The 2011-2012 pilot European Society of Cardiology Sentinel Registry of Transcatheter Aortic Valve Implantation: 12-month clinical outcomes

Martine Gilard[1], MD; Michael Schlüter[2], PhD; Thomas M. Snow[3], MD; Gianni Dall'Ara[4], MD; Helene Eltchaninoff[5], MD; Neil Moat[4], MS, FRCS; Javier Goicolea[6], MD; Gian Paolo Ussia[7], MD; Petr Kala[8], MD, PhD; Peter Wenaweser[9], MD; Marian Zembala[10], MD, PhD; Georg Nickenig[11], MD, PhD; Susanna Price[4], MD; Eduardo Alegria Barrero[12], MD; Bernard Iung[13], MD; Pepe Zamorano[14], MD; Gerhard Schuler[15], MD; Roberto Corti[16], MD; Ottavio Alfieri[17], MD; Bernard Prendergast[18], MD; Peter Ludman[19], MD; Stephan Windecker[9], MD; Manel Sabate[20], MD, PhD; Adam Witkowski[21], MD, PhD; Haim Danenberg[22], MD; Erwin Schroeder[23], MD; Francesco Romeo[7], MD; Carlos Macaya[24], MD, PhD; Geneviève Derumeaux[25], MD, PhD; Cécile Laroche[26], PhD; Michele Pighi[4], MD; Roberta Serdoz, MD[4]; Carlo Di Mario[4]*, MD, PhD; for the TransCatheter Valve Treatment (TCVT) Sentinel Registry Investigators of the EURObservational Research Programme (EORP) of the European Society of Cardiology

1. Centre Hospitalier Universitaire (CHU) Brest, Brest, France; 2. Asklepios Proresearch, Hamburg, Germany; 3. King's College Hospital, London, United Kingdom; 4. NIHR Cardiovascular BRU Royal Brompton Hospital, London, United Kingdom; 5. University Hospital, Rouen, France; 6. Hospital Universitario Puerta de Hierro, Madrid, Spain; 7. Tor Vergata University Hospital, Rome, Italy; 8. Masaryk University, University Hospital Brno, Brno, Czech Republic; 9. Bern University Hospital, Bern, Switzerland; 10. Silesian Centre for Heart Disease, Zabrze, Poland; 11. University Hospital, Bonn, Germany; 12. Hospital Universitario de Torrejon, Madrid, Spain; 13. Bichat Hospital, Paris, France; 14. Hospital Universitario Ramon y Cajal, Madrid, Spain; 15. Department of Cardiology and Angiology, Herzzentrum Leipzig, Leipzig, Germany; 16. Heart Clinic Hirslanden, Zurich, Switzerland; 17. Ospedale San Raffaele, Milan, Italy; 18. John Radcliffe Hospital, Oxford, United Kingdom; 19. Queen Elizabeth Hospital, Birmingham, United Kingdom; 20. Thorax Institute, Hospital Clinic, University of Barcelona, Barcelona, Spain; 21. Institute of Cardiology, Warsaw, Poland; 22. Hadassah-Hebrew University Medical Center, Jerusalem, Israel; 23. UCL de Mont-Godinne, Yvoir, Belgium; 24. Clinico San Carlos University Hospital, Madrid, Spain; 25. University of Lyon, Lyon, France; 26. European Society of Cardiology EORP, Sophia Antipolis, France

This paper also includes supplementary data published online at: http://www.pcronline.com/eurointervention/98th_issue/15

Abstract

Aims: Our aim was to assess one-year outcomes of patients enrolled in the pilot European Sentinel Registry of Transcatheter Aortic Valve Implantation (TAVI).

Methods and results: One-year outcomes of 4,571 patients (81.4±7.2 years, 2,291 [50.1%] male) receiving TAVI with the SAPIEN XT (57.3%) or CoreValve prosthesis at 137 European centres were analysed using Kaplan-Meier and Cox proportional hazards regression techniques. At one year, 3,341 patients were alive, 821 had died, and 409 were lost to follow-up. Of 2,125 patients who underwent functional assessment, 1,916 (90%) were in New York Heart Association (NYHA) Class I/II at one year, with functional improvement from baseline noted in 1,682 patients (88%). One-year survival based on 4,564 patients was estimated at 79.1%. Independent baseline predictors of mortality were increasing age and logistic EuroSCORE, the presence of NYHA III/IV, chronic obstructive pulmonary disease, and atrial fibrillation. Female gender was associated with a 4% survival benefit at one year. Vascular access routes other than transfemoral were associated with poorer survival. Procedural failure and major periprocedural complications had an adverse impact on survival.

Conclusions: Contemporary European experience attests to the effectiveness of routine TAVI in unselected elderly patients.

Corresponding author: NIHR Cardiovascular Biomedical Research Unit, Royal Brompton Hospital, Sydney Street, London, SW3 6NP, United Kingdom. E-mail: c.dimario@rbht.nhs.uk

Introduction

The number of elderly patients with degenerative aortic valve stenosis has increased with ageing of the European population. Advances in science and technology have offered an alternative to conventional surgical valve replacement with the evolution of transcatheter aortic valve implantation (TAVI). There is a need to monitor indications, techniques and outcomes to identify those patients best treated with such devices. However, at present there is no doubt that this technology has greatly improved the symptomatic and prognostic outcomes for patients with an otherwise dismal prognosis[1-4].

The pilot Sentinel Registry of Transcatheter Aortic Valve Implantation of the EURObservational Research Programme (EORP) represents a collaborative effort of 137 centres in 10 European countries. Over a 16-month period, 4,571 patients were recruited. In-hospital outcomes of this cohort have recently been published[5]. Whilst a number of national and industry-sponsored, valve-specific registries have been reported, the EORP pilot Sentinel Registry is unique in its unbiased reflection of national and international variation in patient selection, procedural approach, and choice of valve prosthesis.

In this paper, the one-year follow-up results from the registry with respect to patient selection, procedural technique, and predictors of one-year mortality are presented.

Methods

Between January 2011 and June 2012, 4,571 patients were enrolled at 137 centres in 10 European countries. Full details of this process and data collection have been described before[5]. In brief, patients were consecutively recruited and informed consent was obtained for both the TAVI procedure and the clinical data collection and processing. The valve prostheses used in this study were the balloon-expandable SAPIEN XT (Edwards Lifesciences Inc., Irvine, CA, USA) and the self-expanding CoreValve® (Medtronic, Minneapolis, MN, USA) devices exclusively. Information was obtained either via a web-based electronic case record form (eCRF) or by direct transfer of national registry data. All data collection was monitored centrally at the European Heart House (Sophia Antipolis, France), where the EORP team generated queries to clean the database and validate entries.

At participating centres all consecutive patients receiving TAVI were prospectively entered into the registry. In accordance with national legislation, patients provided written informed consent, including consent for anonymous processing of data. Patients directly entered into the TCVT database signed an individual specific consent approved by the ethics committees of the participating centres.

All recorded variables were defined in accordance with, or as close as possible to, the updated Valve Academic Research Consortium-2 (VARC-2) criteria[6], and attempts were made to align the national databases with the EORP data set. Where ambiguity was a concern, outcomes were limited to recording unequivocal events only (e.g., death).

STATISTICAL ANALYSIS

Continuous variables are reported as mean±standard deviation or as median plus interquartile range (IQR), where appropriate. Between-group comparisons were made using the Kruskal-Wallis test. Categorical variables are presented as absolute numbers and percentages. Between-group comparisons were made using a chi-square test or Fisher's exact test if any expected cell count was less than five. Survival up to 12 months was assessed using the Kaplan-Meier method, with differences between survival curves assessed by the log-rank test. All analyses were performed using SAS statistical software, version 9.2 (SAS Institute, Inc., Cary, NC, USA).

Cox proportional hazards regression analysis was used to explore the association between baseline covariates and mortality up to one year. Baseline covariates were compared in univariate analyses at 12 months between deceased and surviving patients; all covariates statistically significant on univariate analysis were then entered into a "full" multivariate proportional hazards model. Multivariate Cox regression was performed with 100 multiple imputations for missing values using the R software (http://www.Rproject.org/) and the package Hmisc (http://CRAN.Rproject.org/package-Hmisc). Two-tailed p-values <0.05 were considered statistically significant.

Results

Baseline clinical characteristics of the 4,571 patients are given in **Table 1**. Baseline and post-interventional echocardiographic variables are presented in **Online Table 1**.

PROCEDURAL OUTCOMES

Device success was 96.5%. Procedural details and periprocedural complications are listed in **Online Table 2**.

CLINICAL OUTCOMES AT ONE YEAR

Of the 4,571 patients, vital status at one year could be assessed in 4,162 patients (91.1%), with 3,341 patients (73.1%) alive, 821 (18.0%) deceased, and 409 patients (8.9%) lost to follow-up. Of the surviving patients, New York Heart Association (NYHA) functional class at baseline and at one year was available in 2,125 patients **(Figure 1)**. The vast majority of these patients (n=1,916 [90.2%]) were in NYHA Class I or II at one year. Changes in NYHA functional class from baseline to one year are shown for the 2,125 patients in **Online Figure 1**.

Of the 821 patients who had died by one year, in-hospital deaths occurred in 338 (41% **[Figure 2]**). A further 188 patients (23%) had died out of hospital by one month after TAVI, and 295 patients (36%) died between the one-month and one-year time points. It must be noted that the proportion of unknown causes of death increased considerably, reaching 48% (142 of 295) in patients who died between one month and one year after TAVI.

SURVIVAL AT ONE YEAR

Cumulative survival of 4,564 patients initially at risk (follow-up dates were missing in seven patients) is shown in **Figure 3A**. The Kaplan-Meier estimate of cumulative survival at one year was 79.1%.

Table 1. Baseline clinical characteristics.

	Variable	N
Number of patients	4,571	
Male, n (%)	4,571	2,291 (50.1)
Age, years	4,571	81.4±7.2
Age >80 years, n (%)	4,571	2,850 (62.4)
Body mass index, kg/m^2	4,527	26.6±4.9
Logistic EuroSCORE, %	4,394	20.2±13.3
Hypertension, n (%)	3,664	2,709 (73.9)
Diabetes mellitus, n (%)	4,547	1,259 (27.7)
Current smoking, n (%)	4,357	185 (4.3)
Atrial fibrillation/flutter, n (%)	2,773	557 (20.1)
COPD, n (%)	3,844	981 (25.5)
Dialysis, n (%)	3,821	265 (6.9)
Previous stroke, n (%)	4,549	115 (2.5)
Left main coronary artery stenosis >50%, n (%)	3,198	215 (6.7)
Previous MI, n (%)	4,549	769 (16.9)
Previous cardiac surgery, n (%)	4,505	824 (18.3)
Previous PCI, n (%)	2,289	463 (20.2)
Previous pacemaker, n (%)	3,676	430 (11.7)
NYHA functional Class, n (%)	4,571	
I		111 (2.4)
II		940 (20.6)
III		2,894 (63.3)
IV		603 (13.2)
unknown		23 (0.5)

BMI: body mass index; COPD: chronic obstructive pulmonary disease; EuroSCORE: European System for Cardiac Operative Risk Evaluation; MI: myocardial infarction; N: total number of patients in whom respective variable was assessed; NYHA: New York Heart Association; PCI: percutaneous coronary intervention
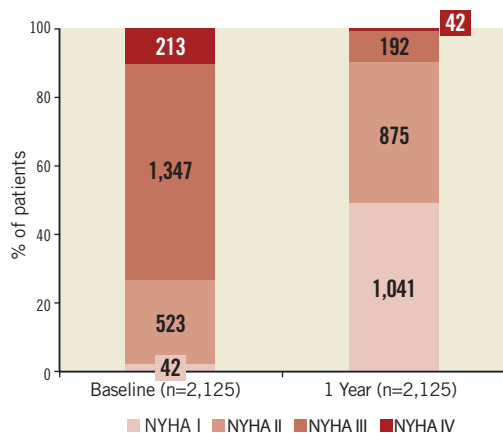
Figure 1. *Functional status according to New York Heart Association (NYHA) class at baseline and one year in the 2,125 patients in whom functional status was assessed at both time points. Numbers in columns denote numbers of patients.*
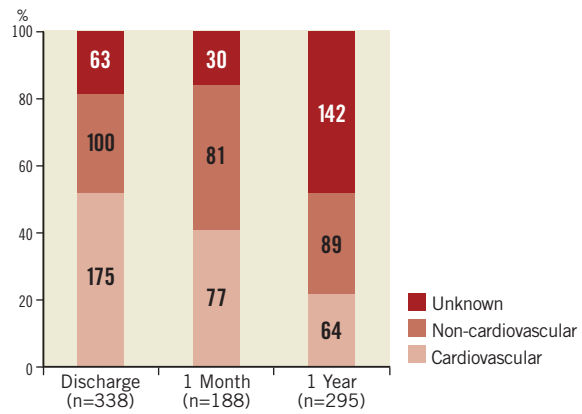
Figure 2. *Classification of death at discharge, one month, and one year after TAVI in 821 patients. Numbers in columns denote numbers of patients.*

Independent predictors of mortality as assessed by multivariate Cox proportional hazards regression analysis are shown in **Table 2**. Covariates statistically significant on univariate analysis and subsequently entered into the multivariate analysis are listed in **Online Table 3**. Of the baseline patient characteristics, expected predictors were age (2% increase in the probability of death per one-year increase in age) and logistic EuroSCORE (7% increase in the

Table 2. Independent predictors of mortality.

Variable	Hazard ratio	95% CI	*p*-value
Baseline patient characteristics			
Age	1.02	1.01-1.03	0.0005
Female gender	0.81	0.70-0.94	0.0063
BMI			0.0012
<32 kg/m^2	0.97	0.95-0.99	
>32 kg/m^2	1.06	1.02-1.11	
Logistic EuroSCORE (per 5% increase)	1.07	1.04-1.10	<0.0001
NYHA I-II vs. III-IV	0.82	0.69-0.99	0.0371
COPD	1.24	1.05-1.46	0.0169
Atrial fibrillation	1.30	1.07-1.58	0.0076
Vascular access			
Other vs. transfemoral	1.32	1.04-1.66	<0.0001
Transapical vs. transfemoral	1.64	1.36-1.98	<0.01
Echo-Doppler parameters			
Mean transvalvular aortic pressure gradient at baseline (per 5 mmHg increase)	0.98	0.95-1.00	0.0493
Post-procedural			
Unsuccessful deployment	3.84	2.92-5.06	<0.0001
Major stroke	2.11	1.33-3.34	0.0010
Cardiac tamponade	2.41	1.48-3.90	0.0004
New haemodialysis	2.54	1.48-4.38	0.0023
Transfusions	1.47	1.19-1.82	0.0003

BMI: body mass index; CI: confidence interval; COPD: chronic obstructive pulmonary disease; EuroSCORE: European System for Cardiac Operative Risk Evaluation; NYHA: New York Heart Association

probability of death per 5% increase in EuroSCORE). Female gender was associated with a 19% lower probability of death at one year. A non-linear relation of body mass index (BMI) with survival was noted, such that, in patients with BMI <32 kg/m^2, a 1-kg/m^2 increase was associated with a 3% decrease in the probability of death, whereas, in patients with BMI >32 kg/m^2, a 1-kg/m^2 increase was associated with a 6% increase in the probability of death. The association of BMI with mortality according to a 20 kg/m^2 cut-off is shown in **Online Table 4**. Not surprisingly, patients with baseline NYHA functional Class I or II (as opposed to III or IV) had a lower probability of death within one year (by 18%), whereas increases in mortality (by 24% and 30%, respectively) were observed in those with chronic obstructive pulmonary disease and atrial fibrillation.

Vascular access routes other than transfemoral were associated with an increased probability of death (by 32% if any "other" route was used and by 64% if the transapical route was used).

Borderline statistical significance was observed for the pre-TAVI mean transvalvular aortic pressure gradient, for which an increase by 5 mmHg was associated with a 2% decrease in the probability of death. Failure to deploy the prosthetic valve increased the probability of death by a factor of nearly four; an increased risk of death was also associated with periprocedural adverse events such as major stroke, cardiac tamponade, the need for haemodialysis, and transfusions.

Of note, neither valve prosthesis type (hazard ratio [CoreValve vs. SAPIEN XT] 0.88 [95% CI: 0.76-1.01], p=0.0693) nor the implantation of a permanent pacemaker (hazard ratio [yes vs. no] 1.16 [95% CI: 0.93-1.45], p=0.1979) was found to impact on survival on univariate Cox regression analysis. Therefore, these covariates were not included in the multivariate model.

The relationship between mortality and any variable is also reflected in the cumulative survival curves. Thus, **Figure 3B** shows a small, yet statistically significant survival benefit for women (estimated one-year survival **[Table 3]** 81.1% vs. 77.1% in men; p [log-rank]=0.0080), and **Figure 3C** shows decreasing one-year survival estimates (from 83.6% to 73.7%; p<0.0001) in terciles of patients with increasing logistic EuroSCORE (from <12.6% to >22.68%, respectively). One-year survival was, at 79.4%, significantly higher (p=0.0002) in patients with a left ventricular ejection fraction (LVEF) >50% than in patients with an LVEF between 30% and 50% or an LVEF <30% in whom survival curves overlapped and one-year estimates were in the order of 73% **(Figure 3D)**.

Patients in NYHA functional Class I or II at baseline had a significantly higher one-year survival (82.4%) than patients in NYHA Class III or IV (78.2%; p=0.0028) **(Figure 3E)**, and transfemoral vascular access was associated with significantly better one-year survival (81.3%; p<0.0001) than transapical access (71.3%) or any other vascular access route (75.7%) **(Figure 3F)**.

With respect to residual aortic regurgitation (AR) severity post TAVI, no statistically significant difference in survival curves was observed between patients with no residual AR vs. those with mild or moderate-severe AR, despite the finding that one-month survival in the few patients with moderate-severe AR appeared to be markedly lower than in the other two patient groups **(Figure 3G)**.

Table 3. Estimates of 1-year survival in selected patient groups.

	N*	1-year survival (%)	95% CI (%)
All patients	4,564	79.1	77.8-80.4
Men	2,290	77.1	75.2-79.0
Women	2,274	81.1	79.3-82.9
Patients with logistic EuroSCORE			
<12.6%	1,459	83.6	81.5-85.7
12.6%-22.68%	1,470	79.6	77.3-81.8
>22.68%	1,459	73.7	71.2-76.2
Patients with baseline LVEF			
<30%	169	74.0	66.1-81.9
30%-50%	1,140	72.7	69.7-75.8
>50%	2,101	79.4	77.4-81.4
Patients with baseline NYHA functional Class			
I-II	1,049	82.4	79.8-85.0
III-IV	3,492	78.2	76.7-79.7
Patients with TAVI via			
transfemoral access	3,383	81.3	79.8-82.7
transapical access	749	71.3	67.8-74.8
other access	432	75.7	71.3-80.1
Patients with			
no AR post TAVI	2,297	80.3	78.3-82.3
mild AR post TAVI	195	75.5	67.6-83.4
moderate-severe AR post TAVI	34	77.4	62.6-92.3
Patients implanted with			
SAPIEN XT	2,602	78.3	76.5-80.1
CoreValve	1,939	80.4	78.4-82.3

*Number of patients initially at risk. AR: aortic regurgitation; CI: confidence interval; EuroSCORE: European System for Cardiac Operative Risk Evaluation; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association

Discussion
THE REGISTRY

This large, contemporary, non-industry-sponsored multinational registry of more than four thousand patients provides a unique opportunity to examine the "real-world" one-year outcomes of unselected patients who were deemed at high surgical risk or inoperable undergoing routine TAVI in Europe. Utilising exclusively the SAPIEN XT or CoreValve prostheses, vascular access was predominantly transfemoral (74%), and device success was achieved in 96.5% of cases. The registry was extremely well balanced with respect to gender (50.1% male vs. 49.9% female), the patients had a mean age of 81.4 years, with 62.4% of patients older than 80 years, and a mean logistic EuroSCORE of 20.2%; before TAVI, 76.5% of patients were in NYHA functional Class III or IV.

MAIN FINDINGS

Based on a total of 4,564 patients, one-year survival was estimated at 79%. With 409 patients lost to follow-up, actual mortality was 18% (821 patients). Thus, the survival rate observed in
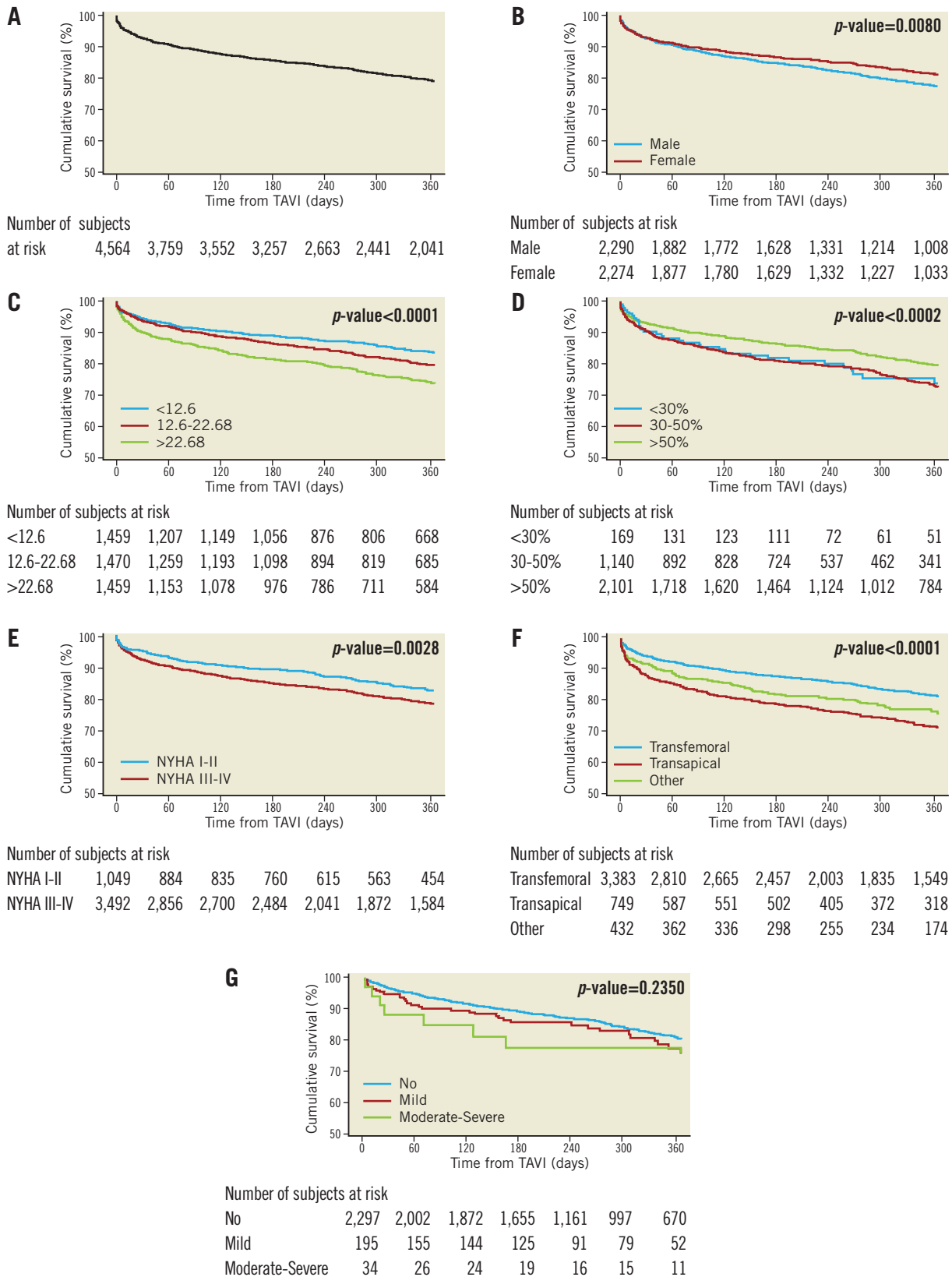
Figure 3. *Cumulative survival for the first 12 months after TAVI. A) Total patient cohort (n=4,564 patients). B) According to gender in 4,564 patients. C) According to terciles of logistic EuroSCORE in 4,388 patients. First tercile (n=1,459) <12.6% (red curve); second tercile (n=1,470) 12.6%-22.68% (green curve); third tercile (n=1,459) >22.68% (blue curve). D) According to left ventricular ejection fraction (LVEF) in 3,410 patients. E) According to New York Heart Association (NYHA) functional class at baseline in 4,541 patients. F) According to vascular access route in 4,564 patients. G) According to residual aortic regurgitation post TAVI in 2,526 patients.*

this registry was similar to the rates reported in previous major national registries[4,7,8]. The vast majority of patients surviving up to one year experienced a significant improvement in functional capacity, with 90% of 2,125 patients in whom functional status was assessed at one year presenting in NYHA Class I or II. This finding confirms the persistent long-term benefits of TAVI.

A number of patient and procedural characteristics associated with mortality were identified. Not surprisingly, increasing age as well as increasing logistic EuroSCORE, a left ventricular ejection fraction ≤50%, and poor functional status at baseline (NYHA Class III or IV) increased mortality.

Interestingly, lower mortality was observed with an increase in BMI up to 32 kg/m², probably reflecting increased physical robustness; however, in patients with a BMI beyond 32 kg/m² – which includes patients regarded as severely or even morbidly obese – the probability of death after TAVI increased with increasing BMI. This finding appears to reflect that reported previously for patients undergoing surgical aortic valve replacement[9-11], yet is not concordant with results from the FRANCE-2 TAVI registry, in which a steady increase in survival with increasing BMI was observed[12].

Regardless of possible differences in baseline characteristics according to gender, lower mortality was observed in female patients, reflected in survival curves that diverge steadily over time and result at one year in a 4% survival benefit for women. This finding confirms previous reports[13-15]. However, female gender has also been associated with higher rates of life-threatening bleeding[16] and major vascular complications[17] after TAVI.

Borderline statistical significance was observed for an increasing mean transvalvular pressure gradient associated with decreasing probability of death, possibly explained by relief of aortic stenosis resulting in an increased left ventricular ejection fraction.

A clear benefit was noted for patients in whom the transfemoral vascular access route was used (81.3% survival at one year), as opposed to the transapical (71.3%) or other access routes (75.7%). These results confirm previous reports assessing the relationship between access route and mortality[2,5,18,19].

In accordance with previous studies reporting no differences in terms of outcomes between different types of valve prosthesis[4,20,21], valve type was not found to affect survival in the patients of this registry.

The severity of residual AR post TAVI did not impact on mortality in this registry, even though distinct survival curves were observed for patients with no residual AR vs. those with mild residual AR and patients with moderate-severe residual AR. However, statistical significance was not reached, possibly because the numbers of patients in the latter two groups were fairly low (195 and 34, respectively). The echocardiographic grading of residual AR (1.4% moderate/severe) was obviously dissociated from the angiographic grading (10.4% moderate/severe). However, the angiographic grading depends on the position of the catheter, the volume of contrast agent, and the fact that it was performed in the catheter laboratory immediately after TAVI. The echocardiographic grading, performed one or two days after the intervention,

is not influenced by these factors. Also, the lack of statistical significance of residual AR post TAVI may be due to the absence of standardisation in the evaluation of AR severity in a large multicentre registry such as ours.

Finally, failure to deploy the valve prosthesis and severe periprocedural complications such as major stroke, cardiac tamponade, new haemodialysis, and the need for transfusion of red blood cells all had an adverse impact on survival.

CLINICAL RELEVANCE

It is becoming increasingly evident that procedural practice significantly impacts on patient prognosis. Whilst we can use clinical characteristics to inform patient selection by the Heart Team, the technique of valve implantation does confer worse outcomes if suboptimal results are achieved. Failure to deploy the valve and major complications are most powerful predictors of mortality. Operators must strive to minimise AR after valve deployment, and the introduction of new valves (Direct Flow Medical®; Direct Flow Medical, Santa Rosa, CA, USA, Lotus™; Boston Scientific, Marlborough, MA, USA, JenaValve; JenaValve Technology, Irvine, CA, USA) or new iterations of the valves used in this study (SAPIEN 3 and CoreValve Evolut) are expected to minimise AR. Previous reports suggested that any level of AR was a marker of worse outcome[5,22]. However, in this registry, mild AR did not influence survival and there were too few patients with more severe AR to draw statistically meaningful conclusions. Recent studies using mainly the CoreValve have shown a reduction of AR in serial echocardiograms which may explain the different result.

LVEF has been demonstrated to impact on outcome, independent of prior myocardial infarction, historical revascularisation, or the presence or extent of coronary artery disease[4,23,24]. The observation in this registry that patients with a baseline LVEF >50% have better survival than patients with an LVEF ≤50% supports these findings.

Our observations add to an already substantial body of work aiming to identify patients most likely to respond well to TAVI and to guide further advances in procedural technique by identifying aspects that have a deleterious impact on survival. As more knowledge and experience is gained, clinical outcomes will probably improve, and TAVI may become a competitive alternative in patients with moderate surgical risk – now currently under investigation in trials such as PARTNER 2A, SURTAVI and UK TAVI[25]. Formulation and validation of TAVI-specific risk scores will aid in the process of patient selection, taking into account patient characteristics that are not traditionally included in surgical risk scores.

Limitations

The TCVT registry is a voluntary pilot registry. Procedural complications, adverse events and echocardiographic parameters are self-reported. With the exception of national audit protocols for some of the registries, no other specific monitoring was performed. We acknowledge the restrictions evident in the direct transfer of national data. Missing values can be generated by national registry data transfer, as the list of collected variables may differ or

definitions vary. We attempted to standardise endpoints, using only unequivocal clinical endpoints. Nonetheless, the analysis of this registry has necessitated the use of statistical techniques to account for missing values, while maintaining the validity of our observations and conclusions. This registry only included patients treated with the SAPIEN XT or CoreValve prostheses, two devices that are in the process of being replaced with more sophisticated new designs and are now joined by a variety of other CE-marked devices due to be assessed in the next (long-term) phase of this registry.

Conclusions

The use of TAVI to treat severe symptomatic aortic stenosis is an effective and safe option, improving symptomatic and prognostic outcome in patients who are unable to undergo surgical intervention or in patients considered at high surgical risk according to the Heart Team.

Impact on daily practice

This follow-up study offers a broad comparison basis from the recent past to understand the rapid improvement of transcatheter aortic valve technology. The higher periprocedural mortality in surgical and especially transapical approaches shows a further increase at one year, justifying the steep increase in the percutaneous transfemoral approach allowed by the miniaturisation of the valve delivery systems. The limited percentage of 18% patients dead at one year with a clear cardiovascular cause of mortality confirms the efficacy of TAVI, but also suggests a more careful selection of cases excluding patients whose general health is too poor to benefit from any intervention.

Acknowledgements

From the EURObservational Research Programme of the European Society of Cardiology, 2035 Route des Colles – Les Templiers, CS 80179 BIOT - 06903 Sophia Antipolis Cedex – France. Tel: +33 492 94 76 00 - Fax: +33 492 94 76 29. E-mail: eorp@escardio.org

Funding

Conflict of interest statement

H. Eltchaninoff served as a proctor for Edwards Lifesciences and received lecture fees from the company. N. Moat served as a consultant and a proctor for Medtronic. P. Wenaweser declares proctoring and lecture fees from Medtronic, Edwards Lifesciences, Boston Scientific, and a research grant to the institution from Medtronic. S. Price declares an educational contract with Medtronic and is part of the medical advisory board of Abbott and MitraClip. B. Iung has received consultant's fees from Abbott, Boehringer Ingelheim, Valtech and speaker's fees from Edwards Lifesciences. B. Prendergast received lecture fees from Edwards Lifesciences. S. Windecker has received research contracts to the institution from Abbott, Biotronik, Boston Scientific, Biosensors, Edwards Lifesciences, Medicines Company, Medtronic and St. Jude, and lecture fees from AstraZeneca, Eli Lilly, Bayer, Abbott, Biotronik, Boston Scientific, Edwards Lifesciences, and Medtronic. A. Witkowski received proctorship fees from Medtronic. H. Danenberg serves as a clinical proctor for Medtronic CoreValve. The other authors have no conflicts of interest to declare.

References

1. Thomas M, Schymik G, Walther T, Himbert D, Lefèvre T, Treede H, Eggebrecht H, Rubino P, Colombo A, Lange R, Schwarz RR, Wendler O. One-year outcomes of cohort 1 in the Edwards SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) registry: the European registry of transcatheter aortic valve implantation using the Edwards SAPIEN valve. *Circulation.* 2011;124:425-33.

2. Davies WR, Thomas MR. European experience and perspectives on transcatheter aortic valve replacement. *Prog Cardiovasc Dis.* 2014;56:625-34.

3. Moat NE, Ludman P, de Belder MA, Bridgewater B, Cunningham AD, Young CP, Thomas M, Kovac J, Spyt T, MacCarthy PA, Wendler O, Hildick-Smith D, Davies SW, Trivedi U, Blackman DJ, Levy RD, Brecker SJ, Baumbach A, Daniel T, Gray H, Mullen MJ. Long-term outcomes after

transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis: the U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry. *J Am Coll Cardiol.* 2011;58:2130-8.

4. Gilard M, Eltchaninoff H, Iung B, Donzeau-Gouge P, Chevreul K, Fajadet J, Leprince P, Leguerrier A, Lievre M, Prat A, Teiger E, Lefevre T, Himbert D, Tchetche D, Carrié D, Albat B, Cribier A, Rioufol G, Sudre A, Blanchard D, Collet F, Dos Santos P, Meneveau N, Tirouvanziam A, Caussin C, Guyon P, Boschat J, Le Breton H, Collart F, Houel R, Delpine S, Souteyrand G, Favereau X, Ohlmann P, Doisy V, Grollier G, Gommeaux A, Claudel JP, Bourlon F, Bertrand B, Van Belle E, Laskar M; FRANCE 2 Investigators. Registry of transcatheter aortic-valve implantation in high-risk patients. *N Engl J Med.* 2012;366:1705-15.

5. Di Mario C, Eltchaninoff H, Moat N, Goicolea J, Ussia GP, Kala P, Wenaweser P, Zembala M, Nickenig G, Alegria Barrero E, Snow T, Iung B, Zamorano P, Schuler G, Corti R, Alfieri O, Prendergast B, Ludman P, Windecker S, Sabate M, Gilard M, Witowski A, Danenberg H, Schroeder E, Romeo F, Macaya C, Derumeaux G, Maggioni A, Tavazzi L; Transcatheter Valve Treatment Sentinel Registry (TCVT) Investigators of the EURObservational Research Programme (EORP) of the European Society of Cardiology. The 2011-12 pilot European Sentinel Registry of Transcatheter Aortic Valve Implantation: in-hospital results in 4,571 patients. *EuroIntervention.* 2013;8:1362-71.

6. Kappetein AP, Head SJ, Généreux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S, Mack MJ, Mehran R, Rodés-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW, Leon MB. Updated standardized end-point definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *Eur Heart J.* 2012;33:2403-18.

7. Abdel-Wahab M, Zahn R, Gerckens U, Linke A, Sievert H, Schäfer U, Kahlert P, Hambrecht R, Sack S, Hoffmann E, Senges J, Schneider S, Richardt G; German TAVI Registry Investigators. Predictors of 1-year mortality in patients with aortic regurgitation after transcatheter aortic valve implantation: an analysis from the multicentre German TAVI registry. *Heart.* 2014;100:1250-6.

8. Sabaté M, Cánovas S, García E, Hernández Antolín R, Maroto L, Hernández JM, Alonso Briales JH, Muñoz García AJ, Gutiérrez-Ibañes E, Rodríguez-Roda J; collaborators of the TAVI National Group. In-hospital and mid-term predictors of mortality after transcatheter aortic valve implantation: data from the TAVI National Registry 2010-2011. *Rev Esp Cardiol (Engl Ed).* 2013;66:949-58.

9. Roberts WC, Roberts CC, Vowels TJ, Ko JM, Filardo G, Hamman BL, Matter GJ, Henry AC, Hebeler RF Jr. Effect of body mass index on survival in patients having aortic valve replacement for aortic stenosis with or without concomitant coronary artery bypass grafting. *Am J Cardiol.* 2011;108:1767-71.

10. Smith RL 2nd, Herbert MA, Dewey TM, Brinkman WT, Prince SL, Ryan WH, Mack MJ. Does body mass index affect

outcomes for aortic valve replacement surgery for aortic stenosis? *Ann Thorac Surg.* 2012;93:742-6.

11. Vaduganathan M, Lee R, Beckham AJ, Andrei AC, Lapin B, Stone NJ, McGee EC Jr, Malaisrie SC, Kansal P, Silverberg RA, Lloyd-Jones DM, McCarthy PM. Relation of body mass index to late survival after valvular heart surgery. *Am J Cardiol.* 2012;110:1667-78.

12. Yamamoto M, Mouillet G, Oguri A, Gilard M, Laskar M, Eltchaninoff H, Fajadet J, Iung B, Donzeau-Gouge P, Leprince P, Leuguerrier A, Prat A, Lievre M, Chevreul K, Dubois-Rande JL, Teiger E; FRANCE 2 Registry Investigators. Effect of body mass index on 30- and 365-day complication and survival rates of transcatheter aortic valve implantation (from the FRench Aortic National CoreValve and Edwards 2 [FRANCE 2] registry). *Am J Cardiol.* 2013;112:1932-7.

13. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Williams M, Dewey T, Kapadia S, Babaliaros V, Thourani VH, Corso P, Pichard AD, Bavaria JE, Herrmann HC, Akin JJ, Anderson WN, Wang D, Pocock SJ; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med.* 2011;364:2187-98.

14. Erez A, Segev A, Medvedofsky D, Fefer P, Raanani E, Goldenberg I, Guetta V. Factors affecting survival in men versus women following transcatheter aortic valve implantation. *Am J Cardiol.* 2014;113:701-5.

15. Sherif MA, Zahn R, Gerckens U, Sievert H, Eggebrecht H, Hambrecht R, Sack S, Richardt G, Schneider S, Senges J, Brachmann J. Effect of gender differences on 1-year mortality after transcatheter aortic valve implantation for severe aortic stenosis: results from a multicenter real-world registry. *Clin Res Cardiol.* 2014;103:613-20.

16. D'Ascenzo F, Gonella A, Moretti C, Omedè P, Salizzoni S, La Torre M, Giordana F, Barbanti M, Ussia GP, Brambilla N, Bedogni F, Gaita F, Tamburino C, Sheiban I. Gender differences in patients undergoing TAVI: a multicentre study. *EuroIntervention.* 2013;9:367-72.

17. Onorati F, D'Errigo P, Barbanti M, Rosato S, Covello RD, Maraschini A, Ranucci M, Santoro G, Tamburino C, Grossi C, Santini F, Menicanti L, Seccareccia F; OBSERVANT Research Group. Different impact of sex on baseline characteristics and major periprocedural outcomes of transcatheter and surgical aortic valve interventions: Results of the multicenter Italian OBSERVANT Registry. *J Thorac Cardiovasc Surg.* 2014;147: 1529-39.

18. Blackman DJ, Baxter PD, Gale CP, Moat NE, Maccarthy PA, Hildick-Smith D, Trivedi U, Cunningham D, DE Belder MA, Ludman PF; National Institute for Cardiovascular Outcomes Research (NICOR). Do outcomes from transcatheter aortic valve implantation vary according to access route and valve type? The UK TAVI Registry. *J Interv Cardiol.* 2014;27:86-95.

19. Svensson LG, Blackstone EH, Rajeswaran J, Brozzi N, Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Tuzcu EM,

Webb JG, Kapadia S, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Thourani VH, Pichard AD, Bavaria JE, Herrmann HC, Williams MR, Babaliaros V, Généreux P, Akin JJ; PARTNER Trial Investigators. Comprehensive analysis of mortality among patients undergoing TAVR: results of the PARTNER trial. *J Am Coll Cardiol.* 2014;64:158-68.

20. Chieffo A, Buchanan GL, Van Mieghem NM, Tchetche D, Dumonteil N, Latib A, van der Boon RM, Vahdat O, Marcheix B, Farah B, Serruys PW, Fajadet J, Carrié D, de Jaegere PP, Colombo A. Transcatheter aortic valve implantation with the Edwards SAPIEN versus the Medtronic CoreValve Revalving system devices: a multicenter collaborative study: the PRAGMATIC Plus Initiative (Pooled-RotterdAm-Milano-Toulouse In Collaboration). *J Am Coll Cardiol.* 2013;61:830-6.

21. Abdel-Wahab M, Mehilli J, Frerker C, Neumann FJ, Kurz T, Tölg R, Zachow D, Guerra E, Massberg S, Schäfer U, El-Mawardy M, Richardt G; CHOICE investigators. Comparison of balloon-expandable vs. self-expandable valves in patients undergoing transcatheter aortic valve replacement: the CHOICE randomized clinical trial. *JAMA.* 2014;311:1503-14.

22. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S; PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med.* 2010;363:1597-607.

23. Wenaweser P, Pilgrim T, Guerios E, Stortecky S, Huber C, Khattab AA, Kadner A, Buellesfeld L, Gloekler S, Meier B, Carrel T, Windecker S. Impact of coronary artery disease and percutaneous coronary intervention on outcomes in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation. *EuroIntervention.* 2011;7:541-8.

24. D'Ascenzo F, Conrotto F, Giordana F, Moretti C, D'Amico M, Salizzoni S, Omedè P, La Torre M, Thomas M, Khawaja Z, Hildick-Smith D, Ussia G, Barbanti M, Tamburino C, Webb J, Schnabel RB, Seiffert M, Wilde S, Treede H, Gasparetto V, Napodano M, Tarantini G, Presbitero P, Mennuni M, Rossi ML, Gasparini M, Biondi Zoccai G, Lupo M, Rinaldi M, Gaita F, Marra S. Mid-term prognostic value of coronary artery disease in patients undergoing transcatheter aortic valve implantation: a meta-analysis of adjusted observational results. *Int J Cardiol.* 2013;168:2528-32.

25. Piazza N, Kalesan B, van Mieghem N, Head S, Wenaweser P, Carrel TP, Bleiziffer S, de Jaegere PP, Gahl B, Anderson RH, Kappetein AP, Lange R, Serruys PW, Windecker S, Jüni P. A 3-center comparison of 1-year mortality outcomes between transcatheter aortic valve implantation and surgical aortic valve replacement on the basis of propensity score matching among intermediate-risk surgical patients. *JACC Cardiovasc Interv.* 2013;6:443-51.

Supplementary data

Online Table 1. Baseline and post-procedural echocardiographic data.
Online Table 2. Procedural details, procedural outcomes and periprocedural complications.
Online Table 3. Covariates entered into the multivariate Cox proportional hazards regression analysis.
Online Table 4. Association of BMI according to a 20 kg/m² cut-off with mortality.
Online Figure 1. Schematic showing TAVI-related changes in NYHA functional class from baseline to one year in 2,125 patients.

The supplementary data are published online at:
http://www.pcronline.com/
eurointervention/98th_issue/15

Supplementary data

Online Table 1. Baseline and post-procedural echocardiographic data.

	N	
Echocardiographic variables pre TAVI		
Aortic valve area, cm^2	3,852	0.7±0.3
Mean transvalvular aortic pressure gradient, mmHg	3,503	49.1±16.3
Left ventricular ejection fraction, %	3,414	54.2±13.8
<30%, n (%)		169 (5.0)
30-50%, n (%)		1,141 (33.4)
>50%, n (%)		2,104 (61.6)
Moderate/severe aortic regurgitation, n (%)	3,103	564 (18.2)
Moderate/severe mitral regurgitation, n (%)	3,104	645 (20.8)
Systolic pulmonary artery pressure >60 mmHg, n (%)	2,365	289 (12.2)
Echocardiographic variables post TAVI		
Aortic valve area, cm^2	1,526	1.8±0.6
Mean transvalvular aortic pressure gradient, mmHg	2,545	11.2±8.2
Left ventricular ejection fraction, %	2,453	55.2±12.7
<30%, n (%)		73 (3.0)
30-50%, n (%)		798 (32.5)
>50%, n (%)		1,582 (64.5)
Aortic regurgitation, n (%)	2,526	
None		2,297 (90.9)
Mild		195 (7.7)
Moderate		32 (1.3)
Severe		2 (0.08)
Moderate/severe mitral regurgitation, n (%)	523	129 (24.7)
Aortic valve aetiology	1,591	
Degenerative		1,532 (96.3)
Degenerated bioprosthesis		50 (3.1)
Rheumatic		9 (0.6)
Aortic valve morphology	559	
Tricuspid		437 (96.1)
Bicuspid		14 (2.5)
Not assessable		8 (1.4)
N=total number of patients in whom respective variable was assessed.		

Online Table 2. Procedural details, procedural outcomes and periprocedural complications.

Periprocedural variables	N		Periprocedural variables	N	
Annular measurement by TOE, n (%)*	4,411	1,345 (30.5)	Emergency		10 (0.6)
Annular measurement by CT, n (%)*	3,654	396 (10.8)	Procedural outcome, n (%)		
Total procedure duration, min	1,362	114±54	Device success	4,441	4,286 (96.5)
Total fluoroscopy time, min	552	26.0±20.4	Conversion to surgery	4,558	194 (4.3)
Valve prosthesis type, n (%)	4,548		Pacemaker implantation required	3,795	407 (10.7)
SAPIEN XT		2,604 (57.3)	Cardiac tamponade	3,757	91 (2.4)
CoreValve		1,943 (42.7)	New onset atrial fibrillation	2,858	166 (5.8)
Vascular access, n (%)	4,571		Cardiogenic shock	2,163	53 (2.5)
Transfemoral percutaneous		2,932 (64.1)	Bail-out PCI	1,473	8 (0.5)
Transapical		749 (16.4)	Major vascular complications	1,332	41 (3.1)
Transfemoral surgical		458 (10.0)	SVT/VF	448	10 (2.2)
Subclavian surgical		161 (3.5)	Angiographic AR moderate/severe	2,168	226 (10.4)
Subclavian percutaneous		61 (1.3)	Procedural failure, n (%)	1,467	
Transaxillary		19 (0.4)	Access-site failure		4 (0.3)
Transaortic		12 (0.3)	Did not navigate to position		13 (0.9)
Other access		179 (3.9)	Aborted due to coronary obstruction		6 (0.4)
Circulatory support, n (%)	1,685	84 (5.0)	Aborted due to other reasons		1 (0.1)
Periprocedural TOE imaging, n (%)	3,750	2,370 (63.2)	Post-procedural		
Local anaesthesia, n (%)	3,818	1,123 (29.4)	Hospital stay, days¶	4,535	8 [6-15]
Vascular closure technique, n (%)	3,737		Haemoglobin, g/dl¶	2,734	10.0 [8.9-11.3]
Manual pressure		131 (3.5)	RBC transfusions, n (%)	3,789	636 (16.8)
Elective surgical closure		1,559 (41.7)	Acute kidney failure, n (%)	2,890	128 (4.4)
Bail-out surgical closure		6 (0.2)	Bleeding, n (%)	2,911	169 (5.8)
Device closure		2,041 (54.6)	New haemofiltration or dialysis, n (%)	3,750	62 (1.7)
Procedure urgency, n (%)	1,602		Stroke, n (%)	3,765	61 (1.6)
Elective		1,468 (91.6)	Valve embolisation, n (%)	3,848	17 (0.4)
Urgent		124 (7.7)	Valve-in-valve, n (%)	3,760	92 (2.5)

*In the vast majority of patients, aortic annuli were measured by transthoracic echocardiography. ¶Median [IQR]. AR: aortic regurgitation; CT: computed tomography; N: total number of patients in whom respective variable was assessed; PCI: percutaneous coronary intervention; RBC: red blood cell; SVT: supraventricular tachycardia; TOE: transoesophageal echocardiography; VF: ventricular fibrillation

Online Table 3. Covariates entered into the multivariate Cox proportional hazards regression analysis.

Baseline characteristics
Age
Gender
BMI
Logistic EuroSCORE
NYHA I-II, NYHA III-IV
Comorbidities
COPD
Previous MI
Atrial fibrillation/flutter
Procedure-related events
Access site
Successful implantation
Complications (major stroke; bleeding; need for transfusion; second valve implanted; tamponade, dialysis, haemoglobin, acute kidney injury)
Type of anaesthesia
Duration of hospital stay
Echocardiographic variables
Moderate/severe mitral regurgitation pre TAVI
Mean transaortic pressure gradient pre TAVI

Online Table 4. Association of BMI according to a 20 kg/m² cut-off with mortality.

BMI	n	Alive	Dead	Lost to follow-up
<20 kg/m²	203	132 (65%)	45 (22%)	26 (13%)
≥20 kg/m²	4,324	3,176 (73%)	768 (18%)	380 (9%)
Total	4,527	3,308 (73%)	813 (18%)	406 (9%)
(44 BMI missing in 44 patients).				

Online Figure 1. *Schematic showing TAVI-related changes in NYHA functional class from baseline to one year in 2,125 patients. Shades of green denote improvement, shades of red denote worsening, e.g., 625 patients with NYHA III at baseline improved to NYHA I within one year, whereas 30 patients with NYHA II at baseline worsened to NYHA III.*