Eetu Syystö

TIMING OF DEBRIDEMENT, ANTIBIOTICS, AND IMPLANT RETENTION FOR EARLY PROSTHETIC JOINT INFECTION: DATA FROM THE FINNISH ARTHROPLASTY REGISTER

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Summary:

Early periprosthetic joint infection (PJI) is a serious complication of knee and hip replacement with an incidence of around 1 %. It may have disastrous consequences. Debridement, antibiotics and implant retention (DAIR) is the method of choice in the treatment of PJI. Optimal timing of DAIR is somewhat unclear. The aim of this study was to compare the failure rate of DAIR between three time intervals: 0-42 days (=6 weeks), 43-84 (=6-12 weeks) and 85-180 days (=12 weeks-6 months) after the primary total hip arthroplasty and total knee arthroplasty based on Finnish Arthroplasty Register (FAR) data from 2014 to 2022 in 1 year follow-up.

There were 178,498 primary total hip and knee replacements from May 2014 to April 2022 recorded in FAR. A total of 1014 DAIR procedures were performed within 6 months postoperatively. Re-revision due to PJI within one year was regarded as failure of the DAIR treatment. We compared the failure rate of DAIR between three time intervals: 0-42 days, 43-84 and 85-180 days after the primary operation.

After total hip arthroplasty, the failure rate of DAIR was 15.1% when performed within the first 42 days, 10% when done between 43 and 84 days, and 31.4% when carried out 85 to 180 days after the primary surgery. Following total knee arthroplasty, the corresponding failure rates were 8.9%, 16.7%, and 9.8%, respectively. Based on the results, the likelihood of DAIR failure may not increase as much as previously thought when more than six weeks have passed since primary surgery.

Timing of debridement, antibiotics, and implant retention for early prosthetic joint infection: data from the Finnish Arthroplasty Register.

Hannes Keemu M.D. [a]; Eetu Syystö, BM.[a]; Riku Klén Ph.D.[b]; Mikko S. Venäläinen, Ph.D.[c]; Matias Hemmilä, M.D.,Ph.D. [a]; Jutta Järvelin, M.D., Ph.D., M.Sc.[d]; Antti P. Eskelinen, M.D., Ph.D.[e]; Keijo T. Mäkelä, M.D., Ph.D.[a]

[a] Department of Orthopaedics and Traumatology, Turku University Hospital, and University of Turku, Turku, Finland

[b] Turku PET Centre, University of Turku, and Turku University Hospital, Turku, Finland

[c] Department of Medical Physics, Turku University Hospital and University of Turku, Turku, Finland

[d] Finnish Institute for Health and Welfare, Helsinki, Finland

[e] Coxa Hospital for Joint Replacement, and Faculty of Medicine and Health Technologies, University of Tampere, Tampere, Finland

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Department of Orthopaedics and Traumatology address: Luolavuorentie 2, 20700 Turku, Finland

Turku Bioscience Centre address: Tykistökatu 6, 20520 Turku, Finland

Department of Medical Physics, Hämeentie 11, FI-20521 Turku, Finland

Finnish Institute for Health and Welfare address: Mannerheimintie 166, 00271 Helsinki, Finland

Coxa Hospital for Joint Replacement address: Niveltie 4, 33520 Tampere, Finland

Address for Correspondence:

Luolavuorentie 2 FI-20700 Turku, Finland

Tel: +35823136210

Email: Hannes.Keemu@varha.fi

Abstract

Background and purpose

Debridement, antibiotics and implant retention (DAIR) is the method of choice in the treatment of acute periprosthetic joint infection (PJI). Optimal timing of DAIR however is somewhat unclear. We assessed success of DAIR in different time intervals performed after primary total hip and knee arthroplasty (THA, TKA) based on data from the Finnish Arthroplasty Register (FAR).

Patients and methods

There were 178.498 primary THA and TKA altogether from May 2014 to April 2022 recorded in FAR. A total of 1014 DAIR procedures were performed within 6 months postoperatively. Re-revision due to PJI within one year was regarded as a failure of the DAIR treatment. We compared the failure rate of DAIR between three-time intervals: 0-42 days, 43-84 and 85-180 days after the primary operation. Cox regression model was used to assess risk factors for re-revision.

Results

After THA, failure rate was 15.1% when DAIR was performed within 42 days, 10% when DAIR was performed 43-84 days and 31.4% when performed 85-180 days after primary operation. After TKA, failure rates where 8.9%, 16.7% and 9.8%, accordingly. Timing of DAIR was not associated with an increased re-revision risk: for THA-DAIR during 43-84 days HR 1.2, 95% CI 0.6-2.2, p=0.63 and during 85-180 days HR 1.4, 95% CI 0.6-3.0, p=0.41, compared to the reference 0-42 days; and for TKA-DAIR during 43-84 days HR 1.0, 95% CI 0.4-2.4, p=0.98 and during 85-180 days HR 1.9, 95% CI 1.0-3.8, p=0.065 compared to the reference.

Interpretation

Failure rate of DAIR may not increase as much as previously thought after 6 weeks of primary total joint arthroplasty. DAIR can be worth considering as a treatment method of PJI also after first 6 weeks depending on the severity of the case.

Level of Evidence III

Key words

Total knee arthroplasty, total hip arthroplasty, periprosthetic joint infection, debridement, antibiotics and implant retention.

Introduction

Early periprosthetic joint infection (PJI) is a serious complication with an incidence of around 1 % (5,12). PJI may have disastrous consequences, and PJI revision always decreases quality of life of the patient (2). With the progressively increased number of hip and knee arthroplasties (THA, TKA) performed worldwide, the number of PJIs is expected to increase in the following years (12).

PJIs can be classified into early (occurring within three months postoperatively), delayed (developing between three-and 24 months post-surgery), and late infections (arising more than 24 months after surgery). According to most guidelines, the primary treatment for acute postoperative PJI is debridement, antibiotic therapy, and implant retention, also known as the DAIR procedure. As part of a DAIR procedure, the exchange of modular polyethylene components is recommended (12).

According to some previous studies, DAIR procedure is efficient when performed during 4 weeks after primary arthroplasty (1). It is still somewhat unclear, how viable option DAIR is with a more delayed presentation. The presence of a mature biofilm at later stages may decrease the effect of DAIR. According to recent systematic review, success rate of DAIR in the treatment of PJI varied from 56% to 90% in single clinic study settings, when DAIR was performed early with varying follow-up times (12). In a two-hospital study, success rate of DAIR after THA and TKA was 84% during the first three months, and 47% after that in one-year follow-up (4). Based on Dutch national registry data, there was no difference in re-revision rates for DAIR procedures performed within 4 weeks or between 4 to 12 weeks with 1-year follow-up (23).

The Finnish Arthroplasty Register (FAR) was established in 1980, and became all-electric in May 2014. Our aim was to compare the failure rate of DAIR between three time intervals: 0-42 days (=6 weeks), 43-84 (=6-12 weeks) and 85-180 days (=12 weeks-6 months) after the primary THA and TKA based on FAR data from 2014 to 2022 in 1 year follow-up. Further, risk factors for re-revision following a DAIR procedure were assessed.

Patients and methods

The FAR is a nationwide register that includes information on THA and TKA in Finland. Finnish health care units are obligated to report arthroplasty surgeries to FAR, which is maintained by Finnish Institute of Health and Welfare (26). Patient and surgery related data like body mass index (BMI), and surgical approach are reported to FAR by a standard online sheet which is filled during and immediately after the operation. Primary and revision arthroplasties are linked to each other by using a personal identification number. Dates of death are obtained from Digital and Population Data Services Agency.

During the study period, the coverage of the Finnish hospitals was 100%. The completeness of the primary THA and TKA data in FAR varied annually between 95-100% compared to the Care Register for Health Care. Completeness of revision THA and TKA varied annually between 82-92% (26).

We included all primary THAs and TKAs in the period of May 2014 - April 2022. There were 178.498 primary operations during that period with at least one-year follow-up time (78.888 THAs and 99.610 TKAs, Figure 1). There were 1014 DAIR operations for PJI or suspected PJI reported to FAR during the same time period (515 THAs, 499 TKAs). 19 vs. 11 deaths after DAIR were registered during the follow-up time in the THA and TKA groups, respectively. DAIR was defined as a deep (not superficial) debridement and irrigation of the joint with or without exchange of the femoral head and acetabular liner in THA, and exchange of the polyethylene insert in TKA. Re-revisions performed for DAIR was our primary endpoint and defined as any re-operation performed for PJI, like re-DAIRs, and one- and two-stage revisions. We compared the failure rate of DAIR between three time intervals: 0-42 days, 43-84 and 85-180 days after the primary operation. Also, a separate time-to-event analysis using Cox proportional hazards regression with spline smoothing was performed to enable more detailed overview on the effects of timing of DAIR on re-revision risk. By estimating a flexible hazard ratio curve for the timing of DAIR as a continuous variable, the analysis provided additional support for the selection of our discrete timing categories (Figure 2).

Cox regression model was used to assess risk factors for re-revision. The risk factors assessed were age group (⩽62, 63-69, 69-75, ⩾76 years), sex, ASA group (1, 2, 3-4), BMI (⩽24, 25-29, 30-34, 35-39, ⩾40), Charlson comorbidity index (1, 2, 3-4, ⩾5), diagnosis (primary osteoarthritis, inflammatory arthritis, fracture, other), mode of anesthesia (spinal, general), and use of local infiltrative anesthesia LIA (yes, no). Charlson comorbidity index was counted based on data of the Care Register for Health Care with which the FAR data was linked.

The statistical analysis was carried out using R version 4.3.1 (18). Unadjusted and adjusted Cox proportional hazards regression models were used to estimate hazard ratios with 95% confidence intervals (CIs) for re-revision. Based on previous literature and clinical practice, we performed a directed graph analysis (DAG, Figure **3**) to organize variables and their supposed relation to re-revision and other variables. The unadjusted Cox proportional hazards regression model was then used to estimate potential risk factors and hazard ratios with CIs to the re-revision due to PJI (Table 3). All variables with potential confounding bias were further scrutinized with Cox adjusted analysis in which adjustment was done according to the DAG analysis. Potential risk factors were adjusted based on their relation toother factors on the DAG. The following 3 risk factors were adjusted with associated covariates on the DAG: anesthesia (age, ASA class, Charlson index), ASA class (age, Charlson index), and Charlson index (age).

The fulfillment of the proportional hazards assumption for the Cox models were assessed visually from the Kaplan–Meier curves and by using a test based on the scaled Schoenfeld residuals (17; 18). Some of the categories had only uncensored subjects and in those few cases the models were not built. These categories were ASA 1 and LIA anesthesia for hip and BMI ⩽24 for knee. For these variables unadjusted models were not constructed for the particular joint. These variables were also omitted from the adjusted models for both joints. In addition, for the adjusted model for the knee the variables inflammatory arthritis and fracture were also dropped out due to too low number of occurrences. The flexible hazard ratio curve for timing of DAIR as a continuous variable was generated using R packages *smoothHR* and *ggplot2*. The level of statistical significance was set at $p < 0.05$.

Results

Demographic data of the DAIR patients are presented in Table 1. In the THA-DAIR group 53.4% and in TKA-DAIR group 55.5% were male. In the THA-DAIR group 21.9% and in the TKA-DAIR group 24.6% had BMI >35. Most common age group was ≤62 years in the THA-DAIR group, and ≥76 years in the TKA-DAIR group.

Of 515 THA-DAIR procedures, 391 were performed during first 42 days (6 weeks), 70 during following 43-84 days (6 to 12 weeks), and 35 during following 85-180 days (12 weeks to 6 months) after primary THA. Of 499 TKA-DAIR procedures, 383 were performed during first 42 days, 54 during following 43-84 days, and 51 during following 85-180 days after primary TKA (Figure 1). There were 77 re-revisions for PJI after THA-DAIR, and 48 re-revisions for PJI after TKA-DAIR.

After THA, failure rate was 15.1% (n=59) when DAIR was performed within 42 days, 10.0% (n=7) when DAIR was performed 43-84 days and 31.5% (n=11) when performed 85-180 days after primary operation. After TKA, failure rates where 8.9% (n=34), 16.7% (n=9) and 9.8% (n=5), accordingly.

In the Cox model, timing of DAIR was not associated with an increased re-revision risk: for THA-DAIR during 43-84 days HR 1.2, 95% CI 0.6-2.2, p=0.63 and during 85-180 days HR 1.4, 95% CI 0.6-3.0, p=0.41, compared to the reference 0-42 days; and for TKA-DAIR during 43-84 days HR 1.0, 95% CI 0.4-2.4, p=0.98 and during 85-180 days HR 1.9, 95% CI 1.0-3.8, p=0.065 compared to the reference (Table 2).

In the additional time-to-event analysis treating timing of DAIR as a continuous variable, re-revision risk did not change significantly over time (Figure 2).

Female sex was associated with decreased risk for re-revision after TKA-DAIR (HR 0.5, 95% CI 0.3-0.8, p=0,007). Superobese patients with BMI ⩾40 had an increased risk of re-revision after THA-DAIR (HR 4, 95% CI 1.3-12.7, p=0,017) (Table 2). In the adjusted Cox model, general anesthesia was associated with an increased risk for re-revision after THA-DAIR (HR 2.0 (1.2-3.5, p=0.008). Charlson index class 3-4 (HR 2.4, 95% CI 1.1-5.0, p=0.02) was associated with an increased risk for re-revision after THA-DAIR (Table 3).

Discussion

We found that failure rate of DAIR may not increase as much as previously thought after 6 weeks of primary total joint arthroplasty. In the Cox model, timing of DAIR was not associated with an increased re-revision risk**,** and not even when time was considered as a continuous variable in a separate analysis. Female sex was associated with a decreased risk for re-revision after TKA-DAIR. Superobese patients with BMI ⩾40 had an increased risk of re-revision after THA-DAIR. According to our data, DAIR can be worth considering as a treatment method of PJI also after early 6-week time period depending on the severity of the case.

According also to previous studies, DAIR procedure is very efficient when performed early after primary arthroplasty. Barros et al. (2019) stated in a single center study with a mean follow-up time of 42 months and with 38 DAIR patients, that the overall success rate was 89% when DAIR was performed mean 23 days (range 6-30) after primary THA/TKA. Tirumala et al (2021) assessed 103 cultures positive PJIs with DAIR treatment in four weeks of the primary procedure and found success rate of 88% at one year.

It is still somewhat unclear, how viable option DAIR is with a more delayed presentation. In a two-hospital study from Netherlands of 84 patients, success rate of DAIR after THA and TKA was 84% during the first three months, and only 47% after that in one-year follow-up (4). Sendi et al. (2017) assessed 46 single center DAIRs with PJI diagnosis within three months after THA in a mean 4-year follow-up. The successful outcome rate was excellent 90%. On the other hand, Chalmers et al. (2021) stated that success rate of DAIR in a single tertiary clinic setting with PJI diagnosis within three months after THA/TKA was only 58% by two years. In that study DAIR was performed always in three weeks from the symptom onset. Lövik et al. (2020) assessed 769 DAIR patients in six hospitals in four countries (USA, Spain, Portugal, the Netherlands) performed within 90 days of index arthroplasty with 1-year follow-up. Treatment failure rate was 42% for weeks 1-2, 38% for weeks 3-4, 29% for weeks 5-6 and 42% for weeks 7-12. However, exchange of modular components occurred very rarely (40-63% of cases) and polymicrobial finding was common (35-42%). Further, methicillin resistant Staphylococcus aureus (MRSA), Staphylococcus epidermidis, Enterococcus and Pseudomonas were often involved. The authors concluded that DAIR can be performed late, but it is important do it within one week after the onset of symptoms.

It is obvious that the diagnostic criteria of PJI, antibiotic regimen, length of the follow-up time, time of performing DAIR from symptom onset, technical performance of DAIR, and micro-organisms present vary considerably between the studies, and certainly explain many of the differences. The proportion of MRSA and other bacteria which are difficult to treat using DAIR is important information. Single or few center studies are usually able to provide with these granular data. Also, completeness of revision operations is usually high in single center studies, but the number of PJIs can be small. A major limitation of our national arthroplasty registry study is that our data does not contain microbiology or antibiotic regimen data, or time from the symptom onset. A delay from the onset of the symptoms of more than 1 - 2 weeks may lead to significantly lower rates of DAIR success. In Finland there has been only a very limited number of PJIs caused by methicillin resistant bacteria so far, which may partly explain relatively high success rate of DAIR in the current study.

The PJI diagnosis in FAR is based on clinical decision making of the orthopaedic surgeon at the first aid, policlinics and in the operative theatre (clinical and laboratory findings). The data to FAR is then inputted electronically in the operative theatre. Often unfortunately the bacterial culture is not ready at this stage. So FAR PJI definition is based on clinical findings, and it is not corrected afterwards when the bacterial culture is ready. Further, PJI diagnosis in FAR is not classified as acute, subacute or chronic, but only as a PJI. Therefore, we are not aware of the exact clinical presentation of the PJI cases (pus in aspiration or not etc). Clinical presentation of PJI is not recorded in FAR.

In Finland modular components are always changed if possible, which certainly helps to gain the successful outcome. Arthroscopic lavage is not used in our country. A strength of our study was the large number of DAIR procedures and re-revisions compared to the previous studies.

Van der Ende et al. (2021) assessed 514 DAIR procedures after THA/TKA based on Dutch national registry data. There was no difference in re-revision rates for DAIR procedures in 1-year follow-up performed within 4 weeks (20% for THA, 21% for TKA) or between 4 to 12 weeks (17% for THA, 20% for TKA) (23). Our results give support to the Dutch results. However, the time periods of the two studies were not directly comparable, because we had special interest also on very late performed DAIRs (3 to 6 months after primary THA/TKA). Further, the completeness of revision surgery in the Dutch Register may be higher than that in FAR (24). Our major limitation is that the completeness of revision THA/TKA in FAR is somewhat lower than that of primary surgery. Especially those revisions performed on call like PJI revisions may be underreported. During some of the study years, even 18% of revision surgery data were missing. This should be taken account of when interpreting our results. However, we think that the distribution of missing revisions is probably equal in relation to the time from primary surgery so there should not be major bias in comparing success rates in different time periods. The success rate of also very late DAIRs was acceptable in our study. We think that sometimes in late PJIs DAIR may be considered instead of 1- or 2-stage revisions, after careful consideration of patient and bacteriological status. DAIR has 68% success rate at two years even when performed after revision arthroplasty (26).

According to van der Ende et al. (2021) male sex was a risk factor for re-revision after THA-DAIR (OR 3.1). Also in our study male sex was a risk factor for re-revision especially after TKA-DAIR. Male sex is a known risk factor for having PJI after THA/TKA (8; 15), and it seems now that the risk of treatment failure for male sex is also considerable, although not all studies have confirmed that (de Vries et al. 2016). Higher ASA-class, which is a crude estimate of patient comorbidity, was not a risk factor for re-revision in our study or in the Dutch study (23). A strength of our study was that we were able to assess Charlson comorbidity index based on the Care Register for Health Care. Charlson index class 3-4 was associated with an increased re-revision risk after THA-DAIR, but not after TKA-

DAIR. The number of re-revisions was relatively small, which may cause some bias. High BMI⩾40 was associated with an increased re-revision risk after THA-DAIR, although Fink et al (2017) and de Vries et al (2016) did not find any such association.

Another limitation of our study is, that in rare cases, long-term antibiotic suppression or even life-long antimicrobial therapy may be used instead of revision surgery. Permanent antibiotic treatment can be interpreted as failed infection treatment, but unfortunately, we were unable to detect those unrevised cases. Further, we are not aware if some of the late PJIs were actually acute hematogenous infections, although the treatment regimen would be the same. Also, the follow-up time - one year - in our study was relatively short. Certainly, there will be some PJI relapses after that time period. However, 1-year follow-up has been used also previously (23).

Conclusion

Failure rate of DAIR may not increase as much as previously thought after 6 weeks of primary total joint arthroplasty. DAIR can be worth considering as a treatment method of PJI also after first 6 weeks depending on the severity of the case.

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Table 1. Patient characteristics of the DAIR patients at the time of the primary procedure. Anesthesia mode and the use of LIA are presented for the DAIR-procedure. (n=1014)		
	THA (n=515)	**TKA (n=499)**
Age group (years)		
⩽62	139 (27%)	125 (25.1%)
62-69	133 (25.8%)	119 (23.8%)
69-75	119 (23.1%)	124 (24.8%)
⩾76	124 (24.1%)	131 (26.3%)
Gender (n, %) male	275 (53.4%)	277 (55.5%)
ASA classification (n, %)		
1	33 (6.4%)	24 (4.8%)
2	204 (39.6%)	209 (41.9%)
3	275 (53.4%)	263 (52.7%)
BMI category (n, %)		
⩽24	60 (11.7%)	51 (10.2%)
25-29	157 (30.5%)	153 (30.7%)
30-34	154 (29.9%)	153 (30.7%)
35-39	89 (17.3%)	93 (18.6%)
⩾40	24 (4.6%)	30 (6%)
Charlson index (n, %)		
1	99 (19.2%)	109 (21.8%)

2	73 (14.2%)	98 (19.6%)
3-4	104 (20.2%)	90 (18.0%)
⩾5	85 (16.5%)	78 (15.6%)
Preoperative diagnosis (n, %)		
Primary osteoarthritis	415 (80.6%)	458 (91.8%)
Inflammatory arthritis	7 (1.4%)	14 (2.8%)
Fracture	38 (7.4%)	27 (5.4%)
Other	55 (7.4%)	0
Anesthesia (spinal)	337 (65.4%)	353 (70.7%)
LIA anesthesia (No)	508 (98.6%)	485 (97.2%)

Table 2. Unadjusted risk factors for risk of re-revision in the Cox model				
Variable	THA		TKA	
	Hazard ratio (95%CI)	P-Value	Hazard ratio (95%CI)	P-Value
Re-revision risk				
0-6 weeks	Reference		Reference	
6-12 weeks	1.2 (0.6-2.2)	0.63	1.0 (0.4-2.4)	0.98
12 weeks- 6 months	1.4 (0.6-3.0)	0.41	1.9 (1-3.8)	0.07
Age				
Age ⩽62	Reference			
Age 63-69	1.1 (0.6-2.1)	0.72	1.1 (0.6-2.3)	0.73
Age 69-75	0.9 (0.5-1.8)	0.84	1.0 (0.5-2.1)	0.99
Age ⩾76	1.2 (0.0-1.6)	0.65	0.7 (0.4-1.6)	0.46
Sex				
Male	Reference		Reference	
Female	1.1 (0.7-1.7)	0.63	0.5 (0.3-0.8)	0.01
ASA Class				
ASA 1	Reference		Reference	
ASA 2	1.8 (0.4-7.5)	0.44	0.7 (0.2-2.5)	0.64
ASA 3-4	3.4 (0.8-13.8)	0.09	1.0 (0.3-3.3)	0.97
BMI				
⩽24	Reference		Reference	
25-29	1.7 (0.6-4.5)	0.29	2.4 (0.5-10.5)	0.25

30-34	2.3 (0.9-5.9)	0.09	4.4 (1.0-18.7)	0.04
35-39	1.8 (0.6-5.1)	0.26	3.5 (0.8-15.7)	0.1
⩾40	4.0 (1.3-12.7)	0.02	1.8 (0.2-12.6)	0.57
Charlson index				
1	Reference		Reference	
2	1.8 (0.8-4.1)	0.16	0.7 (0.3-1.6)	0.40
3-4	2.4 (1.1-5.0)	0.02	1.5 (0.7-3.1)	0.32
⩾5	1.6 (0.7-3.6)	0.29	0.9 (0.4-2.1)	0.77
Anesthesia				
Spinal	Reference		Reference	
General	1.6 (1.0-2.5)	0.05	1.2 (0.7-2.1)	0.48
Local anesthesia (LIA)				
No	Reference		Reference	
Yes	1.0 (0.1-7.1)	0.99	2.8 (1.0-7.6)	0.05
Diagnosis				
Primary osteoarthritis	Reference		Reference	
Inflammatory arthritis	0.7 (0.2-3.0)	0.66	<0.001 (0-inf)	0.99
Fracture	1.3 (0.6-2.8)	0.52	0.9 (0.3-2.9)	0.86
Other	1.4 (0.8-2.4)	0.24	0.9 (0.3-2.9)	0.86

Table 3. Adjusted risk factors for risk of re-revision in the Cox model based on DAG. ASA class was adjusted for age group and Charlson index. Anesthesia mode was adjusted for age group, ASA class and Charlson index. Charlson index was adjusted for age.				
Variable	THA		TKA	
	Hazard ratio (95%CI)	P-Value	Hazard ratio (95%CI)	P-Value
ASA Class				
ASA 1	Reference		Reference	
ASA 2	0.8 (0.1-6.4)	0.83	0.4 (0.05-3.0)	0.36
ASA 3-4	2.4 (0.3-18.4)	0.40	0.5 (0.07-4.2)	0.55
Anesthesia				
Spinal	Reference		Reference	
General	2.2 (1.3-3.7)	0.003	1.3 (0.7-2.5)	0.42
Charlson index				
1	Reference		Reference	
2	1.8 (0.8-4.1)	0.16	0.7 (0.3-1.7)	0.41
3-4	2.4 (1.2-5.1)	0.02	1.4 (0.7-3.0)	0.36
⩾5	1.6 (0.7-3.7)	0.25	0.9 (0.4-2.1)	0.77

Figures

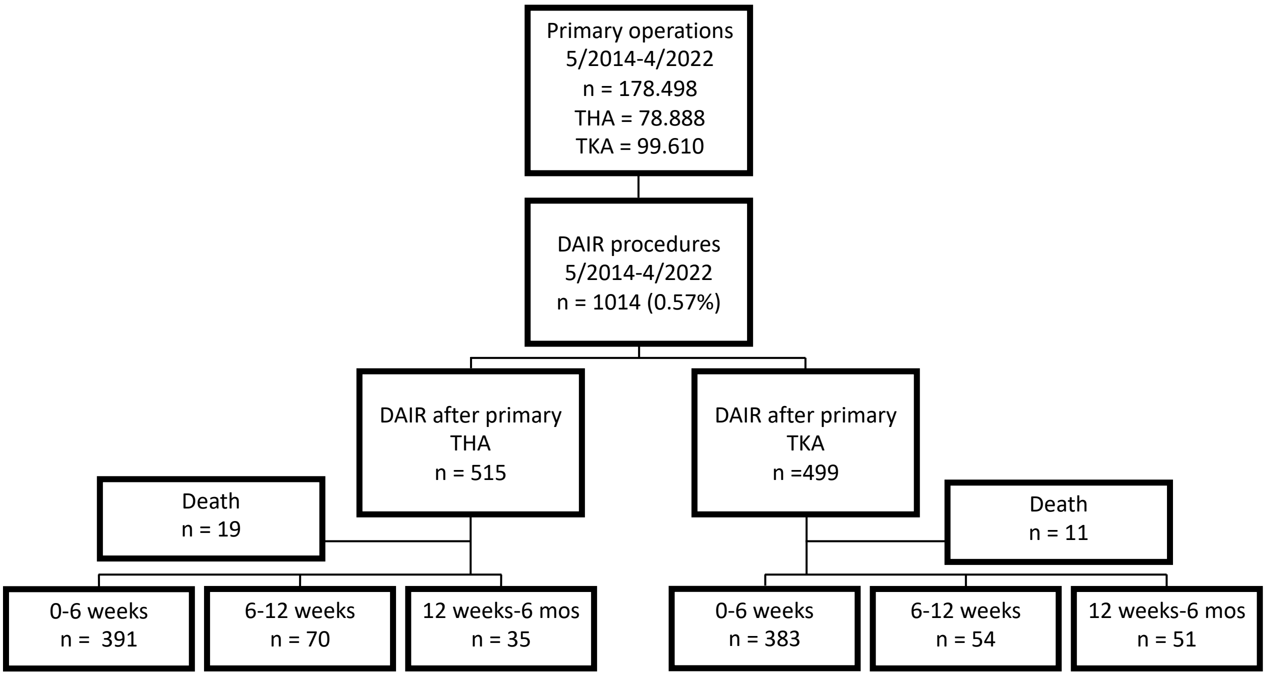

Figure 1. Flow chart of the study patients.

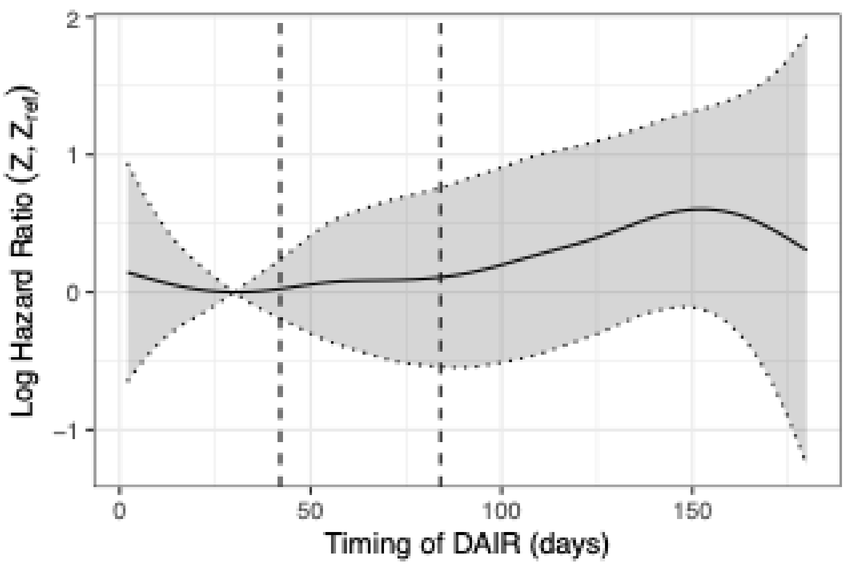

Figure 2. Nonparametric estimates of the dependence of risk of re-revision on the timing of the debridement, antibiotics, and implant retention (DAIR) procedure. Estimates are presented as log hazard ratios with 95% confidence limits with respect to a reference time point of 30 days (minimum of the hazard ratio curve). The vertical dashed lines indicate the cutoffs used for grouping the patients (0-42 days, 43-84 and 85-180 days) for further analysis.

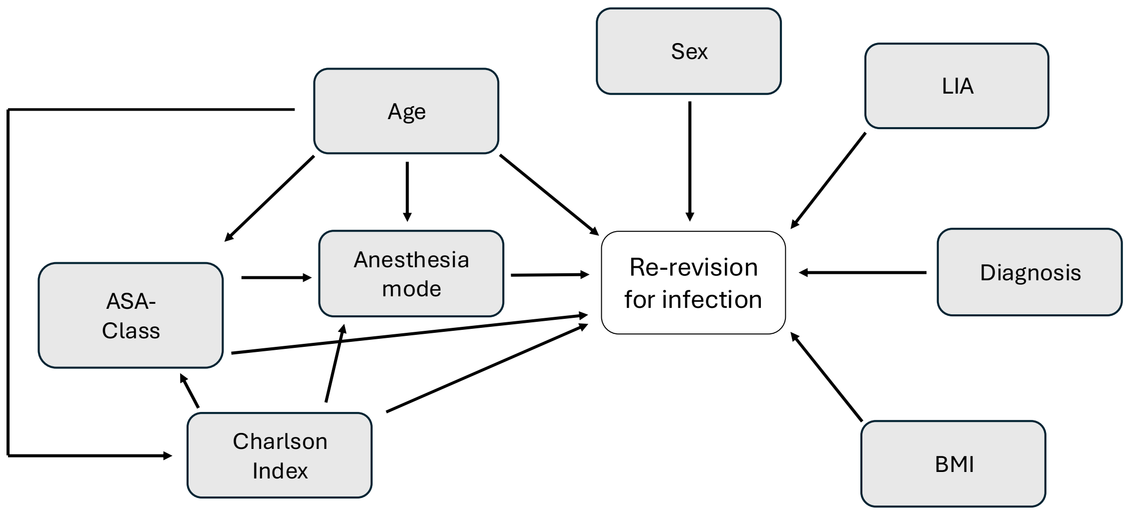

Figure 3. Directed acyclic graph (DAG) for selection of covariates in adjusted Cox proportional hazards regression analysis.

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