

1 **Özet**

2 Aort stenozu tedavisinde kateter yöntemiyle gerçekleştirilen aort kapak implantasyonu [TAVI]
3 hızla yaygınlaşmaktadır. Fakat ileri aort darlığının gold standart tedavi yönteminin halen
4 cerrahi aort valv replasmanı olduğu akılda tutulmalı ve ancak cerrahi olarak opere edilemeyen
5 çok yüksek riskli hastalar TAVI işlemine alınmalıdırlar. Konvansiyonel cerrahi replasmanın
6 komorbid hastalıkları nedeni ile yüksek riskli olduğu yaşlı hasta grubu için TAVI uygun bir
7 alternatif oluşturmaktadır. Endikasyon titizlikle konmalıdır, çünkü bu hastalarda, girişim
8 transkutan olsa da, 30 günlük mortalite yüzde 10 civarındadır. Uzun dönemli takip veriler hala
9 yetersiz olmakla beraber, endikasyon konusunda güncel literatürde 75 yaş üstü hastalar, STS-
10 skoru > 10 veya log Euroskoru > 20 olan hastalarla sınırlı tutulması gerektiği yönünde
11 görüşler olmakla birlikte bu girişim için yaş kesin bir belirleyici değildir. Esas olan hastanın,
12 kardiyolog, girişimsel kardiyolog, anesteziist ve kardiyak cerrahdan oluşan bir kalp takımı
13 tarafından değerlendirilmesi ve bu değerlendirmenin sonuçları bağlamında hareket
14 edilmelidir. Anulus genişliği endikasyonda önemli role sahiptir ve bu girişim anulus genişliği
15 18-27mm arasında olan hastalar ile sınırlandırılmalıdır. Tüm bunların yanında yaşam
16 beklentisi 1 yılın altında olan hastalarda TAVI kontraedikedir. Halen yürütülmekte olan
17 bilimsel çalışmalarda güvenilirlik , verimlilik ve özellikle kapağın uzun dönem dayanıklılığı
18 gibi parametreler araştırılmaktadır. Bu çalışmalar ışığında TAVI endikasyonlarına yeni
19 tanımlamalar ve parametreler eklenmektedir..

20 Biz bu derlemede TAVI ile ilgili genel bilgileri ve kliniğimizin tecrübesini sunuyoruz. Biz
21 kliniğimizde 15 tanesi transapikal ve 7 tanesi transfemoral yaklaşım olmak üzere toplam 22
22 aort valve replasmanı gerçekleştirdik. (Tablo 1-2)

23

24 **Anahtar kelimeler**

25 TAVI, TAVI transfemoral, TAVI transapikal, Kateter yöntemiyle aort kapak implantasyonu,
26 Ağır Aort Kapak Stenozu,

27

28 **Abstract**

29 Transcatheter Aortic Valve Implantation [TAVI] spreads enormously worldwide as an
30 alternative therapy procedure to the patients suffering from severe aortic valve stenosis. But
31 we shouldn't forget that the conventional surgical aortic valve replacement is still gold
32 standart therapy for severe aortic valve stenosis. For the patients who can not be treated
33 conventionally because of high risk comorbid diseases and older age; TAVI is an effective
34 alternative therapy method. The indications should be limited concerning the high mortality
35 rate, 10% within 30 days of intervention. Long term effectivity data are still inadequate.
36 Although the indications are restricted to older patients older with a STS score > 10 or log-
37 Euro Score > 20, age is not a definite indication for this treatment. The patients should be
38 assessed by a heart team including non-interventional cardiologist, interventional cardiologist,
39 cardiac anesthesiologist and cardiac surgeon according to their general status, frailty and STS-
40 Euro score. In other words, assessment and treating the patient by a heart team is the main
41 point besides the limited power of the scoring systems. The treatment should be applied to the
42 patients with aortic annulus diameter between 18-27 mm and a life expectancy of at least
43 more than 1 year. The currently ongoing investigations are focused on the parameters like
44 safety, efficiency and long term reliability of TAVI. The scientific and technical
45 developments lead to new definitions and parameters regarding the treatment indications of
46 severe aortic valve stenosis.

47 In this review, we present the actual data about TAVI and also our own experiences. We
48 performed 15 transapical and 7 transfemoral procedure (totally 22 patients) (Table 1-2)

49

50 **Keywords:** TAVI, TAVI transfemoral, TAVI transapical, Conventional Aortic Valve
51 Implantation, Catheter-based aortic valve implantation

52

53 **INTRODUCTION**

54 Calcified degenerative aortic valve stenosis is the most common valvular heart disease in
55 adults. Prevalence of aortic valve stenosis with aging is around 6-7% over the age 85. Such
56 patients are bringing new medical and economic burdens to the medical care system. TAVI is
57 a new treatment method and in particular patients, ineligible for valve replacement with
58 conservative surgical method or those under high risk group, have the chance to benefit from
59 this method of treatment [1-4].

60 **Diagnosis of aortic valve stenosis and Indications of TAVI**

61 Aortic valve stenosis may not give symptoms for a long period of time. Prognosis of the
62 disease worsens in case of development of typical symptoms such as chest pain, syncope and
63 dyspnea or a decline in the left ventricular ejection fraction [LVEF]. Some studies report up to
64 80% of 2-year mortality in symptomatic aortic valve stenosis. In general, average
65 perioperative mortality is 4% and 3-year survival rate is 80% after following surgical aortic
66 valve replacement procedures. Perioperative complication risk considerably increases in
67 particular in the elderly patients with comorbid diseases such as COPD, pulmonary
68 hypertension, renal failure, heart failure, previous cardiac surgery and consequently
69 perioperative mortality risk also increases. For this reason, 30% of the patients in average
70 were not operated in the past, despite of having first degree indication [5-8].

71 Symptomatic aortic valve stenosis is a first degree indication for aortic valve
72 replacement. Valve replacement indicated for patients with aortic valve stenosis after the
73 development of symptoms such as dyspnea, chest pain, vertigo and syncope. Aortic stenosis
74 patients are mostly the elderly, hypertensive, obese individuals and also those with chronic
75 lung diseases. The auscultation finding is a hard systolic murmur transmitted to the carotid
76 arteries at the right upper sternum at the point of maximal impulse. “Thrill” is sometimes
77 observed at manubrium sterni in the advanced stage. Hemodynamic significance of stenosis

78 should be identified with echocardiography or invasive procedures due to lack of a reliable
79 characteristic finding.

80 Patients have senile degenerative severe aortic valve stenosis with transthoracic
81 echocardiographically derived criteria: mean gradient >40 mmHg or jet velocity greater than
82 4.0 m/s or an initial aortic valve area of < 0.8 cm²

83 Furthermore, patients having left ventricular function impairment with low cardiac
84 output and patients with low aortic valve gradient are also candidates for valve replacement.
85 However, further tests are required for such patients to confirm the indication aortic valve.
86 Percutaneous aortic valve implantation is a new and favorable treatment option for these
87 patients. Valve function can be measured by echocardiography.

88 Patients with advanced aortic valve stenosis and impaired left ventricular function do
89 not comply to the above mentioned aortic valve gradient criteria. These are the patients with
90 LVEF impairment, low cardiac output and low gradient. Significant degree of aortic stenosis
91 is strongly confirmed particularly in these patients during transoesophageal echocardiography
92 at the planimetry measurement. Dobutamine stress echocardiography can be applied to
93 differentiate pseudo-stenosis from a true stenosis and to detect sufficient and insufficient
94 contractile reserve. This test allows predicting perioperative mortality risk. Since insufficient
95 contractile reserve increases the surgical mortality up to 30% in conventional valve
96 replacement, conventional valve replacement procedure is not applied for such patients. At
97 this point, patients can benefit from the TAVI procedure. Protective assist devices should be
98 available because these patients have higher mortality risk due to acute heart failure.

99 TAVI is applied as an “off label” preferential treatment approach for patients with EF
100 $< 20\%$. However, further analyses show that such patients benefit considerably from valve
101 implantation. Valve replacement indication for most of the centers includes the above
102 mentioned aortic stenosis, having EF $< 50\%$ and a positive stress test in echocardiography.

103 **TAVI**

104 **Evolution of TAVI**

105 TAVI was initially tested on animals at the mid 1960's. In 1992, Anderson et al. performed
106 percutaneous valve implantation in pigs. A couple of years later, Bonhoeffer et al.
107 successfully performed the first in-human percutaneous implantation, by inserting the self-
108 expandable valve in the pulmonary valve position. In 2002, Cribier et al. inserted the first
109 balloon-expandable valve in the aorta position, named as the TAVI procedure [1]. During the
110 subsequent years, application of percutaneous transcatheter aortic valve implantation has
111 rapidly evolved in high risk patients. After that, TAVI, which is being applied in various
112 centers worldwide and follow-up results of which is reported (around 11 000 patients), can
113 well be applied with a mortality rate between 6-10%, despite of being a high risk intervention
114 [9,10].

115 **Patients and method:**

116 The TAVI procedures took place in the Coronary Angiography Center at the University
117 Hospital of Giessen and Marburg, Campus Giessen. There were totally 22 cases who
118 underwent TAVI procedure in our clinic at a mean age of 81(\pm 7) with an average Body Mass
119 Index of 26,6 and transapical approach was applied to 15 and transfemoral approach to 7 of
120 these patients. From these 22 cases, 12 of them were females, 15 had Coronary Artery
121 Disease and also 3 of them with transapical approach were Diabetes Mellitus patients. 16
122 were closely followed because of Hypertension, 8 of them were classified as NYHA III and
123 NYHA IV and 4 of them had a LVEF less than 35%. The average Aortic Annulus diameter
124 were 22,23mm.

125 The TAVI procedure can be used in two approaches. Through a minithoracotomy from the
126 cardiac apex; antegrade and through a free preparation of femoral artery; retrograde. In our
127 institute, we have used both of the methods, although the femoral approach seems to be more

128 advantageous in terms of complications, whereas the apical approach is the option to apply
129 TAVI at the patients that expected to have peripheral circulation problems.

130 **How to apply Aortic Valve Implantation**

131 Today, percutaneous aortic valve implantation is performed in a standardized manner in the
132 well-established centers and is consisted of the following steps:

- 133 1. It is required to evaluate the aortic root and the possible accesses mostly with the
134 imaging techniques during the planning phase of the intervention. Access from the
135 pelvic veins is not possible at today's technical devices. Transfemoral access is
136 possible in anatomical terms and there are presently 2 types of valves accepted for use
137 in Europe. These valves differ from each other from technical point of view.
- 138 2. TAVI-transfemoral is an intervention performed in less than 90 minutes with mild
139 sedation in particular in high risk patients, without the need for intubation and local
140 anesthesia. Aortic valve is implanted with retrograde approach from the femoral
141 artery. Subsequent valvuloplasty allows for the positioning and implantation of the
142 valve during "rapid pacing" (explained below). A special suture system is used for
143 closing the artery.
- 144 3. Following the procedure, the patients should be followed in particular for high degree
145 AV-block and local bleeding.
- 146 4. The subsequent treatment follow-up protocol is similar to the drug therapy of the
147 patients with coronary stent treatment.

148 **How to Apply TAVI**

149 During TAVI procedure, the aortic valve is fixated at the tip of the catheter and is moved to
150 the aortic valve area as retrograde TAVI- transfemoral (over the arterial system) or as TAVI-
151 transapical through antegrade minithoracotomy. For balloon-expandable or self-expandable
152 valves, the valve is moved to the aortic valve area and is opened there. The existing valve is

153 not removed and remains in the body, as attached to the aortic wall under the newly implanted
154 valve [17-19].

155 **TAVI-transfemoral (Figure 1)**

156 In cases where vessel size is adequate (>7mm), the procedure is in general performed by a
157 puncture at A. femoralis communis. Surgical opening of the vessel is mostly not required with
158 the use of percutaneous suture system (Pre-Closure, e.g.: ProStar XL, Abbott Vascular).
159 Therefore, general anesthesia is not applied in many of the cases and intervention is
160 performed with analgo sedation (e.g. Midazolam and Propofol) under regular conditions. The
161 major determinant of TAVI- transfemoral intervention is to make a careful puncture in the
162 vessel at an adequate distance to bifurcation. Evolution of the inserted cannulas provides for a
163 decrease in the vascular complications experienced in the past. A steerable catheter is
164 developed for the implantation of SAPIEN valve to facilitate delivery from arcus aorta and
165 the aortic valve. 22-F access set (outer diameter 8,4 mm) for the 23 mm prosthesis or 24F
166 access set (outer diameter 9,1 mm) for 26 mm prosthesis are used for Edwards-SAPIEN
167 interventions, depending on the valve sizes. Smaller 18F-access set (outer diameter 6,5-7 mm)
168 is used for CoreValve prosthesis. Smaller and larger sized access sets are on the way.

169 **TAVI-transapical (Figure 2)**

170 Comparative studies to demonstrate the significance of TAVI-transapical access over TAVI-
171 transfemoral access are inadequate. General anesthesia is required during TAVI- transapical
172 implantation. This method is not favorable for patients with chronic lung disease such as
173 COPD, due to the possibility for longer “weaning” period. For the patients being subject to
174 hypoxia for long time, weaning effect is a syndrome in which the patients become dependent
175 to lung assist device after 100% oxygen, in case the respiratory function is set to pO₂ level
176 rather than pCO₂ level. Myocardial puncture is made through left ventricular apex by way of
177 minithoracotomy. After drilling the aortic valve in aortic valve stenosis, valvuloplasty is
178 performed with the access set (24 F) and the prosthesis is inserted inside the aortic valve.

179 Similar to TAVI- transfemoral intervention, “rapid pacing” is applied during implantation.
180 TAVI- transapical implantation method requires general anesthesia for being a major invasive
181 intervention and it is a method only applied when TAVI- transfemoral approach is not
182 appropriate for any reason.

183 **Indications / Contraindications**

184 Cardiologists and cardiac surgeons should cooperate in determining for the indications.
185 Adequate level of training and a fully-equipped catheterization laboratory (hybrid
186 catheterization laboratory) is essential. It is recommended to be applied only in centers with
187 cardiac surgery department since severe complications such as vessel perforation, tamponade,
188 annulus rupture, aortic dissection may develop in 3% of the cases [9-13-].

189 TAVI criteria:

- 190 1. Confirmation of symptomatic aortic valve stenosis
- 191 2. Risk-scores measured as STS (>10%) or logEuro-Score (>20%)
- 192 3. Evaluation of the anatomy with TEE and/or CT (17-27mm) on the basis of the annulus
193 width

194 Indication should be carefully considered for patients with a life expectancy less than 1 year.
195 The major criterion is to identify the width of the aortic annulus. This can most sensitively be
196 identified with transoesophageal echocardiography [TEE] or CT techniques. TAVI should be
197 limited to patients with an annulus width of 18-29 mm. In case of any coronary heart disease,
198 the patient should be treated with percutaneous coronary intervention at least 14 days prior to
199 TAVI procedure. Immediate and last minute interventions should be avoided due to risk of
200 acute stent thrombosis and bleeding. Besides the anatomical criteria, clinical criteria should
201 also be considered during the decision making process for TAVI indication [12-15].

202 Criteria required to be evaluated in clinical terms include unusual chest malformation,
203 porcelain aorta, previous surgical operations, comorbidities, post-radiotherapy adhesions,
204 elderly patients under risk for surgery and patients with degenerative bio-valve. Indication

205 should be carefully considered for patients with a life expectancy less than 1 year.
206 In principle, the use of this new technology should be limited to inoperable patients or
207 patients over 75 with a risk score STS over 10% or logEuro-Score >20% (clinical indication
208 class IIa).
209 It should be noted for patients with valvular diseases that risk scoring is not updated and is not
210 focused on the valvular disease, because scoring is based on the data from coronary heart
211 disease patients and is adapted to valvular diseases. Therefore, it is inadequate. Euro-score, in
212 particular, indicates high mortality in conventional aortic valve replacement. Given such
213 limitations, each patient should be individualized on the basis of specific risks.
214 There are limitations to the application of TAVI procedures, because the mortality rate within
215 the first 30 days is 10% in all available lists for TAVI. There is no underlying rationale for the
216 application of this procedure in low-risk patients due to high mortality rate and this has never
217 been attempted so far. Results of comparative studies between conventional procedures and
218 TAVI are expected for a comprehensive interpretation on the subject matter.

219 **Pre-TAVI preparations**

220 Invasive diagnostic interventions are inevitable besides TEE for TAVI preparations. Detailed
221 anatomy of the aortic root should be evaluated with aortic root angiography as a part of
222 invasive coronary imaging. Pulmonary hypertension can be ruled out with right heart
223 catheterization and the cardiac output and valve opening area can be measured through
224 thermodilution. In case major stenosis is observed in the coronary vessels, a two-tiered
225 method should apply and first the vessels with coronary stenosis should be stented. TAVI
226 should definitely not be applied within the first following 14 days. Pelvic vessels should also
227 be imaged in addition to invasive diagnostic methods. Finally, Angio-CT (2 mm sections,
228 multiplanar imaging) is recommended. Aortic outflow tract, ascending aorta, arcus aorta,
229 subclavian artery, thoracic aorta, abdominal aorta, iliac arteries and femoral artery should be
230 evaluated for calcification. It should not be applied in patients with acute systemic

231 inflammation (sepsis, endocarditis) and also patients identified to have atrial and ventricular
232 thrombosis. Proper anti-coagulation therapy is required for atrial fibrillation patients prior to
233 the implantation. Patients with TAVI indication should in advance be treated with ASS 100
234 mg and Clopidogrel 75 mg and 300 mg Clopidogrel loading dose should apply 1 day before
235 the implantation.

236 **Valve Types and Use of Valves**

237 There are two types of valves as the balloon-expandable SAPIEN-bioprostheses (Edwards
238 LifeSciences, Irvine, CA, USA, [15]) and self-expandable CoreValve Revalving-system
239 (Medtronic, Minneapolis, MN, USA, [8]). There are also other different valve models at the
240 clinical trial phase (e.g.; Jena Valve, Lotus Valve, Direct Flow, HLT, etc.)
241 Edwards-SAPIEN-THV is a valve with a stainless steel frame and bovine pericardial tissue.
242 Three different sizes as 23, 26 and 29 mm are available in the market; TAVI-transfemoral
243 implantation is performed with 18-F, 22-F and 24-F cannula systems. 33-F cannula system is
244 required for TAVI-transapical procedure (Figure 3). Balloon-expandable SAPIEN valve, used
245 during TAVI-Transfemoral and TAVI-transapical implantation, should be implanted under
246 high frequency right ventricular stimulation [rapid pacing] to allow for its stable insertion in
247 the aortic annulus. On the other hand, self-expandable CoreValve-prosthesis has Nitinol frame
248 of 5 cm and porcine pericardium. Since CoreValve prosthesis is self-expandable (Self
249 Expansion), there is no need for rapid pacing and use of balloon during the implantation.
250 Core-Valve prosthesis is also available in two different sizes as 26 mm and 29 mm, similar to
251 the SAPIEN valve, however, larger and smaller prostheses are expected to be manufactured
252 soon [16-17].

253 **Results:**

254 From these 22 cases, we have no mortality as a major complication at operation room. Only at
255 one of the trans-apical approaches, the incision at the apex is not self-closed. We had to
256 actively close the apex by sewing it. Also at one of the transfemoral approaches, we have

257 detected a leak from one side of the valve. We have electively programmed another procedure
258 and another valve implantation to the area, and this procedure is called valve in valve. Except
259 for this case, we have followed the patients for 3 days in our intensive care and no other major
260 complication occurred during this time period.

261 **How to interpret TAVI results**

262 Hemodynamic parameters start to change right after TAVI procedure. Besides, better
263 hemodynamic results were reported at the annulus of more stenotic aortic valve in anatomical
264 terms [16]. Average transvalvular pressure difference is under 10 mmHg and post-intervention
265 valve opening area reaches to the level of 1,5-1,8 cm². Unfortunately, data comparing long
266 term results of TAVI and conventional valve replacement procedures are lacking. There is
267 patient-prosthesis mismatch in 58 percent of the cases mostly in conventional aortic valve
268 replacement procedure of small aortic annulus. In this case, postoperative mortality rate is
269 around 30 percent [11]. Stable hemodynamic improvements are observed at the end of TAVI
270 procedure in the medium term. No structural valve degeneration was observed so far in
271 SAPIEN and CoreValve prostheses. However, 25 percent of the patients develop prosthesis
272 leakage. In case clinically significant leakage is detected, it can be corrected by way of special
273 occlusion devices. In short, present success rate for both prostheses is around 95-98%. Post-
274 TAVI 30-day mortality rate is reported between 6-10 percent for the high risk patients at the
275 data tables of the industrial companies.

276 **Complications**

277 Cerebrovascular complications [CVE]

278 Incidence of CVE is around 3-4 percent and is not lower than the conventional approach in
279 TAVI interventions. Cerebrovascular complications are slightly lower after TAVI-transapical
280 implantation, with the ratio of 1-2,9 percent. There are differences specific to both of the
281 valve prostheses and differences in coronary stenosis (CoreValve 0,4 percent, SAPIEN 1,0-1,8
282 percent) due to different design structures. Vessel related complications are higher in Edwards

283 systems by 7,4 percent, whereas 2,9 percent in CoreValve prosthesis, as a result of size
284 difference in TAVI-transfemoral catheterization systems (CoreValve 18F, SAPIEN 22-24 F).
285 However, an absolute disadvantage of CoreValve prostheses is the considerable need for
286 pacemaker implantation. Left bundle branch block and high degree AV-block (20-30 percent
287 of the cases) is detected during the intervention. Pacemaker implantation is around 6,7 percent
288 in conventional aortic valve surgery and 6,7-7,3 percent with the SAPIEN systems.

289 In our 22 patients we didn't see operating room and in hospital mortality. We observed 2
290 major complication: the first is in one of the trans-apical approaches, the incision at the apex
291 is not self-closed and the second is one of the transfemoral approaches, we have detected a
292 significant leak from one side of the valve. We didn't observe any CVE.

293 **Complementary therapy**

294 Post-interventional 1 day follow-up is required for the patients at the intensive care unit.
295 Follow-up at the intensive care unit may be extended in case of development of complications
296 such as renal failure, vascular complications or bleeding. Perioperative invasive
297 hemodynamic monitoring is required for each patient to allow for timely identification of
298 changes in blood pressure. In particular after CoreValve implantation, transvenous pacemaker
299 leads should definitely be available for 48 hours. Pacemaker is required in case of
300 development of AV conduction anomalies and in particular post-interventional left bundle
301 branch block (QRS>145 ms). Functionality of the bioprosthesis should be checked during the
302 follow-up by TTE and NT-proBNP, if required. Paraprosthetic leakages may sometimes not be
303 detected by TTE and TEE methods. In case of any suspicion, angiography should be applied
304 immediately and transvalvular hemodynamic values should be measured immediately. Oral
305 double antiaggregant therapy should be administered. 4-week combination therapy (100 mg
306 Aspirin and 75 mg Clopidogrel) is adequate for SAPIEN valve. Combination therapy (100 mg
307 Aspirin and 75 mg Clopidogrel) is recommended for 6 months in CoreValve valves. 100 mg
308 aspirin therapy should be added to the combination therapy.

309

310 **Expectations**

311 TAVI has been applied to around 11.000 high risk patients worldwide. Considerable results
312 are expected from the PARTNER-Trial, comparing conventional valve replacement, TAVI and
313 conservative treatment, in terms of safety, efficiency and comparison to the conventional
314 intervention. In case the trial results in the favor of TAVI, its area of application would be
315 wider. Furthermore, new generation valves and access sets are being developed by the
316 ongoing studies with a view to decrease interventional risk in the near future and to make
317 TAVI procedure safer. In parallel to these developments, TAVI, presently considered to be an
318 alternative treatment method in patients ineligible for conventional valve replacement, may
319 take its place in the literature as an elective treatment method to be recommended in the first-
320 line for high risk group patients in the near future.

321 **References**

- 322 1. Cribier A, Eltchaninoff H, Bash A, Borenstein N, Tron C, Bauer F, Derumeaux G, Anselme
323 F, Laborde F, Leon MB. Percutaneous transcatheter implantation of an aortic valve prosthesis
324 for calcific aortic stenosis: first human case description. *Circulation* 2002;106:3006–3008
- 325 2. Piazza N, Wenaweser P, van Gameren M, Pilgrim T, Tsikas A, Otten A, Nuis R, Onuma Y,
326 Cheng JM, Kappetein AP, Boersma E, Juni P, de Jaegere P, Windecker S, Serruys PW.
327 Relationship between the logistic EuroSCORE and the Society of Thoracic Surgeons
328 Predicted Risk of Mortality score in patients implanted with the CoreValve ReValving
329 System – A Bern–Rotterdam Study. *Am Heart J* 2010;159:323–329. 310
- 330 3. Kalvrouziotis D, Li D, Buth KJ, Le´gare´ J-F. The European System for cardiac Operative
331 Risk Evaluation (EuroSCORE) is not appropriate for withholding surgery in high-risk patients
332 with aortic stenosis: a retrospective cohort study. *J Cardiothorac Surg* 2009;4:32 doi:
333 10.1186/1749-8090-4-32.
- 334 4. Zajarias A, Cribier AG. Outcomes and safety of percutaneous aortic valve replacement. *J*
335 *Am Coll Cardiol* 2009;53:1829–1836.
- 336 5. Piazza N, van Gameren M, Ju´ni P, Wenaweser P, Carrel T, Onuma Y, Gahl B, Hellige G,
337 Otten A, Kappetein AP, Takkenberg JJ, van Domburg R, de Jaegere P, Serruys PW,
338 Windecker S. A comparison of patient characteristics and 30-day mortality outcomes after
339 transcatheter aortic valve implantation and surgical aortic valve replacement for the treatment
340 of aortic stenosis: a two-centre study. *EuroIntervention* 2009;5:580–588.
- 341 6. Ramaraj R, Sorrell VL. Degenerative aortic stenosis. *Br Med J* 2008;336:550–555.
- 342 7. Iung B, Cachier A, Baron G, et al. Decision-making in elderly patients with severe aortic
343 stenosis: Why are so many denied surgery? *Eur Heart J* 2005;26:2714–2720.
- 344 8. Walther T, Kempfert J, Borger MA, Fassel J, Falk V, Blumenstein J, Dehdashtian M,
345 Schuler G, Mohr FW. Human minimally invasive off-pump valve-in-a-valve implantation.
346 *Ann Thorac Surg* 2008;85:1072–1073.

- 347 9. Schäfer U., Frerker C., Schewel D., Schneider C., Malisius R., Blaschke K., Köktürk B.,
348 Kuck K. H., Bergman M. W. Perkutane Aortenklappenimplantation, *Der Kardiologe* 2007;
- 349 10. Hara H, Pedersen WR, Ladich E, Mooney M, Virmani R, Nakamura M, et al.
350 Percutaneous balloon aortic valvuloplasty revisited: Time for a renaissance? *Circulation* 2007;
351 **115**: e334 – e338.
- 352 11. Iung B, Baron G, Butchart EG, Delahaye F, Gohlke-Bärwolf C, Levang OW, et al. A
353 prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey
354 on Valvular Heart Disease 1. *Eur Heart J* 2003; **24**: 1231 – 1243.
- 355 12. Cribier A, Eltchaninoff H, Tron C, Bauer F, Agatiello C, Sebah L. et al. Early experience
356 with percutaneous transcatheter implantation of heart valve prosthesis for the treatment of
357 end-stage inoperable patients with calcific aortic stenosis. *J Am Coll Cardiol* 2004; **43**: 698 –
358 703.
- 359 13. Grube E, Laborde JC, Gerckens U, Felderhoff T, Sauren B, Buellesfeld L, et al.
360 Percutaneous implantation of the CoreValve self-expanding valve prosthesis in high-risk
361 patients with aortic valve disease: The Siegburg first-in-man study. *Circulation* 2006; **114**:
362 1616 – 1624.
- 363 14. Heistad DD, Wakisaka Y, Miller J, Chu Y, Pena-Silva R. Novel aspects of oxidative stress
364 in cardiovascular diseases. *Circ J* 2009; **73**: 201 – 207.
- 365 15. Linhartová K, Veselka J, Sterbáková G, Racek J, Topolcan O, Cerbák R. Parathyroid
366 hormone and vitamin D levels are independently associated with calcific aortic stenosis. *Circ*
367 *J* 2008; **72**: 245 – 250.
- 368 16. Ross J Jr, Braunwald E. Aortic stenosis. *Circulation* 1968; **38**(Suppl): 61 – 67.
- 369 17. Roberts WC, Ko JM, Filardo G. Comparison of heavier versus lighter operatively excised
370 stenotic aortic valves in adults with aortic stenosis and implications for percutaneous aortic
371 valve implantation without replacement. *Am J Cardiol* 2009; **104**: 393 – 405.
- 372 18. Webb JG, Chandavimol M, Thompson CR, Ricci DR, Carere RG, Munt BI, et al.

373 Percutaneous aortic valve implantation retrograde from the femoral artery. *Circulation* 2006;
374 **113**: 842 – 850.

375 19. Thomas M, Schymik G, Walther T, Himbert D, Lefèvre T, Treede H, et al. Thirty-day
376 results of the SAPIEN aortic bioprosthesis european outcome (SOURCE) Registry: A
377 European registry of transcatheter aortic valve implantation using the Edwards SAPIEN
378 valve. *Circulation* 2010; **122**: 62 – 69.

379 20. Piazza N, Grube E, Gerckens U, den Heijer P, Linke A, Luha O, et al. Procedural and 30-
380 day outcomes following transcatheter aortic valve implantation using the third generation
381 (18Fr) CoreValve ReValving system: Results from the multicentre, expanded evaluation
382 registry 1-year following CE mark approval. *EuroIntervention* 2008; **4**: 242 – 249.

383 21. Piazza N, Onuma Y, Jesserun E, Kint PP, Maugeness AM, Anderson RH, et al. Early and
384 persistent intraventricular conduction abnormalities and requirements for pacemaking after
385 percutaneous replacement of the aortic valve. *JACC Cardiovasc Interv* 2008; **1**: 310 – 316.

386 22. Fraccaro C, Napodano M, Tarantini G, Gasparetto V, Gerosa G, R, Bonato R, et al.
387 Expanding the eligibility for transcatheter aortic valve implantation the trans-subclavian
388 retrograde approach using: The III generation CoreValve ReValving system. *JACC*
389 *Cardiovasc Interv* 2009; **2**: 828 – 833.

390 23. Olsen LK, Engstrøm T, Søndergaard L. Transcatheter valve-in-valve implantation due to
391 severe aortic regurgitation in a degenerated aortic homograft. *J Invasive Cardiol* 2009; **21**:
392 E197 – E200.

393 24. Hara H., Schwarz RS., Transcatheter aortic valve implantation in high-risk patients with
394 severe aortic stenosis. *Circulation Journal* 2010 Aug;74(8):1513-7. Epub 2010 Jul 17.

395 **Tables and Figure Legends**

396 **Table 1.** Clinical data of patients with TAVI procedure at Giessen University.

Patient characteristics	Total N=22	Transapical N=15	Transfemoral N=7
Age, year	81 (±7)	81(±6)	84 (±3)
BMI (kg/m ²)	26,6		
Gender, M/F	10/12	8/7	2/5
Creatinine (mg/dl)	1,1	1,11	1,08
Renal Failure (n)	8	6	2
Diabetes Mellitus (n)	3	3	0
Hyperlipidemia (n)	9	9	3
Hypertension (n)	16	13	3
Smokers (n)	9	7	2
NYHA > III (n)	8	6	2
Coronary Artery Disease Pt (n)	15	12	3
Atrial Fibrillation (n)	6	5	1
Pacemaker (n) post-op	2	1	1
LVEF < %35 (n)	4	3	1
Aortic Annulus, mm	22,23	22,59	21,13

397

398

399 **Table 2.** Data on TAVI procedures performed at Giessen University.

Procedural data	Total N=22	Transapical N=15	Transfemoral N=7
Contrast agent	124,71	122,67	140
X-ray time (min.)	9,96	9,96	17,55
X-ray area (cGy/cm ²)	8011,76	8011,76	10000
Time (min.)	100,12	100,12	112

