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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

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ABSTRACT

Background: Prosthetic joint infection (PJI) is one of the most devastating complications after total hip arthroplasty (THA), and comorbidities increase the risk. We examined whether there was a temporal change in the demographics, especially regarding comorbidities, of patients who have PJIs and were treated over a 13-year study period at a high-volume academic joint arthroplasty center. In addition, the surgical methods used and the microbiology of the PJIs were assessed.

Methods: Revisions (n = 423, 418 patients) due to PJI of the hip performed at our institution between 2008 and September 2021 were identified. All included PJIs fulfilled the 2013 International Consensus Meeting diagnostic criteria. The surgeries were categorized into one of the following categories: debridement, antibiotics, and implant retention, 1-stage revision, and 2-stage revision. Infections were classified as early, acute hematogenous, and chronic infections.

Results: There was no change in the median age of the patients, but the proportion of ASA-class 4 patients increased from 10.5% to 20%. The incidence of early infections increased from 0.11 per 100 primary THAs in 2008 to 1.09 in 2021. The incidence of 1-stage revisions increased the most, rising from 0.10 per 100 primary THAs in 2010 to 0.91 per 100 primary THAs in 2021. Furthermore, the proportion of infections caused by *Staphylococcus aureus* increased from 26.3% in 2008 to 2009 to 40% in 2020 to 2021.

Conclusion: The comorbidity burden of PJI patients increased during the study period. This increase may present a treatment challenge, as comorbidities are known to have a negative effect on PJI treatment outcomes.

Prosthetic joint infection (PJI) is one of the most devastating complications after total hip arthroplasty (THA). Moreover, PJI is not only a tremendous burden for the individual patient, but also for the global health care industry, as it is associated with recurrent surgeries, increased mortality risks, and inferior patient-reported outcomes [1–3].The incidence of PJI after THA has been reported to range between 0.5% and 0.7% at 1-year follow-up. For late infections, the cumulative incidence has been reported to range from 0.04% to 0.06% per prosthesis-year [4–6]. The incidence of PJI has increased during recent decades [6–10]. Over this period, the comorbidity burden of patients undergoing primary THA has also increased and is expected to increase further [11,12]. Indeed, an increased prevalence of diabetes and obesity, both of which are known risk factors for PJI [13,14], may lead to an even greater increase in the incidence of PJI [11].

Traditionally, the surgical treatment of PJI has been based on treatment algorithms, where early infections are preferably treated with debridement, antibiotics, and retention (DAIR), and delayed

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infections in 2-stage revision surgery [15,16]. Early or acute hematogenous PJIs are mainly caused by *Staphylococcus aureus* and delayed infections by coagulase-negative staphylococci (CNS) [17,18]. However, high rates of CNSs have also been observed in early infections [19]. The proportion of culture-negative infections has been reported to be around 5% to 15% [19,20]. Culture-negative PJIs, in particular, might present a challenge for treatment, as microbiological treatment cannot be targeted [21].

To our best knowledge, no previous study has examined how the demographics of patients with PJI, the strategy for surgical treatment, and the distribution of pathogens have changed during the past decade. In the present study, we aimed to assess the following: (1) Has there has been a change in the demographics of PJI patients? (2) Has there been any change in the surgical treatment of PJI?, and (3) Have microbiological findings changed?

Materials and Methods

Our institution is a high-volume academic referral center focused on joint arthroplasty surgery, with an annual volume of more than 2,500 primary and over 300 revision THAs. In this retrospective cohort study, we identified all revision surgeries performed for PJI at our institution between January 1st, 2008, and September 12th, 2021, by searching the ICD-10 (International Classification of Diseases 10th revision) code T84.5 (Infection and inflammatory reaction due to internal joint prosthesis). After excluding superficial wound infections and 2-stage operations, where the information on the first surgery was not available, the PJI diagnosis was confirmed with 2013 International Consensus Meeting diagnostic criteria [22]. If the criteria were not fulfilled, the hip was 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 2 separate operations.

The patient data were obtained using our institution's electronic data lake as well as electronic health records (EHR). Our institution's electronic data lake is a prospectively filled database, where specific details of every treatment period (eg, details of surgery, prosthesis, laboratory results, medication, comorbidities) are collected and documented. The EHRs contain information related to patient care, whereas the data base contains more comprehensive information on surgical details. The following patient demographics were collected from the data lake and EHRs: age, sex, body mass index (BMI), American Society of Anesthesiology (ASA) classification, and comorbidities. Charlson comorbidity indexes (CCI) were calculated separately for each patient [23]. In addition, we also recorded the date of the primary surgery, the date of the last non-infectious operation to the ipsilateral joint, and the date from the beginning of the symptoms before revision surgery. Information on the presence of the fistula and intraoperative microbiological findings from tissue specimens were also collected from the EHRs. All the microbiology analyses were performed in the accredited microbiology 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 based on the intention to treat principle: Debridement, antibiotics, and implant retention (DAIR); 1-stage revision; or 2-stage revision. The DAIR included all surgeries where the joint capsule was opened, acetabular liner and/or femoral head possibly replaced, but the femoral stem or acetabular component were not replaced or removed. In 1-stage revision, all the components were replaced in 1 operation, whereas in 2-stage revision, the components were sequentially removed and replaced in 2 operations with a period of resection arthroplasty or spacer prosthesis in between. To reflect the pathogenesis of the PJI and to produce results that are applicable in the clinical setting, 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 to chronic infections (>90 days from the previous surgery AND ≥28 days of symptoms) [16,18,24].

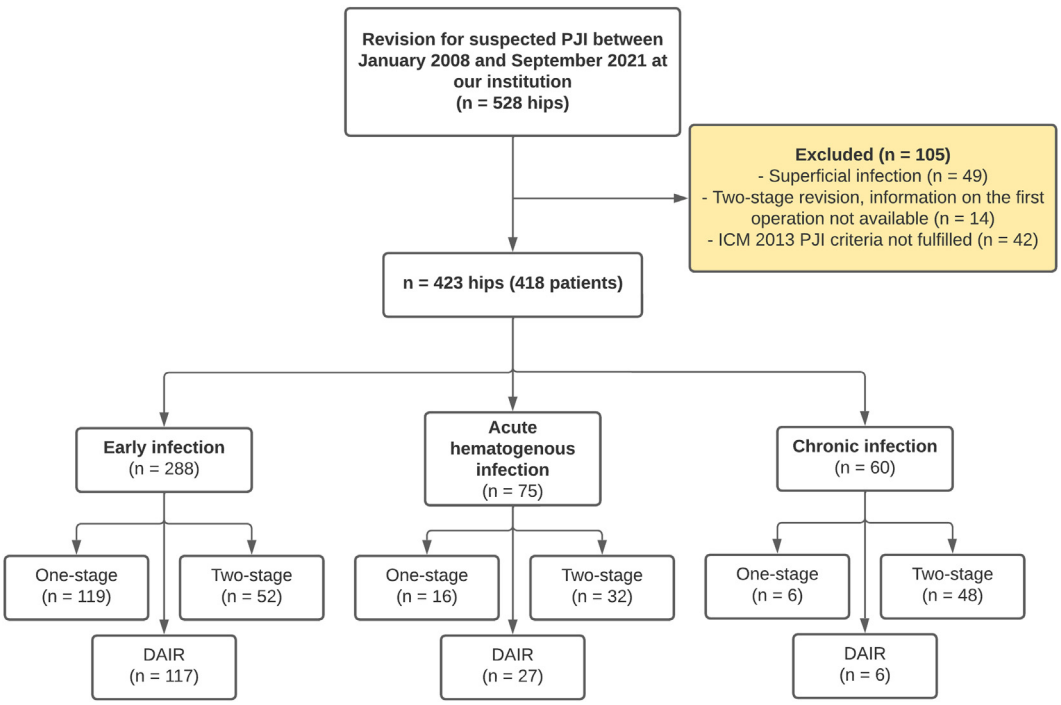

Fig. 1. Infections are classified as early (≤3 months from the previous surgery), acute hematogenous (>3 months from the previous surgery with <28 days of symptoms), and chronic (≥3 months from the previous surgery with ≥28 days of symptoms). PJI, prosthetic joint infection; DAIR, debridement, antibiotics, and implant retention.

Table 1
PJI Patient Characteristics and Preoperative Risk Factors, Stratified by the Type of the Infection.

Variable	Early (n = 288)	Acute Hematogenous (n = 75)	Chronic (n = 60)
Patient characteristics			
Women, n (%)	157/288 (54.5)	38/75 (50.7)	31/60 (51.7)
Age, y, median (IQR)	72 (63-79)	70 (64-78)	75 (63-79)
BMI, mean (sd)	29.3 (6.0)	28.5 (6.5)	26.8 (4.7)
BMI ≥30, n (%)	109/272 (40.1)	23/66 (34.8)	15/54 (27.8)
BMI ≥35, n (%)	49/272 (18)	11/66 (16.7)	3/54 (5.6)
CCI, median (range)	3 (0-7)	3 (0-6)	3 (0-6)
CCI ≥3, n (%)	192/288 (66.7)	43/75 (57.3)	41/60 (68.3)
ASA-class, n (%)			
1	9 (3.1)	2 (2.7)	1 (1.7)
2	68 (23.6)	14 (18.7)	14 (23.3)
3	169 (58.7)	40 (53.3)	34 (56.7)
4	38 (13.2)	19 (25.3)	10 (16.7)
5	2 (0.7)	0	0
NA	2 (0.7)	0	1 (1.7)
Co-morbidities, n (%)			
Diabetes mellitus	59/276 (21.4)	9/65 (13.8)	11/57 (19.3)
Rheumatoid arthritis	23/272 (8.5)	4/65 (6.2)	8/56 (14.3)
Chronic kidney disease	11/275 (4)	0	3/56 (5.4)
Operation type, n (%)			
DAIR	117 (40.6)	27 (36)	6 (10)
One-stage revision	119 (41.3)	16 (21.3)	6 (10)
Two-stage revision	52 (18.1)	32 (42.6)	48 (80)
Spacer usage	12/52 (23.1)	3/32 (9.4)	9/48 (18.8)
Surgical characteristic			
Time since previous operation, median (IQR), d	18 (13-26)	2,163 (891-3,675)	1,133 (392-2441)
Symptom duration, median (IQR), d	14 (7-20)	7 (3-13)	158 (61-369)
Sinus tract, n (%)	208/284 (73.2)	7/74 (9.5)	18/60 (30)

Infections are classified as early (≤3 mo from the previous surgery), acute hematogenous (>3 mo from the previous surgery with <28 d of symptoms), and chronic (>3 mo from the previous surgery with ≥28 d of symptoms).
DAIR, debridement, antibiotics, and implant retention; d, days; y, years; IQR, interquartile range; sd, standard deviation; CCI, charlson comorbidity index; ASA, American Society of Anesthesiology; BMI, body mass index.

Table 2
PJI Patient Characteristics and Preoperative Risk Factors, Stratified by the Operation type.

Variable	DAIR (n = 150)	One-Stage (n = 141)	Two-Stage (n = 132)
Patient characteristics			
Women, n (%)	93/150 (62)	70/141 (49.6)	63/132 (47.7)
Age, median (IQR), y	73 (66-80)	71 (59-79)	72 (64-78)
BMI, mean (sd)	28.9 (6.1)	29.9 (6.6)	27.5 (4.9)
BMI ≥30, n (%)	51/135 (37.8)	59/131 (45)	37/126 (29.4)
BMI ≥35, n (%)	23/135 (17)	27/131 (20.6)	13/126 (10.3)
CCI, median (range)	3 (0-7)	3 (0-7)	3 (0-7)
CCI ≥3, n (%)	105/150 (70)	85/141 (60.3)	86/132 (65.2)
ASA-class, n (%)			
1	4 (2.7)	6 (4.3)	2 (1.5)
2	35 (23.3)	33 (23.4)	28 (21.2)
3	78 (52)	77 (54.6)	88 (66.7)
4	32 (21.3)	23 (16.3)	12 (9.1)
5	1 (0.7)	1 (0.7)	0
NA	0	1 (0.7)	2 (1.5)
Co-morbidities, n (%)			
Diabetes mellitus	27/139 (19.4)	29/133 (21.8)	23/126 (18.3)
Rheumatoid arthritis	14/139 (10.1)	7/129 (5.4)	14/125 (11.2)
Chronic kidney disease	5/140 (3.6)	4/131 (3.1)	5/125 (4)
Infection type, n (%)			
Early	117 (78)	119 (84.4)	52 (39.4)
Acute hematogenous	27 (18)	16 (11.3)	32 (24.2)
Chronic	6 (4)	6 (4.3)	48 (36.4)
Surgical characteristic			
Time since previous operation, median (IQR), d	18 (13-47)	21 (15-37)	248 (34-1733)
Symptom duration, median (IQR), d	12 (6-17)	15 (8-22)	19 (7-80)
Sinus tract, n (%)	92/148 (62.2)	91/138 (65.9)	50/132 (37.9)
Spacer usage, n (%)	-	-	24/132 (18.2)

Infections are classified as early (≤3 mo from the previous surgery), acute hematogenous (>3 mo from the previous surgery with <28 d of symptoms), and chronic (>3 mo from the previous surgery with ≥28 d of symptoms).
DAIR, debridement, antibiotics, and implant retention; d, days; y, years; IQR, interquartile range; sd, standard deviation; CCI, charlson comorbidity index; ASA, American Society of Anesthesiology; BMI, body mass index.

Table 3
Patient Demographics Within Our Study Period, Stratified by the Year of Operation Infections are Classified as Early (≤3 mo From the Previous Surgery), Acute Hematogenous (>3 mo From the Previous Surgery With <28 d of Symptoms), and Chronic (>3 mo From the Previous Surgery With ≥28 d of Symptoms).

Variable	2008-09 (n = 19)	2010-11 (n = 35)	2012-13 (n = 33)	2014-15 (n = 64)	2016-17 (n = 91)	2018-19 (n = 76)	2020-21 (n = 105)
Patient characteristics							
Female, n (%)	10/19 (52.6)	19/35 (54.3)	19/33 (57.6)	33/64 (51.6)	51/91 (56)	39/76 (51.3)	55/105 (53.4)
Age, median (IQR), y	71 (64-79)	69 (62-77)	75 (70-78)	73 (64-80)	73 (66-80)	72 (63-79)	70 (60-78)
BMI, mean (sd)	25.6 (3.6)	28.2 (4.5)	25.9 (3.8)	29.4 (6.4)	28.7 (6.3)	29.6 (6.2)	29.4 (6.3)
BMI ≥30, n (%)	4/18 (22.2)	15/34 (44.1)	3/23 (13)	23/62 (37.1)	33/84 (39.3)	27/73 (37)	42/98 (42.9)
BMI ≥35, n (%)	0	2/34 (5.9)	1/23 (4.3)	13/62 (21)	13/84 (15.5)	13/73 (17.8)	21/98 (21.4)
CCI, median (range)	3 (1-6)	3 (1-6)	3 (1-6)	3 (0-7)	3 (0-7)	3 (0-6)	3 (0-7)
CCI ≥3, n (%)	12/19 (63.2)	19/35 (54.3)	26/33 (78.8)	42/64 (65.6)	64/91 (70.3)	47/76 (61.8)	66/105 (62.9)
ASA-class, n (%)							
1	0	0	1 (3)	2 (3.1)	3 (3.3)	2 (2.6)	4 (3.8)
2	6 (31.6)	10 (28.6)	5 (15.2)	16 (25)	23 (25.3)	14 (18.4)	22 (21)
3	9 (47.4)	24 (68.6)	23 (69.7)	39 (60.9)	45 (49.5)	45 (59.2)	58 (55.2)
4	2 (10.5)	1 (2.9)	4 (12.1)	7 (10.9)	19 (20.9)	13 (17.1)	21 (20)
5	0	0	0	0	1 (1.1)	1 (1.3)	0
NA	2 (10.5)	0	0	0	0	1 (1.3)	0
Comorbidities, n (%)							
Diabetes mellitus	1/17 (5.9)	5/34 (14.7)	11/32 (34.4)	11/61 (18)	17/86 (19.8)	13/67 (19.4)	21/101 (20.8)
Rheumatoid arthritis	2/17 (11.8)	4/34 (11.8)	3/31 (9.7)	6/61 (9.8)	8/86 (9.3)	5/65 (7.7)	7/99 (7.1)
Chronic kidney disease	1/17 (5.9)	2/34 (5.9)	0	3/61 (4.9)	4/86 (4.7)	2/67 (3)	2/100 (2)
Infection type, n (%)							
Early	7 (36.8)	16 (45.7)	16 (48.5)	37 (57.8)	63 (69.2)	62 (81.6)	87 (82.9)
Acute hematogenous	6 (31.6)	5 (14.3)	8 (24.2)	18 (28.1)	18 (19.8)	8 (10.5)	12 (11.4)
Chronic	6 (31.6)	14 (40)	9 (27.3)	9 (14.1)	10 (11)	6 (7.9)	6 (5.7)
Operation type, n (%)							
DAIR	0	8 (22.9)	10 (30.3)	29 (45.3)	41 (45.1)	31 (40.8)	31 (29.5)
One-stage revision	0	5 (14.3)	5 (15.2)	11 (17.2)	29 (31.9)	32 (42.1)	59 (56.2)
Two-stage revision	19 (100)	22 (62.9)	18 (54.5)	24 (37.5)	21 (23.1)	13 (17.1)	15 (14.3)
Spacer usage	3 (15.8)	4 (18.2)	2 (11.1)	10 (41.7)	4 (19)	0	1 (6.7)

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

Patient and Surgical Demographics

A total of 423 PJI revisions (418 patients) were performed at our institution between January 1st, 2008 and September 12th, 2021. Of these, 288 (68.1%) were early infections, 75 (17.7%) acute hematogenous infections, and 60 (14.2%) chronic infections (Fig. 1). A total of 150 (35.5%) DAIRs, 141 (33.3%) 1-stage revisions, and 132 (31.2%) 2-stage revisions were performed. Most of the DAIRs (n = 117, 78%) and 1-stage operations (n = 119, 84.4%) were performed for early infections. Most of the 2-stage revisions were performed because of early (n = 52, 39.4%) or chronic infection (n = 48, 36.4%). The median age of the patients was 72 years (range, 34 to 94) and 53.9% (n = 226) were women. Further details on the demographics and surgical treatments are presented in Tables 1 and 2.

Data Analyses

Means with standard deviations (SD) were presented for normally distributed variables and medians with interquartile ranges (IQRs) for variables with non-Gaussian population. Categorical variables were presented as counts and percentages. To examine the changes during our study period, patient demographics and microbiology of the PJIs were compared in a longitudinal setting using descriptive statistics. Moreover, to avoid selection bias, patient demographics and microbiology of the PJIs were compared in 2-year admission groups, rather than in yearly groups.

As our institution is a tertiary referral center, not all revisions were performed on patients whose primary-THA was performed at our institution. Therefore, incidences were calculated based on the number of primary THAs performed at our institution, and the number of PJIs of which the primary arthroplasty was performed at our institution. Referral PJIs, and PJIs that occurred after revision THA, were not included in the incidence calculations. All analyses were performed using R (version 4.1.2; R Foundation for Statistical Computing, Vienna, Austria). The results of this study are reported according to the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) guidelines [25].

Results

Trends in Demographics and Surgical Treatment

While the median age of the patients did not change during the study period, the comorbidity burden of the patients increased markedly; the proportion of ASA-class 4 patients increased from 10.5% in 2008 to 2009 to over 20% in 2016 to 2017 and remained approximately that level till the end of the study period (Table 3).

Furthermore, the incidence of PJI operations increased over 12-fold: from 0.11 per 100 primary THAs in 2008 to 1.34 per 100 primary THAs in 2021. The largest increase was observed in early infections. In 2008, the incidence of early infection was 0.11 per 100 primary THAs, whereas in 2021 it was 1.09 per 100 primary THAs. During our study period, 1-stage revision became the most common surgical treatment. In the years 2008 to 2009, no 1-stage revisions were performed, but in the years 2020 to 2021, the proportion of 1-stage revisions was 56.2% (n = 59). (Tables 3 and 4, Figs. 2 and 3).

Microbial Findings

Staphylococcus aureus was the most identified pathogen, accounting for 157 (37.1%) infections. A further 107 (25.3%) infections were caused by coagulase-negative staphylococci (CNS), 10 (9.3%) of which were further identified as *Staphylococcus lugdunensis*. There were 75 culture-negative infections (17.7%), which were the most common among acute hematogenous infections, with 19.7%

Table 4
Yearly Incidence of the PJI Revisions at Our Institution Between 2008 and 2021.

Variable	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Operation type, n														
Primary THA	944	1,033	986	958	928	1,020	1,078	1,188	1,445	1,565	1,892	2,038	2,063	1,646
PJI revision	1	6	7	12	4	2	11	19	16	29	23	16	41	22
Infection type, n														
Early	1	3	4	6	0	1	6	10	12	21	20	14	37	18
Acute hematogenous	0	3	0	2	3	0	5	6	2	5	0	1	2	3
Chronic	0	0	3	4	1	1	0	3	2	3	3	1	2	1
Type of the revision, n														
DAIR	0	0	1	2	1	1	5	10	9	12	11	4	4	6
One-stage revision	0	0	1	3	2	0	2	5	4	11	8	10	31	15
Two-stage revision	1	6	5	7	1	1	4	4	3	6	4	2	6	1
Incidence per 100 primary THAs														
Overall	0.11	0.58	0.71	1.25	0.43	0.20	1.02	1.60	1.11	1.85	1.22	0.79	1.99	1.34
Early infections	0.11	0.29	0.41	0.63	0	0.10	0.56	0.84	0.83	1.34	1.06	0.69	1.79	1.09
Acute hematogenous infections	0	0.29	0	0.21	0.32	0	0.46	0.51	0.14	0.32	0	0.05	0.10	0.18
Chronic infections	0	0	0.30	0.42	0.11	0.10	0	0.25	0.14	0.19	0.16	0.05	0.10	0.06
DAIR	0	0	0.10	0.21	0.11	0.10	0.46	0.84	0.62	0.77	0.58	0.20	0.19	0.36
One-stage revision	0	0	0.10	0.31	0.22	0	0.19	0.42	0.28	0.70	0.42	0.49	1.50	0.91
Two-stage revision	0.11	0.58	0.51	0.73	0.11	0.10	0.37	0.34	0.21	0.38	0.21	0.10	0.29	0.06

The number of PJI revisions are calculated based on the number of PJIs, whose previous operation was primary arthroplasty performed at our institution. Therefore, referral PJIs or PJIs that occurred after revision arthroplasty are not included. infections are classified as early (≤3 mo from the previous surgery), acute hematogenous (>3 mo from the previous surgery with <28 d of symptoms), and chronic (≥3 mo from the previous surgery with ≥28 d of symptoms).
THA, total hip arthroplasty; DAIR, debridement, antibiotics, and implant retention.

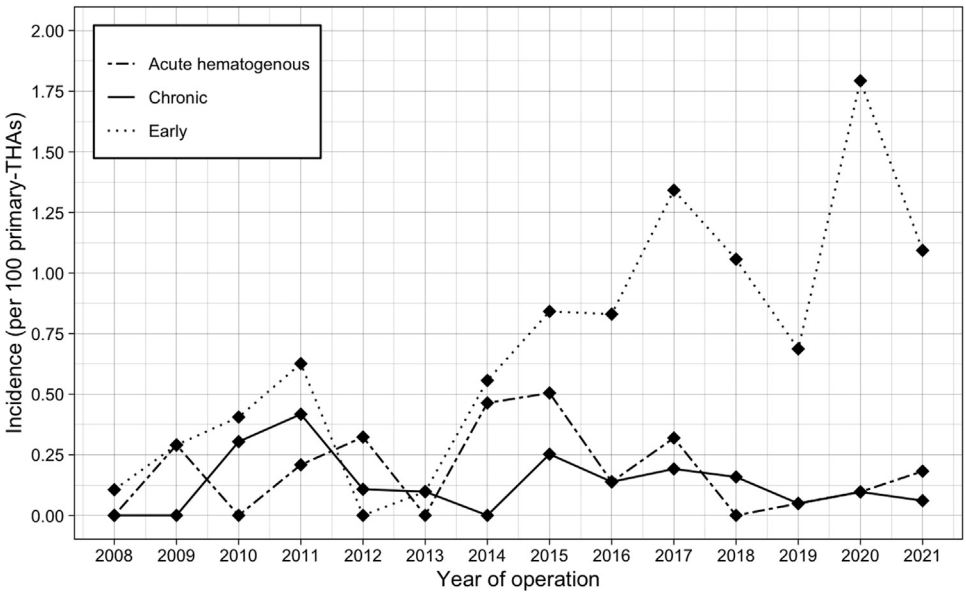

Fig. 2. Infections are classified as early (≤3 months from the previous surgery), acute hematogenous (>3 months from the previous surgery with <28 days of symptoms), and chronic (≥3 months from the previous surgery with ≥28 days of symptoms). Incidences are calculated based on the number of primary THAs at our institution and number of PJI revisions, whose previous operation was primary arthroplasty performed at our institution. Therefore, referral PJIs or PJIs that occurred after revision arthroplasty are not included. THA, total hip arthroplasty.

(n = 15) of them identified as culture negative. In addition, a total of 38 (9%) infections were polymicrobial. (Tables 5 and 6).

During the study period, the proportion of *S. aureus* increased the most. In 2008 to 2009, the proportion of *S. aureus* was 26.3% (n = 5). However, in 2020 to 2021, the proportion had increased to 40% (n = 46). The proportion of negative cultures decreased remarkably in this period. Also, the proportion was 31.6% (n = 6) in 2008 to 2009, but only 16.5% (n = 19) in 2020 to 2021 (Table 7).

Discussion

The results of the present study reveal that there was a notable increase in the comorbidity burden of patients with PJI during the study period. At the beginning of our study period, 2-stage revision was the most performed surgical procedure. However, 1-stage revision became the most performed procedure later. In addition, we also observed a more than 10-fold increase in the incidence of early infections and, perhaps reflecting this increase, the proportion of PJIs caused by *S. aureus* also increased notably.

The median age of the patients did not change during the study period. However, the proportion of ASA-class 4 patients more than doubled from approximately 10 to around 20%. The same trend was observed for patients with ASA-class 3 or greater, as the proportion increased from 57.9% to 75.2%. The same trend of increased comorbidity burden has previously been reported by O'Toole et al. They reported that rates of obesity and diabetes in THA patients has

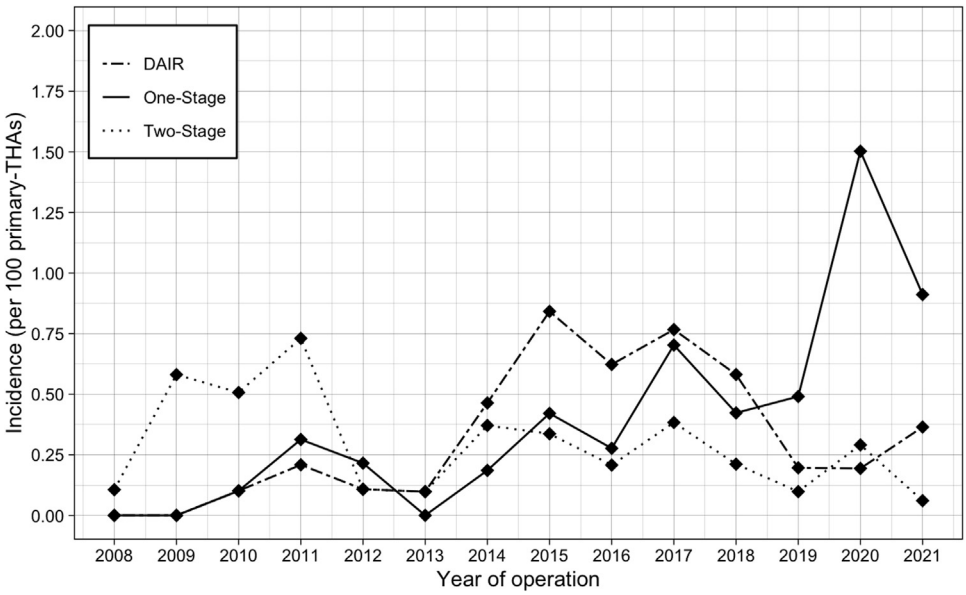

Fig. 3. Incidences are calculated based on the number of primary THAs performed at our institution and number of PJI revisions, whose previous operation was primary arthroplasty performed at our institution.

Table 5
Microbiological Results From Tissue Specimens, Stratified by the Type of the Infection.

Pathogen	All (n = 461)		Early (n = 319)		Acute Hematogenous (n = 76)		Chronic (n = 66)	
	N	%	N	%	N	%	N	%
Staphylococcus aureus	157	*34.1*	116	*36.4*	32	*42.1*	9	*13.6*
CNS	107	*23.2*	80	*25.1*	4	*5.3*	23	*34.8*
Streptococcus beta-hemolyticus	40	*8.7*	28	*8.8*	10	*13.2*	2	*3*
Other streptococcus species	14	*3*	0	*0*	6	*7.9*	8	*12.1*
Gram-negative aerobic	24	*5.2*	15	*4.7*	6	*7.9*	3	*4.5*
Enterococcus species	20	*4.3*	15	*4.7*	0	*0*	5	*7.6*
Anaerobic	13	*2.8*	5	*1.6*	3	*3.9*	5	*7.6*
Other	11	*2.4*	9	*2.8*	0	*0*	2	*3*
Negative culture	75	*16.3*	51	*16*	15	*19.7*	9	*13.6*

Microbiological findings from the polymicrobial infections (n = 38) are included, and therefore the total N is greater than the total N of the surgeries performed (n = 423). *Bacillus cereus* (n = 2), *Candida parapsilosis* (n = 1) and *Corynebacterium species* (n = 8) are included in the other group.
Italics: No statistical testing of significance (eg, T-Test or Mann-Whitney U) were performed, as described in the methods section "microbiology of the PJIs were compared in a longitudinal setting using descriptive statistics".
CNS, Coagulase-Negative Staphylococci.

increased significantly and was projected to increase even more [11]. This increase in the comorbidity burden can be partly explained by the increases in the proportion of patients who had diabetes or BMI over 35. Furthermore, as the increased comorbidity burden is a risk factor for PJI, we might assume that it has had an effect on the observed increase in the incidence of PJIs [6,13,14,26].

In addition to the increase in the incidence of early infection, there was also an over 120% increase in the proportion of early infections over the study period. During the same period, the number of primary THAs in our institution increased from 944 in 2008 to 2,063 in 2020, an increase of 118.5%. Therefore, the observed increase in the proportion of early PJIs is at least partly due to the increased number of primary THAs performed. In addition to that, as our institution is a tertiary referral center, not all revisions were performed on patients, whose primary THA was performed at our institution. This might be the reason why the number of revisions due to early infections performed at our institution increased more than the number of primary THAs.

The increase in the incidence of 1-stage revisions and the subsequent decrease in the incidence of DAIRs might be considered surprising because DAIR is less invasive than 1-stage revision and is considered as a suitable option for the treatment of early or acute hematogenous infections [16,27]. The differences in incidence rates can be explained by the adoption of a more aggressive approach to PJI treatment, as the 1-stage operation is also considered as a suitable treatment for early and acute infections [16,27]. In addition, our institution is a high-volume center, and we currently prefer to perform 1-stage revision to as many patients as possible. Increased comorbidity might also be a reason, why the incidence of 1-stage operations has increased. We might, therefore, end up performing the 1-stage revision rather than DAIR for patients with multiple comorbidities, because the eradication rates of 1-stage operations have been reported to be better [27]. With 2-stage revisions, we observed no trend in the number of operations or in the incidences, as both remained at approximately the same level during the entire study period.

Staphylococcus aureus is reported to cause between 24 and 28% of PJIs, and the most common pathogen among early infections and responsible for causing approximately one-third of them [17–19,28]. Similarly, in our study, *S. aureus* was the most isolated pathogen and the most prevalent among early and acute hematogenous infections. In contrast, chronic PJI was most commonly caused by CNS. The proportion of *S. aureus* had a temporal trend, however, and it became the most common pathogen during our study period. At the same time, the proportion of early infections increased from 36.8 to 82.9%. Furthermore, the proportion of acute hematogenous infections caused by *S. aureus* was also high in our study, which is in line with the findings of Benito et al. (2019) [17].

The proportion of negative cultures also decreased during the study period from 31.6% to 16.5%. This finding might be explained by the more accurate microbiological diagnostic techniques used. Furthermore, an increasing trend in the mean number of

Table 6
Microbiological Results From Polymicrobial Infections (n = 38) Stratified by the Type of the Infection.

Pathogen	All (n = 76)		Early (n = 62)		Acute Hematogenous (n = 2)		Chronic (n = 12)	
	N	%	N	%	N	%	N	%
Staphylococcus aureus	11	*14.5*	10	*16.1*	0	*0*	1	*8.3*
CNS	26	*34.2*	22	*35.5*	0	*0*	4	*33.3*
Streptococcus beta-hemolyticus	8	*10.5*	7	*11.3*	0	*0*	1	*8.3*
Other streptococcus species	3	*3.9*	0	*0*	1	*50*	2	*16.7*
Gram-negative aerobic	10	*13.2*	9	*14.5*	0	*0*	1	*8.3*
Enterococcus species	4	*5.3*	3	*4.8*	0	*0*	1	*8.3*
Anaerobic	5	*6.6*	3	*4.8*	1	*50*	1	*8.3*
Other	9	*11.8*	8	*12.9*	0	*0*	1	*8.3*

Bacillus cereus (n = 1), *Candida parapsilosis* (n = 1) and *Corynebacterium species* (n = 7) are included in the other group.
Italics: No statistical testing of significance (eg, T-Test or Mann-Whitney U) were performed, as described in the methods section "microbiology of the PJIs were compared in a longitudinal setting using descriptive statistics".
CNS, Coagulase-Negative Staphylococci.

Table 7
Microbiological Results From Tissue Specimens During Our Study Period.

Pathogen	2008-09 (n = 19)		2010-11 (n = 36)		2012-13 (n = 35)		2014-15 (n = 67)		2016-17 (n = 101)		2018-19 (n = 88)		2020-21 (n = 115)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Staphylococcus aureus	5	*26.3*	8	*22.2*	13	*37.1*	19	*28.4*	32	*31.7*	34	*38.6*	46	*40*
CNS	6	*31.6*	10	*27.8*	6	*17.1*	17	*25.4*	23	*22.8*	18	*20.5*	27	*23.5*
Streptococcus beta-hemolyticus	0	*0*	4	*11.1*	3	*8.6*	5	*7.5*	11	*10.9*	8	*9.1*	9	*7.8*
Other streptococcus species	1	*5.3*	2	*5.6*	0	*0*	4	*6*	3	*3*	2	*2.3*	2	*1.7*
Gram-negative aerobic	1	*5.3*	1	*2.8*	1	*2.9*	3	*4.5*	7	*6.9*	6	*6.8*	5	*4.3*
Enterococcus species	0	*0*	1	*2.8*	3	*8.6*	5	*7.5*	6	*5.9*	4	*4.5*	1	*0.9*
Anaerobic	0	*0*	2	*5.6*	1	*2.9*	2	*3*	3	*3*	2	*2.3*	3	*2.6*
Other	0	*0*	0	*0*	0	*0*	1	*1.5*	2	*2*	5	*5.7*	3	*2.6*
Negative culture	6	*31.6*	8	*22.2*	8	*22.9*	11	*16.4*	14	*13.9*	9	*10.2*	19	*16.5*

Microbiological findings from the polymicrobial infections (n = 38) are included, and therefore the total N is greater than the total N of surgeries performed (n = 423).
Italics: No statistical testing of significance (eg, T-Test or Mann-Whitney U) were performed, as described in the methods section "microbiology of the PJIs were compared in a longitudinal setting using descriptive statistics".
DAIR, debridement, antibiotics, and implant retention; CNS, Coagulase-Negative Staphylococcus.

intraoperative tissue specimens per patient was observed. In the years 2008 to 2009, the mean number was 5.26, but the corresponding number had increased to 5.90 in 2020 to 2021. This arguably decreases the risk of "false-negative" diagnosis. The decreased proportion of acute hematogenous infections may also be the reason, as the largest proportion of culture-negative infections was among those. Sepsis is often presented within patients with acute infection, and therefore the antimicrobial treatment may have been started before the revision surgery, thus causing the intraoperative tissue cultures being negative.

Our study has several potential limitations that should be considered. Due to the rare nature of PJI, our findings might be prone to selection bias. However, as the total number of patients was over 400 and each patient was treated in the same institution by the same surgeons, rather than in a multicenter setting, we believe that the potential risk for selection bias was minimized. Furthermore, as we analyzed the surgeries in 2-year admission groups, rather than in yearly groups, we managed to minimize the effect of patient selection on the observed results and temporal trends. Another potential limitation of our study is that in some cases microbiological treatment may have started before the surgery. Therefore, the intraoperative findings might have been negative, and thus may have affected the results. Moreover, as the definition of PJI does not require positive microbiological cultures [20,22], and all our PJIs were confirmed with validated criteria, we cannot be sure whether some of the PJIs were culture-negative only because of previous antimicrobial treatment. In addition, there might be inaccuracy in the used databases, and therefore for example, the diagnosis of diabetes mellitus or rheumatoid arthritis might have been missing in some patients. However, as the EHRs were screened thorough for the history of comorbidities, we believe, that this possible bias that missing information regarding the comorbidities might have to our results, was minimized. Furthermore, the classification of the infection was based on the combination of time from the previous surgery and duration of symptoms, and it is evident, that different classification strategies might have produced different results. However, this limitation is common in PJI research, as there is no standardized protocol for the infection classification. In addition, we also included multiply operated hips, if no infection-related revisions were performed previously, and this might also have effected to our results. The strengths of our study are the large number of patients combined with accurate records from our high-quality prospectively maintained datalake. In addition, the length of the study period made it possible to examine temporal trends in a single-center setting.

In conclusion, the comorbidity burden among PJI patients increased markedly over the last decade at our institution. This clearly presents a formidable treatment challenge, as comorbidities have a negative effect on PJI treatment outcomes. Furthermore, the incidence of revisions due to early infections has increased remarkably, perhaps reflecting the change in the distribution of the pathogens that cause PJIs.

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