Evaluation of heart valve prosthesis implantations, infections and related extrapolated costs.

Claudia Schrimpf[1], Miriam Schaper[1], Julia Umminger[1], Saad Rustum[1], Christian Kuehn[1], Michaela Wilhelmi[2], Axel Haverich[1] and Mathias Wilhelmi[1,3*]

[1]Department of Cardiothoracic, Transplantation, and Vascular Surgery, Hannover Medical School, Hannover, Germany
[2]Department of Trauma Surgery, Hannover Medical School, Hannover, Germany
[3]Center of Competence for Cardiovascular Implants, Hannover Medical School, Hannover, Germany

Abstract

Background: Prosthetic heart valve implantations are standard in cardiac surgery. Transcatheter procedures gained popularity within the last decade for multi-morbid patients. However, approximately 5% of implants develop infections, causing a life-threatening event. We aimed to analyze if procedure-codes suffice to link implantation and infection, to dissect the impact of transcatheter valve implantations on infections and to calculate the financial burden valve infections cause.

Methods: Nationwide data on heart valve implantations and infections between 2005 and 2012 were acquired through operation procedure and disease related ICD-10-GM codes. One-way ANOVA analyzed infection prevalence in dependency from age. Contingency testing for consecutive years compared infected and non-infected implants. Pearson correlation of infections and 1) transcatheter 2) conventional and 3) minimal invasive valve implantations was performed. We analyzed costs for valve infections in our own institution in 2012 and extrapolated those nationwide.

Results: Age (p<0.001) was a predictor for implantations (n=100,681), infections (n=3,224) and infections/implantations (p<0.05). Most cases could be observed in patients >65 years. Transcatheter procedures (p=0.007; r=0.851) and minimal invasive procedures in the elderly (p=0.009; r=0.836) were associated to infections. Surgical implantation was negatively correlated (p<0.0001; r=-0.9847). In 2012 we could identify 33,396.00€ as average treatment costs of an infected prosthesis at our institution, causing costs of 16,898,376.00€ nationwide.

Conclusion: Prosthetic heart valve infections burden the health care system with over 16 million €/year. Transcatheter valve implantations were associated with infections, while conventional surgery showed negative correlation. Until now, it remains unclear if transcatheter methods will hold up to conventional results.

Keywords: Infection, heart valve surgery, heart valve transapical, health economics.

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Introduction

Prosthetic heart valve implantations represent a standard procedure to treat heart valve diseases otherwise leading to decompensated heart failure or even death [1-5]. Although the classical open surgical procedure (i.e. valve replacement (VR)) belongs to the standard of care, minimally invasive methods such as transapical and transcatheter valve replacements (TVR) have gained popularity [5,6], especially for patients with multiple comorbidities and high surgical risk [7].

The incidence of surgical prosthetic valve endocarditis (PVE) has been reported with 0.3% to 1.2% /patient year [8]. Older reports show that 1% of implants develop a PVE within the first year after surgery [9] and approximately 3% within 5 years [9]. For transcatheter procedures information is inconsistent. Some groups report an infection incidence of 3.1% within the first year which is higher than for surgical implanted valves [10] others report an incidence of only 0.5% [11]. In transcatheter aortic valve replacements (TAVR) the majority of infections occur within the first year of implantation [12].

So far it remains unclear if transcatheter valve replacement reduces or increases the risk of PVE. To make matters worse unspecific symptoms often result in late diagnosis, leading to complex medical treatment [7,9], and increasing mortality [8].

We aimed to analyze the relation of conventional and transcatheter valve replacements to infections through analysis of nationwide datasets (i.e. OPS and ICD-10 GM codes; 2005-2012). Furthermore, we collected data from our institution to calculate heart valve prosthesis related infection rates and to extrapolate the financial burden for the German health care system.

Patients and Methods

Federal data acquisition

Federal data on prosthetic heart valve implantations were acquired by an online search for the specific German procedure classification code (OPS=operation procedure code) that is annually released by the German Institute for Medical Documentation and Information (DIMDI) (Table 1). Data on prosthetic heart valve infections were collected from the German modification of the latest version of the "International Statistical Classification of Diseases and Related Health Problems (ICD-10-GM)", The federal statistical office was contacted and provided data on total numbers and age distribution, assigned to the corresponding OPS and ICD-10-GM codes from 2005 to 2012.

Retrospective analysis of patient data at a primary care institution

Data from patients who underwent prosthetic heart valve implantation as well as those who were diagnosed with a PVE at a tertiary care university hospital in 2012 were retrospectively collected after approval of the local ethics committee, (approval number: 2585-2015) who waived patient´s consent. All files were analyzed for implant infection and causative germ. Cases without clear identification of the infected implant were excluded. Information on total costs per case (Euro) was accounted to the implant infection by identifying "diagnosis related group (DRG) codes". Re-admission to the hospital for treatment of the implant infection lead to summary of costs, the infection was counted only once.

Statistical analyses

Statistical analysis of heart valve implantations and their infections with regard to age group were analyzed using one-way ANOVA, followed by Bonferroni's comparison of groups (graph pad Prism, San Diego California, USA). For consecutive years and for 2005 vs. 2012 the number of implantations and the number of infected and non-infected implants were quantified and compared by Chi^2-test (Yates correction). We assumed that infection and implantation occurred in the same year.

Pearson correlation between overall implant-infections and *1. minimally invasive operations (OPS 5-35a),* 2. all clearly transcatheter coded procedures and 3.subgroup correlation between OPS 5-35a and infections in patients ≥65 years was performed. In consequence we performed the adverse correlation linking conventional procedures to infections.

To estimate the burden for the German Health care system an extrapolation of "heart valve prosthesis infection" related costs was performed based on data acquired at a tertiary care hospital for 2012. The mean of these costs was multiplied by the total number of patients coded with this specific ICD-10-GM nationwide. Analyses were performed according to advice of the department for statistics and biometrics at the university hospital.

Limitations

As no federal data exists on year of infection and corresponding year of implantation all calculations were performed assuming that infections occurred in the same year as implantations.

Table 1*: OPS codes for implantations of heart valve prostheses.*

5-351	**Replacement of a heart valve by prosthesis**
5-351.04	Aortic valve
5-351.14	Mitral valve, open replacement
5-351.24	Mitral valve, thoracoscopic
5-351.34	Pulmonary valve
5-351.44	Tricuspid valve
5-351.xx	others
5-351.y	Not otherwise specified (NOS)
5-352	**Exchange of Heart valve prostheses**
5-352.00	Aortic valve
5-352.10	Mitral valve
5-352.20	Pulmonary valve
5-352.30	Tricuspid valve
5-352.y	NOS
5-354	**Other Operations on heart valves**
5-354.08	Implantation valve bearing vascular prosthesis, mechanical
5-354.09	Implantation valve bearing vascular prosthesis, biological
5-354.0a	Aortic root reconstruction with Implantation of a vascular prosthesis (David operation)
5-354.0b	Aortic root reconstruction with implantation of a vascular prosthesis (Yacoub operation)
5-354.0x	Others
5-354.1	**Mitral valve**
5-354.1x	Others
5-354.28	Implantation valve bearing vascular prosthesis, mechanical
5-354.29	Implantation valve bearing vascular prosthesis, biological
5-354.2	**Pulmonary valve**
5-354.2x	Others
5-354.3	**Tricuspid valve**
5-354.3x	Others
5-354.x	Others
5-354.y	NOS
5-35a	**Minimally invasive operations on heart valves**
5-35a.00	Endovascular
5-35a.01	Transapical
5-35a.0	Implantation of an aortic valve replacement
5-35a.1	Endovascular implantation of a pulmonic valve replacement
5-35a.2	Endovascular mitral valve anuloplasty
	Incl.: percutaneous mitral valve anulorrhaphy with Clip
	excl.: trans arterial or trans venous mitral valve reconstruction (5-35a.40, 5-35a.41)
5-35a.3	Implantation of a mitral valve replacement
5-35a.30	Endovascular
5-35a.31	Transapical
5-35a.x	Others
5-35a.y	NOS
5-35a.5	Endovascular Tricuspid valve reconstruction
5-35a.x	Others
5-35a.y	NOS

The extrapolation of treatment costs relies on single-center data from 2012. The number of infections within this timeframe was rather low, therefore costs can only be regarded as an approximation.

Results

Identification of procedure classification codes (OPS) for prosthetic heart valves

A detailed description of all OPS codes identified for prosthetic heart valve implantations including all relevant subcodes can be found in Table1. The primary codes included replacements of a heart valve by a prosthesis (code 5-351), the exchange of a heart valve prosthesis (code 5-352), other operations on heart valves (code 5-354) and minimally invasive operations on heart valves (code 5-35a).

In total 100,681 heart valves were implanted in Germany from 2005 to 2012. This total number of implantations could be subdivided into the following procedures (codes):

5-351 replacement of a heart valve by prosthesis:
44,843 patients

5-352 exchange of heart valve prostheses:
4,074 patients

5-354 other operations on heart valves:
20,332 patients

5-35a: minimally invasive operations on heart valves:
31,432 patients

Overall, the above-mentioned codes were distributed during the observational period as following:

2005: 10,838 implantations

2006: 20,217 implantations

2007: 9,568 implantations

2009: 11,790 implantations

2010: 14,319 implantations

2011: 15,374 implantations

2012: 17,711 implantations

A detailed description of the individual code/year can be found in Table 2.

Age distribution of prosthetic heart valve implantations

Statistical analysis of implantation numbers revealed an age-related increase (p<0.0001). Figure 1a shows an overview of all prosthetic heart valve implantations between 2005 and 2012. Highest implantation numbers were recorded between 55 and 85 years (Figure 1a). A group with an absolute maximum of implantations was not visible. Subgroup analysis of elderly patients showed differences in implantation numbers (p<0.001; Figure 1a). Patients older than 90 years had less implantations than patients between 55 and 89 years. In detail we could find a statistical significant differences (p<0.001) in implantation rates in the following age-groups:

60-<65 vs. 90-<95

60-<65 vs. ≥95

65-<70 vs. 90-<95

65-<70 vs. ≥95

70-<75 vs. 90-<95

70-<75 vs. ≥95.

Age distribution of minimally invasive (5-35a) and conventional heart valve implantations (5-351; 5-352; 5-354)

Consistent with its medical indication for predominantly multi-morbid patients Figure 2a shows that minimally invasive techniques, (i.e. code 5-35a) are mostly responsible for the increase in implantation numbers seen in elderly patients (Figure 2d). The OPS code 5-35a did not exist in 2005 and increased steadily thereafter (Table 2 and Figure 2d). When 5-35a was excluded from the analysis, revealing only conventional heart valve implantations, numbers decreased in patients older than 65 years (Figure 2b). Minimally invasive techniques increased in elderly patients starting at 65 years, (maximum at 80-85 years) (Figure 2d) and most implantations within this subgroup were performed endovascular (Figure 2f). Within 5-35a approximately 90% of all codes represented minimal invasive **aortic** valve replacements (Figure 2c) through 1) transapical or 2) endovascular surgical access (Figure 2e and 2f).

ICD-10-GM code for infections of prosthetic heart valves

Only one code exists in the ICD-10-GM system (i.e. T82.6: "Infections of prosthetic heart valves"). In Germany a total number of 3,224 patients were coded with T82.6 from 2005 to 2012 (Table 2). Unfortunately, T82.6 does not provide any information on the implanting procedure.

Age distribution of total prosthetic heart valve infections according to ICD-10-GM T82.6

Age group 70-75 years showed the maximum of prosthetic heart valve infections. Age was a predictor for infection (p<0.0001; Figure 1b). Patients older than 80 years showed a reduction of overall infections (p<0.001) compared to patients between 65 and 75 years.

In total, following absolute numbers of coded prosthetic heart valve infections could be identified during the whole observational period in the corresponding age groups:

< 1year 1 infection coded 1 - < 5 years 5 infections coded

Table 2: *Distribution of OPS codes and ICD-10-GM code T82.6 between 2005 and 2012.*

Year code	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**Total all years**
5-351	8,375	7,233	6,432	5,931	4,827	4,325	3,980	3,740	44,843
5-352	460	547	468	439	522	572	501	565	4,074
5-354	2,003	2,364	2,399	2,526	2,678	2,748	2,839	2,775	20,332
5-35a	n.a.	73	269	1,608	3,763	6,674	8,414	10,631	31,432
Total	**10,838**	**10,217**	**9,568**	**10,504**	**11,790**	**14,319**	**15,734**	**17,711**	**1,00,681**
T82.6	191	287	340	376	457	521	546	506	**3224**
(%)	1.80%	2.80%	3.60%	3.60%	3.90%	3.60%	3.50%	2.90%	3.20%
Delta Δ		1.00%	0.80%	0.00%	0.30%	-0.30%	-0.10%	-0.60%	1.10%

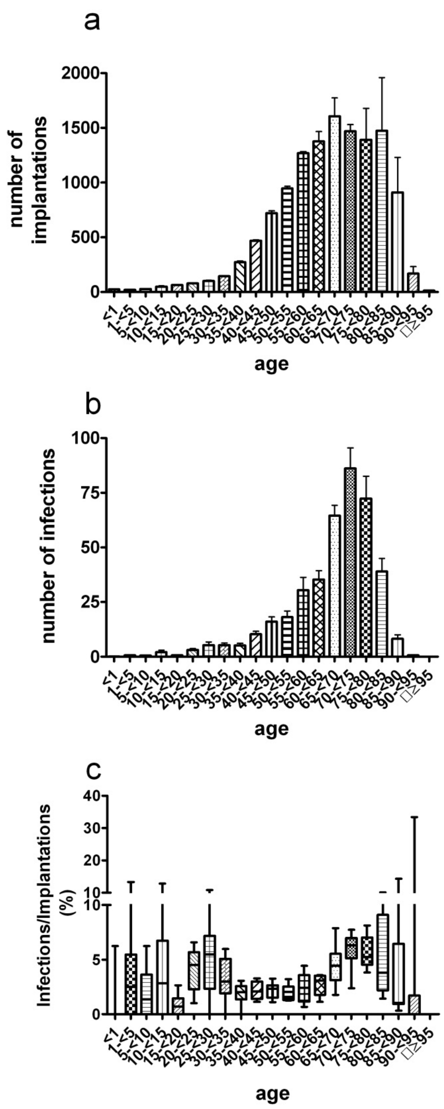

Figure 1: *Distribution of heart valve implantations (a), infections (b) and their relation (c) Age predicted valve implantations (p<0.0001) and infections (p<0.0001). Values are depicted as mean and standard error of mean. Following subgroup comparisons were significantly different (p<0.001) in implantation rates 60-<65 vs. 90-<95, 60-<65 vs. ≥95, 65-<70 vs. 90-<95, 65-<70 vs. ≥95, 70-<75 vs. 90-<95 and vs. ≥95.*
(c): Boxplot showing percentage of infections in relation to number of implantations, line within the box represents median, box represents 25th -75th percentile, whiskers represent full range of values, one way ANOVA revealed age as a predictor (p<0.05) for infection.

5-<10 years 4 infections coded 10-<15 years 17 infections coded

15-<20 years 5 infections coded 20-<25 years 25 infections coded

25-<30 years 42 infections coded 30-<35 years 37 infections coded

35-<49 years 41 infections coded 40-<45 years 82 infections coded

45-<50 years 128 infections coded 50-<55 years 145 infections coded

55-<60 years 243 infections coded 60-<65 years 283 infections coded

65-<70 years 516 infections coded 70-<75 years 689 infections coded

75-<80 years 578 infections coded 80-<85 years 312 infections coded

85-<90 years 66 infections coded 90-<95 years 5 infections coded

≥ 95 years 0 infections coded

Relation of prosthetic heart valve implantations to infections

The total number of infections per year, was divided by the number of implantations within the same year (Figure 1c). Again, age (p<0.05) was as a predictor for infection. The Mean of prostheses infections was 3.19% with a minimum of 1.8% in 2005 and a maximum of 3.9% in 2009 (Table 2). During the observational period we could identify an increase of infections of 1.1% from 2005 compared to 2012 (Table 2).

As the analysis above did not take into account whether there was an in- or decrease in regard of infections or implantations per age group and year, we looked for these specific characteristics in more detail (Figure 3). An increase of implantation numbers starting at 70 years of age could be identified (Figure 3a), while a decline could be seen in patients between 60 and 70 years. At the same time infection numbers of patients older than 70 years and of patients between 60 and 70 years increased (Figure 3b).

Independent of age and OPS code, a statistical analysis of overall heart valve prosthesis infections in relation to non-infected prostheses within each year was performed and results of consecutive years compared with each other using a Chi^2-test with Yates correction (Figure 4).

While there was an overall increase of implant-infections in 2005 vs. 2006 (code did not exist in 2005) and 2006 vs. 2007, infections declined (p=0.0015) in comparison of 2011 with 2012 (Figure 4).

Correlation of implant-infections and OPS 5-35a (minimally invasive operations including transcatheter procedures)

Methods in heart valve implantation changed during the last years, with a trend towards minimally invasive techniques. Therefore, we specifically looked at code 5.35-a between 2005 and 2012, dividing it into endovascular (i.e. transcatheter) and non-endovascular procedures according to Table 1. Codes 5-35a.00 (endovascular); 5-35a.1 (endovascular implantation of a pulmonic valve replacement); 5-35a.2 (endovascular mitral valve anuloplasty); 5-35a.30 (endovascular); 5-35a.5 (endovascular tricuspid valve reconstruction) clearly define endovascular procedures and were taken into account for subgroup analysis. Within 5-35a, endovascular procedures were responsible for 93.2% in 2006 but only for 66.3% in 2012 with a minimum of 55.7% in 2009 (Table 3 and Figure 2d).

As only one ICD-10-GM code (T82.6) for infections exists, and it is not divided into sub-codes, there are no insights regarding the amount of implant-infections due to 5-35a (minimally

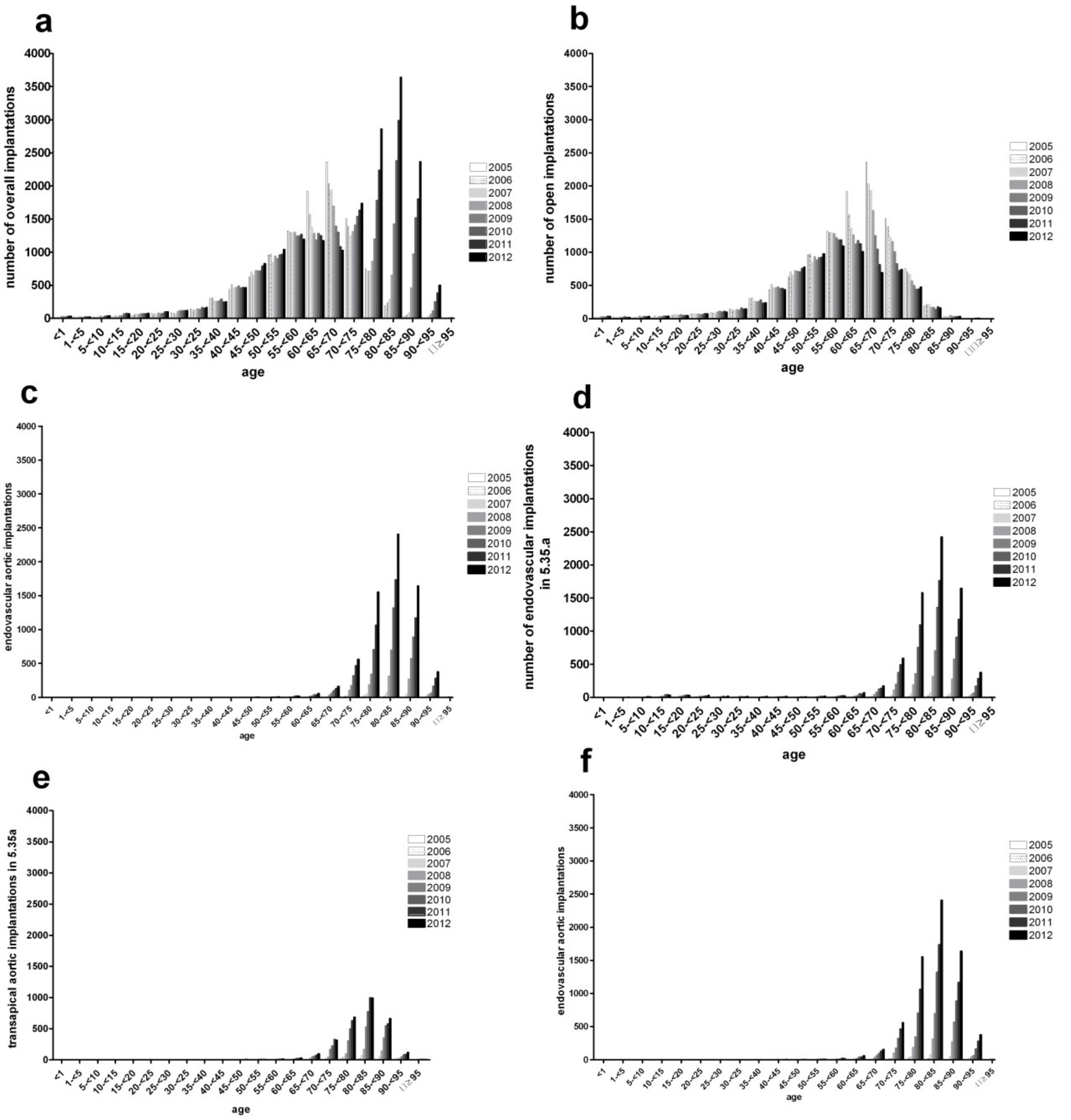

Figure 2: *Bar graph showing the distribution of all (a), conventional (open) (b), endovascular aortic (c) and all minimally invasive (d) heart valve implantations, coded as endovascular between 2005 and 2012. (e) represents transapical and (f) transcatheter aortic implantations.*

Table 3*: Percentage of endovascular procedures within OPS 5-35a.*

Years	Percentage of endovascular procedures in OPS 5-35a (minimal invasive operations on heart valves)
2005	n.a.
2006	93.20%
2007	96.70%
2008	66.10%
2009	55.70%
2010	58.80%
2011	61.50%
2012	66.30%

invasive operations on heart valves including endovascular procedures).

Figure 3b shows an increase of implant-infections at 65 years and older, similar to the increase seen in OPS 5-35a (Figure 2c,). We hypothesized that both inclinations might be connected. Correlation of number of infections and numbers in 5-35a showed a positive correlation ($p=0.004$; $r=0.876$). In older patients (>65 years) infections and code 5-35a were also positively correlated ($p=0.009$; $r=0.836$). Interestingly, correlation of infection numbers to endovascular procedures also showed a positive correlation, with a high coefficient ($p=0.007$; $r=0.851$) while conventional open surgery was negatively correlated to infection ($p<0.0001$; $r=-0,9847$) (Figure 5).

Extrapolated Costs for heart valve prostheses infections in 2012

The coding system, does not give insights into specific heart valve prosthesis infection related costs. This is rooted in the fact that each patient "produces" specific costs as a function of his/her individual comorbidities. The Case mix index accounts for this variability, so that individual treatment, besides the operation, will cause different cost. To acquire an approximation to yearly produced costs due to heart valve prosthesis infections, we did a retrospective analysis of patients who were admitted in 2012. In total, 8 patients were treated at our institution due to heart valve prosthesis infection. Total DRG proceeds for each case ranged from 11,509.94€ to 121,436.24€ with an average of 33,396.00€

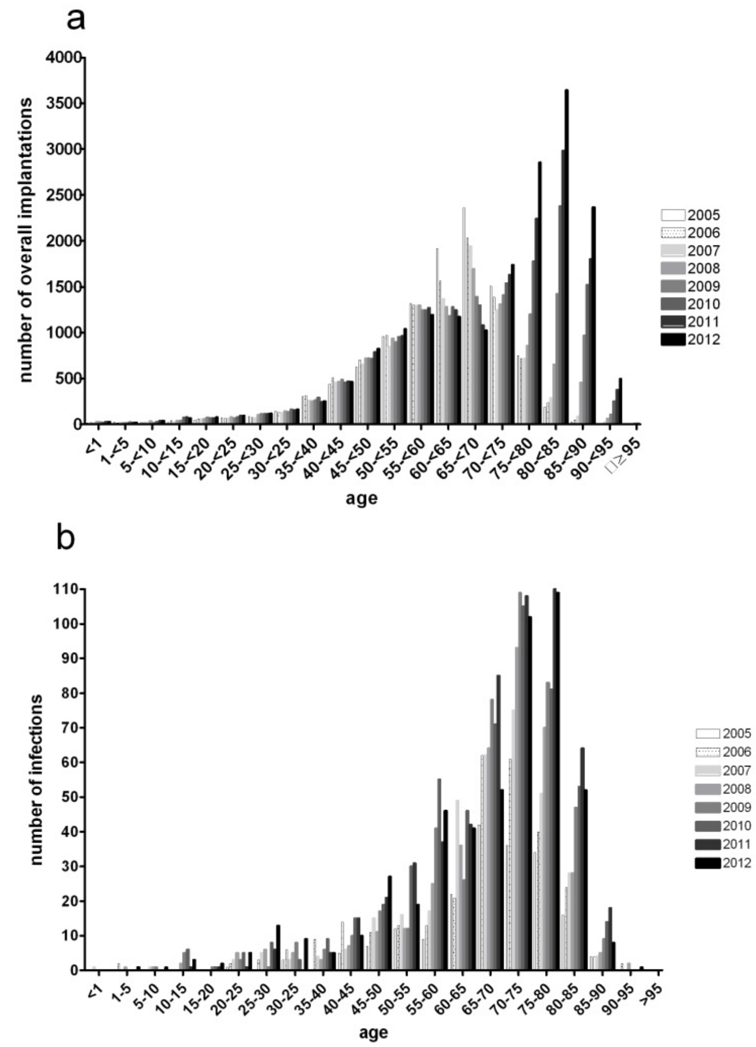

Figure 3: *(a) Bar graph of age distribution and number of implantations for each year between 2005 and 2012. Of note: implantations increased steadily in ages 70 and up. (b) shows the distribution of infections within the same timeframe in the German population.*

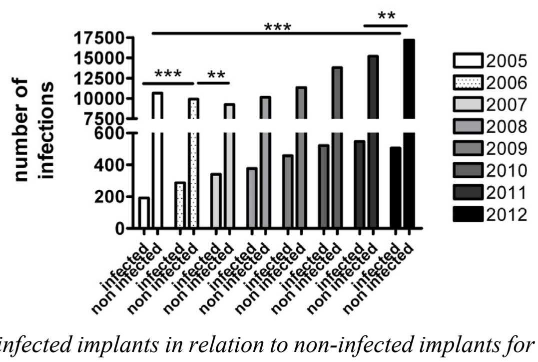

Figure 4: *Bar graph showing the number of infected implants in relation to non-infected implants for all age groups between 2005 and 2012. Chi²-test with Yates correction and two tailed p-value revealed significance for comparison of consecutive years 2005-2006, 2006-2007, 2011-2012 and 2005 vs. 2012. Asterix marks significant values: * p<0.05, **p<0.01, ***p<0.001.*

and a median of 20,923.82€. Extrapolating those proceeds to a total of 506 heart valve prosthesis infections in Germany in 2012 resulted in an average of 16,898,376.00€ (min=5,822,005.64€ to max=61,446,740.00€).

Discussion

In this study we analyzed the relation of prosthetic heart valve implantations and their infections in Germany between 2005 and 2012. We could show that although there was an increase of overall infections, the numbers have decreased between 2011 and 2012. Within the observational period we could detect a mean of infections in relation to implantations of 3.19%. This finding is in accordance to others who have reported infection rates of 3.1% within the first year [9] of implantation.

Germany is lacking compulsory federal registers on prosthetic heart valve implantations. Therefore, we had to generate federal data by asking for (i) information on total numbers of implantation and (ii) information on total numbers of

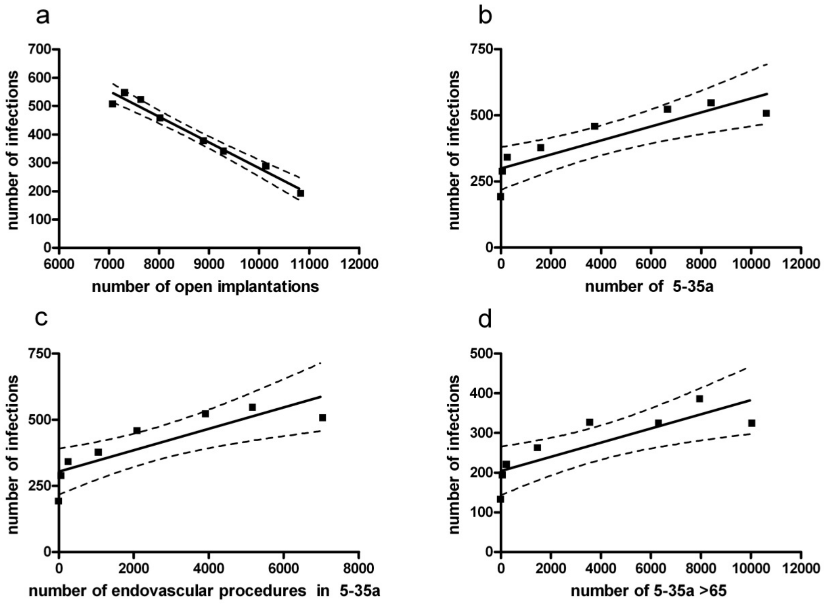

Figure 5: *(a) Pearson correlation of number of infections to number of open surgeries performed/year between 2005 and 2012. Each point represents values of the corresponding year starting at 2005. The dotted line represents the 95% confidence interval; the continuous line shows the regression line (linear regression) (p<0.0001; r=-0.9847). (b) Correlation of number of infections to total number of implantations coded as 5-35a (p=0.004; correlation coefficient r=0.876), (c) represents a correlation of total number of infections between 2005 and 2012 and total number of implantations coded clearly as endovascular/transcatheter procedure within 5-35a (p=0.007; r=0.851). (d) represents a correlation of total number of infections between 2005 and 2012 to total number of implantations coded as 5-35a but only for patients with 65 years of age and higher. The dotted line represents the 95% confidence interval; the continuous line represents the regression line (p=0.009; r=0.836).*

infections in relation to age. Our analysis showed that ICD-10-GM code T82.6 summarized infections related to a prosthetic heart valves, regardless of the type of valve or implantation technique. A subdivision into these categories is impossible so far but would be desirable for the future, so that putative causes of infections (for example the procedure itself) and a correlation to comorbidities would be possible. This could help to stratify patients before valve implantation into groups with high or low risk for infection and adapt treatment strategies in advance [13,14].

We could demonstrate that heart valve implantations and infections in elderly patients have increased. Bearing in mind that the German federal statistical office expects an increase of 33% in habitants over 65 years of age comparing 2011 to 2030 [15] this reflects a major future problem as a further increase of implantations within the elderly and a consecutive increase in infections is likely.

Transcatheter valve implantations (sub-grouped in OPS code 5-35a) are a new technique that is coded in Germany since 2006. We could demonstrate that 5-35a mainly reflects valve implantations in the elderly, and that 5-35a is correlated to implant infections. Interestingly, conventional valve implantations showed negative correlation to infection. The fact that transcatheter procedures accounted for the majority of implantations (55.7% to 96.7%) in 5-35a and were also positively associated to infections, suggests that this technique also accounts for the majority of infections seen especially when bearing in mind that open surgery showed negative correlation.

Approximately 90% of all procedures in 5-35a, were located at the aortic valve. Hence, our results may be comparable to literature concerning transcatheter aortic valve replacements. From a clinician point of view, the increase of transcatheter procedures in the elderly makes sense, as it is mainly performed on patients with multiple comorbidities and high surgical risk [5-7], for whom surgery is not an option.

Olsen et al. reported an increase of infections in patients treated with a "transcatheter valve" [10]. These results are similar to our findings were transcatheter procedures accounted for the majority of elderly patients and were positively correlated to infections. They also reported that infections mainly occur within the first year of implantation [10], so that the major limitation of our analysis (i.e. equality of infection and implantation year) corresponds well to reality. Based on the detected insufficiency in the coding system the analysis performed in this study, so far is the only approximation possible from the national data set.

The lack of a direct link between implantation procedure and infection is also caused by this insufficiency. To proof equality to surgery a compulsory federal register for transcatheter valve placement should be implemented.

An independent registry was initiated in 2009. First results were reported in 2011 [16]. A total of 697 cases were analyzed, including transapically and transaortally implanted valves. The total number for these procedures in 2009 was 3,411 cases. Hence, the registry analysis only represents 20,4%. This low inclusion rate highlights the urgent need for further federal data acquisition to acquire meaningful datasets. The German Society of Thoracic- Heart- and Vascular Surgery and the German Society of Cardiology addressed this need by initiation of "GARY" the German aortic valve registry in 2010. This registry includes valve implantations at the aortic valve regardless of implantation procedure [17]. A recent publication of this register, focused on transcatheter aortic valve replacements (TAVR) in 15,964 patients between 2011 and 2013 [18]. The huge number of patients within this study highlights the acceptance of the register; most high volume centers in Germany participate. 3,945 TAVR patients in 2011 and 5,531 patients in 2012 were included, representing 51.3% and 56.9% coded for endovascular and transapical aortic valve replacement in Germany respectively.

We found further insufficiencies from a surgeon's point of view: Open transapical replacements in 5-35a can only be encoded as 5.35a.x (Others). This code is not exclusive, analysis difficult and calculations performed from the GARY registry might underrepresent actual numbers. As GARY is not compulsory, patients declining to participate and patients treated in non-participating institutions are missing. Unfortunately the authors did not give any information about prosthetic valve endocarditis, possibly due to the insufficiency in the coding system we could detect in the here presented study. In a published 1-year follow up, no additional information on infections was given, but repeated in hospital stays for complications were approximately 6% [19]. Interestingly, Bouleti et al. could identify infectious complications as a predictive factor for early death after TAVI. Unfortunately, the study summarized all infectious complications, not only infections of the aortic valve [20].

Finally, we have extrapolated costs caused by prosthesis infections based on a single center analysis, in a high volume university hospital. We found an average of approximate 33,400€ (38,300 US$) per patient to be associated with prosthetic valve infection, with an immense range from 11,509.94€ to 121,436.24€. Based on these calculations total costs of an average of more than 16 million € (more than 19 million US$) each year burdens the German health care system. Others have looked into hospital charges for native infective endocarditis and valve surgery [21]. Although these results, from the US, are not 100% comparable as they deal with native infective endocarditis and charges for valve surgery, they found a median of 60,072 US$ per patient. In addition, Darouiche estimated an average of 50,000 US$ annual costs per patient with prosthetic heart valve infection based on market reports, data provided by medical and surgical organizations and published studies [22]. In a retrospective single center study Kuehn et al. have looked at costs caused by prosthetic valve endocarditis in patients during 2006 [23]. As far as we know, the federal statistical office was not contacted in any other work for information on T82.6. Kuehn et al. could identify approximately 72,096€ per case resulting in 28,838,400€ burden for the German health care system in 2006. For 2012 we could identify an average burden of 16,898,376€ (min. 5,822,005€ to max. 61,446,740€). Taking into account, that we, within this study, asked for the exact number of valvular prosthesis infections in Germany in 2006 (i.e. 287 cases coded T82.6) we could correct the former published estimation to 20,691,552 €. The remaining discrepancies are due to coding changes between 2006 and 2012.

Conclusion

Although prosthetic valve infections represent a rare complication, treatment is extremely expensive with expenditures of more than 16 million €/year. Infection rates have increased in the elderly during the first few years after introduction of catheter-based methods and could be positively correlated to endovascular implantation, in contrast open surgery showed a negative correlation. A compulsory register should be implemented to proof the equality of transcatheter and open surgical procedures.

We could demonstrate that predominately elderly patients are prone to infections and due to demographical changes, treatment of elderly patients will represent an ongoing and aggravating challenge in the future. The missing link of implantation procedure code to the corresponding infection code makes a stringent analysis impossible. The current coding system should be revised, subdividing the ICD-10-GM code T82.6 according to the type of implant, the anatomic implant location and procedure applied.

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References

1. Carpentier A, Chauvaud S, Fabiani JN, et al. Reconstructive surgery of mitral valve incompetence: ten-year appraisal. J Thorac Cardiovasc Surg. 1980;79:338-48.

2. Izumoto H. Aortic valve repair for aortic insufficiency in adults: a contemporary review and comparison with replacement techniques. Eur J Cardiothorac Surg. 2006;29:854.

3. Rader F, Sachdev E, Arsanjani R, et al. Left ventricular hypertrophy in valvular aortic stenosis: mechanisms and clinical implications. Am J Med. 2015;128:344-52.

4. Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012). Eur Heart J. 2012;33:2451-96.

5. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129:2440-92.

6. Volodarsky I, Shimoni S, George J. The current status of transcutaneous aortic valve implantation. Expert Rev Cardiovasc Ther. 2014;12:1205-18.

7. Doebler K, Boukamp K, Mayer ED. Indication and structures and management of transcatheter aortic valve implantation: a review of the literature. Thorac Cardiovasc Surg. 2012;60:309-18.

8. Habib G, Hoen B, Tornos P, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the

European Society of Cardiology (ESC). Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for Infection and Cancer. Eur Heart J. 2009;30:2369-413.

9. Mylonakis E, Calderwood SB. Infective endocarditis in adults. N Engl J Med. 2001;345:1318-30.
10. Olsen NT, De Backer O, Thyregod HG, et al. Prosthetic valve endocarditis after transcatheter aortic valve implantation. Circ Cardiovasc Interv. 2015;8.
11. Amat-Santos IJ, Messika-Zeitoun D, Eltchaninoff H, et al. Infective endocarditis after ranscatheter aortic valve implantation: results from a large multicenter registry. Circulation. 2015;131:1566-74.
12. Latib A, Naim C, De Bonis M, et al. TAVR-associated prosthetic valve infective endocarditis: results of a large, multicenter registry. J Am Coll Cardiol. 2014;64:2176-88.
13. Wang TK, Choi DH, Haydock D, et al. Comparison of Risk Scores for Prediction of Complications following Aortic Valve Replacement. Heart Lung Circ. 2015;24:595-601.
14. Vranken NP, Weerwind PW, Barenbrug PJ, et al. The role of patient's profile and allogeneic blood transfusion in development of post-cardiac surgery infections: a retrospective study. Interact Cardiovasc Thorac Surg. 2014;19:232-38.
15. DESTATIS. Demographischer Wandel in Deutschland. In: Deutschland sAdBudL, editor: statistische Aemter des Bundes und der Laender 2011:8-9pp.
16. Zahn R, Gerckens U, Grube E, et al. Transcatheter aortic valve implantation: first results from a multi-centre real-world registry. Eur Heart J. 2011;32:198-204.
17. Beckmann A, Hamm C, Figulla HR, et al. The German Aortic Valve Registry (GARY): a nationwide registry for patients undergoing invasive therapy for severe aortic valve stenosis. Thorac Cardiovasc Surg. 2012;60:319-25.
18. Walther T, Hamm CW, Schuler G, et al. Perioperative Results and Complications in 15,964 Transcatheter Aortic Valve Replacements: Prospective Data From the GARY Registry. J Am Coll Cardiol. 2015;65:2173-80.
19. Holzhey D, Mohr FW, Walther T, et al. Current Results of Surgical Aortic Valve Replacement: Insights From the German Aortic Valve Registry. Ann Thorac Surg. 2016;101:658-66.
20. Bouleti C, Chauvet M, Franchineau G, et al. The impact of the development of transcatheter aortic valve implantation on the management of severe aortic stenosis in high-risk patients: treatment strategies and outcome. Eur J Cardiothorac Surg. 2017;51:80-88.
21. Kemp CD, Arnaoutakis GJ, George TJ, et al. Valve surgery for infective endocarditis is associated with high hospital charges. J Heart Valve Dis. 2013;22:110-17.
22. Darouiche RO. Treatment of infections associated with surgical implants. N Engl J Med. 2004;350:1422-29.
23. Kuehn C, Graf K, Heuer W, et al. Economic implications of infections of implantable cardiac devices in a single institution. Eur J Cardiothorac Surg. 2010;37:875-79.

[*]Correspondence to
Prof. Dr. med. Mathias Wilhelmi
Department of Cardiothoracic, Transplantation and Vascular Surgery
Division of Vascular- and Endovascular Surgery, Hannover Medical School
Carl-Neuberg-Strasse 1
30625 Hannover, Germany
Tel: +49-511-532-6592
Fax: +49- 511-532-5404
E-mail: Wilhelmi.Mathias@mh-hannover.de