Research Article

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Complications and associated healthcare costs of transvenous cardiac pacemakers in Germany

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Aim: This study evaluated the occurrence and associated costs of pacemaker complications in Germany from 2010 to 2013. **Patients & methods:** Patients with a *de novo* or replacement implantation of a single or dual chamber pacemaker between 2010 and 2013 were followed for 12 months post-implant using German health insurance claims data. A case–control analysis was performed using propensity score matching to estimate the costs of complications. **Results:** Out of 12,922 implanted patients, 12.0% had a complication in the year following the implant. Complications related to lead and pocket were found in 10.2% of all implanted patients; infections occurred in 1.7% patients. Healthcare costs up to 36 months post complication were on average €4627 higher than for pacemaker patients without a complication. **Conclusion:** Pacemaker complications are common and represent a burden for patients and healthcare systems generating substantial costs. Most of the pacemaker complications involved the pacing lead or pacemaker pocket.

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Bradycardia, defined as an abnormally slow heartbeat, occurs when there is improper conduction of electrical impulses from the atria to the ventricles or sinus node dysfunction [1]. Associated symptoms include fatigue, dizziness, confusion, syncope, angina and palpitations. If untreated, symptomatic bradycardia results in impaired functioning and poor health-related quality of life [2].

Permanent cardiac pacing is the only effective treatment for symptomatic and non-reversible bradycardia [1]. Pacemakers are being used with increasing frequency with an estimated 1 million patients implanted worldwide per year [3]. Conventional pacemakers consist of a generator typically implanted in a subcutaneous pocket in the chest wall, and one or two leads threaded through the subclavian or cephalic vein into the heart. Despite being an established and frequently used therapy, the benefits of pacing therapy are limited by complications. Most pacemaker complications are acute, procedural events that occur at the time of implant or peri-operatively such as pneumothorax, hematoma, tamponade or cardiac injuries. However, other complications such as pocket and lead infections, lead fracture, lead dislodgement, lead or device malfunctions and upper extremity deep venous thrombosis can happen multiple time over the lifespan of a device [4–8].

The rates of pacemaker complications vary in the published literature. Two recent large real-world studies have shown that pacemaker complications are still common. The Dutch study FOLLOWPACE, a large study (1517 patients) with an average follow-up of 5.8 years, reported a complication rate of 12.4% at 2 months and 9.2% thereafter for new implants [5]. In the Danish pacemaker registry the rate of complications was 8.4% at 6 months (4189 patients). The Danish pacemaker registry includes all device implants and replacements for single- and dual-chamber pacemaker patients in Denmark [6].

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Many of these complications are inherent to the design of the device, and are particularly related to the leads and pocket. The leads are the most vulnerable component of the system, as they can fracture, develop insulation defects, connector issues or become infected [9,10]. In addition, certain comorbidities such as renal disease and malignancies are recognized risk factors for a device complication [11]. Patients with end-stage renal disease or patients receiving chemotherapy will for example be subject to the use of indwelling dialysis catheters. The combination of impaired immunity coupled with the need for repeat intravascular access is likely to lead to a significantly elevated risk of device infection as has been reasoned in various studies regarding renal dysfunction [12–15].

The economic burden of pacemaker complications is not well known, but longer hospital stays, use of intensive care unit and higher mortality are likely to pose a substantial burden [7]. Complications may result in multiple hospital admissions and surgical procedures for a patient. Infections, for example, are among the most serious complications and most expensive to treat as they generally involve a system extraction, re-implantation and long stay in hospital, as well as sometimes a stay in the intensive care unit [16–18]. Patients with an infection from a cardiac device are five times more likely to die during a hospital admission than comparable patients without infection and their mortality is still twice as high in the long term [19]. The objective of this study was therefore to study pacemaker complications and their associated costs in the German healthcare system.

Methods

Data source

Health insurance is mandatory in Germany, roughly 90% of the population in Germany are members of Statutory Health Insurances. There were 110 different statutory health insurances in 2018. Residents can choose the type of insurance (statutory or private) once they surpass a certain yearly income (59,400 Euros in 2018).

In order to be reimbursed, healthcare providers submit claims to the Statutory Health Insurances. Statutory Health Insurances track the healthcare resource utilization and costs of services of all insured people. A part of the data can be accessed for research purposes. The research database used for this analysis comprises healthcare claims data from up to 75 different health insurances (corresponding to approximately two-thirds of the overall number of health insurances in Germany). The dataset is a sample from approximately 3 million people, representing almost 4% of the nationwide population. Individuals in the database can be followed for a maximum period of 6 years. To obtain a representative sample of the German population, the dataset has been adjusted for age and gender. Moreover, the research database has proven to have good external validity to the German population in terms of morbidity, mortality and drug use [20].

Healthcare claims result from combining certain diagnosis codes with procedure codes. The claims data include the ICD-10-GM (International Statistical Classification of Diseases and Related Health Problems, 10th revision, German Modification) codes for the classification of diseases, the German version of the International Classification of Procedures in Medicine codes (OPS). When diagnosis and procedure codes are combined, they are mapped into a final code which determines the final reimbursement. In the inpatient setting these codes are called German Diagnosis Related Groups (G-DRG), in the outpatient setting these codes result from the Einheitlicher Bewertungsmassstab (EBM). Similarly, there are codes for outpatient drugs prescribed (German national drug codes, ATC codes).

Total healthcare costs include inpatient care (hospitalization), outpatient care, prescribed pharmaceuticals (outpatient setting), sick leave pay (salary replacement after 42 days of absence), remedies and medical aids (such as shoe inserts, walkers). Data were available for 6 consecutive years, from 2009 to 2014 and allowed to track patients based on a unique patient identifier.

Study population

Patients included in the analysis had a record of a *de novo* pacemaker implant (single or dual chamber) or replacement during 2010–2013 (OPS codes 5–377* for *de novo* implantations and 5–378* for replacements). A sub-analysis of single versus dual chamber pacemaker patients was not performed due to sample size constraints.

Data were extracted for 12 months prior to implant to ensure comparability pre-implant for a case–controlled cost analysis. Patients without continuous insurance coverage 1 year prior to implantation were excluded from the analysis. All patients had a minimum of 1-year follow-up time after the implant.

The total available follow-up time per patient depended on the year of the pacemaker implant/replacement. Up to 36 months follow-up time was available for patients implanted in 2010 and 2011 while patients implanted in

2013 had only 1 year of follow-up. These different follow-up time allowed to include the maximum number of patients in the analysis.

The average follow-up time was 1.66 years per patient. Complications were analyzed over a follow-up time of 12 months after the pacemaker implant. While 12 months is an arbitrary term as complications may occur later as well it allowed to maximize the sample of patients analyzed. It furthermore reduces mortality bias. Selection bias due to mortality is a well-recognized issue in medical research. In this study, complication rates are likely to be underestimated if based on survivors as patients with comorbidities are at higher risk of pacemaker complications and at the same time at higher risk of death [11,21,22]. Mortality data were not available in the dataset and it was therefore not feasible to adjust for it.

In contrast, the maximum follow-up available was used to estimate the healthcare costs of these complications to account for the total costs for the healthcare system. Healthcare costs of complications could arise over a longer time period than 12 months depending on how severe the complication was. Infections, for example, have been shown to lead to higher morbidity and thus would have an impact beyond 1 year [16].

Definition of complications

De novo implants versus replacements

For *de novo* implants, complications were considered related to the device if they occurred within 365 days of the implantation. In case of a replacement, coding does not allow to discern whether a patient underwent a replacement procedure in response to a complication or if the complication arose because of the replacement procedure. If a complication was coded when a device was replaced, it was assumed that the replacement was performed to treat a complication. To avoid double counting, complications were only counted if they occurred after the index device replacement stay.

Complication coding

ICD-10 diagnosis codes were used to identify pacemaker complications in the database. A list of pacemaker complications was defined based on complications reported in published clinical studies of pacemaker patients. Diagnosis codes were found for all clinical pacemaker complications (Supplementary Table 1). However, not all complications reported in clinical studies could be found in the database. Claims data are likely to be not as detailed in terms of complication reporting as clinical studies. Claims are coded for reimbursement purposes and thus generally focus on major procedures or severe events which impact the final reimbursed costs. Moreover, the wording of some diagnosis codes is rather general, for example 'other infection' and 'other complications'. To be relevant to our analysis, these codes were only considered if associated to a procedure code for an initial implantation, a replacement or revision of a pacemaker.

The following complication codes were found in the database:

- Mechanical complications caused by an electronic cardiac device (T82.1);
- Other complications (T82.8), coded in combination with a procedure code for a device implant or replacement OPS 5–377* or OPS 5–378*;
- Infection or inflammatory reaction through a device, implants or transplants in the heart and in the vessels (T82.7);
- Other infections (e.g., endocarditis: I33; or pericarditis: I30), coded in combination with a procedure code for a device implant or replacement (OPS 5–377* or OPS 5–378*).

A mechanical complication caused by an electronic cardiac device generally refers to a lead or pocket complication such as lead dislodgments, dislocations, displacements, fractures, insulation breaches. However, which of these complications occurred cannot be tracked in a claims database analysis.

Statistical analysis

The objectives were to estimate the incidence of pacemaker-related complications and associated healthcare costs. A case–controlled analysis was performed to compare incremental costs for patients with and without a complication using a Propensity Score Matching (PSM) methodology. The date of pacemaker implant or replacement served as the index date for this analysis. Covariates considered for matching included age, sex, procedure type and date, type of device, comorbidities and pre-implant costs.

Table 1. Complications in pacemaker implantations between 2010 and 2013.

	All patients (%)	*De novo* (%)	Replacement (%)
Number of patients	12,922	9339	3583
Complication	1549 (12.0)	1075 (11.5)	474 (13.2)
– Infection	223 (1.7)	150 (1.6)	73 (2.0)
– Mechanical complication or other complications	1326 (10.3)	925 (9.9)	401 (11.2)
Complications requiring a device removal	341 (2.6)	253 (2.7)	88 (2.5)

For the cost data analysis, a payer perspective was taken, in other words, amounts reimbursed by payers to healthcare providers. Depending on available follow-up years, cost data were analyzed up to 3-years from the date when the complication occurred.

Three types of statistical tests were employed. T-tests were used for calculating differences in means. Fisher's exact test was used for analysis of contingency tables. Binomial tests were used for dichotomous data. Data were stored and analyzed using Microsoft Office Excel® 2014 (Microsoft Corporation, WA, USA) and SAS® (Version 9.4; SAS Institute Inc., NC, USA).

To estimate incremental costs, pacemaker patients with a complication were matched to patients who did not experience a complication during the follow-up time. The rational of matching was to balance potential confounding variables between the two groups. The matching technique used was a kernel matching with an Epanechnikov function. Kernel matching is a non-parametric matching estimator that uses weighted averages of all individuals in the control group to construct the counterfactual outcome. Using a weighted average instead of matching individual patients generally results in a lower variance. Weights depend on the distance between patients in the two groups. Paired patients had their index event in the same year and the same duration of follow-up. The defined covariates for the matching were set as follows: Age, sex, *de novo* or replacement implantation, ambulatory or in-hospital implantation, mean costs measured over the 12 months period prior to device implant and comorbidities.

Results

Complication rates

Between 2010 and 2013, 12,922 patients received a pacemaker implantation (9339 *de novo* implants and 3583 replacements) (Table 1). The number of implants included in this study is estimated to represent 3.1% (12,900) of the total number of pacemakers implanted in Germany in the period 2010 to 2013 (415,000).

Complications occurred in 12.0% of patients during a follow-up of 1 year (1549 patients). Complication rates were similar for *de novo* and replacement procedures. (13.2%, 474/3583 patients for replacement procedures and (11.5%, 1075/9339 patients in *de novo* implants). Mechanical complications were found in 10.2% of all implanted patients (1321/12,922); infections occurred in 1.7% (223/12,922) of patient, including 1.6% (150/9339) patients in *de novo* implants and 2.1% (75/3,583) patients for replacement procedures. Mechanical complications and infections accounted for 99.7% of complications in our study. 22% of complications required a device removal (341/1549 patients). Out of the 223 patients with an infection, 32.3% of patients (72/223) had the device removed.

Costs of complications: case–control analysis

Out of 11,373 patients without complications, 8313 had 3 years follow-up time after the implant and were included in the pool of patients for the matching analysis. Pre-matching, patients with complications were more likely to have renal disease malignancies, chronic obstructive pulmonary disease (COPD), or be on oral anticoagulant therapy (Supplementary Table 2). Through PSM methodology, complication and control groups of equal size (1287 patients each) were created.

From the initial cohort of patient with complications, 262 patients with a complication could not be matched to a patient without complication. Postmatching, characteristics of the two matched groups were well balanced (Supplementary Table 3).

Healthcare utilization was higher in patients with complications compared with the matched control group (Table 2). On average, patients with complications had 1.4 hospitalisations per year compared with 0.89 in the control group ($p < 0.0001$) and the hospitalizations was nearly twice as long as patients without complications

Table 2. Average annual healthcare utilization.

	Control group	With complications	Complications without device removal	Complications with device removal
Inpatient stays	0.9 (95% CI:0.8–1.0)	1.4 ($p < 0.0001$) (95% CI:1.3–1.5)	1.2 ($p < 0.0001$) (95% CI:1.1–1.3)	2.1 ($p < 0.0001$) (95% CI:2.0–2.3)
Length of stay (days)	7.7 (95% CI:6.8–8.6)	14.0 ($p < 0.0001$) (95% CI: 12.7–15.4)	12.0 ($p < 0.0001$) (95% CI:10.7–13.4)	21.2 ($p < 0.0001$) (95% CI:17.0–25.3)
Outpatient visits	34.2 (95% CI:32.9–35.5)	39.2 ($p < 0.0001$) (95% CI:37.9–40.5)	39.5 ($p < 0.0001$) (95% CI:38.0–41.0)	38.2 ($p = 0.1$) (95% CI:35.3–41.0)

Table 3. Average healthcare expenditure with up to 36 months follow-up.

	Control group	With complications	Difference in total costs [95% CI]	p-value
12 months	n = 936	n = 936		
Inpatient	€ 7249 (65.5%)	€ 10,550 (72.3%)		
Outpatient	€ 976 (8.8%)	€ 1091 (7.5%)		
Drugs	€ 1184 (10.7%)	€ 1134 (7.8%)		
Remedies	€ 1627 (14.7%)	€ 1777 (12.2%)		
Aids and sick pay	€ 25 (0.2%)	€ 28 (0.2%)		
Total	€ 11,060	€ 14,579	€ 3519 [2375–4663]	$p < 0.0001$
24 months	n = 604	n = 604		
Inpatient	€ 9184 (54.5%)	€ 12,676 (63.4%)		
Outpatient	€ 2016 (12.0%)	€ 1980 (9.9%)		
Drugs	€ 2418 (14.3%)	€ 2419 (12.1%)		
Remedies	€ 3214 (19.1%)	€ 2822 (14.1%)		
Aids and sick pay	€ 20 (0.1%)	€ 112 (0.6%)		
Total	€ 16,852	€ 20,009	€ 3157 [1257–5057]	$p = 0.001$
36 months	n = 311	n = 311		
Inpatient	€ 12,174 (54.7%)	€ 16,125 (60.0%)		
Outpatient	€ 2482 (11.1%)	€ 2877 (10.7%)		
Drugs	€ 2989 (13.4%)	€ 3490 (13.0%)		
Remedies	€ 4550 (20.4%)	€ 4052 (15.1%)		
Aids and sick pay	€ 59 (0.3%)	€ 335 (1.2%)		
Total	€ 22,253	€ 26,880	€ 4627 [1017–8236]	$p = 0.01$

(14.0 days vs 7.7 days; $p < 0.0001$). Patients with a device removal had a higher number of hospital stays (2.1 per year) with longer length of stay (21.1 days). Patients with complications also incurred more outpatient visits per year compared with matched patients (39.2 vs 34.2; $p < 0.0001$).

Expenditure in the 12 months following the complication were on average €3519 higher than for patients in the control group (95% confidence interval [CI]: 2375–4663; $p < 0.0001$). For patients with a device removal, the difference in costs was €10,371 (95% CI: 7414–13,328; $p < 0.0001$). When considering 36 months post complication, the difference in healthcare expenditure was €4627 (95% CI: 1017–8236; $p = 0.01$), and €10,684 for patients with device removal (95% CI: 3197–18,170; $p = 0.006$). Inpatient costs represented the highest part of healthcare expenditure. The different components of the total healthcare expenditures are reported in Table 3, as well as Figures 1 and 2.

Discussion

The results from this large retrospective analysis of the German claims database reveal a 12% rate of pacemaker complications during a follow-up of 1 year. As claims data are likely to underreport clinical complications since coding is often based on reimbursement, the rate of 12% can be considered as an estimate of more severe complications. This is evident from the fact that not all pacemaker complications reported in clinical trials are visible in the claims dataset.

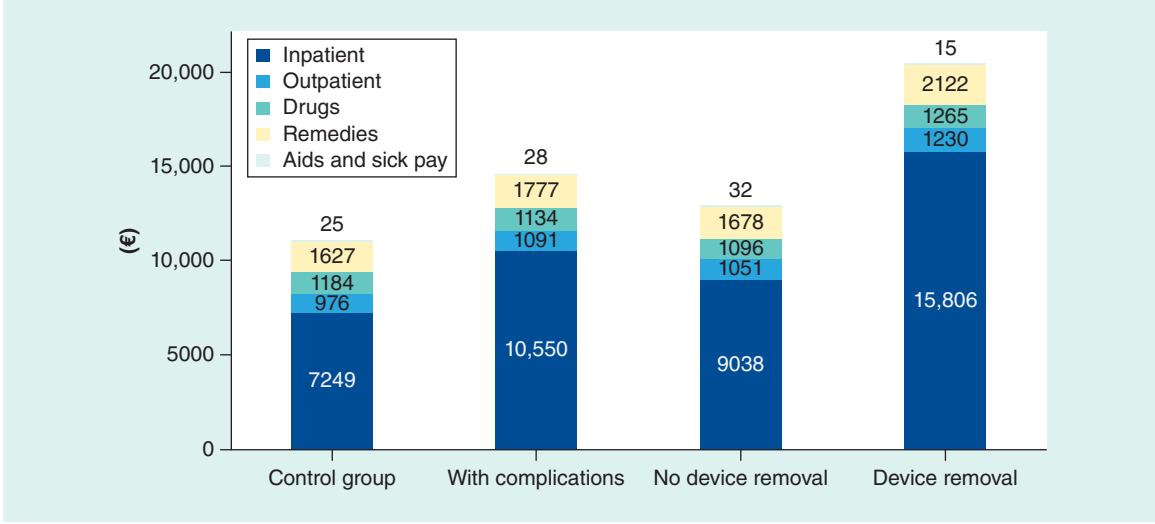

Figure 1. Average healthcare expenditures through 12 months follow-up.

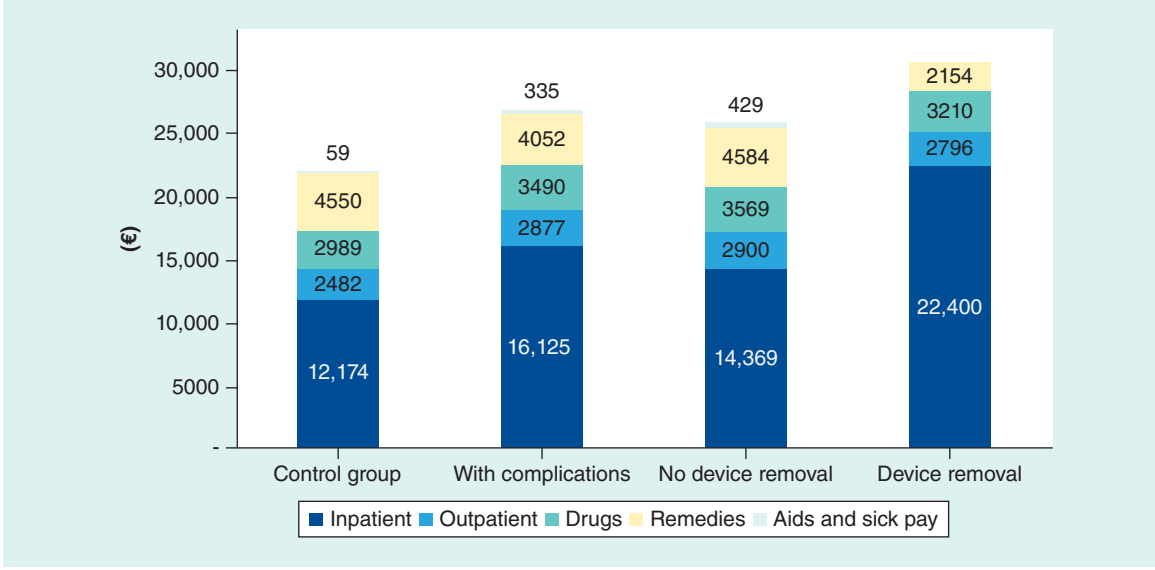

Figure 2. Average healthcare expenditures through 36 months follow-up.

The results confirm that although pacemakers are an established therapy with proven benefits, the rate of complications remains high. This is consistent with the results of large recent pacemaker studies. In the Dutch study FOLLOWPACE, the complication rate was 12.4% at 2 months, and 9.2% after a mean follow-up of 5.8 years. In the Danish pacemaker registry, the complication rate was 8.4% at 6 months [5,6]. In FOLLOWPACE, lead related complications were common as well which is in line with this study revealing a mechanical complications rate of 10.2%. The results are also in line with a recent large US healthcare claims data analysis. Among 72,701 implantations, the acute rate of complication (up to 1 months follow-up) was 7.7% of single- and 9.1% in dual-chamber pacemakers and long-term complications (1–36 months) were 6.4 and 5.9%, respectively [23].

Complications are a burden both for patients and healthcare systems with significant morbidity and mortality risks. As permanent cardiac pacing is the only effective treatment for symptomatic and nonreversible bradycardia, technological advances to decrease pacemaker complications are important. To reduce lead and pocket complications, leadless pacing options have long been of interest [24–26]. Recently introduced leadless chamber pacemaker systems are delivered via a catheter through the femoral vein and implanted directly inside the right ventricle of

the heart. These devices are currently only available as single chamber system. As the new leadless pacemakers are implanted in an entirely different procedure, they are associated to different implant procedure complications. As leadless pacemakers are introduced through the femoral vein using an 18-F vascular delivery catheter, they might be associated with more vascular events. The most serious complications reported for leadless pacemakers are cardiac perforation and pericardial effusion. These complications occur with both technologies and more evidence regarding difference in severity is needed [27–29]. Limited follow-up is available for the new leadless systems and thus complications cannot be fully evaluated yet. In case–control analysis, the rates of serious complication have been shown to be lower for leadless pacemakers than for transvenous devices for a follow-up of up to 800 days [30,31]. In conclusion, by avoiding the need for a device pocket and the insertion of a pacing lead, many serious complications associated with traditional pacing systems may be eliminated.

This analysis has confirmed that patients with comorbidities such as renal disease, malignancies and COPD are more likely to have complications. Numerous studies have highlighted a higher rate of device infection for these patients [11]. The higher risk of systemic infections is likely to stem from the chronic conditions and required treatment such as dialysis or chemotherapy [12–14]. For these patients leadless pacemakers could reduce the risk of infection due to the elimination of leads. Leadless pacemakers are fully encapsulated in fibrous tissue over time, thus removing any direct contact with blood and possibly reducing the risk of long-term infections. The safety results for leadless pacemakers for patients with limited venous anatomy access or conventional pacemaker contraindication have shown promising results [32,33].

Limitations

Claims data were primarily designed to enable appropriate hospital financing and not for epidemiological purposes. Moreover, performed healthcare services and the underlying health condition of the patient are often coded to reach a certain reimbursement and not necessarily to provide a comprehensive summary of clinical actions taken. The accuracy of the data thus depends on coding practices and may differ between healthcare providers. Moreover, the costs of complications are based on the reimbursement associated to the G-DRG codes and do not reflect the actual costs of treating a specific complication. Moreover, only one device procedure is reimbursed within 30 days. Thus, if a revision or explant is needed within 30 days of an implantation or replacement, only one DRG can be charged. Consequently, the reimbursement may not cover the total costs incurred by the hospital. The costs reported in this study may therefore underestimate the actual costs.

The complication definition used may underestimate the complication rate for replacement procedures, and conversely overestimate the rate for *de novo* implants. If a complication was coded during a replacement procedure, it was not possible to identify whether the replacement was performed to treat a complication or whether the complication occurred as a result of the replacement procedure. Therefore, complications were only attributed to the replacement if they occurred after the replacement. If a complication was coded during a replacement procedure it was assumed that the replacement was the result of the complication.

Conclusion

The rate of complications was 12.0% in patients implanted with a pacemaker in Germany over a follow-up period of 1 year. Patients with a complication were more likely to have comorbidities such as renal disease, malignancies and COPD. The average cost of a complication was €3519 ($p < 0.0001$) after 1 year of follow-up and €4627 ($p = 0.01$) at 3-years follow-up; €10,371 and €10,684, respectively, at 1-year and 3-years for complications requiring a device removal. A total of 10.2% of the pacemaker complications were mechanical complications involving the lead or pocket.

Financial & competing interests disclosure

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No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: www.futuremedicine.com/doi/suppl/10.2217/cer-2018-0114

Summary points

- Study confirms that despite being an established therapy, complications in cardiac pacing are common in clinical practice.
- Incidence of complications with transvenous pacemakers was 12% overall – complications related to lead and pocket were found in 10.2% of all implanted patients; infections occurred in 1.7%.
- Healthcare costs up to 36 months post-complication were on average €4627 higher than for pacemaker patients without a complication.
- This difference in costs was mainly driven by increased hospitalization costs.
- Patients with a *de novo* or replacement implantation of a single or dual chamber pacemaker between 2010 and 2013 were followed for 12 months post-implant using German health insurance claims data.
- Propensity score matching was used to compare total healthcare costs of pacemaker patients with and without complication.
- Although pacemakers are a well-established therapy; benefits may be limited by complications following implantation, with both clinical and economic impact for the patient and the healthcare system.
- This study reinforces that strategies to prevent complications of cardiac implanted electronic devices should be a priority for healthcare providers and payers.

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