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ORIGINAL ARTICLE

National trends and differences in morbidity among surgical approaches for radical prostatectomy in Germany

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Abstract
Objective In this study, we document trends in radical prostatectomy (RP) employment in Germany during the period 2005–2012 and compare the morbidity of open (ORP), laparoscopic and robotic-assisted RP based on nationwide administrative data of Allgemeine Ortskrankenkassen (AOK) German local healthcare funds.
Materials and methods Administrative claims data of all AOK patients subjected to RP during 2005–2012 (57,156 cases) were used to evaluate the employment of minimally invasive RP (MIRP) procedures, pelvic lymph node dissection (PLND) and nerve-sparing approaches during this period. In addition, data from the most recent three-year period of our dataset (2010–2012) were used to compare the morbidity among the different surgical approaches. Study end points comprised 30-day mortality, 30-day transfusion, 1-year reintervention and 30-day adverse events, as well as 1-year overall complications.
Results A 20 % reduction in RP utilization from 2007 to 2012 was documented. ORP remained the predominant RP approach in Germany. MIRP approaches carried a lower risk of 30-day transfusions, 1-year reinterventions and 1-year overall complications than ORP when adjusting for confounding factors. PLND was associated with an increased risk of complications, while age in the highest quintile and the presence of comorbidities were independent risk factors for morbidity and mortality. Lack of pathological data was the main limitation of the study.
Conclusions RP utilization in Germany is dropping, but the use of MIRP has risen steadily during the years 2005–2012, which is expected to have a positive impact on the morbidity of the operation.

Keywords Open radical prostatectomy · Laparoscopic radical prostatectomy · Robotic assisted · Radical prostatectomy · Complications · Morbidity · Germany

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Introduction

Open (ORP), conventional laparoscopic (LRP) and robotic-assisted (RARP) radical prostatectomy (RP) represent the mainstay surgical treatment options in the management of localized and locally advanced prostate cancer (PCa). Still, the literature regarding comparative studies among these techniques is characterized by a low level of evidence due to lack of large-scale randomized trials. In addition, reported surgical outcomes are mostly derived by high-volume academic centers and as a result the actual morbidity of the respective operations at nationwide levels is largely unknown. Nationwide administrative databases such as those of insurance companies represent an important source of information that can depict the true impact of

different surgical techniques, given that the average nationwide outcomes of all performed operations over a specific period can be compared.

In this work, we used the nationwide administrative data of Allgemeine Ortskrankenkassen (AOK) German local healthcare funds. The AOK is one of the largest providers of statutory health insurance and covers roughly 30 % of the German population [1, 2]. The aim of the study was to document trends in RP utilization in the German health care system, to evaluate the overall morbidity and quality of surgery of RP in Germany and to examine differences in morbidity and mortality between ORP, LRP and RARP.

Patients and methods

Database characteristics

We used anonymized nationwide administrative claims data for inpatient episodes (including diagnoses, procedures, length of stay, transfers and discharge type) and core data (including age, sex, insurance status and survival status) of all AOK patients subjected to RP during the period 2005–2012 (based on date of discharge, 57,156 patients). In addition, we used data provided by the German Federal Statistical Office [3] to evaluate the total number of RPs in the same time period.

In the second part of the analysis, the morbidity and mortality outcomes of RPs covered by the AOK during the most recent 3-year period of our dataset (2010–2012; 20,067 patients) were used to compare the overall morbidity of ORP, LRP and RARP. For this part of the analysis, we excluded patients under the age of 40, patients without PCa as a primary diagnosis, patients who underwent salvage RP and patients with comorbid neuromuscular dysfunction of bladder, to rule out any influence of rare cases with a divergent risk of complication.

Study endpoints

The endpoints in the analysis are complications corresponding to the definitions of hospital quality indicators for RP which were developed by the Research Institute of the Local Health Care Funds (WIdO). These endpoints comprise 30-day mortality, 30-day transfusions, 1-year reinterventions and 30-day adverse events, as well as 1-year overall complications, which combine the four separate indicators. Details can be found in the WIdO report on RP quality indicators [4]. Comorbid conditions were identified using the definitions proposed by Elixhauser and colleagues, which identify 31 chronic conditions, and entered as separate variables [5].

Statistical analysis

To analyze the effect of RP approach on outcome, we used multiple logistic regression models with random intercepts for hospitals. The models were adjusted for pelvic lymph node dissection (PLND), nerve-sparing (NS) procedure, age (entered as a dummy-coded categorical variable expressing patient quintiles), antithrombotic medication prior to the operation and comorbid conditions. Model selection was done manually for each endpoint. Elixhauser categories which were not significant at the 5 % level of significance were subsequently eliminated from the respective model. Likelihood ratio tests were then performed which confirmed that removing these sets of predictors did not result in a loss in predictive power for any of the models. All analyses were performed using STATA 11.2 (StataCorp, College Station, Texas).

Results

Trends during 2005–2012 in RP in Germany

The employment of RP in Germany during the 8-year period of this study (2005–2012) accounted for 25–30,000 operations/year (Fig. 1a). Around 25 % (values from 24.8 to 26.6 %) of operated patients were covered by the AOK during the same period, and their data were available for further analysis. A notably stable rate of PLND utilization (values from 81.6 to 83.8 % of RPs) was evidenced throughout study period. In contrast, the employment of a unilateral or bilateral NS approach demonstrated a constant increase from 23.1 % of RP in 2005 to 45.3 % in 2012 (Fig. 1b). A marked change in favor of minimally invasive approaches was also noted in the same period. The employment of ORP dropped from 88.2 % of RPs in 2005 to 71.2 % in 2012. The use of laparoscopy remained relative stable accounting for 11.8–15.3 % of operations while a notable increase in robotic procedures was evident, overtaking the number of performed laparoscopic approaches in 2012 and reaching a level of 15.5 % of RP operations (Fig. 1c). Of notice, during the period 2010–2012 conventional laparoscopic approach was associated with lower employment of PLND (62.65 vs 85 % for ORP and RARP), while RARP was associated with higher employment of a NS approach (58.2 vs 42 % for both ORP and LRP) as compared with the other two techniques (Table 1).

Differences in morbidity among ORP, LRP and RARP

During study period, a higher unadjusted incidence of overall complications and risk of 1-year reintervention for ORP was documented (Table 1). Multiple regression analysis

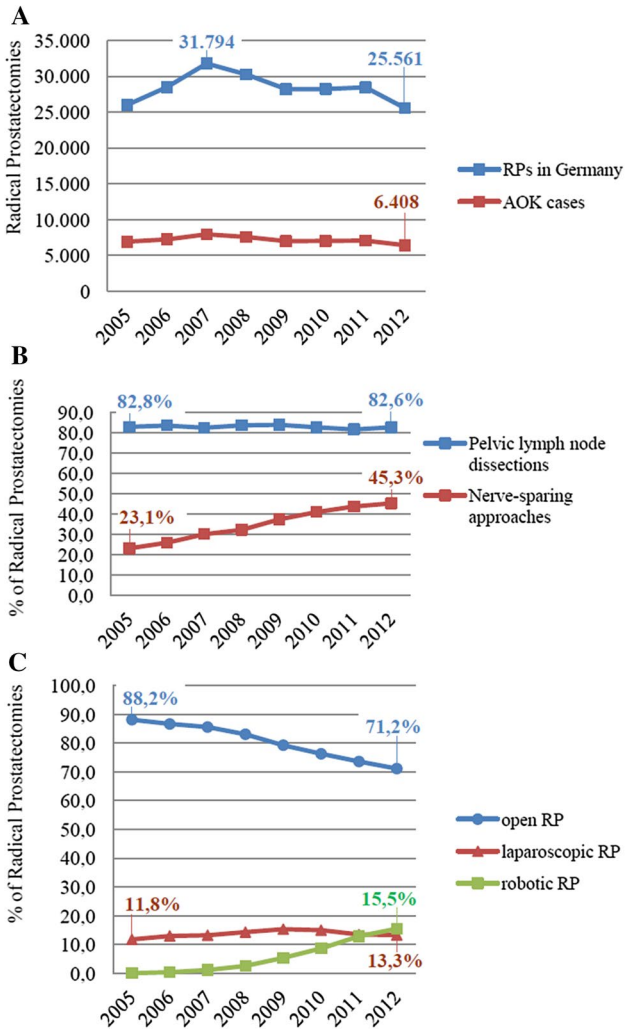

Fig. 1 **a** Number of radical prostatectomies (RPs) performed in the period 2005–2012 in Germany, based on data provided by the German Federal Statistical Office and AOK claims data, respectively. **b** Radical prostatectomies employing a pelvic lymph node dissection or a nerve-sparing (unilateral or bilateral) approach in AOK patients during the period 2005–2012. **c** Radical prostatectomies performed via an open, a laparoscopic or a robotic-assisted approach in AOK patients during the period 2005–2012

showed that both laparoscopic and robotic RP carry a significantly lower risk than open RP for 30-day transfusions, 1-year reinterventions and 1-year overall complications when adjusting for potentially confounding factors (Table 2).

Other factors affecting morbidity of RP

Apart from surgical approach, morbidity outcomes were consistently negatively influenced by PLND, which was associated with an increased risk of 30-day transfusion and 30-day adverse events as well as 1-year reintervention (Table 2). It should be stressed that the protective role of minimally invasive (MI) procedures in terms of lower morbidity was evidenced even when only patients subjected to PLND were analyzed. In this subgroup of patients, the odds ration (OR) for overall complications were 0.45 for laparoscopic and 0.42 for robotic RP. For 30-day transfusions, the OR were 0.21 (laparoscopic RP) and 0.17 (robotic RP), while for 1-year reinterventions, the OR were 0.75 (laparoscopic RP) and 0.60 (robotic RP), respectively (data not shown).

Interestingly, cases subjected to NS had a lower risk of 30-day transfusion, 1-year reintervention, 30-day adverse events and overall 1-year complications as compared with non-NS approaches (Table 2). Age effects were also largely consistent across outcomes, with higher risks of complications in higher age, particularly in the highest quintile (73–87 years). Antithrombotic medication was associated with a higher risk of 30-day transfusions and 1-year overall complications. With regard to comorbidities, findings differ according to the type of complication. The effect of selected comorbidities on RP morbidity is documented in Table 2.

Mortality in RP

During the study period 34 out of 20,067 AOK patients (0.17 %) died within 30 days of the operation. There was no significant association of 30-day mortality with RP approach, employment of PLND or use of antithrombotic medication. The only independent risk factors for mortality were age in the highest quintile (73–87 years, OR: 6.94) and the presence of comorbidities. The risk of 30-day mortality was significantly increased in the presence of coagulopathy (OR: 3.8), anemia (OR: 9.58), congestive heart failure (OR: 3.52) and pulmonary circulatory disorders (OR: 26.47) (data not shown).

Discussion

The employment of RP in Germany demonstrated a stable drop since 2007 which has led to a 20 % reduction in case volume up to 2012. The latter parallels changes in the surgical management of PCa in other European countries such as France and Sweden, where a similar decrease was noted [6, 7]. The stabilization of PCa incidence and the introduction of new guidelines addressing alternative treatment options such as active surveillance and brachytherapy have been proposed to explain this phenomenon [6, 8].

Upon introduction of RARP in Germany in 2005, an exponential increase in its utilization was evident, at the expense of open approach. In 2012, 15.5 % of RPs had been performed with robotic assistance, surpassing the laparoscopic approaches. Due to adaptation of RARP,

Table 1 Descriptive statistics, unadjusted complication rates and 1-year reintervention rates of AOK radical prostatectomy patients operated during 2010–2012

	Approach		
	Open	Laparoscopic	Robotic
Descriptive data			
Cases	14.741	2.831	2.495
Age mean (SD, range)	65.9 (6.6, 40–87)	65.5 (6.6, 41–80)	64.2 (7.1, 56–73)
Pelvic lymph node dissection % (*N*)	85.9 % (12.658)	62.6 % (1.773)	85.5 % (2.132)
Nerve-sparing procedure % (*N*)	41.8 % (6.160)	41.8 % (1.184)	58.2 % (1.451)
Complications			
30-day mortality % (*N*)	0.18 % (27)	0.21 % (6)	0.04 % (1)
30-day transfusion % (*N*)	12.36 % (1.814)	3.80 % (107)	2.57 % (64)
1-year reintervention % (*N*)	10.07 % (1.460)	7.38 % (206)	6.23 % (153)
30-day adverse events % (*N*)	5.36 % (788)	3.93 % (111)	4.58 % (114)
1-year overall complications % (*N*)	23.49 % (3.422)	13.39 % (375)	11.96 % (294)
Reinterventions (1 year)			
Ureteral stent (1 year)	1.10 %	1.18 %	1.02 %
Procedures involving the urethra (90 days)	0.94 %	0.36 %	0.20 %
Bladder neck incision (1 year)	2.85 %	0.43 %	0.45 %
Dilatation of the urethra (1 year)	0.50 %	0.04 %	0.12 %
Procedure for a lymphocele (1 year)	4.29 %	4.13 %	1.88 %
Procedure for an incisional hernia (1 year)	0.49 %	0.18 %	1.63 %
Laparotomy (30 days)	0.06 %	0.04 %	0.04 %
Placement of an enterostoma (30 days)	0.39 %	0.67 %	0.12 %
Rectal reconstruction (1 year)	0.86 %	0.93 %	1.10 %

utilization of ORP dropped by 17 % during our study period. Still, with more than 70 % of operations in 2012 performed via an open access, ORP remained the predominant surgical treatment of PCa in Germany. In contrast, according to the British Association of Urological Surgeons database, in 2011 ORP accounted for only 25.8 % of RPs in the UK with laparoscopy being the predominant approach accounting for 54.6 % of operations [9]. In Sweden, in 2008 around 40 % of RPs were performed via robotic assistance while in France in 2010 MIRP surpassed ORP employment and has remained at a higher level ever since [6, 7]. Similarly, in the USA the adaptation of MI RP was responsible for the decrease in ORP use from 89.4 % in 2003 to 52.9 % in 2007 and in 2008 MI RP procedures surpassed open approaches [10, 11]. Based on the trends depicted by our study, it is expected that the employment of RARP in Germany will keep rising, but further analysis of data from the year 2012 onward is required to estimate the level at which RARP employment may finally stabilize.

Following the introduction of robotic technology, there have been reports documenting an underutilization of PLND during periods of rapid uptake of RARP. Based on the SEER cancer registry in the US, during the period 2003–2007 the odds of undergoing a PLND were more than five times greater in men who had ORP compared with patients subjected to MIRP [12]. This phenomenon was not observed in Germany where the employment of PLND during RARP introduction remained similar to ORP rates. Still, a lower rate of PLND was evident in the laparoscopic group.

A stable increase in utilization of NS procedures accounting for a rise of more than 20 % during the period 2005–2012 was evident in our data. Stage migration of RP patients toward patients with more favorable disease allowing for a NS approach could be a potential explanation for this increase. Yet, concurrent data from Germany document the opposite. The rate of low-risk cancers subjected to RP in the Martini Clinic, a high-volume center in Germany with more than 2000 RPs per year, declined from 60 % in 2004 to 27 % in 2011–2013 [13]. Consequently, the rise in NS utilization in Germany is more likely a result of progress in overall surgical experience and operating technique as well as a result of improvements in our understanding on the effect of NS in postoperative continence, rather than an effect of PCa stage migration. It should be noted that in this study, NS operations demonstrated lower complication and reintervention rates than non-NS procedures. Whether the latter is due to differences in baseline characteristics of the two groups of patients not captured by our analysis (patients subjected to NS RP usually have low-risk cancer) or an outcome of the better preservation of the integrity of pelvic structures in NS approach warrants further investigation.

Table 2 Multivariate analysis: access-related risk of complications after radical prostatectomy and effect of pelvic lymph node dissection, nerve-sparing procedures and selective comorbidities on the morbidity of AOK patient operated during 2010–2012

	OR	95 % CI lower	95 % CI upper
Effect of access (open, laparoscopic, robotic assisted) on complications			
Transfusion (30 days)			
Approach (ref.: open)			
Laparoscopic	0.22*	0.17	0.30
Robotic	0.18*	0.13	0.25
Reintervention (1 year)			
Approach (ref.: open)			
Laparoscopic	0.69*	0.55	0.85
Robotic	0.57*	0.45	0.72
Adverse events (30 days)			
Approach (ref.: open)			
Laparoscopic	0.90	0.68	1.20
Robotic	0.94	0.71	1.26
Overall complications (1 year)			
Approach (ref.: open)			
Laparoscopic	0.45*	0.37	0.53
Robotic	0.41*	0.34	0.49
Effect of PLND and NS approach on complications			
Transfusion (30 days)			
PLND (ref.: no PLND)	1.36*	1.12	1.64
NS (ref.: no NS)	0.69*	0.61	0.79
Reintervention (1 year)			
PLND (ref.: no PLND)	1.96*	1.63	2.37
NS (ref.: no NS)	0.76*	0.68	0.85
Adverse events (30 days)			
PLND (ref.: no PLND)	1.66*	1.31	2.10
NS (ref.: no NS)	0.83*	0.71	0.97
Overall complications (1 year)			
PLND (ref.: no PLND)	1.68*	1.47	1.92
NS (ref.: no NS)	0.74*	0.67	0.80
Effect of selected comorbidities on 1-year overall complications			
Overall complications (1 year)			
Age (ref.: 40–60 years)			
61–65 years	1.18*	1.05	1.33
66–68 years	1.30*	1.15	1.48
69–72 years	1.33*	1.18	1.49
73–87 years	1.76*	1.55	2.01
Antithrombotic medication (ref: none)	1.14*	1.02	1.28
Comorbidities (ref: absent)*			
Psychoses	3.28*	1.36	7.91
Depression	1.43*	1.14	1.80
Metastatic cancer	1.32*	1.12	1.55
Coagulopathy	7.64*	6.13	9.52
Obesity	1.17*	1.01	1.34
Diabetes	1.17*	1.05	1.31
Blood loss anemia	3.03*	1.73	5.29
Neurological diseases	1.84*	1.33	2.54
COPD	1.26*	1.08	1.46
Renal failure	1.66*	1.40	1.97
Paralysis	2.65*	1.62	4.33

OR odds ratio, *CI* confidence interval, *PLND* pelvic lymph node dissection, *NS* unilateral or bilateral nerve-sparing, *COPD* chronic obstructive pulmonary disorder

* Statistically significant differences

Our analysis documented that MIRP in Germany was associated with a favorable safety profile. As depicted by the multivariate analysis, lower overall morbidity of endoscopic procedures was not only due to the well-documented lower blood loss and transfusion rates of LRP and RARP (as compared with ORP) but also due to lower rates of 1-year reinterventions observed in the MIRP groups. In particular, unadjusted analyses suggest a role of lower reintervention rates associated with urethra and bladder neck contraction in the endoscopic groups. Our outcomes are consistent with similar studies in the literature. Kowalczyk et al. [10] documented that MIRP was associated with fewer genitourinary, miscellaneous, perioperative and late complications than ORP in an analysis of all US patients over the age of 65 subjected to RP from 2003 to 2007.

Given that preoperative and postoperative oncological data are not included in medical claims records of insurance companies, risk adjustment of RP outcomes is missing from current study. Nevertheless, whether high preoperative Gleason score and PSA as well as the presence of pT3 disease represent an independent risk factor for complications remains a matter of controversy. Ward et al. [14] reported similar morbidity between pT3 and pT2 cases in a series of 5652 RPs. In contrast, Agarwal et al. [15] showed that preoperative PSA as well as high Gleason score were independent predictors of complications using a standardized report of complications in 3317 patients. As a result, it is possible that a part of the differences in morbidity between the approaches in our study may be due to differences in operated cases.

Morbidity outcomes in the RP literature are characterized by great heterogeneity given that they are significantly affected by surgical experience, hospital volume as well as from potential selection bias in the reported cases [16]. In addition, most RP literature is derived from high-volume academic centers. As a result, reported complication rates can differ from the reality of surgical morbidity in the general population. For example, weighted mean of postoperative complication rates after ORP was calculated 10.3 % in a review of outcomes reported by high-volume centers, which is nearly half from overall complication

rates calculated for ORP in our database (23.49 %) [17]. Taking the above into consideration, it can be concluded that nationwide surgeon independent databases such as the one presented in this study can depict the true morbidity of a surgical approach observed in a large treated population on a given period that physicians and patients can consult in order to make a realistic informed decision for their treatment.

Conclusions

RP utilization in Germany is dropping, but the use of MIRP (laparoscopic and robotic assisted) has risen during the years 2005–2012, which is expected to have a positive impact on the morbidity of the operation.

Author contribution Stolzenburg was involved in protocol/project development/data analysis/study supervision. Kyriazis contributed to data analysis/manuscript writing/editing. Fahlenbrach, Gilfrich, Günster, Jeschke, Popken, Weißbach, von Zastrow, Hanna Leicht were involved in data collection/data analysis/manuscript editing.

Compliance with ethical standards

Conflict of interest All authors have no conflict of interest to declare.

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