

Transapical aortic valve implantation in 100 consecutive patients: comparison to propensity-matched conventional aortic valve replacement

Thomas Walther^{1,*}, Gerhard Schuler², Michael A. Borger¹, Jörg Kempfert¹, Jörg Seeburger¹, Yvonne Rückert¹, Jörg Ender³, Axel Linke², Markus Scholz⁴, Volkmar Falk¹, and Friedrich W. Mohr¹

¹Department of Cardiac Surgery, Heartcenter, University Leipzig, Herzzentrum, Klinik für Herzchirurgie, Strümpellstrasse 39, Leipzig 04289, Germany; ²Department of Cardiology, University Leipzig, Leipzig, Germany; ³Department of Anaesthesia, Heartcenter, University Leipzig, Leipzig, Germany; and ⁴Department of Medical Informatics, Statistics and Epidemiology, Leipzig, Germany

Received 14 July 2009; revised 15 December 2009; accepted 19 January 2010; online publish-ahead-of-print 16 March 2010

Aims

To evaluate the outcome of transapical aortic valve implantation (TA-AVI) in comparison to conventional surgery.

Methods and results

One hundred consecutive high-risk patients with symptomatic aortic valve stenosis received TA-AVI using the Edwards SAPIENTM pericardial xenograft between February 2006 and January 2008. Patient age was 82.7 ± 5 years, 77 were females, logistic EuroSCORE predicted risk of mortality was $29.4 \pm 13\%$ and Society Thoracic Surgeons score risk for mortality was $15.2 \pm 8.3\%$. Propensity score analysis was used to identify a control group of patients that underwent conventional aortic valve replacement (C-AVR). Transapical aortic valve implantation was performed successfully in 97 patients, whereas three patients required early conversion. There were no new onset neurological events in the TA-AVI group and early extubation was performed in 82 patients. Echocardiography revealed good valve function with low transvalvular gradients in all patients. Thirty-day survival was 90 ± 3 vs. $85 \pm 4\%$ for TA-AVI vs. C-AVR, and 1-year survival was 73 ± 4 vs. $69 \pm 5\%$ ($P = 0.55$).

Conclusion

Transapical aortic valve implantation is a safe, minimally invasive, and off-pump technique to treat high-risk patients with aortic stenosis. Results of the initial 100 patients are good and compare favourably to conventional surgery.

Keywords

Aortic valve • Aortic stenosis • Transcatheter • Transapical aortic valve implantation • Aortic valve replacement

Introduction

Aortic valve replacement (AVR) is a standard and relatively low-risk procedure indicated in patients with symptomatic aortic stenosis (AS)^{1–2}. Good surgical outcome can be expected even in octogenarians³. However, a substantial number of patients are not being referred due to an operative risk that is presumed to be too high⁴. Such observations of real world clinical practice underline the need for further improvements, a reduction in the invasiveness of the procedure, avoidance of a sternotomy, and elimination of the need for cardioplegic myocardial arrest and cardiopulmonary bypass. This can be accomplished by transfemoral or transapical (TA) minimally invasive aortic valve implantation (AVI),

which has been recently introduced into clinical practice with encouraging early results in high-risk patients^{5–9}. The aim of this study was to evaluate the results of the initial 100 patients receiving TA-AVI and to compare their outcomes to a control group of conventional AVR (C-AVR).

Methods

A total of 102 patients received TA-AVI between February 2006 and January 2008 at our centre. Two patients with haemodynamic instability were excluded from further analysis. The study was approved by the local Ethics Committee and all patients gave written informed consent. Patients were considered eligible for TA-AVI in the presence

* Corresponding author. Direktor der Abteilung Herzchirurgie, Kerckhoff-Klinik, Benekestr., 2-8, 61231 Bad Nauheim, Germany. Tel.: +49 6032 996 2501, Fax: +49 6032 996 2567, Email: t.walther@kerckhoff-klinik.de

of stable symptomatic AS and high surgical risk, defined by age ≥ 75 years and an additive EuroSCORE ≥ 9 . Exclusion criteria consisted of an aortic annulus larger than 24 mm (for TA-AVI patients only), requirement for concomitant cardiac surgical procedures or preoperative haemodynamic instability.

Only those patients with an aortic annulus diameter ≤ 24 mm were eligible for TA-AVI in order to allow for oversizing of the implanted valve by 2–4 mm. In a previous study performed between December 2004 and August 2005, three patients were treated unsuccessfully at our centre without the use of an oversizing technique. We therefore modified our valve sizing protocol and restarted TA-AVI procedures in February 2006.

Transapical aortic valve implantation was performed in a hybrid operative theatre by a team of cardiac surgeons and cardiologists under fluoroscopic and transesophageal echocardiographic control using the Edwards SAPIEN™ transcatheter xenograft. Key steps of the procedure have been previously outlined in detail.⁹

Patients older than 75 years of age who underwent isolated C-AVR using standard surgical techniques served as controls. Propensity matching was used to select 100 C-AVR patients with a similar risk profile to TA-AVI patients. Clinical and echocardiographic follow-up was performed 6 months and 1 year postoperatively and was 100% complete. Follow-up was truncated for all patients at 1 year.

Statistical analysis

All TA-AVI patients were analysed intent to treat. Propensity matching was performed in order to derive a comparable group of C-AVR patients. A total of 777 patients that were 75 years of age or older underwent isolated C-AVR at our institution between September 1996 and January 2008. Data were taken from the prospective hospital database. The large cohort of C-AVR patients enabled 1:1 propensity score matching on many variables.

The propensity score represented the probability of a patient being assigned to the case group given the covariables of that patient. It was calculated for each patient using a logistic regression model which included the following variables: age, gender, body mass index, logistic EuroSCORE, left ventricular ejection fraction, NYHA functional class, urgency of the procedure (elective vs. urgent, where urgent means therapy during the same hospital stay), chronic obstructive pulmonary disease (use of bronchodilators or steroids due to lung disease), previous myocardial infarction, syncope, congestive heart failure, hyperlipidaemia, arterial hypertension, pulmonary hypertension (systolic pulmonary pressure >60 mmHg), diabetes, smoking, previous cardiac surgery, peripheral vascular disease, stroke/transitory ischaemic attack, renal dysfunction (serum creatinine >200 μ mol/L), and liver dysfunction (hepatitis, cirrhosis and/or cholinesterasis >1000 U/L). Matching was performed by selecting a patient randomly from the case group and looking for a partner in the control group who had the nearest logit-transformed propensity score^{10,11}. Balance of matching variables was assessed by formal statistical comparison (Kolmogorov–Smirnov test for continuous variables and Fishers exact test for categorical variables). *P*-values >0.05 were considered as evidence for balance of the quantity.

Categorical outcomes are displayed as proportions throughout the manuscript and were compared with χ^2 or Fisher's exact test for unpaired samples and with McNemar test or exact binomial test for comparison of matched samples. Continuous outcomes are displayed as mean \pm standard deviation throughout the manuscript and were compared with Mann–Whitney *U* test for unpaired samples or Wilcoxon signed rank test for matched samples, respectively. Survival analyses were performed using the Kaplan–Meier method. Comparison of survival curves was performed with Cox regression stratified on

matched pairs. We additionally adjusted our analysis with respect to time of treatment using regression techniques and propensity. A probability of *P* < 0.05 was considered significant. All calculations were performed using the statistical software package R (version 2.7.0, www.r-project.org).¹² Exact logistic regression has been performed with LogXact-8 (Cytel, Inc.).

Results

Transapical aortic valve implantation perioperative results

Patient details including the incidence of specific risk factors are displayed in *Table 1*. Additional risk factors present in the TA-AVI cohort were peripheral vascular disease in 33%, history of preoperative stroke in 21%, and previous cardiac surgery in 22% of the patients. Vital capacity was $79 \pm 25\%$ and forced expiratory capacity within 1 s was $91 \pm 43\%$ of normal in these patients.

Transapical aortic valve implantation was successfully performed in 97 patients, three patients required conversion to full sternotomy due to secondary aortic root dissection after selective coronary artery imaging, left main stem occlusion, and proximal valve dislocation in the presence of eccentric calcification causing severe mitral regurgitation (one patient each). Two of the converted patients were discharged alive from the hospital. Two rethoracotomies were required: one for diffuse chest wall bleeding in a patient who was on preoperative Plavix® therapy and one for a secondary apical tear 6 h postoperatively treated by additional suturing during femoral cardiopulmonary bypass (CPB) support. The mean implanted valve size was 25.3 ± 1.3 mm. A total of 75 patients received a 26 mm valve and 25 patients a 23 mm valve. The aortic annulus measured 22.7 ± 1.3 mm leading to an oversizing of

Table 1 Patient characteristics and risk factors for the transapical (TA-AVI) and the conventional (C-AVR) groups

	TA-AVI	C-AVR
<i>n</i>	100	100
Age	82.7 \pm 5	82.4 \pm 4
Female	77	70
NYHA	3.2 \pm 0.4	3.1 \pm 0.6
LVEF (%)	54.0 \pm 15	56.3 \pm 18
Logistic EuroScore (%)	29 \pm 13	30 \pm 13
STS score	15.2 \pm 8.3	n/a
COPD	27	30
Hypercholesterolaemia	35	41
Arterial hypertension	86	85
Diabetes	40	37
Smoking	25	19
Renal insufficiency	14	17

The control group was generated by means of propensity score analysis. All statistical comparisons between groups are not significant. TA-AVI, transapical aortic valve implantation; NYHA, New York Heart Association functional class; STS, Society Thoracic Surgeons.

2.6 mm. Mean duration of fluoroscopy was 419 ± 248 s and a total of 101 ± 92 mL of contrast medium was required.

Femoral CPB was used intentionally in 10 patients at the beginning of our series. Subsequent patients received only femoral wires as preparation for emergency CPB cannulation, if required⁹. Secondary CPB was required in 10 patients due to conversion to full sternotomy as described above (three patients), for suturing of the apex (two patients—one during the operation and one during a rethoracotomy), for temporary reperfusion secondary to haemodynamic instability (four patients—two of who required additional coronary artery stenting) and for valve in a valve implantation due to upside down positioning of the initial prosthesis (one patient). All but one of the patients treated with CPB were weaned successfully. One patient required extracorporeal membrane oxygenation support for 2 days and was weaned successfully thereafter.

Patients were intubated postoperatively for a median of 5 h. A total of 89 patients were extubated within the first 24 postoperative hours. Renal function was preserved (creatinine level <1.7 mg/dL with adequate diuresis) in 88 patients postoperatively. Twelve patients required temporary haemofiltration. The mean preoperative creatinine level was 2.8 ± 1.7 mg/dL in these patients and five of them had been on chronic haemodialysis preoperatively. None of the patients had clinical evidence of a new onset stroke in the perioperative period.

Preoperatively, 11 of the 100 patients had a pacemaker. Of the remaining 89 patients, nine (10.1%) required new onset pacemaker implantation, all due to high-grade atrioventricular block, four of them with delayed (1–5 days) onset. Laboratory evaluation revealed no significant increase in myocardial enzymes (CK-MB) immediately and 24 h postoperatively in all patients, with the exception of the one patient suffering left main stem occlusion who required subsequent coronary artery bypass grafting. At 30 days, 10 patients died after TA-AVI due to the following causes: respiratory dysfunction ($n = 3$), abdominal complications ($n = 3$), low-cardiac output syndrome ($n = 2$), sudden death ($n = 1$), and other ($n = 1$).

Transapical aortic valve implantation follow-up results

During follow-up, another 18 of the remaining 90 patients (20%) died, all except one with good valve function at most recent echocardiographic examination. This patient with a porcelain aorta and moderate paravalvular leak at discharge was readmitted with severe paravalvular leakage 6 weeks postoperatively. After

unsuccessful redilatation of the valved stent, the patient underwent aortic root replacement via conventional surgery. She recovered and was discharged, but subsequently died suddenly on postoperative day 71 for unknown reasons. Follow-up mortality in TA-AVI patients occurred at a mean of 119 ± 73 (range 48–280) days after valve implantation. Outcome after TA-AVI in relation to preoperative risk profile is displayed in *Table 2*. Patients are grouped according to increasing logistic EuroSCORE, whereas Society Thoracic Surgeons Score is supplied for comparisons.

Preoperatively New York Heart Association (NYHA) class was III (76) or IV (24). At 3–6 months follow-up, NYHA class was I for 7.8%, II for 56.3%, and III for 35.9% of the patients and all but seven patients had improved by at least one NYHA class. No patient remained in NYHA class IV during follow-up. At 1-year follow-up, NYHA class was I for 8.8%, II for 47.1%, and III for 44.1% of the patients.

Echocardiography revealed good valve function with low transvalvular gradients in all patients early postoperatively (*Table 3*). Ventricular function was stable with a slight increase in left ventricular ejection fraction at follow-up examinations. Paravalvular leakage was present in 48 patients, which was trivial to mild in all but three patients. There were no clinical signs of haemolysis in any of the patients postoperatively. A summary of echocardiographic results is given in *Table 3*.

Transapical aortic valve implantation vs. conventional aortic valve replacement patients

Patient characteristics of the control group receiving C-AVR are given in *Table 1*. The prevalence of all preoperative risk factors was similar between the two patient groups. Postoperative outcomes were also similar as shown in *Table 4*, with the exception of a higher proportion of patients that were managed without any stay in the ICU and a lower rate of new neurological events in the TA-AVI group. Survival was $90 \pm 3\%$ at 30 days, $75 \pm 4\%$ at 6 months, and $73 \pm 4\%$ at 1 year in the TA-AVI group. Comparisons between TA-AVI group and control population revealed no significant differences for 30-day survival [odds ratio = 0.46, 95% CI (0.14; 1.30), $P = 0.17$ for the unadjusted analysis and odds ratio = 0.32, 95% CI (0.03; 3.38), $P = 0.34$ for the analysis adjusted for time of treatment and propensity] and overall survival [unadjusted: hazard ratio = 0.83, 95% CI (0.46; 1.51), $P = 0.55$; adjusted: hazard ratio = 1.00, 95% CI (0.29; 3.47), $P = 1.00$]. Kaplan–Meier survival curves are displayed in *Figure 1*.

Table 2 Outcome after transapical aortic valve implantation in relation to the preoperative risk profile

	n	STS (%)	ES _{log} (%)	30-Day mortality	1-Year mortality
Total	100	15.2 ± 8	29.6 ± 13	10	18
ES _{log} ≤ 20	32	11.2 ± 5	16.4 ± 3	6.3% ²	13.3% ⁴
20 < ES _{log} ≤ 30	32	13.6 ± 8	25.9 ± 3	6.3% ²	16.7% ⁵
30 < ES _{log} ≤ 50	27	19.1 ± 8	40 ± 6	11.1% ³	29.2% ⁷
ES _{log} ≥ 50	9	23.4 ± 10	58 ± 6	33.3% ³	33.3% ²

STS, Society of Thoracic Surgeons. ES_{log}, logistic EuroScore.

Table 3 Echocardiographic results at predischarge, 6-months, and 1-year follow-up in transapical aortic valve implantation patients

	Post-OP	6 Months	1 Year
V_{max} (m/s)	1.9 ± 0.4	1.9 ± 0.5	2 ± 0.4
P_{max} (mmHg)	15 ± 7	16 ± 7	17 ± 7
LVEF (%)	56 ± 13	59 ± 12	58 ± 12
AI (grade)	0.5 ± 0.5	0.6 ± 0.5	0.7 ± 0.5

TA-AVI, transapical aortic valve implantation; V_{max} , maximum transvalvular velocity; P_{max} , maximum transvalvular pressure gradient; LVEF, left ventricular ejection fraction; AI, aortic insufficiency.

Table 4 Comparison of patient outcomes for transapical aortic valve implantation vs. conventional aortic valve replacement surgery

	TA-AVI	C-AVR	P-value
n	100	100	
Respiratory support (h)	93 ± 194	118 ± 275	0.6
PACU*	58	5	<0.0001
Temporary neurological event**	3	6	0.4
Stroke	–	2	0.5

The control group was generated by means of propensity score analysis. PACU, postanaesthetic care unit—patients not managed in intensive care unit.

*Available for only 25 control patients (see text).

**Postoperative seizure or delirium.

Discussion

Transcatheter AVI has become a clinical reality for the minimally invasive treatment of AS in high-risk patients. Our initial results in 100 patients treated transapically are acceptable, particularly when considering the overall high-risk profile of the patients and when comparing to early feasibility results^{5–8} as well as to results of recently published series.^{13–18} We strongly believe that a team approach involving the expertise of cardiac surgeons, cardiologists, and cardiac anaesthetists—which is strongly supported by a recent consensus statement¹⁹—was important for the relatively good outcome in high-risk patients in this study.

Comparative trials

At present, no prospectively randomized trials comparing transcatheter techniques to C-AVR are available. Our study is again a retrospective analysis underlying the limitation of a non-random selection of treatment arms. This source of bias is reduced as far as possible by our propensity score matching which comprised a large set of possible confounding variables. We were thus able to collect evidence that TA-AVI in the initial 100 high-risk patients was as good as C-AVR. Therefore, we can conclude that TA-AVI can be performed safely when performed under optimal imaging by an expert team. Whether further advancements in transcatheter techniques will lead to outcomes that are even better than conventional surgery remains to be seen.

Stroke risk

The initial goals of TA-AVI therapy have been achieved in the present study: safety, feasibility, capacity to be performed through a minimally invasive approach, and capability to avoid sternotomy and use of CPB. In addition, an acceptably low morbidity with an extremely low stroke risk has been demonstrated. The

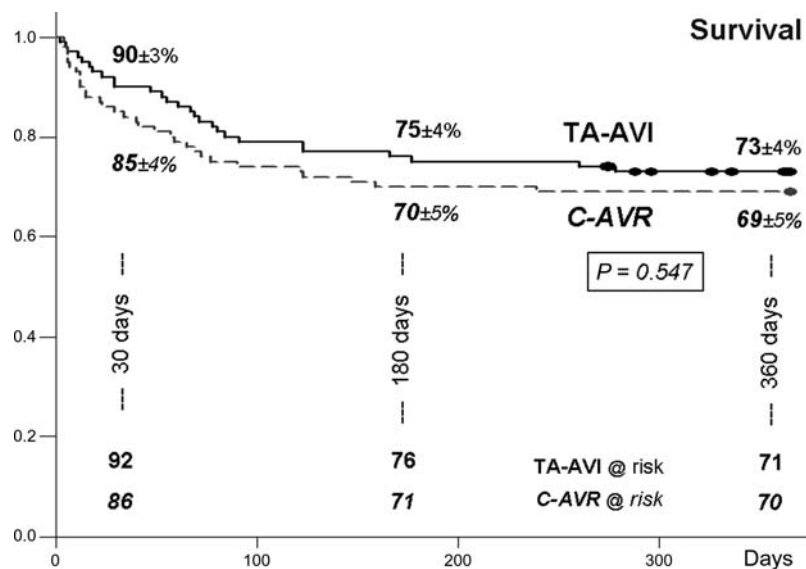


Figure 1 Survival analysis for the 100 patients receiving transapical aortic valve implantation (TA-AVI) compared with a propensity matched control group (C-AVR). No significant differences in survival up to 1 year were found.

low stroke rate may be due to the antegrade TA approach with minimal manipulation of the ascending aorta and aortic arch. The ascending aorta and arch have a high burden of atherosclerosis in elderly, high-risk patients, increasing their risk of stroke during conventional aortic surgery.²⁰ As stroke is a devastating complication associated with a significantly increased risk of perioperative morbidity, mortality, and resource utilization, the observed very low stroke rate is an important observation.

Risk assessment

Preoperative risk assessment can be difficult in patients with multiple comorbidities. We used the EuroSCORE to obtain risk quantification in the current study, despite knowing that operative risk may be overestimated with this scoring system in higher risk subgroups. In addition, the high-risk profile of our TA-AVI patients was confirmed using the STS risk score.²¹ Using both of these scoring systems, together with clinical judgement, clinicians may be able to target patients that may benefit most from the new transcatheter minimally invasive procedures while directing patients with lower risk profiles, even if they are in their 80 or 90, to a conventional surgical approach. Use of the logistic EuroSCORE, however, may still be helpful to differentiate between high-risk and very high-risk patients and it may be an indicator for potential longer-term outcome as shown in *Table 2*.

Valve positioning

Causes of death in TA-AVI patients and the lack of significant cardiac enzyme release indicate that risk of coronary artery obstruction was low with this procedure. We may therefore conclude that valve positioning can be performed safely when good imaging techniques are used. Furthermore, the risk of subsequent valve dislocation can be assumed to be minimal, as we did not observe this event in any patient and as no reports of such events have occurred to date in the world-wide experience. However, further improvements in imaging, such as the use of perioperative rotational angiography to render a three-dimensional reconstruction of aortic root anatomy and then online overlay (Dyna CT, Siemens, Inc., Erlangen, Germany) or additional computerized lines to depict the landmarks for exact valve positioning, may prove to be helpful in the near future.

Transapical access

The TA access was secured safely in all but one patient. Sufficiently deep bites when positioning the apical purse-string suture are essential, especially in presence of very soft tissue. Cardiac rhythm may be of some concern with a 10% rate of pacemaker implantations, most certainly due to calcifications that are squeezed into the peri-annular space during valve implantation. We therefore suggest that TA-AVI patients are monitored with telemetry for 1 week after their procedure. Differences in the frequency of postoperative postanaesthetic care unit (PACU) treatment between the two groups were due to a more frequent off-pump treatment together with shorter operative duration in the TA-AVI patients and due to the availability of the PACU unit.

Mortality and morbidity

Mortality during follow-up in the TA-AVI group was in general related to patient comorbidities, underscoring the overall risk profile of these patients. It has been our observation that patients with severe respiratory dysfunction are of particular concern. In contrast, neither low ejection fraction nor pulmonary hypertension was associated with a worse outcome in this series. More specific assessment of respiratory dysfunction may be warranted in high-risk patients with AS, particularly as it can be difficult to differentiate between dyspnoea due to AS or due to underlying pulmonary disease. Performing a thoracotomy may be an influencing factor for the observed poor outcomes in patients with respiratory dysfunction. However, we were able to extubate most such patients early after their procedure. Echocardiography revealed good valve function with low transvalvular gradients and low transvalvular blood flow velocities in all TA-AVI patients (*Table 3*). Paravalvular incompetence was frequent but usually of minor degree without any clinically relevant consequences such as heart failure or haemolysis.

Future aspects

Future aspects for transcatheter valve implantation should focus on a further reduction of paravalvular leakage by second generation stent designs, by increasing the size of available prostheses or by simply adding a cuff to existing stents. Future systems should also address mechanisms to reposition a device which has already been deployed, in cases of malposition or embolization.

Study limitations

The main limitation of the present study is its retrospective design comparing the new technique of TA-AVI vs. data from C-AVR patients that were identified through our hospital registry. The hospital registry data, however, were acquired in a prospective manner. A prospectively randomized clinical trial would be the best method for comparing these two groups of patients. At present, however, no randomized clinical trial data is available. We therefore believe that our propensity matching study, which resulted in two patient groups with very similar risk profiles, may provide some valuable information. Although control patients underwent their procedures over a longer time period than TA-AVI patients, time of treatment had no discernible effect on our results when it was included as a covariable.

Summary

Current results of minimally invasive off-pump TA-AVI in high-risk patients are promising. TA-AVI in the initial 100 patients was proven to be as good as C-AVR by means of propensity score analysis. The overall survival and functional quality of life of these patients is good.

Acknowledgements

We would like to acknowledge the technical support of Reinhardt Becht and Mark Dehdashtian of Edwards Lifesciences during valve implantation procedures.

Conflict of interest: T.W. is receiving minor honorarium for lectures at Edwards seminars infrequently and F.W.M. is a consultant advisor for Edwards Lifesciences. All other authors declare that they have no conflict of interest in relation to the topic of the manuscript.

References

- Bonow RO, Carabello BA, Chatterjee K. ACC/AHA 2006 Guidelines for the management of patients with valvular heart disease: Executive summary. *Circulation* 2006;**1**:450–527.
- Gummert JF, Funkat A, Beckmann A, Schiller W, Hekmat K, Ernst M, Krian A. Cardiac Surgery in Germany during 2006: a Report on Behalf of the German Society for Thoracic and Cardiovascular Surgery. *Thorac Cardiovasc Surg* 2007;**1**: 343–350.
- Chukwuemeka A, Borger MA, Ivanov J, Armstrong S, Feindel CM, David TE. Valve surgery in octogenarians: a safe option with good medium-term results. *J Heart Valve Dis* 2006;**1**:191–196.
- lung B, Baron G, Butchart EG, Delahaye F, Gohlke-Bärwolf C, Levang OW, Tornos P, Vanoverschelde JL, Vermeer F, Boersma E, Ravaud P, Vahanian A. A prospective survey of patients with valvular heart disease in Europe: the Euro Heart Survey on valvular heart disease. *Eur Heart J* 2003;**1**:1231–1243.
- Cribier A, Eltchaninoff H, Tron C, Bauer F, Agatiello C, Nercolini D, Tapiero S, Litzler PY, Bessou JP, Babaliaros V. Treatment of calcific aortic stenosis with the percutaneous heart valve: mid-term follow-up from the initial feasibility studies: the French experience. *J Am Coll Cardiol* 2006;**1**:1214–1223.
- Grube E, Schuler G, Buellesfeld L, Gerckens U, Linke A, Wenaweser P, Sauren B, Mohr FW, Walther T, Zickmann B, Iversen S, Felderhoff T, Cartier R, Bonan R. Percutaneous aortic valve replacement for severe aortic stenosis in high risk patients using the second- and current third- generation self-expanding Core-Valve prosthesis. Device success and 30-day clinical outcome. *J Am Coll Cardiol* 2007;**1**:69–76.
- Webb JG, Pasupati S, Humphries K, Thompson C, Altwegg L, Moss R, Sinhal A, Carere RG, Munt B, Ricci D, Ye J, Cheung A, Lichtenstein SV. Percutaneous transarterial aortic valve replacement in selected high-risk patients with aortic stenosis. *Circulation* 2007;**1**:755–763.
- Walther T, Simon P, Dewey T, Wimmer-Greinecker G, Falk V, Kasimir MT, Doss M, Borger MA, Schuler G, Glogar D, Fehske W, Wolner E, Mohr FW, Mack M. Transapical minimally invasive aortic valve implantation: multicenter experience. *Circulation* 2007;**116**(Suppl. 1):I240–I245.
- Walther T, Dewey T, Borger MA, Kempfert J, Linke A, Becht R, Falk V, Schuler G, Mohr FW, Mack M. Transapical aortic valve implantation (TA-AVI): Step by Step. *Ann Thorac Surg* 2009;**1**:276–283.
- D'Agostino RB Jr. Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. *Statist Med* 1998;**1**: 2265–2281.
- Rosenbaum PR, Rubin DB. Constructing a control group using multivariate matched sampling methods that incorporate the propensity score. *American Statistician* 1985;**1**:33–38.
- Ihaka R, Gentleman R. R a language for data analysis and graphics. *J Comp Graph Stat* 1996;**1**:299–314.
- Ye J, Cheung A, Lichtenstein SV, Altwegg LA, Wong DR, Carere RG, Thompson CR, Moss RR, Munt B, Pasupati S, Boone RH, Masson JB, Ali A, Webb JG Al. Transapical transcatheter aortic valve implantation: 1-year outcome in 26 patients. *J Thorac Cardiovasc Surg* 2009;**1**:167–173.
- Al-Attar N, Himbert D, Descoutures F, lung B, Raffoul R, Messika-Zeitoun D, Brochet E, Francis F, Ibrahim H, Vahanian A, Nataf P. Transcatheter aortic valve implantation: selection strategy is crucial for outcome. *Ann Thorac Surg* 2009;**1**: 1757–1762.
- Zierer A, Wimmer-Greinecker G, Martens S, Moritz A, Doss M. Is transapical aortic valve implantation really less invasive than minimally invasive aortic valve replacement? *J Thorac Cardiovasc Surg* 2009;**1**:1067–1072.
- Bleiziffer S, Ruge H, Mazzitelli D, Hutter A, Opitz A, Bauernschmitt R, Lange R. Survival after transapical and transfemoral aortic valve implantation: talking about two different patient populations. *J Thorac Cardiovasc Surg* 2009;**1**: 1073–1080.
- Thielmann M, Wendt D, Eggebrecht H, Kahlert P, Massoudy P, Kamler M, Erbel R, Jakob H, Sack S. Transcatheter aortic valve implantation in patients with very high risk for conventional aortic valve replacement. *Ann Thorac Surg* 2009;**1**: 1468–1474.
- Osten MK, Feindel C, Greutmann M, Chamberlain K, Meineri M, Rubin B, Mezodi M, Ivanov J, Butany J, Horlick EM. Transcatheter aortic valve implantation for high risk patients with severe aortic stenosis using the Edwards Sapien balloon-expandable bioprosthesis. A single centre study with immediate and medium-term outcomes. *Cath Cardiovasc Interv* 2009; doi:10.1002/ccd.22291. Published online ahead of print 6 October 2009.
- Vahanian A, Alfieri O, Al-Attar N, Antunes M, Bax J, Cormier B, Cribier A, De Jaegere P, Fournial G, Kappetein AP, Kovac J, Ludgate S, Maisano F, Moat N, Mohr F, Nataf P, Piérard L, Pomar JL, Schofer J, Tornos P, Tuzcu M, van Hout B, Von Segesser LK, Walther T, European Association of Cardio-Thoracic Surgery; European Society of Cardiology; European Association of Percutaneous Cardiovascular Interventions. Transcatheter valve implantation for patients with aortic stenosis: a position statement from the European Association of Cardio-Thoracic Surgery (EACTS) and the European Society of Cardiology (ESC), in collaboration with the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J* 2008;**1**:1463–1470.
- Borger MA, Ivanov J, Weisel RD, Rao V, Peniston CM. Stroke during coronary bypass surgery: principal role of cerebral macroemboli. *Eur J Cardiothorac Surg* 2001;**19**:627–632.
- Dewey TM, Brown D, Ryan WH, Herbert MA, Prince SL, Mack MJ. Reliability of risk algorithms in predicting early and late operative outcomes in high risk patients undergoing aortic valve replacement. *J Thorac Cardiovasc Surg* 2008;**1**: 180–187.