■ HIP

Re-revision and mortality rate following revision total hip arthroplasty for infection

AN UNDERESTIMATED PROBLEM

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Aims

This study compares the re-revision rate and mortality following septic and aseptic revision hip arthroplasty (rTHA) in registry data, and compares the outcomes to previously reported data.

Methods

This is an observational cohort study using data from the German Arthroplasty Registry (EPRD). A total of 17,842 rTHAs were included, and the rates and cumulative incidence of hip re-revision and mortality following septic and aseptic rTHA were analyzed with seven-year follow-up. The Kaplan-Meier estimates were used to determine the re-revision rate and cumulative probability of mortality following rTHA.

Results

The re-revision rate within one year after septic rTHA was 30%, and after seven years was 34%. The cumulative mortality within the first year after septic rTHA was 14%, and within seven years was 40%. After multiple previous hip revisions, the re-revision rate rose to over 40% in septic rTHA. The first six months were identified as the most critical period for the re-revision for septic rTHA.

Conclusion

The risk re-revision and reinfection after septic rTHA was almost four times higher, as recorded in the ERPD, when compared to previous meta-analysis. We conclude that it is currently not possible to assume the data from single studies and meta-analysis reflects the outcomes in the 'real world'. Data presented in meta-analyses and from specialist single-centre studies do not reflect the generality of outcomes as recorded in the ERPD. The highest re-revision rates and mortality are seen in the first six months postoperatively. The optimization of perioperative care through the development of a network of high-volume specialist hospitals is likely to lead to improved outcomes for patients undergoing rTHA, especially if associated with infection.

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Introduction

Despite the steadily growing number of primary total hip arthroplasties (THAs), the revision rate is not rising similarly. However, the frequency of periprosthetic joint infections (PJIs) in THA is increasing and gaining more importance.[1,2] This change in indications for revision total hip arthroplasty (rTHA) might be explained due to improvements in the bearing wear characteristics and a reduction in aseptic loosening in recent years.[3,4] The frequency and proportion of rTHA due to PJI is increasing and is between 16% and 25% according to previously reported registry data.[5-8] Moreover, rTHA secondary to infection is associated with a increased mortality compared to its aseptic revision.[9] A meta-analysis reports that reinfection rates following one- and two-stage revisions for infection are between 5.7% and 8%, respectively.[10] Even when excellent results with infection eradication of up to 100% have been reported, the re-revision rate and mortality in literature differ widely, with others reporting an eradication rate of approximately 70%.[6-8,11-15] These wide differences raise the question of whether different definitions or criteria for revision and infection eradication are being applied. Different

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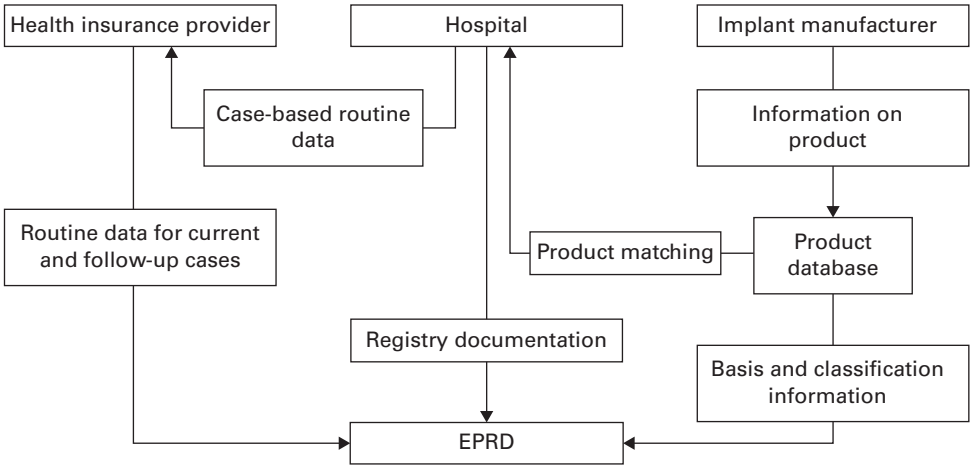

Fig. 1

The flow of data from hospitals, health insurers, and implant manufacturers to the German Arthroplasty Registry (EPRD).

Table I. Demographic characteristics of hip revisions.

Variable	First rTHA (n = 16,349)		Multiple rTHA (n = 1,493)	
	Aseptic (n = 10,406)	Septic (n = 5,943)	Aseptic (n = 530)	Septic (n = 963)
Median age, yrs (IQR)	73 (63 to 80)	74 (64 to 80)	73 (63 to 80)	72 (64 to 79)
Sex, n (%)				
Female	6,775 (65)	3,366 (57)	326 (62)	535 (56)
Male	3,631 (35)	2,577 (43)	204 (38)	428 (44)
BMI, kg/m², n (%)				
Underweight (< 18.5)	78 (1.8)	29 (1.1)	7 (1.5)	4 (0.5)
Normal (18.5 to 24.99)	1,394 (32)	572 (22)	133 (29%)	164 (21)
Pre-obese (25.0 to 29.99)	1,526 (35)	831 (32)	166 (36)	234 (30)
Obese 1 (30.0 to 34.99)	872 (20)	622 (24)	91 (20)	176 (23)
Obese 2 (35.0 to 39.99)	347 (8.0)	318 (12)	39 (8.6)	119 (15)
Obese 3 (≥ 40)	141 (3.2)	221 (8.5)	19 (4.2)	81 (10)
Unknown	6,048	3,350	75	185
Elixhauser score, n (%)				
< 0	772 (14)	458 (14)	82 (15)	124 (13)
0	2,119 (38)	805 (25)	150 (28)	167 (17)
1 to 4	548 (9.8)	341 (11)	52 (9.8)	118 (12)
5+	2,154 (39)	1,643 (51)	246 (46)	554 (58)
Unknown, n	4,183	2,696		
Recurrent PJI, %	0	26	0	27
Indications for rTHA, %				
Periprosthetic fracture	26	3.4	8.1	0.8
Loosening	25	5.7	22.6	3.1
Dislocation	24	3.8	40	5.7
Infection	0	62	0	51
Other	25	25.1	29.3	39.4

IQR, interquartile range; PJI, periprosthetic joint infection; rTHA, revision total hip arthroplasty.

national registries use varying definitions for revisions as shown by Liebs et al.[16] Moreover, single-centre retrospective cohort studies or national registries apply different criteria for the inclusion or exclusion of patients. This can lead to a systematic underestimation of the revision rate due to biased patient selection and inconsistent reporting of re-revision rates and complications by surgeons.[17] The German Arthroplasty Registry (EPRD), by contrast, obtains its data directly from the health insurance provider, so that every procedure performed in the participating clinics is evaluated directly by the registry. The registry records and accounts for approximately 70% of the annual hip arthroplasties, primary and revision, undertaken in Germany. The purpose of this study is to present re-revision and mortality rates following rTHA due to infection compared to aseptic revision in an unselected population, as recorded in the EPRD.

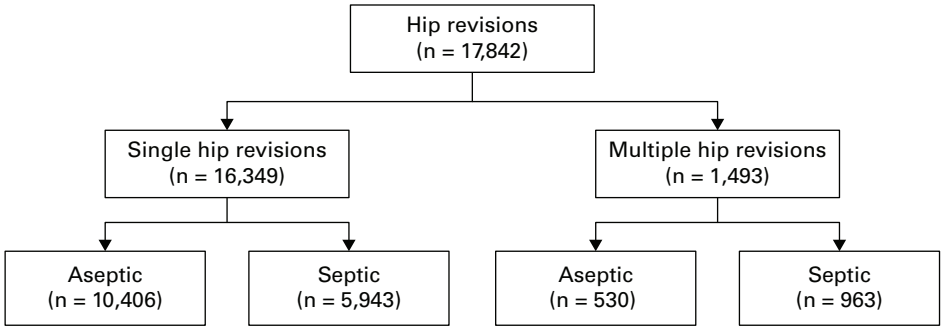

Fig. 2

Hip revision data overview of patients included in the German Arthroplasty Registry (EPRD) from 2015 until 2022.

Methods

Data source. The EPRD has collected data from almost 2.5 million hip and knee arthroplasty procedures since 2012. This dataset represents the world's third largest national registry. Data are generated by documentation of each case from the participating 747 clinics, the product database of the participating implant suppliers, and the routine data captured by the participating health insurance companies. Linking these three data sources creates a robust follow-up mechanism of the registered patients (Figure 1), regardless of whether their revision procedure is performed at another hospital, unless the revision surgery was performed outside Germany or undertaken by non-participating clinics or funded by non-contributing insurance companies. The Elixhauser Comorbidity Index (ECI) classifies comorbidities using a weighted algorithm based on the association between comorbidity and death, and is more comprehensive and robust than the American Society of Anesthesiologists (ASA) grade.[12,18,19]

The revision arthroplasty in the EPRD is defined as the exchange of any component of the hip arthroplasty, including the modular head and the acetabular liner. Every procedure with an exchange or removal of components and followed by reimplantation is counted as a re-revision. In re-revision THAs, the starting point is either the date of the most recent one-stage rTHA or the date of the reimplantation of the prothesis in two-stage rTHA. In EPRD documentation protocol, a revision arthroplasty is defined as septic when either the ICD-T84.5 'infection and inflammatory reaction due to joint arthroplasty' code is recorded,[20] or 'infection' is stated in the operation records as the indication for surgery. In case of multiple revision arthroplasties in one patient, whether multiple rTHAs are classified as septic or aseptic is based on whether or not the indication for the most recent revision arthroplasty was recorded as an infection.

The EPRD received general institutional review board approval (approval number D 473/11).

Patient cohort. The EPRD provided data on 17,842 rTHAs from 2015 to 2022, of which 16,349 (92%) were first-time rTHA and 1,493 (8%) were multiple rTHA. Of the 16,349 rTHAs, 5,943 (36%) were listed as septic and 10,406 (64%) were listed as aseptic. Of the 1,493 multiple rTHAs, 963 (65%) were listed as septic and 530 (35%) were listed as aseptic (Figure 2). The demographic details and Elixhauser scores of the cohorts are shown in Table I.

Statistical analysis. We used the R v.1.0.7 package 'comorbidity' (R Foundation for Statistical Computing, Austria) to compute the weighted ECI scores, which provides a systematic way to quantify the presence of 29 different comorbidities that may affect patient outcomes within a single score. The rate of re-revision and mortality in first-time revised and multiple-hip revised data were analyzed, with sub-division into septic and aseptic groups. To determine the cumulative probability of re-revision and mortality for rTHA, we used the Kaplan-Meier estimates. The cumulative mortality rate and the implant survival time were calculated by the difference in time between the date of the rTHA and death.

Results

Re-revision rate after rTHA. At seven years' follow-up, the re-revision rate of 34.0% was observed for patients undergoing septic rTHA (Figure 3). For aseptic rTHA, a significantly lower re-revision rate of about 16.4% was found. However, the study groups differ not only in the absolute percentage re-revision rate, but also their distribution over time. For septic revisions, 89.4% of the re-revisions occur within the first year. Thereafter, only minimal increase is detected. For aseptic revisions, 63.4% of all re-revisions were documented within the first year.

For multiple rTHA, the number of further re-revisions is higher. For septic multiple rTHA, a rate of 35.8% within one year requiring further revision can be observed, as shown in Figure 4. After six years, 42.2% show a further re-revision after multiple rTHA for infection. Thus, the re-revision rate following septic multiple rTHA is slightly higher than the rate for septic primary rTHA. However, patients with aseptic multiple rTHA also demonstrate a re-revision rate at one year of 22.9% and a re-revision rate after six years of 32.8%, a significantly increased risk for re-revision compared to aseptic primary rTHA.

Mortality rate after rTHA. rTHAs for infection show a cumulative mortality rate within one year of 13.5%, and aseptic rTHA of 8.4%. Within the first year, a difference of 5.1% in the cumulative mortality rate after rTHA is observed between septic and aseptic rTHA. From the one-year timepoint, the cumulative mortality rates rise parallel to each other, with a mean difference of cumulative mortality rate between septic and aseptic revision of 5.8%. The cumulative mortality rate of first-time septic

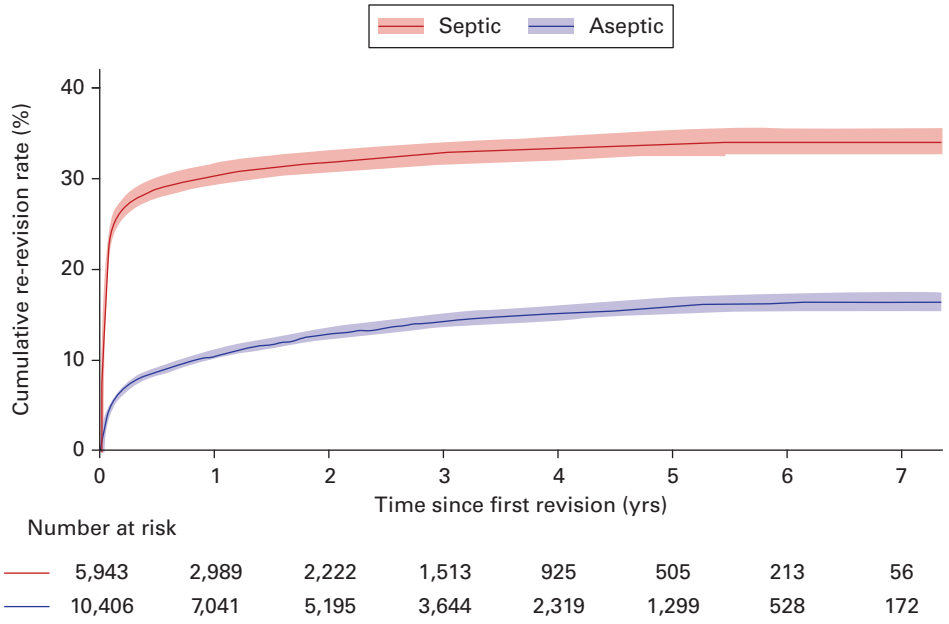

Fig. 3

Cumulative re-revision rate for any reason in first revision total hip arthroplasty.

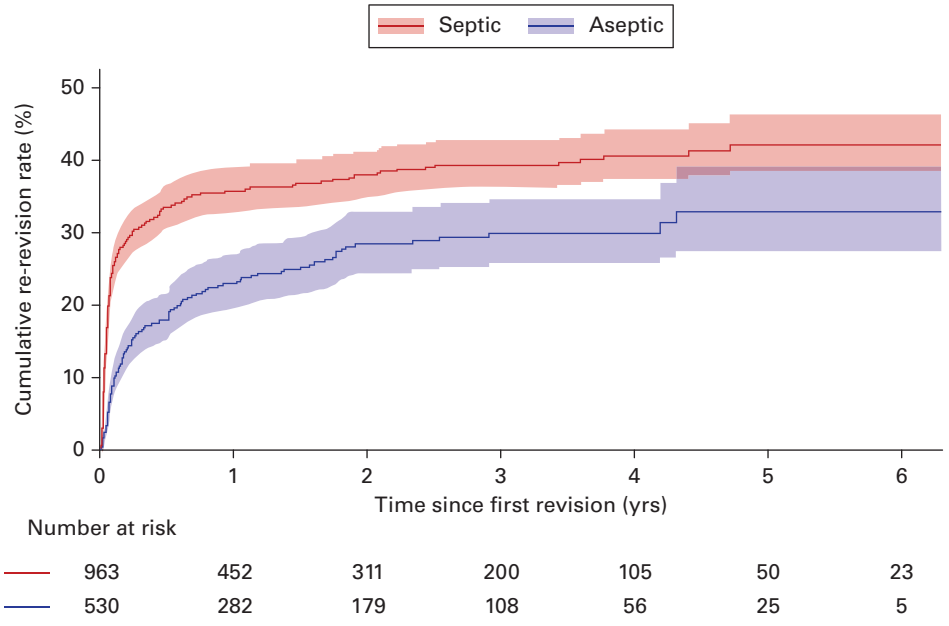

Fig. 4

Cumulative re-revision rate for any reason in multiple revision total hip arthroplasty.

rTHA reaches 39.6% after seven years of follow-up, whereas aseptic revisions present a cumulative mortality of 33.0% after seven years (Figure 5).

In multiple rTHA, in the first year a mortality of 12.5% for septic multiple rTHA and of 8.8% for aseptic multiple rTHA was recorded. After six years of follow-up, patients after septic multiple rTHA exhibited a cumulative mortality rate of 32.5% and after aseptic multiple rTHA a cumulative mortality rate of 39.8%, at variance to the cumulative mortality rates following first-time rTHA (Figure 6).

Kaplan-Meier estimates for re-revision and mortality for first and multiple rTHA are given in Supplementary Tables i to iv.

Discussion

Despite the improvements in the care of patients undergoing rTHA over the past decades, PJI is still a major life-threatening

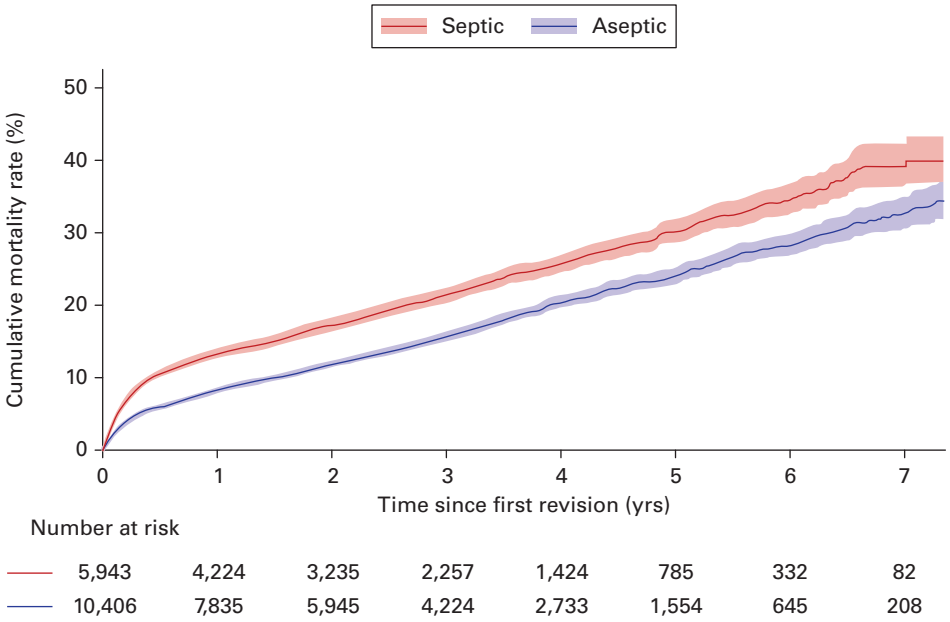

Fig. 5

Cumulative mortality rate after first-time hip revision.

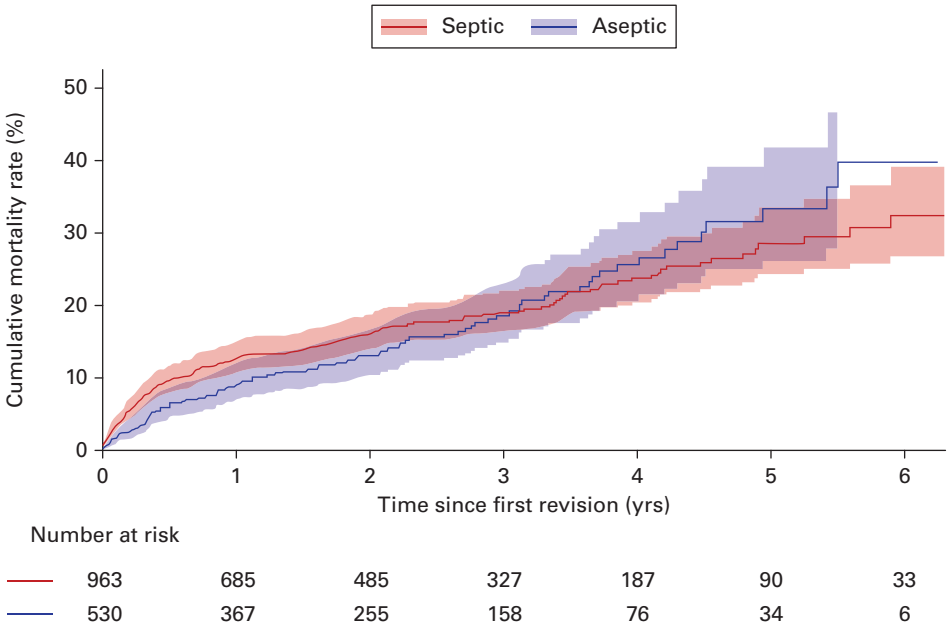

Fig. 6

Cumulative mortality rate for multiple hip revision.

complication of this procedure. Contrary to previous investigations,[21,22] the current study shows a very high re-revision rate of 30.4% at one year, and a high cumulative mortality rate of 13.5%. After seven years' follow-up for first-time septic rTHA, a re-revision rate of 34% and cumulative mortality of 39.6% is seen, which far exceeds the results from previous studies. The recurrence of PJI was recorded septic first-time rTHA in 26% of cases, and in septic multiple rTHA in 27%.

A recent meta-analysis by Goud et al[10] reported significantly lower reinfection rates after septic rTHA, at 5.7% for one-stage revision and 8.4% for two-stage revision, compared to the reinfection rate in the present study. Data from a specialist German

tertiary centre for septic two-stage rTHA show a reinfection rate of 9% for two-stage revision in complex cases with massive bone loss at five-year follow-up, which is comparable to the literature, and a five-year Kaplan-Meier implant survival, free of any revision, of 80.4%.[23] For one-stage revision for PJI, excellent data from another tertiary centre show a reinfection rate of 6% and revision-free survival of 75.9% in a ten-year follow-up.[24] Our results clearly show that data from specialist single-centre studies do not reflect the experience across the German healthcare system as a whole.

Reviewing the results from other centres outside Germany: Ong et al[25] reported a five-year re-revision rate of 19% for rTHA using healthcare data from the USA. The National Joint Registry (NJR) for England, Wales, Northern Ireland, the Isle of Man, and Guernsey reported a 15-year re-revision rate following first-time rTHA of 21.3%.[26] In a single-centre study investigating two-stage hip revision secondary to PJI, Petis et al[27] reported a five-year re-revision rate of 15%. Lie et al[28] reported a ten-year re-revision rate of 26% from data obtained from the Norwegian Arthroplasty Register. Even taking these selected studies with relatively high re-revision rates into account, they are at variance with the re-revision rate in tthis study. The studies by Ong et al,[25] Deere et al,[26] and Lie et al[28] reported their re-revision rates for all causes and not solely for PJI, making the difference in our results all the more startling. Relevant comorbidities are associated with a higher risk of failure of rTHA.[21] In our data, half of the septic rTHAs had ECIs of 5+. Besides the high prevalence of comorbidities in our cohort, the mean age for rTHA in the NJR of 71.4 years,[29] and in the Swedish registry of 71.9 years,[6] is slightly younger compared to the present cohort's mean age of 73 years, and age is a recognized risk factor for prosthetic failure.[30] These differences may explain some of the variation in re-revision and mortality compared to our data.

This study used the ECI due to its higher accuracy and quantity of recorded comorbidities compared to the ASA grade and Charlson Comorbidity Index (CCI).[12,31] We used the R comorbidity package of the ECI, which is a weighting system based on ICD codes and includes 29 comorbidities.[32] Varady et al[12] recorded an area under the curve (AUC) for one-year mortality of 0.755 (95% confidence interval (CI) 0.722 to 0.788) for ECI and 0.685 (95% CI 0.656 to 0.714) for ASA. Furthermore, Menendez et al[31] found ECI (AUC 0.86; 95% CI 0.86 to 0.86) outperformed CCI (AUC 0.83; 95% CI 0.83 to 0.84) as a predictor of in-hospital mortality after major orthopaedic surgery.

Besides the demographic differences noted between this study and other reports, there are additional systematic issues which might have contributed to the differences from our results. Single-centre and multicentre cohort studies are susceptible to exclusion of a relevant part of the patient population, they may underestimate the revision rate as dissatisfied patients may choose an alternative hospital for revision, and mortality may be unreliable due to loss to follow-up.[33] National registries have systematic divergencies; therefore, the patient inclusion as shown by Sabah et al[17] for the NJR analysis of failed metal-on-metal bearings might be biased and may underestimate the revision rates. However, one significant problem in the comparison of all revision data is that there is no consistent or clear definition of revision surgery, and the registration of revision procedures can differ significantly.[16] This may lead to significant differences in data; whereas most registries count the exchange of a head or a liner as a revision, wound revision without exchange of any prosthesis components is only documented as revision in a few national registries.[16] In addition, the differences in the cumulative re-revision and mortality rates between other registries and ours might stem from differing definitions of a PJI or revision surgery and varying inclusion criteria, but could also be a result of differences in patient populations and healthcare systems. The majority of our patient population had a high ECI and higher mean age (73 years), which could explain some of the differences.

Regarding cumulative mortality, the registry data shows that within one year, one in eight of the patients undergoing first-time rTHA for infection had died, and approximately one in 12 in the aseptic rTHA cohort. Our results show that there is a much higher mortality in the septic rTHA group within the first six months in comparison to the aseptic rTHA group. There is controversy in the literature about mortality rates after rTHA. Whereas Rullán et al[21] reported a 30-day mortality rate after rTHA of 1.0% in patients with infection and 0.7% in aseptic revisions, Yao et al[22] reported about 2% mortality after one year. The cumulative mortality recorded in the EPRD is much higher than from these single-centre series. However, at five years' follow-up Kildow et al[34] report a mortality rate of 41%, which is comparable to our results. In a recent European Federation of National Associations of Orthopaedics aand Traumatology (EFORT) review, a five-year mortality rate of 26% and a ten-year mortality rate of 45% were reported.[35] Similar to our results, Day et al[36] reported mortality of 43% after initial rTHA following chronic PJI. The relevant differences in short-term mortality might be explained by the significantly younger patients in the included cohorts, as well as their lower rates of PJI. These findings are supported by the fact that results of studies which only include revisions for PJI are more in line with our results.[34] The cumulative mortality rate of some single-centre studies might also be underestimated due to loss to follow-up.[33]

Beyond one year, we found that mortality increases at a similar rate between the septic and aseptic rTHA groups, with a mean difference in mortality of 5.8%. The greatest difference in increase in mortality between septic and aseptic rTHA is observed within the first six months, suggesting that PJI in rTHA contributes significantly to mortality in the acute phase. The highest impact in changing the process of care is likely to be achieved by improvements in the perioperative care, treatment in high-volume centres, standardized antibiotic regimes, preoperative cardiopulmonary assessment, readily available intensive care facilities, and specialist teams of surgeons and physicians highly experienced in the multidisciplinary care these patients require.[37,38] As shown in registry data, hospitals with higher case numbers perform above average, with reduced re-revision rates and lower mortality. It is likely that patients with PJI will achieve better results if treated in specialist units who can meet the care requirements highlighted.[8 39]

When comparing the cumulative mortality rates of first-time and multiple rTHA, it is striking that first-time rTHAs have a higher mortality rate from the first year (13.5%) to the seventh

year (39.6%) in contrast to multiple rTHAs (12.5%; 32.5%). Contrary to what might be expected, mortality rates for patients undergoing septic rTHA have a higher ECI of 5+ (58%) than patients undergoing first-time rTHA for infection (51%). The higher ECI in multiple revised patients might predict higher mortality rates, but this was not observed. In addition, the multiple revised patients with infection have higher BMIs, which might also predict an increased risk of mortality, but this was similarly not observed. It may be that patients requiring re-revision for infection are being referred more selectively to specialist high-volume units, which have better resources to manage these complex cases and achieve better outcomes.

A limitation of the study is that the EPRD includes only about 70% of the primary and revision arthroplasty procedures performed in Germany. Participation in the EPRD is voluntary. However, most of the hospitals that perform high volumes of arthroplasty surgery do participate, and this may influence complication rates and mortality. Due to the nature of registry studies with a large number of included patients, a fully comprehensive record of specific details on patients, infection, and surgical factors is not feasible, but this study indicates the broad reality of rTHA practice and outcomes in Germany. A strength of this study is that the EPRD collects patient data from three independent sources (registry documentation of participating hospitals, product database of participating implant suppliers, routine data from participating health insurance companies), and the entry of diagnosis is not surgeon- or institution-dependent and follows an independent and a comprehensive follow-up process. Using the data from the EPRD, we can ensure almost 100% follow-up of 16,349 rTHA patients with a follow-up period of up to seven years.[8]

In conclusion, this registry-based study has shown that the risk of re-revision after either aseptic or septic first-time revision, along with associated mortality, is higher and at variance from previously reported outcomes from single-centre series and meta-analyses. The mortality and re-revision rates are significantly increased in the presence of infection in the first year postoperatively. The finding of a re-revision rate for septic rTHA after seven years of 34% is notably higher compared to the rate of around 8% in a recent meta-analysis.[10] Outcomes and results achieved at large specialist centres are not reflected in the outcomes achieved, on average, across the hospital care system in Germany.[40] Better outcomes might be anticipated if complex revision surgery, and especially cases with infection, are managed through specialist centres with resources to support high volumes of complex cases.

Take home message

- The numbers of re-revision rates and mortality after septic revision total hip arthroplasty (rTHA) presented in the registry data are much higher than in single-centre studies and meta-analysis.
- A comparison with the five-year survival rates of oncological tumours underlines the relevance of septic rTHA.
- The critical first year after septic rTHA seems to be the challenging component of revision arthroplasty, and optimization of perioperative management is crucial.

Supplementary material

Tables displaying statistics from Kaplan-Meier estimates of re-revison rates and mortality for index and multiple, septic and aseptic, revision total hip arthroplasty.

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