



ELSEVIER

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Clinical Outcomes After Revision Hip Arthroplasty due to Prosthetic Joint Infection—A Single-Center Study of 369 Hips at a High-Volume Center With a Minimum of One Year Follow-Up

Rasmus Liukkonen, BM^{a,*}, Meeri Honkanen, MD, PhD^b, Eerik Skyttä, MD, PhD^a, Antti Eskelinen, MD, PhD^a, Matti Karppelein, MD, PhD^b, Alekski Reito, MD, PhD^a

^a Coxa Hospital for Joint Replacement, Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland

^b Department of Internal Medicine, Tampere University Hospital, Tampere, Finland

ARTICLE INFO

Article history:

Received 8 July 2023

Received in revised form

22 August 2023

Accepted 27 August 2023

Available online xxx

Keywords:

arthroplasty

hip

revision

infection

PJI

ABSTRACT

Background: Prosthetic joint infection (PJI) treatment decisions are traditionally based on treatment algorithms. There is, however, a lack of evidence to support the choice of these treatment algorithms. Therefore, we aimed to assess the one-year survival after PJI revision and compared different surgical strategies in a single-center setting.

Methods: Revisions of the hip due to PJI performed at our institution between January 2008 and September 2021 with at least one-year of follow-up were identified. In total, 134 debridement, antibiotics, and implant retentions (DAIRs), 114 one-stage revisions, and 121 two-stage revisions were performed. Infections were classified as early, acute hematogenous, and chronic. Survival was calculated using the Kaplan-Meier method and cumulative incidence function. Predictors of outcomes were examined with Fine-Gray regressions and Cox proportional hazards regressions. Subdistribution hazard ratios and hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated.

Results: At one-year follow-up, 26.6% (CI 22.2 to 31.2%) of the patients had undergone reoperation and 7.9% (CI 5.4 to 10.9%) had died. The risk for reoperation was highest after DAIR (36.6%, CI 28.5 to 44.7%) and lowest after one-stage revision (20.2%, CI 13.4 to 28%). Within the early infections, the one-stage revision almost halved the risk of reoperation (HR 0.51, CI 0.31 to 0.84) with no added mortality risk (HR 1.05, CI 0.5 to 2.2), when compared to DAIR.

Conclusion: By utilizing 1-stage revision over DAIR in early infections, it might be possible to improve the prognosis by decreasing the risk of reoperation without increasing mortality. However, as the patient selection is undeniably difficult, more research is warranted.

© 2023 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

Funding: This study was supported by the Päivikki and Sakari Sohlberg Foundation, the Finnish Research Foundation for Orthopedics and Traumatology, the Finnish Medical Foundation, and the competitive research funds of Pirkanmaa Hospital District, Tampere, Finland (representing governmental funding). The sources of funding had no role at any stage of the study.

One or more of the authors of this paper have disclosed potential or pertinent conflicts of interest, which may include receipt of payment, either direct or indirect, institutional support, or association with an entity in the biomedical field which may be perceived to have potential conflict of interest with this work. For full disclosure statements refer to <https://doi.org/10.1016/j.arth.2023.08.078>.

* Address correspondence to: Rasmus Liukkonen, BM, Coxa Hospital for Joint Replacement, Faculty of Medicine and Health Technology, Tampere University, Nivelitie 4, 33520, Tampere, Finland.

<https://doi.org/10.1016/j.arth.2023.08.078>

0883-5403/© 2023 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

Prosthetic joint infection (PJI) is one of the most devastating complications after total hip arthroplasty (THA). The key to successful treatment of PJI is a thorough debridement with the removal of all infected material and the eradication of any possible biofilm [1]. Prosthetic joint infection can also be treated surgically with debridement, antibiotics, and implant retention (DAIR), where the implant is retained in the joint, but the acetabular liner and femoral head are replaced [1,2]. If DAIR is not considered appropriate, the components can be removed and replaced either in a one-stage operation or in 2 separate operations [1,2].

The decision on which type of operation to perform has traditionally been based on treatment algorithms [1–3]. However, there is a lack of clear scientific evidence to support the choice of the treatment algorithm, and no universal consensus on the optimal

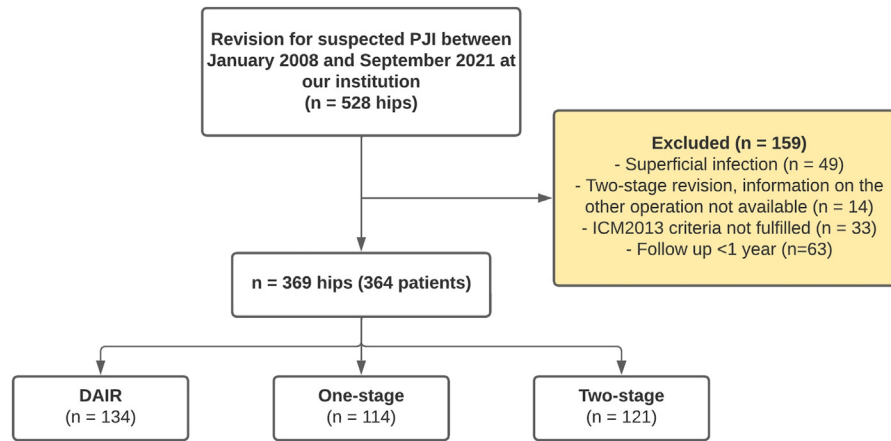


Fig. 1. Flowchart of the patients at our institution between January 2008 and September 2021. PJI, prosthetic joint infection, DAIR, debridement, antibiotics, and implant retention.

method exists [3–5]. Previous clinical studies have been based on case series of small heterogeneous cohorts where patients have either been treated in a multi-center setting or no comparison between surgical strategies has been performed [6–14]. Furthermore, the outcomes of PJI revisions have not improved over time and a definitive consensus for treatment selection has not been achieved [4,15].

To be able to plan future treatment strategies, more evidence on the differences between surgical strategies is needed. In the present study, we assessed: (1) What is the short-term survival after PJI revision? and (2) How do the outcomes of the surgical strategies differ?

Materials and Methods

In this retrospective study, we identified all revision surgeries performed for PJI of the hip at our institution between January 1, 2008, and September 12, 2021, by searching the ICD-10 (International Classification of Diseases 10th revision) code T84.5 (Infection and inflammatory reaction due to internal joint prosthesis). Superficial wound infections and two-stage operations, where information on the first operation was not available, were excluded. Only the first revisions due to PJI were included, and those patients who underwent revision due to PJI in both hips were analyzed as having undergone 2 separate operations. The 2013 International Consensus Diagnostic Criteria [16] were used to confirm the PJI diagnosis. In addition, all patients with less than one year of follow-up were excluded (Figure 1).

Our institution's electronic data lake and electronic health records (EHRs) were used to obtain the patient data. The EHRs contain information related to patient care, whereas the data lake contains more comprehensive information on surgical details (eg, details of the surgery and prosthesis). The following patient demographics were collected: age, sex, body mass index, American Society of Anesthesiology (ASA) classification, and comorbidities. In addition, the date of the last noninfectious operation to the ipsilateral joint, and the date the symptoms started before the revision surgery were recorded. Detailed information on the presence of a fistula and intraoperative microbiological findings acquired from tissue specimens were also collected from the EHRs. All the microbiology analyses were performed in the accredited laboratory of the local university hospital. In accordance with Finnish legislation, no institutional review board hearing was required because of the retrospective register-based study design and because the patients were not contacted.

The surgeries were categorized into one of the following 3 categories: DAIR, one-stage revision, or two-stage revision. The infections were classified as early (≤ 90 days from the previous surgery), acute hematogenous (>90 days from the previous surgery AND <28 days of symptoms), and chronic infections (>90 days from the previous surgery AND ≥ 28 days of symptoms) [2,17,18].

The treatment decisions were based on international consensus, where the early and hematogenous infections are preferably treated with either DAIR or one-stage revision [1,2,19]. Within those, the one-stage revision was the preferred method if the hip was uncemented or if the time from the previous operation was on the edge of the optimal timeframe (within the first 3 to 4 post-operative weeks from the index procedure) for DAIR. For chronic infections, the two-stage revision was the preferred treatment method. If the two-stage revision was contraindicated, then the one-stage ($n = 5$) or even DAIR ($n = 6$) was utilized. In addition, each of the hips were evaluated individually and treated according to the up-to-date consensus.

According to the microbiological results from the preoperative and intraoperative tissue specimens, postoperative antimicrobial treatments were designed by infectious-disease specialists. Since 2014, the usual practice has been to administer postoperative antibiotic therapy intravenously for 2 weeks followed by 4 weeks of oral therapy regardless of the surgical modality. From 2008 to 2014, total duration of treatment may have been longer; up to 3 months. However, parenteral treatment very rarely exceeded 4 weeks if highly bioavailable oral treatment could be used. The antibiotic-free interval before the 2nd stage operation has been variable, but most often not less than 2 weeks. Also, antibiotics have been discontinued after the 2nd stage operation with negative intra-operative cultures and no patient-specific indication for prolonged suppressive antibiotic treatment. In staphylococcal infections, a rifampin-based combination was used when not contraindicated (drug interactions or high risk of adverse reactions) except in two-stage revisions without any foreign material left *in situ*.

Primary and Secondary Outcomes

Follow-up started from the day of the revision surgery due to PJI and ended when the patient was lost to our institution's regular follow-up program (eg, death or patient moved to another area) or on the date of data collection, whichever came first. Reoperation was defined as a new surgical procedure on the previously operated joint. Furthermore, the outcomes of the revision surgeries were categorized according to the Musculoskeletal Infection Society

(MSIS) categorization scheme [20]. In the case of two-stage revision, the first operation was the starting point for the follow-up period, as recommended by the MSIS [20]. In survival analyses, our primary outcome was reoperation due to any reason (MSIS tiers 3A to 3E). It has been suggested that aseptic revision performed within one year from the initial surgery for the treatment for PJI represents a failure secondary due to PJI. Therefore, these revisions were also included [20]. Death from any cause (MSIS tiers 4A and 4B) was considered as a competing risk, as we did not have access to the causes of death, and it was not possible to classify whether the death was PJI-related or not [21,22].

Data Analyses

Means with standard deviations were presented for normally distributed variables and medians with ranges or interquartile ranges for variables with non-Gaussian populations. Cumulative incidences of reoperations and deaths were calculated as described by Scrucca et al. [23]. The risk of any-cause failure was calculated using the Kaplan-Meier estimator. Results are presented with 95% confidence intervals (CIs).

A Fine-Gray regression model was used to identify potential predictors for reoperation or death, as the model has been reported to be more accurate than cause-specific Cox regression when estimating a single patient's clinical prognosis [24]. However, the cause-specific Cox models for both reoperation and death were calculated and the results from those analyses are also presented [25]. In the Cox models, the proportional hazards assumptions were tested using Schoenfeld's residuals, and the assumptions were not violated in any tested model.

To assess the effect of confounding factors and to predict the outcomes more accurately, multivariable analyses were performed. Due to the many possible predictors of outcome, variable selection processes were performed (Appendix 1). First, global models were formed based on known risk factors and clinically relevant factors (Appendix 2). The variables included in these global models were selected for the final Fine-Gray regression models using backward elimination with a significance level of 0.157 (Akaike Information Criteria selection). For the cause-specific Cox regression models, the variables were selected based on the combination of backward elimination with $P < .10$ as a level of significance. Thereafter, model stabilities were assessed by bootstrap stability investigation with 200 repetitions. Based on these 2 investigations, the final variables for the regression analyses were selected. Results from multivariable analyses were presented with either adjusted subdistributed hazard ratios (sdHRs) or adjusted hazard ratios (aHRs). All analyses were performed using R (version 4.1.2; R Foundation for Statistical Computing, Vienna, Austria).

Patient Demographics

A total of 369 revisions (364 patients) with at least one year of follow-up were identified. Of these, 134 (36.3%) were DAIRs, 114 (30.9%) were one-stage revisions, and 121 (32.8%) were two-stage revisions (Figure 1). Most of the PJIs were early infections (245 of 369, 66.4%). A total of 103 (42%) DAIRs and 94 (38.4%) one-stage revisions were performed for early infections. *S. aureus* was the most frequently identified pathogen, causing 134 infections (36.3%). The median age of the patients was 72 years (range, 34 to 94) and 53.4% ($n = 197$) were women. Further details on patient demographics are presented in Table 1.

Results

Outcomes after PJI Revision

At one-year follow-up, 26.6% (CI 22.2 to 31.2%) of the patients had undergone a reoperation and 7.9% (CI 5.2 to 10.9%) had died. The risk for reoperation and death was highest after DAIR (reoperation 36.6%, CI 28.5 to 44.7%; death 10.4%, CI 6 to 16.3%). However, the risk for death between one-stage (7%, CI 3.3 to 12.7%) and two-stage (5.8%, CI 2.5 to 11%) revisions was nearly the same. Compared to the other strategies, time to failure was the shortest when DAIR was performed (Figure 2). When the MSIS criteria were applied, the highest rate of optimal outcome was after one-stage revision (53.5%), and the lowest after DAIR (34.3%) (Table 2, Appendix 3, and Figure 2).

Type of PJI and Risk for Failure

The risk for failure within one year after PJI was highest after early infection (37.1%, CI 30.8 to 42.9%) and lowest after chronic infection (26.8%, CI 14.2 to 37.5%). The risk for failure was highest when DAIR was performed, both after early (45.6%, CI 35.1 to 54.4%) and acute hematogenous infections (48%, CI 24.2 to 64.3%). The risks for failure after one-stage or two-stage revision due to early infections were comparable within the first 30 postoperative days. However, after one year of follow-up, the one-stage revision was superior to the other strategies. Further details of the failure risks are presented in Table 3.

Risk Factors for Failure

Compared to DAIR, one-stage revision more than halved the risk for reoperation (adjusted subdistributed hazard ratios [sdHRs] 0.44, CI 0.26 to 0.75; aHR 0.48, CI 0.29 to 0.79). For early infections, the one-stage revision almost halved the risk of reoperation (HR 0.51, CI 0.31 to 0.84) with no added mortality risk (HR 1.05, CI 0.5 to 2.2) (Appendix 4). The effect of two-stage revision on the risk for reoperation compared with DAIR was similar (adjusted sdHR 0.72, CI 0.43 to 1.19; aHR 0.55, CI 0.34 to 0.89), but the results were imprecise and CIs included the zero change.

Higher ASA scores increased both the risk for reoperation (adjusted sdHR 1.55, CI 1.16 to 2.05; aHR 1.63, CI 1.19 to 2.24 per one-unit increase) and the risk for death (adjusted sdHR 2.98, CI 1.86 to 4.77; aHR 4.54, CI 2.66 to 7.77) (Table 4, and Appendices 5 and 6).

Discussion

The results of the present study revealed that treatment of PJIs is associated with a high risk for reoperation and death. The risk for reoperation was associated with the type of operation, being lowest after one-stage revision and highest after DAIR.

A previous meta-analysis reported that mortality after PJI revision is approximately 4.2% at one-year follow-up [26]. However, only two-stage revisions were included in that analysis. In the present study, one-year mortality differed according to the type of surgery. For example, after a two-stage revision, one-year mortality was 5.8%, whereas after a one-stage revision, it was 7% and, interestingly, after DAIR it was the highest at 10.4%. In multivariable analyses, the type of operation was not related to the risk for death, so the differences between the mortality rates are mostly due to the patient-related factors that contributed to the choice of treatment modality. In addition, as the higher ASA-class was associated to the increased mortality, with the groups not similar regarding the distribution of ASA-classes, this might partly explain this difference between the

Table 1
PJI Patient Characteristics and Preoperative Risk Factors Stratified by the Surgical Technique.

Variable	DAIR n = 134, (%)	One-Stage n = 114, (%)	Two-Stage n = 121, (%)
Patient characteristics			
Women, n	83/134 (61.9)	54/114 (47.4)	60/121 (49.6)
Age, median (range), y	73 (36 to 94)	70 (37 to 93)	72 (34 to 88)
BMI, mean (range)	29.1 (18 to 46)	30.0 (15 to 50)	27.5 (18 to 41)
CCI, median (range)	3 (0 to 7)	3 (0 to 7)	3 (0 to 7)
ASA-class, n			
1	4 (3)	6 (5.3)	2 (1.7)
2	35 (26.1)	29 (35.4)	27 (22.3)
3	67 (50)	63 (55.3)	78 (64.5)
4	27 (20.1)	14 (12.3)	12 (9.9)
5	1 (0.7)	1 (0.9)	0
NA	0	1 (0.9)	2 (1.7)
Comorbidities, n			
Diabetes mellitus	25/124 (20.2)	22/106 (20.8)	22/115 (19.1)
Rheumatoid arthritis	13/125 (10.4)	5/104 (4.8)	12/104 (11.5)
Chronic kidney disease	4/125 (3.2)	3/105 (2.9)	5/114 (4.4)
Infection type, n			
Early	103 (76.9)	94 (82.5)	48 (39.7)
Acute hematogenous	25 (18.7)	15 (13.2)	28 (23.1)
Chronic	6 (4.5)	5 (4.4)	45 (37.2)
Surgical characteristic			
Time since previous operation, median (IQR), d	18 (12 to 50)	21 (15 to 37)	230 (34 to 1,620)
Symptom duration, median (IQR), d	11 (6 to 16)	15 (8 to 22)	20 (7 to 77)
Sinus tract, n	83 (61.9)	72 (63.2)	45 (37.1)
Spacer usage, n	-	-	24 (19.8)
Duration of the antibiotic treatment, mean (SD), wk	7.8 (3.7)	8.0 (5.2)	8.1 (3.2)
Rifampin usage, n	55/130 (42.3)	60/111 (54.1)	41/119 (34.5)
Previous indication, n			
Osteoarthritis	60 (44.8)	85 (74.5)	76 (62.8)
Aseptic revision	41 (30.6)	12 (10.5)	27 (22.3)
Fracture	30 (22.4)	16 (14)	14 (11.6)
Other	3 (2.2)	1 (0.9)	4 (3.3)
Cemented prosthesis	91 (67.9)	60 (52.6)	55 (45.4)
Unstable prosthesis	0	17 (12.3)	20 (16.5)
Microbial findings, n (%)^a			
<i>Staphylococcus aureus</i>	41 (26.6)	50 (40.3)	43 (33.9)
CNS	37 (24)	26 (21)	33 (26)
<i>Streptococcus beta-hemolyticus</i>	15 (9.7)	14 (11.3)	8 (6.3)
Other streptococcus species	3 (1.9)	3 (2.4)	7 (5.5)
Gram-negative aerobic	11 (7.1)	7 (5.6)	4 (3.1)
Enterococcus species	6 (3.9)	8 (6.5)	6 (4.7)
Anaerobic	6 (3.9)	2 (1.6)	4 (3.1)
Other	6 (3.9)	0	2 (1.6)
Negative culture	29 (18.8)	14 (11.3)	20 (15.7)
Polymicrobial	20 (14.9)	10 (8.8)	6 (5)

Infections were classified as early (≤ 90 d from the previous surgery), acute hematogenous (>90 d from the previous surgery AND <28 d of symptoms), and chronic infections (>90 d from the previous surgery AND ≥ 28 d of symptoms).

ASA, American Society of Anesthesiology; BMI, body mass index; CCI, Charlson comorbidity index; d, days; DAIR, debridement, antibiotics, and implant retention; IQR, interquartile range; SD, standard deviation; wk, weeks; y, years.

^a Microbiological findings from the polymicrobial infections (n = 36) are included; therefore, the total N is greater than the total N of surgeries performed (n = 369).

observed mortalities. There is a scarcity of previously published data on the differences between mortality rates after different PJI revision strategies. Tirumala et al. reported that 90-day mortality rates do not differ between one-stage and two-stage revisions [10]. Our results were similar, but we had a larger sample size.

A two-stage revision has been advocated to be the most successful method for the treatment of PJI [1,3]. However, there is a lack of data in the literature for a comparison between the one-stage and two-stage approaches [27]. In our study, one-stage revision had as high a risk for reoperation and death as two-stage revision. The risk for any-cause failure after chronic infection was the lowest after two-stage revision. However, as the findings from the one-stage revisions were imprecise due to the small number of patients, we cannot make definitive conclusions on whether the one-stage revision is effective for chronic infection.

After early infection, the risk for failure at one-year follow-up was lowest after one-stage revision and highest after DAIR. There is still a scarcity of data available on the differences between DAIR and one-stage revisions [28–30]. In a recent study, Riemer et al. reported excellent results after one-stage revision for early PJI, suggesting that one-stage revision might be at least comparable with DAIR in the treatment of early infections [28]. However, their study had a small sample size and no direct comparison between treatment strategies was performed. In addition to the high risk for failure after DAIR, the mean time to failure was remarkably short when DAIR was performed since most of the failures occurred within the first 40 days. Some studies have reported that 6 to 8 weeks of antimicrobial treatment is noninferior to twelve weeks of antimicrobial treatment [31–33]. This finding is in accordance with our results, as most of the failures occurred within the first weeks.

Table 2
Risk for Failure After PJI Revision Surgery Stratified by the Surgical Technique.

Revision Type	30 d Survival (CI)	1 y Survival (CI)
Any-cause failure		
All revisions (n = 369)	21.1% (16.9 to 25.2%)	34.4% (29.4 to 39.1%)
DAIR (n = 134)	33.6% (25.1 to 41.1%)	47% (37.9 to 54.8%)
One-stage (n = 114)	15.8% (8.8 to 22.2%)	27.2% (18.5 to 34.9%)
Two-stage (n = 121)	12.4% (6.3 to 18.1%)	27.3% (18.9 to 34.8%)
Reoperation		
All revisions (n = 369)	19.5% (15.6 to 23.7%)	26.6% (22.2 to 31.2%)
DAIR (n = 134)	32.1% (24.3 to 40.1%)	36.6% (28.5 to 44.7%)
One-stage (n = 114)	14% (8.4 to 21.1%)	20.2% (13.4 to 28%)
Two-stage (n = 121)	10.7% (6 to 17%)	21.5% (14.6 to 29.2%)
Death		
All revisions (n = 369)	1.6% (0.7 to 3.4%)	7.9% (5.4 to 10.9%)
DAIR (n = 134)	1.5% (0.3 to 4.8%)	10.4% (6 to 16.3%)
One-stage (n = 114)	1.8% (0.3 to 5.6%)	7% (3.3 to 12.7%)
Two-stage (n = 121)	1.7% (0.3 to 5.3%)	5.8% (2.5 to 11%)

Any-cause failure rates were calculated with the Kaplan-Meier estimator, and cause-specific failure rates using cumulative incidences. Results are presented with 95% confidence intervals.

DAIR, debridement, antibiotics, and implant retention.

Thus, prolonging the duration of the antimicrobial treatment would not have affected the outcome.

We observed a high risk for reoperation and death after DAIR. To our best knowledge, no previous study has compared outcomes between DAIR and one-stage revision [3]. The one-stage strategy is not suitable for everyone. Indeed, when the femoral stem is well-cemented and the overall situation is suitable for DAIR, it might not be worth risking intraoperative complications. Furthermore, as one-stage revision did not increase the risk for death compared to DAIR, further research on patient selection between these 2 strategies is warranted, preferably in a randomized controlled trial setting. In addition, in the future it would be necessary to evaluate how the results from the nontraditional revision strategies, such as cement-in-cement revisions, compared to the traditional strategies, as the results from those have been reported to be rather good [34].

We are aware that our study has several potential limitations that are mainly due to the retrospective setting of the study. It should be noted about the rare and diverse nature of PJI and that the patient selection process between the different treatment strategies is not completely definitive, possibly resulting in selection bias. However, this is a common limitation in the field of PJI research, and it can only be addressed in a prospective setting. In addition, the patient profile might have changed during our long study period, hence affecting the selection processes and distribution of used techniques [35]. Furthermore, all patients were managed by the same surgeons in a single-center setting, and we believe that the potential selection bias was as low as possible. Another limitation is that we did not examine the effect of antimicrobial therapy on the outcomes because some of the PJIs were referrals and information on treatments was not accurate in all cases. In contrast, a clear advantage of the present

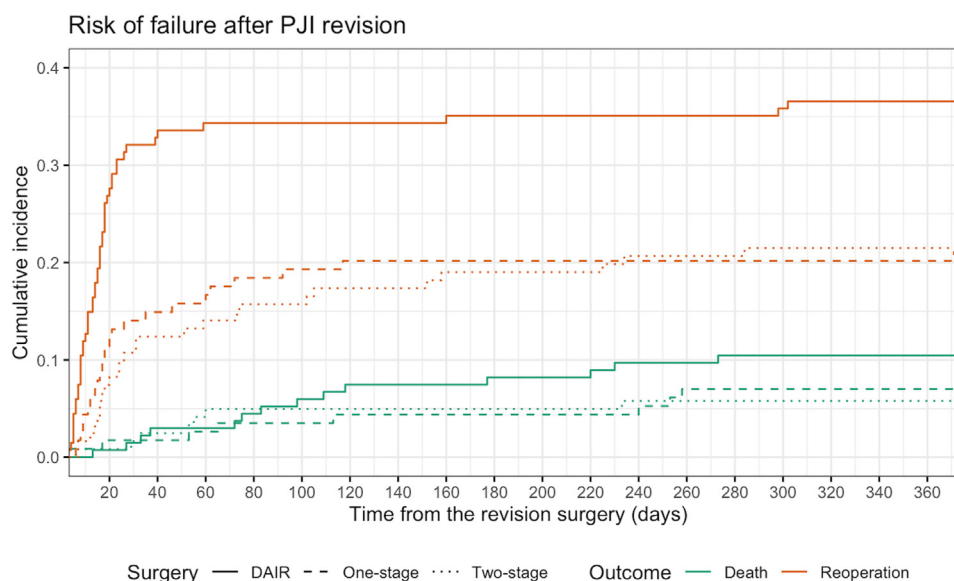


Fig. 2. The surgical technique stratified cumulative incidences of different failure types after prosthetic joint infection revision surgery. DAIR, debridement, antibiotics, and implant retention.

Table 3
Risk for Any-Cause Failure After PJI Revision Surgery Stratified by the Surgical Technique and Infection Type.

Revision Type	30 d Survival (CI)	1 y Survival (CI)
Early infection		
All revisions (n = 245)	24.9% (19.3 to 30.1%)	37.1% (30.8 to 42.9%)
DAIR (n = 103)	35% (25.1 to 43.5%)	45.6% (35.1 to 54.4%)
One-stage (n = 94)	18.1% (9.9 to 25.5%)	26.6% (17.1 to 35%)
Two-stage (n = 48)	16.7% (5.4 to 26.6%)	39.6% (24 to 51.9%)
Acute hematogenous infection		
All revisions (n = 68)	23.5% (12.8 to 33%)	30.9% (19 to 31%)
DAIR (n = 25)	36% (14.1 to 52.3%)	48% (24.2 to 64.3%)
One-stage (n = 15)	6.7% (0 to 18.5%)	13.3% (0 to 28.9%)
Two-stage (n = 28)	21.4% (4.7 to 35.2%)	25% (7.1 to 39.4%)
Chronic infection		
All revisions (n = 56)	1.8% (0 to 5.2%)	26.8% (14.2 to 37.5%)
DAIR (n = 6)	0%	76.7% (0 to 89.2%)
One-stage (n = 5)	0%	80% (0 to 96.5%)
Two-stage (n = 45)	2.2% (0 to 6.4%)	15.6% (4.3 to 25.5%)

Failure is determined as a reoperation or death. Failure rates were calculated with the Kaplan-Meier estimator. Results are presented with 95% confidence intervals. DAIR, debridement, antibiotics, and implant retention.

study was the large study sample. Previous PJI studies have been mainly based on small case series or heterogenous multicenter cohorts. Although the sample size might be larger in a multicenter setting, if the treatment decisions are not made by the same surgeons, the risk for selection bias will be higher than in a single-center setting. Moreover, because our study had a large sample size, we were also able to perform diverse methodological analyses to compare different treatment strategies and to further examine patient-specific factors that can be used in future decision-making.

In conclusion, revision arthroplasty for PJI of a primary total hip arthroplasty is a complex operation with a high risk of reoperation and mortality. However, by preferring 1-stage revision over DAIR in early infections, it might be possible to improve the prognosis by decreasing the risk of reoperation without increasing mortality. However, as the patient selection is undeniably difficult, more research is warranted.

Acknowledgments

The authors would like to thank Mari Karsikas for the data collection and Peter Heath for the language editing of the manuscript.

Table 4
Cox Proportional Hazard Regression Hazard Ratios for Failure With 95% Confidence Intervals.

Cox Cause-specific Regression (n = 295)	Adjusted HR (95% CI)
Hazard ratios for reoperation	
Age	0.98 (0.96 to 0.99)
ASA-score	1.63 (1.19 to 2.24)
One-stage revision ^a	0.48 (0.29 to 0.79)
Two-stage revision ^a	0.55 (0.34 to 0.89)
Hazard ratios for death	
Age	1.02 (0.98 to 1.06)
ASA-score	4.54 (2.66 to 7.77)
Diabetes mellitus	1.77 (0.94 to 3.34)
BMI	0.91 (0.85 to 0.97)

Italics values indicate, if the confidence intervals exclude the 1.0 value, the result is statistically significant.

ASA, American Society of Anesthesiologists; BMI, body mass index; CI, confidence interval; DAIR, debridement, antibiotics, and implant retention; HR, hazard ratio.

^a DAIR was used as the reference.

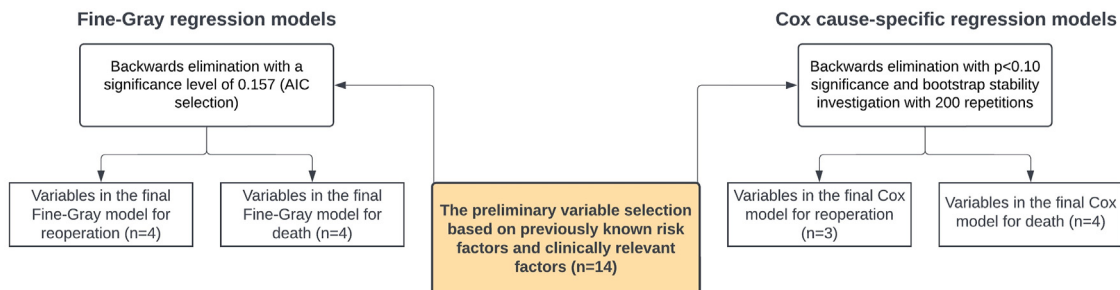
References

- Izakovicova P, Borens O, Trampuz A. Periprosthetic joint infection: current concepts and outlook. *EFORT Open Rev* 2019;4:482–94. <https://doi.org/10.1302/2058-5241.4.180092>.
- Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. *N Engl J Med* 2004;351:1645–54. <https://doi.org/10.1056/NEJMra040181>.
- Karachalios T, Komnos GA. Management strategies for prosthetic joint infection: long-term infection control rates, overall survival rates, functional and quality of life outcomes. *EFORT Open Rev* 2021;6:727–34. <https://doi.org/10.1302/2058-5241.6.210008>.
- Li C, Renz N, Trampuz A. Management of periprosthetic joint infection. *Hip Pelvis* 2018;30:138–46. <https://doi.org/10.5371/hp.2018.30.3.138>.
- Bialecki J, Bucsi L, Fernando N, Foguet P, Guo S, Haddad F, et al. Hip and knee section, treatment, one stage exchange: Proceedings of International Consensus on Orthopedic Infections. *J Arthroplasty* 2019;34:S421–6. <https://doi.org/10.1016/j.arth.2018.09.026>.
- Nurmohamed FRHA, van Dijk B, Veltman ES, Hoekstra M, Rentenaar RJ, Weinans HH, et al. One-year infection control rates of a DAIR (debridement, antibiotics and implant retention) procedure after primary and prosthetic-infection-related revision arthroplasty - a retrospective cohort study. *J Bone Jt Infect* 2021;6:91–7. <https://doi.org/10.5194/jbji-6-91-2021>.
- Bourgonjen YP, Hooning van Duyvenbode JFF, van Dijk B, Nurmohamed FRHA, Veltman ES, Vogely HC, et al. Long-term outcome of two-stage revision surgery after hip and knee prosthetic joint infections: an observational study. *J Bone Jt Infect* 2021;6:379–87. <https://doi.org/10.5194/jbji-6-379-2021>.
- Grammatopoulos G, Kendrick B, McNally M, Athanasou NA, Atkins B, McLardy-Smith P, et al. Outcome following debridement, antibiotics, and implant retention in hip periprosthetic joint infection—an 18-year experience. *J Arthroplasty* 2017;32:2248–55. <https://doi.org/10.1016/j.arth.2017.02.066>.
- Kang J-S, Shin E-H, Roh T-H, Na Y, Moon KH, Park J-H. Long-term clinical outcome of two-stage revision surgery for infected hip arthroplasty using cement spacer: culture negative versus culture positive. *J Orthop Surg* 2018;26:2309499017754095. <https://doi.org/10.1177/2309499017754095>.
- Tirumala V, Klemm C, van den Kieboom J, Xiong L, Kwon Y-M. Comparison of patient reported outcome measures after single versus two-stage revision for chronic infection of total hip arthroplasty: a retrospective propensity score matched cohort study. *Arch Orthop Trauma Surg* 2021;141:1789–96. <https://doi.org/10.1007/s00402-021-03810-6>.
- Ilchmann T, Zimmerli W, Ochsner PE, Kessler B, Zwicky L, Graber P, et al. One-stage revision of infected hip arthroplasty: outcome of 39 consecutive hips. *Int Orthop* 2016;40:913–8. <https://doi.org/10.1007/s00264-015-2833-4>.
- Kuiper JWP, Rustenburg CME, Willems JH, Verberne SJ, Peters EJG, Saouti R. Results and patient reported outcome measures (PROMs) after one-stage revision for periprosthetic joint infection of the hip: a single-centre retrospective study. *J Bone Jt Infect* 2018;3:143–9. <https://doi.org/10.7150/jbji.24366>.
- Grammatopoulos G, Bolduc M-E, Atkins BL, Kendrick BJL, McLardy-Smith P, Murray DW, et al. Functional outcome of debridement, antibiotics and implant retention in periprosthetic joint infection involving the hip. *Bone Jt J* 2017;99-B:614–22. <https://doi.org/10.1302/0301-620X.99B5.BJJ-2016-0562.R2>.
- Kandel CE, Jenkinson R, Daneman N, Backstein D, Hansen BE, Muller MP, et al. Predictors of treatment failure for hip and knee prosthetic joint infections in the setting of 1- and 2-stage exchange arthroplasty: a multicenter retrospective cohort. *Open Forum Infect Dis* 2019;6:ofz452. <https://doi.org/10.1093/ofid/ofz452>.
- Xu C, Goswami K, Li WT, Tan TL, Yayac M, Wang S-H, et al. Is treatment of periprosthetic joint infection improving over time? *J Arthroplasty* 2020;35:1696–1702.e1. <https://doi.org/10.1016/j.arth.2020.01.080>.
- Diagnosis of periprosthetic joint infection. *J Orthop Res* 2014;32:S98–107. <https://doi.org/10.1002/jor.22553>.
- Triffault-Fillit C, Ferry T, Laurent F, Pradat P, Dupieux C, Conrad A, et al. Microbiological epidemiology depending on time to occurrence of prosthetic joint infection: a prospective cohort study. *Clin Microbiol Infect* 2019;25:353–8. <https://doi.org/10.1016/j.cmi.2018.04.035>.
- Kapadia BH, Berg RA, Daley JA, Fritz J, Bhavne A, Mont MA. Periprosthetic joint infection. *Lancet* 2016;387:386–94. [https://doi.org/10.1016/S0140-6736\(14\)61798-0](https://doi.org/10.1016/S0140-6736(14)61798-0).
- Osmon DR, Barbari EF, Berend AR, Lew D, Zimmerli W, Steckelberg JM, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* 2013;56:e1–25. <https://doi.org/10.1093/cid/cis803>.
- Fillingham YA, Della Valle CJ, Suleiman LI, Springer BD, Gehrke T, Bini SA, et al. Definition of successful infection management and guidelines for reporting of outcomes after surgical treatment of periprosthetic joint infection: from the workgroup of the musculoskeletal infection Society (MSIS). *J Bone Joint Surg Am* 2019;101:e69. <https://doi.org/10.2106/JBJS.19.00062>.
- Boddapati V, Fu MC, Mayman DJ, Su EP, Sculco PK, McLawhorn AS. Revision total knee arthroplasty for periprosthetic joint infection is associated with increased postoperative morbidity and mortality relative to noninfectious revisions. *J Arthroplasty* 2018;33:521–6. <https://doi.org/10.1016/j.arth.2017.09.021>.
- Zmistowski B, Karam JA, Durinka JB, Casper DS, Parvizi J. Periprosthetic joint infection increases the risk of one-year mortality. *J Bone Joint Surg Am* 2013;95:2177–84. <https://doi.org/10.2106/JBJS.L00789>.

- [23] Scrucca L, Santucci A, Aversa F. Competing risk analysis using R: an easy guide for clinicians. *Bone Marrow Transplant* 2007;40:381–7. <https://doi.org/10.1038/sj.bmt.1705727>.
- [24] Austin PC, Lee DS, Fine JP. Introduction to the analysis of survival data in the presence of competing risks. *Circulation* 2016;133:601–9. <https://doi.org/10.1161/CIRCULATIONAHA.115.017719>.
- [25] Latouche A, Allignol A, Beyersmann J, Labopin M, Fine JP. A competing risks analysis should report results on all cause-specific hazards and cumulative incidence functions. *J Clin Epidemiol* 2013;66:648–53. <https://doi.org/10.1016/j.jclinepi.2012.09.017>.
- [26] Natsuhara KM, Shelton TJ, Meehan JP, Lum ZC. Mortality during total hip periprosthetic joint infection. *J Arthroplasty* 2019;34:S337–42. <https://doi.org/10.1016/j.arth.2018.12.024>.
- [27] Lange J, Troelsen A, Thomsen RW, Søballe K. Chronic infections in hip arthroplasties: comparing risk of reinfection following one-stage and two-stage revision: a systematic review and meta-analysis. *Clin Epidemiol* 2012;4:57–73. <https://doi.org/10.2147/CLEP.S29025>.
- [28] Riemer K, Lange J. Early periprosthetic hip joint infection managed by cementless one-stage revision – a case series. *J Bone Jt Infect* 2022;7:43–50. <https://doi.org/10.5194/jbj-7-43-2022>.
- [29] Hansen E, Tetreault M, Zmistowski B, Della Valle CJ, Parvizi J, Haddad FS, et al. Outcome of one-stage cementless exchange for acute postoperative periprosthetic hip infection. *Clin Orthop* 2013;471:3214–22. <https://doi.org/10.1007/s11999-013-3079-3>.
- [30] Wolf M, Clar H, Friesenbichler J, Schwantzer G, Bernhardt G, Gruber G, et al. Prosthetic joint infection following total hip replacement: results of one-stage versus two-stage exchange. *Int Orthop* 2014;38:1363–8. <https://doi.org/10.1007/s00264-014-2309-y>.
- [31] Chaussade H, Uçkay I, Vuagnat A, Druon J, Gras G, Rosset P, et al. Antibiotic therapy duration for prosthetic joint infections treated by debridement and implant retention (DAIR): similar long-term remission for 6 weeks as compared to 12 weeks. *Int J Infect Dis* 2017;63:37–42. <https://doi.org/10.1016/j.ijid.2017.08.002>.
- [32] Manning L, Metcalf S, Dymock M, Robinson O, Clark B, Nelson R, et al. Short-versus standard-course intravenous antibiotics for peri-prosthetic joint infections managed with debridement and implant retention: a randomised pilot trial using a desirability of outcome ranking (DOOR) endpoint. *Int J Antimicrob Agents* 2022;60:106598. <https://doi.org/10.1016/j.ijantimicag.2022.106598>.
- [33] Lora-Tamayo J, Euba G, Cobo J, Horcajada JP, Soriano A, Sandoval E, et al. Short- versus long-duration levofloxacin plus rifampicin for acute staphylococcal prosthetic joint infection managed with implant retention: a randomised clinical trial. *Int J Antimicrob Agents* 2016;48:310–6. <https://doi.org/10.1016/j.ijantimicag.2016.05.021>.
- [34] Fishley WG, Selvaratnam V, Whitehouse SL, Kassam A-AM, Petheram TG. Cement-in-cement revision of the femur in infected hip arthroplasty in 89 patients across two centres. *Bone Jt J* 2022;104-B:212–20. <https://doi.org/10.1302/0301-620X.104B2.BJJ-2021-0598.R1>.
- [35] Liukkonen RJ, Honkanen M, Reito AP, Skyttä ET, Karppelin M, Eskelinen AP. Trends in revision hip arthroplasty for prosthetic joint infection: a single-center study of 423 hips at a high-volume center between 2008 and 2021. *J Arthroplasty* 2023;38:1151–9. <https://doi.org/10.1016/j.arth.2023.02.061>.

Appendix

Appendix 1



Supplementary Fig. 1. The flow chart summarizing the predictor variable choice for Fine-Gray and Cox regression models. AIC, Akaike Information Criteria.

Appendix 2

Supplementary File 1. Variables included in the global models before variable selection processes applied.

Previously known risk factors and clinically relevant factors included in the global models

1. Age
2. Sex
3. Charlson's comorbidity index
4. Diabetes mellitus
5. ASA score
6. C-reactive protein (serum)
7. Presence of fistula
8. Indication of the previous surgery (primary THA/revision THA)
9. Rheumatoid arthritis
10. Chronic kidney disease
11. Body mass index
12. Pathogen
13. Type of the revision (DAIR/1-stage revision/2-stage revision)
14. Type of the infection (early/acute hematogenous/chronic)

Appendix 3

Supplementary Table 1

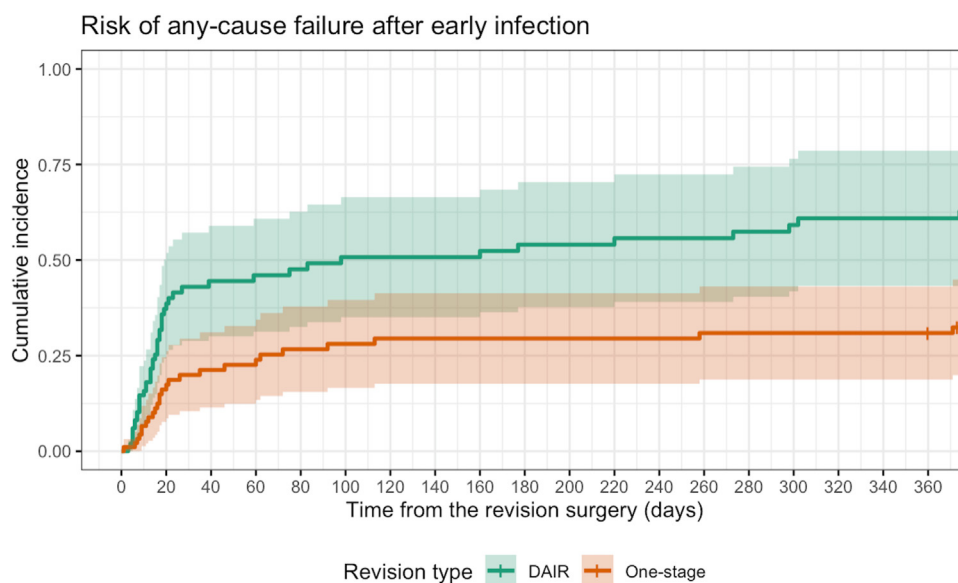
Prosthetic Joint Infection Treatment Outcomes According to Musculoskeletal Infection Society Categorization Scheme.

Outcome	All Revisions (n = 369)		DAIR (n = 134)		One-Stage (n = 114)		Two-Stage (n = 121)	
	N	%	N	%	N	%	N	%
Tier 1: Infection control with no continued antibiotic therapy	166	45	46	34.3	61	53.5	59	48.8
Tier 2: Infection control with the patient on suppressive antibiotic therapy	14	3.8	8	6	5	4.4	1	0.8
Tier 3: Need for reoperation and/or revision and/or spacer retention								
3A: Aseptic revision at >1 y from initiation of PJI treatment	6	1.6	1	0.7	1	0.9	4	3.3
3B: Septic revision (including DAIR) at >1 y from initiation of PJI treatment	2 (50) ^a	0.5	1 (0) ^a	0.7	0	0	1 (100) ^a	0.8
3C: Aseptic revision at ≤1 y from initiation of PJI treatment	16	4.3	5	3.7	4	3.5	7	5.8
3D: Septic revision (including DAIR) at ≤1 y from initiation of PJI treatment	41 (54) ^a	11.1	20 (60) ^a	14.9	4 (25) ^a	3.5	17 (53) ^a	14
3E: Amputation, resection arthroplasty, or arthrodesis	46	12.5	27	20.1	16	14	3	2.5
3F: Retained spacer	2	0.5	-	-	-	-	2	1.7
Tier 4: Death								
4A: ≤1 y from initiation of PJI treatment	29	7.9	14	10.4	8	7	7	5.8
4B: >1 y from initiation of PJI treatment	47	12.7	12	9	15	13.2	20	16.5

DAIR, debridement, antibiotics, and implant retention.

^a Percentage of cases that are reinfected with the same initial organism.

Appendix 4



Supplementary Fig. 2. The risk of any-cause failure after early infection. DAIR, debridement, antibiotics, and implant retention.

Appendix 5

Supplementary Table 2

Fine-Gray Regression Subdistribution Hazard Ratios for Failure With 95% Confidence Intervals.

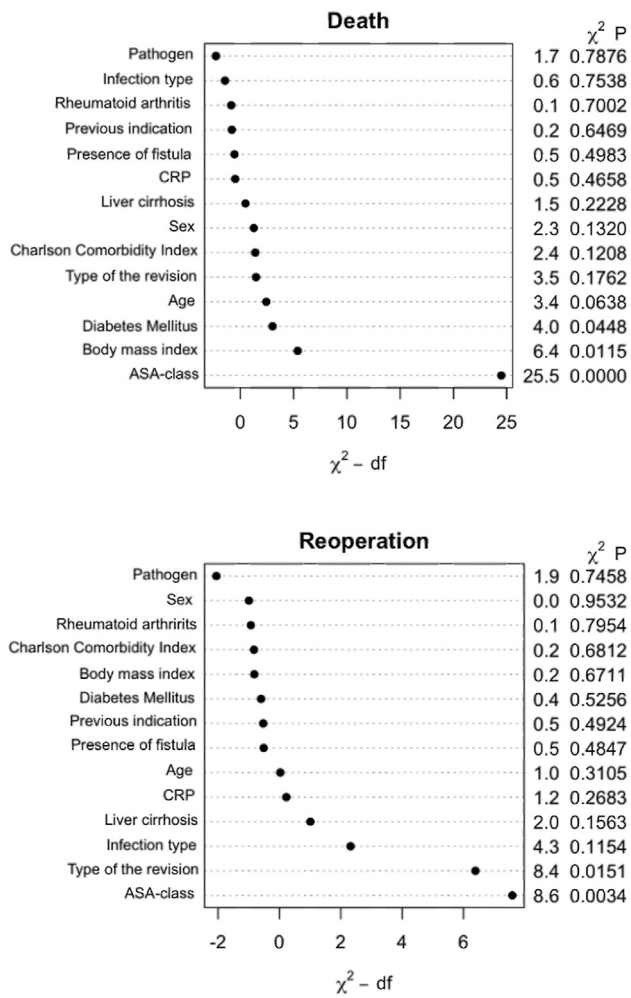
Fine-Gray Regression (n = 295)	
	Adjusted sdHR (95% CI)
Subdistribution hazard ratios for reoperation ^a	
Age	0.97 (0.96 to 0.99)
ASA-score	1.55 (1.16 to 2.05)
One-stage revision ^b	0.44 (0.26 to 0.75)
Two-stage revision ^b	0.72 (0.43 to 1.19)
Subdistribution hazard ratios for death	
Age	1.05 (1.01 to 1.09)
ASA-score	2.98 (1.86 to 4.77)
Diabetes mellitus	1.80 (0.97 to 3.35)
BMI	0.91 (0.86 to 0.98)

DAIR, debridement, antibiotics, and implant retention; HR, hazard ratio; sdHR, subdistribution hazard ratio.

^a DAIR was used as the reference.

^b Type of infection is adjusted for this model.

Appendix 6



Supplementary Fig. 3. The *Chi*-squared regression coefficients for the predictors in the Cox regression models. The American Society of Anesthesiologists (ASA) -class was the most important predictor of reoperation and death. ASA, American Society of Anesthesiology; BMI, body mass index; CCI, Charlson comorbidity index; DM, diabetes mellitus.