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Effect of cardiac rehabilitation on functional and emotional status in patients after transcatheter aortic-valve implantation

Heinz Völler[1,2], Annett Salzwedel[1], Aischa Nitardy[2], Hermann Buhlert[2], András Treszl[3] and Karl Wegscheider[3]

Abstract

Background: Transcatheter aortic-valve implantation (TAVI) is an established alternative therapy in patients with severe aortic stenosis and a high surgical risk. Despite a rapid growth in its use, very few data exist about the efficacy of cardiac rehabilitation (CR) in these patients. We assessed the hypothesis that patients after TAVI benefit from CR, compared to patients after surgical aortic-valve replacement (sAVR).

Methods: From September 2009 to August 2011, 442 consecutive patients after TAVI ($n = 76$) or sAVR ($n = 366$) were referred to a 3-week CR. Data regarding patient characteristics as well as changes of functional (6-min walk test. 6-MWT), bicycle exercise test), and emotional status (Hospital Anxiety and Depression Scale) were retrospectively evaluated and compared between groups after propensity score adjustment.

Results: Patients after TAVI were significantly older ($p < 0.001$), more female ($p < 0.001$), and had more often coronary artery disease ($p = 0.027$), renal failure ($p = 0.012$) and a pacemaker ($p = 0.032$). During CR, distance in 6-MWT (both groups $p \leq 0.001$) and exercise capacity (sAVR $p \leq 0.001$, TAVI $p \leq 0.05$) significantly increased in both groups. Only patients after sAVR demonstrated a significant reduction in anxiety and depression ($p \leq 0.001$). After propensity scores adjustment, changes were not significantly different between sAVR and TAVI, with the exception of 6-MWT ($p = 0.004$).

Conclusions: Patients after TAVI benefit from cardiac rehabilitation despite their older age and comorbidities. CR is a helpful tool to maintain independency for daily life activities and participation in socio-cultural life.

Keywords

Cardiac rehabilitation, emotional status, functional capacity, surgical aortic valve replacement (sAVR), transcatheter aortic valve implantation (TAVI)

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Introduction

Aortic stenosis is a common valve disease in elderly patients, associated with a high risk of death, when untreated.[1] Surgical aortic valve replacement (sAVR) improves prognosis in patients with low surgical risk.[2] But many elderly patients with comorbidities are not appropriate candidates for sAVR.[3] Transcatheter aortic-valve implantation (TAVI) is an alternative option in these high-risk patients[4–9] and is now routinely available for many patients.

In the PARTNER study, TAVI was superior to standard medical therapy in patients with severe aortic stenosis, who were not suitable for surgery.[5] It reduces rates of death and hospitalization,[6,7] improves significantly health-related quality of life,[10] and is associated with an increase in functional status,[11–13] even in patients aged ≥80 years.[14] According to the German Aortic Valve Registry,

[1]University of Potsdam, Potsdam, Germany
[2]Rehabilitation Centre for Cardiovascular Diseases, Rüdersdorf, Germany
[3]University Medical Centre, Hamburg-Eppendorf, Germany

Corresponding author:
Heinz Völler, Centre of Rehabilitation Research, University of Potsdam, Am Neuen Palais 10, D-14469 Potsdam, Germany.
Email: heinz.voeller@uni-potsdam.de

there has been a rapid growth in its use, accounting for 38.5% of patients who underwent an aortic valve replacement in 2011.[15]

Cardiac rehabilitation (CR) and physical activity are recommended treatments after cardiac valve surgery,[16–18] which positively improves morbidity, exercise capacity, and quality of life.[19,20] Despite an increasing number of patients undergoing TAVI, there are very few data available about the efficacy of CR in these often multimorbid patients.

Therefore, the aim of this study was to evaluate the effect of CR on functional and emotional parameters in patients after TAVI in comparison to patients after sAVR in a propensity score-adjusted model.

Methods

Patients

From September 2009 to August 2011, 442 consecutive patients (69.94 ± 11.08 years; 61.3% men) after aortic-valve replacement due to severe aortic stenosis were referred for a 3-week inpatient CR to the Klinik am See, Germany, a rehabilitation centre for cardiovascular diseases. The patients had undergone a transcatheter approach ($n = 76$: 42 transfemoral and 33 transapical) or a surgical aortic-valve replacement ($n = 366$) in four different heart centres. In Germany all eligible patients after aortic valve replacement are offered a cardiac rehabilitation after discharge from hospital.

Data collection

Sociodemographic data, medical history, and clinical status of the admitted patients as well as all results of medical investigations, done in the rehabilitation centre, are recorded and stored in an electronic database. The stored data regarding patient characteristics as well as functional and emotional status of these patients were extracted and evaluated for this study retrospectively.

Rehabilitation programme

All patients underwent a structured rehabilitation programme, including individualized physical training, education, and psychological support.[18] Additional treatment during the rehabilitation stay was done depending on its necessity. Aerobic exercise consisted of training on a bicycle ergometer in different workload classes, depending on the initial exercise intensity, outdoor walking, gymnastics in groups or single, and resistance training of the lower extremities. All sessions were controlled by approved physical therapists and were performed each four or five times per week. Additionally, patients received an individual psychological support. The number of sessions depended on the need and wish of the patients. Psychological education also included stress management, Tai Chi, and progressive muscle relaxation.

Functional evaluation

The functional evaluation of the study patients comprised a 6-min walk test (6-MWT) and a cycle-exercise test, which are performed in all cardiac patients at admission and at discharge from CR.

Standardized 6-MWT was performed with a distance-measuring device (Nestle Rolltachometer, Dornstetten, Germany). To evaluate the maximal exercise capacity, patients performed an individualized symptom-limited cycle test on a cycle ergometer (Cardiovit CS-200; Schiller, Germany) up to the submaximal predicted heart rate (85% of age-adjusted maximum heart rate). Under the supervision of a physician, the stress-test protocol started with 25 W followed by 25 W increase every 2 min until exhaustion. During the exercise test, a 3-lead ECG was recorded continuously to detect ischaemia or arrhythmias. Additionally, blood pressure was controlled every 2 min. The test was stopped, when the standard criteria for termination were reached.

Prior to the exercise test, all patients received a 12-lead ECG and underwent a two-dimensional echocardiography to evaluate left ventricular function and valve haemodynamics using a 3S probe of Vivid 7 (GE Ving Med, Horten, Norway).

Emotional evaluation

The emotional status was evaluated using the validated German version of the standardized Hospital Anxiety and Depression Scale (HADS) at the beginning and end of CR.[21,22] Patients with a HADS score ≥ 11 were offered an individual psychological support.

Statistical analysis

Qualitative (discrete) variables are reported as count and percentage, continuous variables as mean $\pm$ standard deviation. Baseline comparisons between groups were performed using chi-squared tests for discrete and t-tests for continuous variables. For better comparability, changes were expressed in percentage from baseline and analysed based on differences of log-transformed measurements. Changes within groups were tested using paired-sample t-tests for continuous variables. Since this was an observational study and

patients were not randomized to treatment groups, we aimed to control for selection bias when evaluating the effect of treatment. Thus, following a backward variable selection procedure propensity scores (i.e. probability of a patient being assigned into the TAVI treatment group) were calculated based on the baseline variables and multivariable analyses were adjusted for this score. p-values ≤ 0.05 were considered significant. Statistical analyses were calculated using SAS 9.2 (Cary, NC, USA).

Results

Patient characteristics

Patients after TAVI were significantly older and more female than patients after sAVR (80.30 ± 6.15 vs. 67.78 ± 10.66 years and 57.9 vs. 33.7%; $p < 0.001$, respectively). They revealed more often a coronary heart disease (64.5 vs. 50.5%; $p = 0.027$) or markedly renal failure with a glomerular filtration rate < 60 ml/min (42.7 vs. 31.7%; $p = 0.067$), underwent more often a pacemaker implantation (15.8 vs. 7.9%; $p = 0.032$), and had a higher NYHA stage ($p_{trend} = 0.003$). Other comorbidities, such as chronic obstructive pulmonary disease (COPD), diabetes mellitus, and atrial fibrillation, were not significantly different between the two groups (Table 1).

The patients revealed no significantly different length of hospital stay (TAVI 15.55 ± 15.38 vs. sAVR 17.3 ± 11.28 days) or time frame from the index procedure to admission to the rehabilitation centre (TAVI 24.05 ± 15.82 vs. sAVR 26.91 ± 18.71 days). The mean stay in the rehabilitation centre was 20.33 ± 4.03 days with a significantly shorter duration in patients after TAVI (TAVI 19.17 ± 4.54 vs. sAVR 20.58 ± 3.88 days; $p = 0.013$). Patients after TAVI spent more time in the intermediate care unit, needed more monitoring support (due to paroxysmal atrial fibrillation or volume balance in patients with renal failure) compared to the patients after sAVR (sAVR 3.74 ± 4.21 vs. TAVI 5.29 ± 4.21 days; $p = 0.216$). But all patients could complete the CR without a severe complication.

Functional and emotional status at the beginning of cardiac rehabilitation

Patients after sAVR achieved a significantly longer mean distance in the 6-MWT (sAVR 300.74 ± 102.36 vs. TAVI 262.45 ± 90.44 m; $p = 0.010$) and a higher maximal exercise capacity compared to patients after TAVI (sAVR 69.15 ± 26.63 vs. TAVI

Table 1. Patient characteristics at admission to CR

Characteristic	sAVR ($n = 366$)	TAVI				p-value
		Total ($n = 76$)	Transfemoral ($n = 42$)	Transapical ($n = 33$)	Total ($n = 442$)	
Gender (male, n)	239 (66.3)	32 (42.1)	18 (42.9)	13 (39.4)	271 (61.3)	<0.001
Age (years)	67.78 ± 10.66	80.30 ± 6.15	80.29 (6.21)	80.30 (6.27)	69.94 ± 11.08	<0.001
BMI (kg/m^2)	27.21 ± 4.68	26.10 ± 4.44	26.20 (4.71)	25.97 (4.22)	27.02 ± 4.66	0.0591
Stay in CR (days)	20.58 ± 3.88	19.17 ± 4.54	19.43 (4.35)	18.79 (4.87)	20.33 ± 4.03	0.013
COPD	45 (12.3)	11 (14.5)	6 (14.3)	5 (15.2)	56 (12.7)	0.603
Diabetes mellitus	98 (26.8)	27 (35.5)	14 (33.3)	12 (36.4)	125 (28.3)	0.123
CHD	185 (50.5)	49 (64.5)	29 (69.1)	19 (57.6)	234 (52.9)	0.027
GFR (ml/min)	68.80 ± 19.15	62.73 ± 18.21	62:80 (17.63)	62.00 (19.14)	67.77 ± 19.11	0.012
<60	116 (31.7)	32 (42.7)	17 (40.5)	15 (46.9)	148 (33.6)	0.067
<30	12 (3.3)	2 (2.7)	2 (4.8)	0 (0)	14 (3.2)	0.783
Atrial fibrillation	58 (15.9)	12 (15.8)	8 (19.1)	4 (12.1)	70 (15.8)	0.990
Sinus rhythm	265 (72.4)	51 (67.1)	28 (66.7)	22 (66.7)	316 (71.5)	0.352
Pacemaker	29 (7.9)	12 (15.8)	9 (21.4)	3 (9.1)	41 (9.3)	0.032
LVEF (%)	56.19 ± 8.12	57.11 ± 9.19	57.95 (10.20)	56.70 (6.95)	56.35 ± 8.31	0.384
≤40	24 (6.6)	4 (5.3)	3 (7.1)	0 (0)	28 (6.4)	0.670
NYHA (I/II/III/IV)	125/145/94/2	14/32/29/1	10/16/15/1	4/16/13/0	139/177/123/3	0.003*

Values are n (%) or mean ± standard deviation.; *Cochrane-Armitage trend test.; BMI, body mass index; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; CR, cardiac rehabilitation; GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; sAVR, surgical aortic-valve replacement; TAVI, transcatheter aortic-valve implantation.

53.66 ± 22.65 W; $p < 0.001$) at admission of cardiac rehabilitation.

Regarding emotional status, the two study groups showed no significant difference in the anxiety and depression score at baseline (anxiety: sAVR 5.29+/−3.95 vs. TAVI 4.37+/−3.26; $p = 0.157$; depression: sAVR 5.40+/−4.15 vs. TAVI 5.00+/−3.82; $p = 0.550$).

Calculation of propensity scores

For calculation of the propensity scores, a backward variable selection procedure was performed with all baseline variables. Weight at admission and age remained significant in the model and were used to calculate propensity scores.

Effect of cardiac rehabilitation on functional status

Following CR, the 6-MWT increased in both groups (Figure 1 and Table 2). In the propensity score-adjusted model, the change in the distance walked in the 6-MWT between admission and discharge was significantly lower in the TAVI group compared to sAVR patients (median, range: −15.89%, −5.53 to −25.09%; $p = 0.004$).

Regarding exercise capacity, both groups profited from CR, showing significant increases (sAVR 26.72%, 21.62 to 32.02%, TAVI 19.84%, 4.76 to 37.08%; $p < 0.001$ and $p = 0.010$, respectively; Figure 2, Table 2). Comparing the two groups in the propensity score-adjusted model, however, there

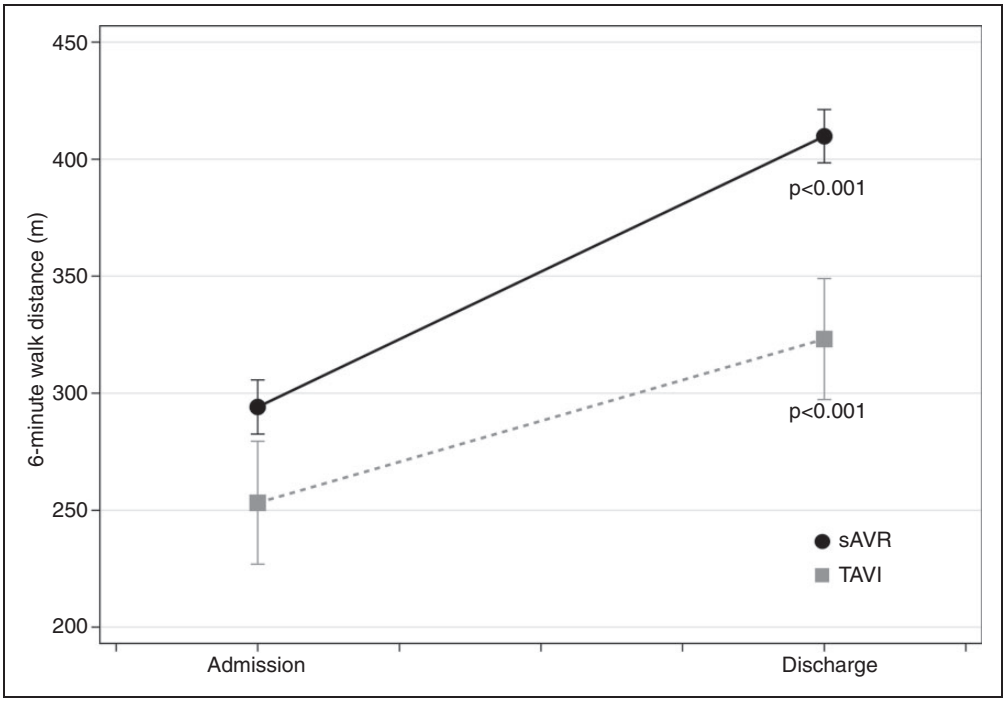

Figure 1. Effect of CR on 6-min walk test in patients after TAVI and sAVR.
CR, cardiac rehabilitation; sAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation.

Table 2. Changes in functional and emotional status from baseline after CR in patients after surgical and transcatheter aortic valve replacement

	Changes during CR			
Variable	sAVR	TAVI	Propensity score-adjusted difference	*p*-value
6-MWT	45.51 (38.87 to 50.38)**	28.13 (20.59 to 36.15)**	−15.89 (−5.53 to −25.09)	0.004
Exercise capacity	26.72 (21.62 to 32.02)**	19.84 (4.76 to 37.08)*	−11.26 (−22.24 to 1.28)	0.076
Anxiety score	−23.60 (−30.09 to −16.51)**	−17.1 (−35.45 to 6.40)	−6.22 (−22.00 to 44.66)	0.700
Depression score	−23.36 (−29.11 to −17.12)**	−17.10 (−34.61 to 5.11)	−0.92 (−23.96 to 29.12)	0.946

Values are % from baseline (95% confidence interval).; *p*-values for improvement measurement: *$p < 0.05$; **$p < 0.001$.; 6-MWT, 6-min walk test; CR, cardiac rehabilitation; sAVR, surgical aortic-valve replacement; TAVI, transcatheter aortic-valve implantation.

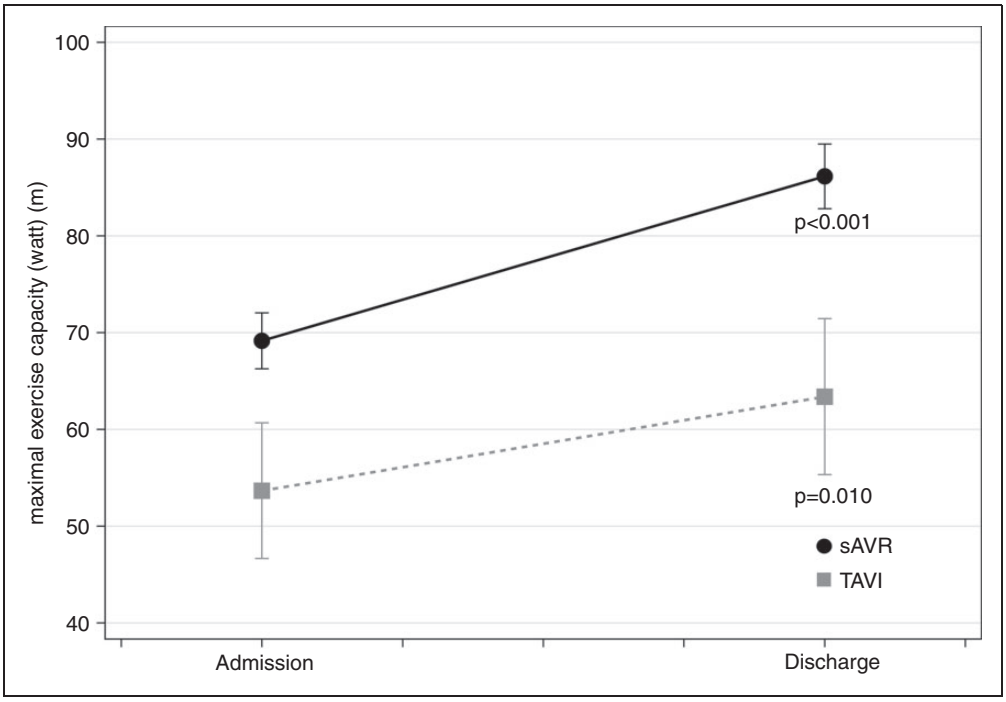

Figure 2. Effect of CR on maximal exercise capacity in W in patients after TAVI and sAVR.

was no significant difference between the two procedures ($p = 0.076$).

Effect of cardiac rehabilitation on emotional status

The evaluation of depression and anxiety in the two groups using HADS revealed a significant reduction in depression and anxiety at the end of CR after sAVR (–23.36%, −29.11 to −17.12% and −23.60%, −30.09 to −16.51%; $p < 0.001$ for both scores). Patients after TAVI showed no significant difference ($p = 0.117$ and 0.134, respectively). After propensity score adjustment, there was no significant difference in depression symptoms in either group comparing the scores at admission and discharge from CR.

Discussion

According to the literature available, very few data have reported about the effect of CR on functional and emotional status in patients after TAVI. The main finding of our observational propensity-matched study was that CR was safe, feasible, and improved physical performance significantly, tested using 6-MWT and maximal exercise capacity, in these elderly, often multimorbid patients. These findings correlate with those reported recently in the only existing small observational single-centre study, which also showed that patients after TAVI improved in 6-MWT after CR.[23]

Effect of cardiac rehabilitation on functional status

In our study, the mean distance in the 6-MWT was significantly improved during CR in both groups. In the propensity score-adjusted model, the change in the distance walked in the 6-MWT between admission and discharge was significantly lower in the TAVI group compared to sAVR patients.

The 6-MWT was chosen as a functional and an outcome measure test because the test is safe and feasible, even in elderly patients and after cardiac surgery.[24–27] As a measure of functional capacity, the 6-MWT reflects more the requirements of activities of daily living when compared with other tests.[28] Patients after TAVI were significantly older, more often female, and had more concomitant diseases than patients after sAVR and therefore showed a significantly shorter mean distance in the 6-MWT at admission. Recent data from the PARTNER trial show that the baseline distance predicts long-term mortality.[29] Other studies have reported that the distance walked in the 6-MWT is inversely related to age[30,31] and is affected by comorbidities[25,32] and gender.[31] Altogether, both groups showed an improvement of more than 50 m, a margin, which was found to be representative for a clinically significant change in functional status in a former study.[33]

At admission to rehabilitation, patients after sAVR showed higher exercise capacity compared to the patients after TAVI. Both groups increased their

exercise intensity during rehabilitation significantly. However, the direct comparison of the groups after propensity score adjustment revealed a strong but non-significant trend in favour of sAVR. Compared to the 6-MWT, the exercise test requires more aerobic performance and this might be the reason for the different results regarding significance in the improvement in the two groups. This could be due to the older age and higher rate of comorbidities in patients after TAVI, which leads to a decline in maximal capacity exercise, but may also result from the different sample sizes of the two groups. In future studies, the functional decline should be assessed on the basis of a composite of variables (e.g. malnutrition, cognition, gait speed, or activities of daily living) to generate the frailty index which is most predictive of functional decline (e.g. prognosis).[34]

Effect of cardiac rehabilitation on emotional status

HADS was reported to be suitable in assessing symptom severity of anxiety disorders and depression.[35] In this study, the average levels of depressive and anxiety symptoms according to HADS-Scale at admission were relatively low (Table 2) in conformity to usual values in cardiovascular patients.

Only patients after sAVR showed a significant improvement in anxiety symptoms during CR. At admission, patients after sAVR showed a trend of higher level of anxiety compared to patients after TAVI. This may be due to the fact that patients consider surgery as a more life-threatening event than interventional therapy. These patients showed a significant recovery at the end of CR. The provided education and psychological support during rehabilitation could have be a substantial impact on this process. Again, different sample sizes may be an alternative explanation. The direct comparison of the groups did not support the assumption of differences between the groups.

Regarding depressive symptoms, there was an improvement at discharge from CR in both groups, but without significance in the TAVI-Group. Depression score was relatively low at admission. For the majority of patients, a specific psychological therapy was not indicated. Therefore, no statistically significant reduction in depression score was to be expected, especially after only 3 weeks of rehabilitation. These results are in accordance with data of a former study in patients with coronary heart disease, which also revealed a nonsignificant improvement of depression symptoms during CR.[36]

Limitations

The description of the patients was focused on variables with functional consequences. Echocardiographic haemodynamic parameters were not reported. Although patients after TAVI were more morbid and older in comparison to sAVR, we did not include the EuroScore or STS score, as the scores are not appropriate for selecting the patients for TAVI.[37]

This study was an observational, nonrandomized study. Since the data for this study were extracted and evaluated retrospectively from a database of our rehabilitation centre, one can assume that it reflects the effect of a usual rehabilitation programme offered.

Conclusions

The mostly elderly patients after TAVI with multiple comorbidities benefit from CR predominantly in functional performance. Although the improvement at the end of CR was less significant in comparison with younger patients after sAVR, CR is a helpful tool to maintain independency for daily-life activities and participation in socio-cultural life in patients after TAVI. For these patients, prospective multicentre studies including geriatric multidimensional evaluation (e.g. disability, cognitive and nutritional status, and frailty) are required to estimate the improvement of prognosis by CR more accurately.

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Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Carabello BA and Paulus WJ. Aortic stenosis. *Lancet* 2009; 373: 956–966.
2. Schwarz F, Baumann P, Manthey J, et al. The effect of aortic valve replacement on survival. *Circulation* 1982; 66: 1105–1110.
3. Varadarajan P, Kapoor N, Bansal CR, et al. Clinical profile and natural history of 453 nonsurgically managed patients with severe aortic stenosis. *Ann Thorac Surg* 2006; 82: 2111–2115.
4. Grube E, Laborde JC, Gerckens U, et al. Percutaneous implantation of the CoreValve self-expanding valve prosthesis in high-risk patients with aortic valve disease: the Siegburg first-in-man study. *Circulation* 2006; 114: 1616–1624.
5. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Eng J Med* 2010; 363: 1597–1607.
6. Makkar RR, Fontana GP, Jilaihawi H, et al. Transcatheter aortic valve replacement for inoperable severe aortic stenosis. *N Eng J Med* 2012; 366: 1696–1704.

7. Kodali SK, Williams MR, Smith CR, et al. Two-year outcomes after transcatheter or surgical aortic-valve replacement. *N Eng J Med* 2012; 366: 1686–1695.
8. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic valve replacement in high risk patients. *N Engl J Med* 2011; 364: 2187–2198.
9. Holmes DR Jr, Mack MJ, Kaul S, et al. ACCF/AATS/SCAI/STS expert consensus document on transcatheter aortic valve replacement. *J Am Coll Cardiol* 2012; 59: 1200–1254.
10. Reynolds MR, Magnuson EA, Lei Y, et al. Health-related quality of life after transcatheter aortic valve replacement in inoperable patients with severe aortic stenosis. *Circulation* 2011; 124: 1964–1972.
11. Bagur R, Rodes-Cabau J, Dumont E, et al. Performance-based functional assessment of patients undergoing transcatheter aortic valve implantation. *Am Heart J* 2011; 161: 726–734.
12. Webb JG, Altwegg L, Boone RH, et al. Transcatheter aortic valve implantation. Impact on clinical and valve-related outcomes. *Circulation* 2009; 119: 3009–3016.
13. Gotzmann M, Hehen T, Germing A, et al. Short-term effects of transcatheter aortic valve implantation on neurohumoral activation, quality of life and 6-minute walk test in severe and symptomatic aortic stenosis. *Heart* 2010; 96: 1102–1106.
14. Bekeredjian R, Krumsdorf U, Chorianopoulos E, et al. Usefulness of percutaneous aortic valve implantation to improve quality of life in patients >80 years of age. *Am J Cardiol* 2010; 106: 1777–1781.
15. Deutsche Herzstiftung e.V. (ed.) Deutscher Herzbericht 2011. Frankfurt am Main: Deutsche Herzstiftung e.V., 2012.
16. Butchart EG, Gohlke-Bärwolf C, Antunes MJ, et al. Recommendations for the management of patients after heart surgery. *Eur Heart J* 2005; 26: 2463–2471.
17. Horstkotte D, Lengyel M, Mistiaen WP, et al. Recommendations for post-discharge patient follow up after cardiac valve interventions: a position paper. *J Heart Valve* 2007; 16: 575–589.
18. Karoff M, Held K, Bjarnason-Wehrens B, et al. Cardiac rehabilitation in Germany. *Eur J Cardiovasc Prev Rehabil* 2007; 14: 18–27.
19. Alter DA, Oh PI and Chong A. Relationship between cardiac rehabilitation and survival after acute cardiac hospitalization within a universal health care system. *Eur J Cardiovasc Prev Rehabil* 2009; 16: 102–113.
20. Kiel MK. Cardiac rehabilitation after heart valve surgery. *PM R* 2011; 3: 962–967.
21. Hermann C. International experiences with the hospital anxiety and depression scale: a review of validation data and clinical results. *J Psychosom Res* 1997; 42: 17–41.
22. Zigmond AS and Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983; 67: 361–370.
23. Russo N, Compostella L, Tarantini G, et al. Cardiac rehabilitation after transcatheter versus surgical prosthetic valve implantation for aortic stenosis in the elderly. *Eur J Prev Cardiol* 2013; (Epub ahead of print).
24. De Feo S, Tramarin R, Lorusso R, et al. Six-minute walking test after cardiac surgery: instructions for an appropriate use. *Eur J Cardiovasc Prev Rehabil* 2009; 16: 144–149.
25. Fiorina C, Vizzardi E, Lorusso R, et al. The 6-min walking test early after cardiac surgery. Reference values and the effects of rehabilitation programme. *Eur J Cardiothorac Surg* 2007; 32: 724–729.
26. De Feo S, Mazza A, Camera F, et al. Distance covered in walking test after cardiac surgery in patients over 70 years of age: outcome indicator for the assessment of quality of care in intensive rehabilitation. *Monaldi Arch Chest Dis* 2003; 60: 111–117.
27. Enright PL, McBurnie MA, Bittner V, et al. The 6-min walk test: a quick measure of functional status in elderly adults. *Chest* 2003; 123: 387–398.
28. Solway S, Brooks D, Lacasse Y, et al. A quantitative systematic overview of the measurement properties of functional walk tests used in the cardiorespiratory domain. *Chest* 2001; 119: 256–270.
29. Green P, Cohen DJ, Généreux P, et al. Relation between six-minute walk test performance and outcomes after transcatheter aortic valve implantation (from the PARTNER trial). *Am J Cardiol* 2013; 112: 700–706.
30. Harada ND and Chiu V and Stewart AL. Mobility-related function in older adults: assessment with a 6-minute walk test. *Arch Phys Med Rehabil* 1999; 80: 837–841.
31. Steffen TM, Hacker TA and Mollinger L. Age- and gender-related test performance in community-dwelling elderly people: Six-Minute Walk Test, Berg Balance Scale, Timed Up & Go Test, and Gaited Speed. *Phys Ther* 2002; 82: 128–137.
32. Opasich C, De F, eo S, Pinna GD, et al. Distance walked in the 6-minute test soon after cardiac surgery. Toward an efficient use in the individual patient. *Chest* 2004; 126: 1796–1801.
33. Reibis RK, Treszl A, Wegscheider K, et al. Exercise capacity is the most powerful predictor of 2-year mortality in patients with left ventricular systolic dysfunction. *Herz* 2010; 35: 104–110.
34. Schoenenberger AW, Stortecky S, Neumann S, et al. Predictors of functional decline in elderly patients undergoing transcatheter aortic valve implantation (TAVI). *Eur Heart J* 2013; 34: 684–692.
35. Bjelland I, Dahl AA, Haug TT, et al. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002; 52: 69–77.
36. Egger E, Schmid JP, Schmid RW, et al. Depression and anxiety symptoms affect change in exercise capacity during cardiac rehabilitation. *Eur J Cardiovasc Prev Rehabil* 2008; 15: 704–708.
37. Van Mieghem NM and Serruys PW. The art of risk stratification in TAVI. *Eur Heart J* 2013; 34: 1859–1861.