are

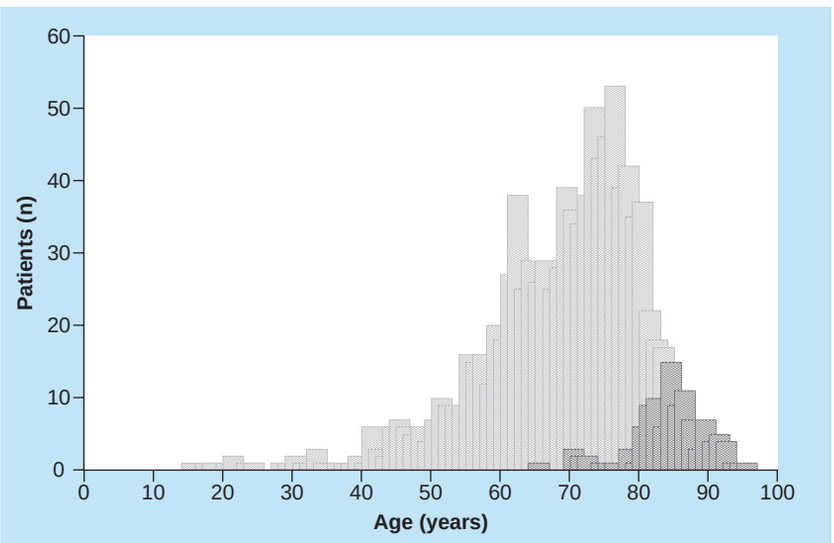


Figure 5. Distribution of age in the transcatheter aortic valve implantation and surgical aortic valve replacement cohort of the matching study (light gray: surgical aortic valve replacement; dark gray: transcatheter aortic valve implantation).
Data taken from [71].

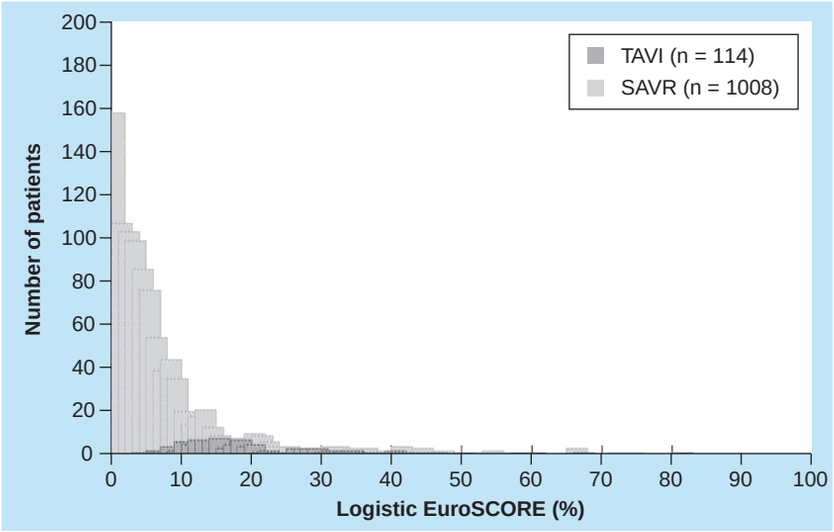


Figure 6. Distribution of estimated perioperative risk in the transcatheter aortic valve implantation and surgical aortic valve replacement cohort of the matching study.
Light gray: SAVR; dark gray: TAVI.
SAVR: Surgical aortic valve replacement; TAVI: Transcatheter aortic valve implantation.
Data taken from [62].

accumulating long-term data are currently lacking. Using the Edwards SAPIEN prosthesis, Webb and colleagues reported 1- and 2-year survival rates of 74 and 61%, respectively, and identified transapical access and chronic renal failure as predictors for increased mortality [57]. The incidence of valve-related adverse events during follow-up was rather low. In the PARTNER EU study, a similar 1-year survival rate of 78% was observed [70]. Using the Medtronic CoreValve Revalving system, Grube and colleagues reported a survival rate of 68% at 1 year [58].

Symptomatic and functional improvement following TAVI is impressive. An increase in functional class has been shown as early as 30 days after the intervention and appeared sustained over time. Thus, 77 (78%) of 99 patients were found to be in NYHA functional class I or II at 1-year follow-up in the study of Webb *et al.* [57]. These findings have been corroborated by a similar improvement of NYHA functional status from 3.3 ± 0.5 preprocedure to 1.7 ± 0.7 postprocedure in the cohort reported by Grube *et al.*, which remained stable over the duration of 12 months [58].

Direct comparison of SAVR & TAVI

Comparing crude, unadjusted outcome in contemporary studies point to similar perioperative mortality in high-risk patients undergoing SAVR and TAVI (Figure 4). A small registry of 66 consecutive patients (mean age of 83 ± 6 years) with severe aortic stenosis reported outcome according to treatment allocation to conservative management, SAVR, TAVI or balloon valvuloplasty following a multidisciplinary consensus. A total of 27 patients were considered low-risk and underwent SAVR. Among the remaining 39 high-risk patients, 12 underwent TAVI, seven balloon valvuloplasty, four SAVR and 16 medical treatment. There were three hospital deaths in patients undergoing TAVI, two in those treated medically, and one following SAVR without

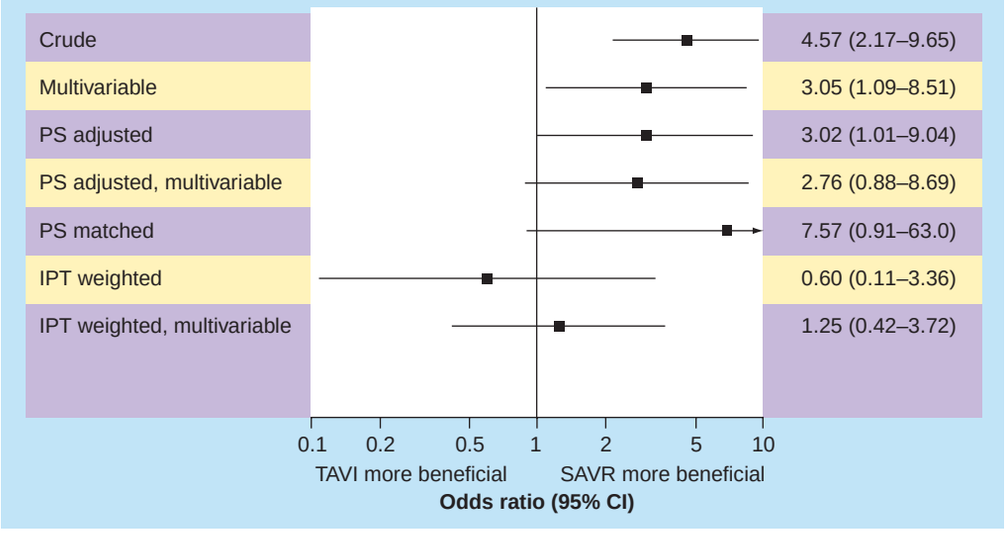


Figure 7. Impact of different approaches used to control for confounding on mortality estimates.
SAVR: Surgical aortic valve replacement; TAVI: Transcatheter aortic valve implantation.
Data taken from [71].

significant differences among groups [70]. A two-center, prospective cohort study compared baseline characteristics and 30-day mortality between TAVI and SAVR in consecutive patients undergoing invasive treatment for aortic stenosis. A total of 1122 patients were included with 114 patients undergoing TAVI and 1008 patients undergoing SAVR. The crude mortality rate was higher in the TAVI group (9.6 vs 2.3%) yielding an odds ratio (OR) of 4.57 (95% CI: 2.17–9.65). Compared with patients undergoing SAVR, patients with TAVI were older, more likely to be in NYHA class III and IV, and had a considerably higher logistic EuroSCORE and more comorbid conditions. In patients with sufficient overlap of propensity scores, adjusted OR ranged from 0.35 (0.04–2.72) to 3.17 (0.31–31.9). In patients with insufficient overlap, an increased odds of death was associated with TAVI compared with SAVR irrespective of the method used to control confounding, with adjusted OR ranging from 5.88 (0.67–51.8) to 25.7 (0.88–750). Approximately a third of patients undergoing TAVI were found to be potentially eligible for a randomized comparison of TAVI versus SAVR. The authors concluded that TAVI could be associated with either substantial benefits or harms and that randomized comparisons of TAVI versus SAVR were warranted to address these issues (Figures 5–7) [71].

One randomized trial assessing the role of TAVI is currently underway. The Placement of Aortic Transcatheter Valve Trial Edwards-SAPIEN Transcatheter Valve (PARTNER US) study completed enrollment of more than 1000 patients who underwent assessment of operability for SAVR and technical feasibility to implant an Edwards-SAPIEN prosthesis. Patients deemed operable were allocated to cohort A and subsequently screened for feasibility of transfemoral access. If transfemoral access was deemed feasible, patients were randomly assigned to treatment with SAVR or TAVI using the Edwards SAPIEN prosthesis implanted via the transfemoral route. In case transfemoral access was not possible, patients were randomly assigned to SAVR or TAVI using the Edwards-SAPIEN prosthesis implanted via the transapical route (patients deemed no longer operable were allocated to cohort B and subsequently assessed for feasibility of transfemoral access. In case of the latter, patients were randomly assigned to conservative, medical treatment or TAVI using the Edwards-SAPIEN prosthesis implanted via the transfemoral route. Preliminary results are expected to be released by the end of 2010.

Conclusion & future perspective

The concept of TAVI is appealing and disruptive with the potential to revolutionize the field of interventional cardiology to a similar degree as the advent of percutaneous transluminal coronary angioplasty more than three decades ago. Smaller delivery catheters, larger prostheses, ability to reposition and retrieve devices, and alternative access routes will all but eliminate technical barriers for TAVI in the near future. Randomized clinical trials are either underway or in the planning phase in order to establish the scientific foundation for the appropriate use of TAVI vis-à-vis both SAVR and medical treatment in various patient populations. The possibility for transcatheter valve-in-valve implantation is not only an attractive treatment for degenerated bioprostheses, but will also permit surgeons to more liberally use bioprostheses instead of mechanical heart valves in younger patients.

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Executive summary

- The prevalence of valvular heart disease increases substantially as the population ages.
- Surgical aortic valve replacement is the established gold standard and provides the therapeutic armamentarium for all complex valvular pathologies.
- Perioperative outcome of high-risk populations, such as octogenarians, patients with reduced left ventricular ejection fraction, or previous sternotomy is associated with a considerably higher perioperative mortality risk ranging from 5 to 19%.
- Transcatheter aortic valve implantation for severe aortic stenosis, which circumvents the need for cardiopulmonary bypass and general anesthesia, was initially restricted to non-operable or high-risk patients and is slowly being extended to less complex patient populations as peri-interventional outcomes improve.
- Randomized clinical trials are underway to establish the scientific foundation for the appropriate use of transcatheter aortic valve implantation vis-à-vis surgical aortic valve replacement.

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