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Influence of Gender on Occurrence of Aseptic Loosening and Recurrent PJI after Revision Total Knee Arthroplasty

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Abstract: Background: Periprosthetic joint infection (PJI) is a common yet severe complication after total knee arthroplasty (TKA). Surgical intervention and antibiotic therapy are obligatory to achieve successful, infection-free outcome. Compared to the outcomes after primary TKA, prosthesis failure rates are drastically increased after PJI-dependent revision surgery. Recurrent PJI and aseptic loosening are the most common reasons for prosthesis failure after revision TKA. An open question is the influence of the patients' gender on long-term prosthesis survival after revision surgery. Additionally, it is unknown whether gender-related parameters and risk factors or differences in treatment are responsible for potential differences in outcome after revision arthroplasty. **Patients and Methods:** In this report, 109 patients that received TKA revision surgery due to PJI were retrospectively analyzed. We used clinical, paraclinical and radiological examinations to study the influence of gender on the long-term complications aseptic loosening and recurrent PJI after PJI-dependent revision arthroplasty. **Results:** While overall prosthesis failure rates and risk of recurrent PJI did not differ between genders, the long-term risk of aseptic loosening was significantly elevated in female patients. Postoperative coronal alignment was significantly more varus for women later diagnosed with aseptic loosening. Besides coronal alignment, no gender-dependent differences in clinical presentation or treatment were observed. **Conclusions:** Female patients displayed a significantly increased risk for aseptic loosening after PJI-dependent revision TKA. The observed gender-dependent differences in long-term outcome in our study support theories surrounding the role of bone metabolism in the development of aseptic loosening. Our data suggest that further research on a female design for PJI-dependent revision prostheses is warranted.

Keywords: aseptic loosening; periprosthetic joint infection; knee arthroplasty; revision arthroplasty; sex differences; gender differences

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1. Introduction

As life expectancy continually increases, the demand for knee joint replacements is rising [1]. Despite use of antibiotic prophylaxis and improved aseptic surgical techniques, PJI is still a common yet severe complication after TKA [2,3]. Surgical intervention and antibiotic therapy are obligatory to achieve a successful, infection-free outcome [4,5]. Current treatment guidelines dictate one, two or multiple-stage revision surgery depending on individual risk factors [6]. Two or multiple-stage revision surgery comprises removal of the infected prosthesis, debridement, irrigation and introduction of a temporary arthrodesis followed by reimplantation of a new prosthesis in a second-stage surgery [6].

With incidences of 1–5% after primary TKA, PJI and aseptic loosening are the most common indications for revision arthroplasty [7,8]. After revision arthroplasty, incidence of both aseptic loosening and PJI is increased to up to approximately 20% [9–11]. The role of patient-specific factors; bone loss due to revision surgery; mechanical factors of the prosthesis and bone–cement interface; and immune system-depended changes in the bone metabolism in long-term prosthesis survival is an ongoing discussion but remains largely unclear [12–14]. An open question is the influence of the patients' gender on long-term prosthesis survival after revision surgery. Additionally, it is unknown whether gender-related parameters and risk factors or differences in treatment may be responsible for potential differences in outcome after revision arthroplasty.

Gender-dependent differences in coronal and sagittal knee alignment are well known [15,16]. Even so, as previous studies found no evidence for short or long-term advantages in gender-dependent designs for primary TKA, the use of gender-dependent prostheses is neither recommended nor common [17,18]. However, there is paucity of data on the potential impact of gender-dependent alignment and the concordant role of prosthesis design in the outcome after PJI-dependent revision surgery.

In this study, we retrospectively analyzed 109 patients receiving cemented revision arthroplasty due to PJI to recognize a gender-dependent difference in prevalence for aseptic loosening or recurrent PJI, and to identify potential gender-related differences responsible for these differences in long-term prosthesis outcome.

2. Materials and Methods

2.1. Patients

This study was approved by the local ethics committee (EA2/083/19; 25 February 2020) and completed in accordance with the Declaration of Helsinki. We retrospectively studied all patients that underwent PJI-dependent TKA revision surgery in between 1 January 2012 and 1 January 2018 at our hospital and were successfully treated at the time of final discharge (Figure 1). In total, 109 patients were included in this study. Clinical, paraclinical and radiological parameters were evaluated for all patients. EBJIS criteria were used to define PJI, and modified Delphi criteria were used to define successful treatment at time of final discharge as previously described [19,20]. Exclusion criteria were: (I) treatment with DAIR or permanent arthrodesis; (II) no implantation of a new prosthesis after implant removal or one-stage exchange TKA; (III) primary TKA due to infection; (IV) primary TKA or revision due to trauma without any pretraumatic signs of infection; (V) incomplete postoperative clinical or radiological examination; (VI) no follow-up after revision surgery. In total, 22 patients were excluded based on these criteria. There were no further exclusions.

2.2. Treatment

All patients received centralized and interdisciplinary treatment in a specialized department for total joint infections. Antimicrobial therapy was initiated as soon as PJI was diagnosed and lasted for up to 6 weeks after reimplantation [6]. Antibiotic treatment was chosen based on bacterial susceptibility, the recommendations of Zimmerli [21], and in consultation with our department for microbiology and infectiology.

For revision surgery, two or multiple-stage exchange surgery was performed as previously described [6,22]. After removal of the infected prosthesis, thorough debridement, and irrigation, patients received a temporary, antibiotics-loaded cement spacer between stages. Prosthesis reimplantation was performed at least six weeks after removal when no clinical and laboratory signs of infection were apparent. Surgical procedures were conducted by high-volume surgeons specialized in the treatment of PJI and revision TKA. At reimplantation, in almost all cases a stemmed rotating-hinge or full-hinged prothesis was used (>95%): 97 patients received a stemmed rotating-hinge prothesis (60 Endo-Modell, LINK, Hamburg, Germany; 36 RT-Plus, Smith and Nephew, Tuttlingen, Germany; one Enduro, Aesculap, Tuttlingen, Germany), seven patients received a stemmed full-hinged prothesis (Endo-Modell, LINK, Hamburg, Germany) and five patients received a stemmed condylar constrained knee prosthesis-type prosthesis (TC3, DePuy Synthes, Johnson & Johnson, West Chester, PA, USA).

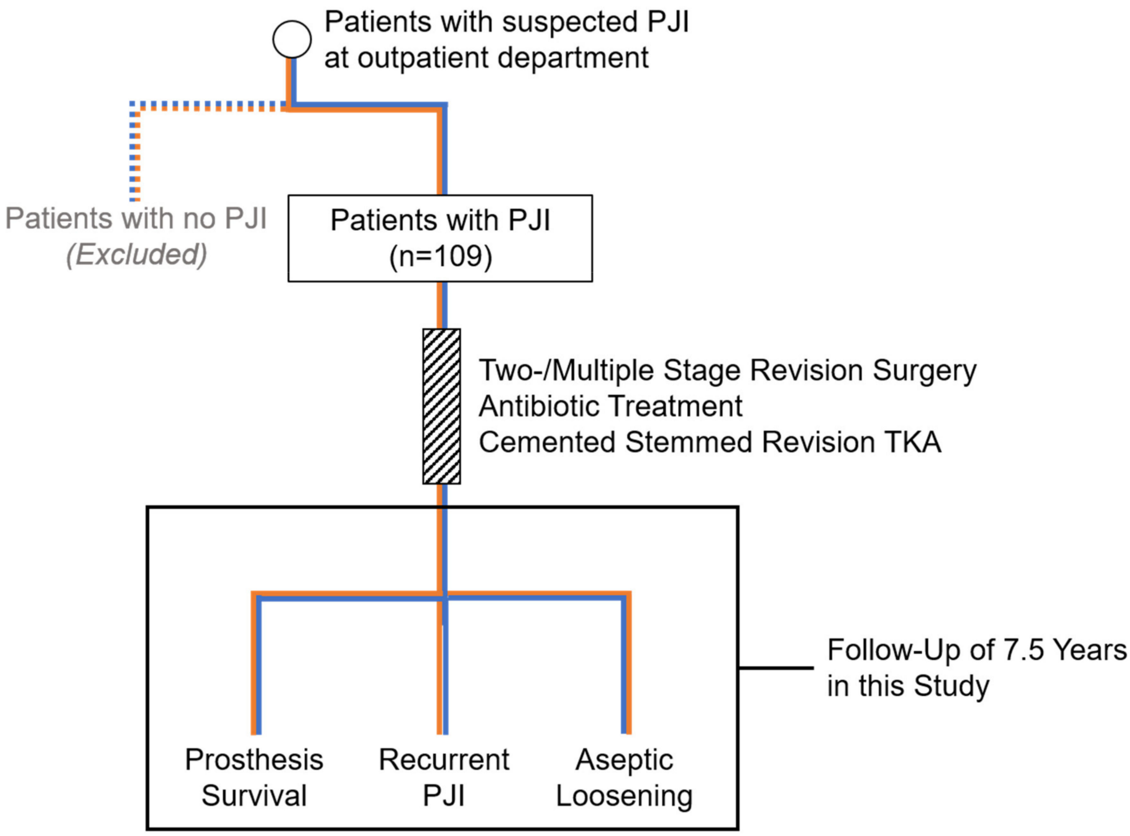

Figure 1. Patient collection and follow-up overview. 60 female (orange line) and 49 male patients that underwent periprosthetic joint infection (PJI)-dependent revision total knee arthroplasty (TKA) were included in this study for a total follow-up of up to 7.5 years.

2.3. Microbiology

Joint aspirate and intraoperative samples were assessed by our microbiology department. Pathogens were grouped depending on rate of occurrence and their characteristic features: *Coagulase-negative staphylococci*; *Staphylococcus aureus*; *Propionibacterium acnes*; *Streptococci*; *Gram-negative bacteria*. Rarely diagnosed pathogens were subsumed as "other" and included *Enterococcus faecalis*, *Bacillus cereus*, *Enterococcus faecium*, *Peptostreptococcus micros*, *Micrococcus luteus*, *Clostridium perfringens*, *Dermabacter hominis* and *Candida parapsilosis*.

2.4. Follow-Up

All patients were regularly invited to our outpatient department for follow-up examinations. For the first postoperative year, patients were invited every three months. Afterward, the follow-up was offered annually. Complications of revision arthroplasty comprise, among others, aseptic loosening, recurrent PJI, instability, pain, patellar maltracking, arthrofibrosis and limited range of motion. For this study, prosthesis survival was defined as the abstinence of diagnosed aseptic loosening or recurrent PJI. Diagnosis of aseptic loosening was dependent upon radiological criteria while taking into account patient-reported clinical symptoms pain and instability. Recurrent PJI was diagnosed using EBJIS and modified Delphi criteria [19,20].

2.5. X-ray Analysis

Implant positioning and aseptic loosening were determined radiologically using long leg standing anterior-posterior and 30-degree flexion true lateral X-ray scans. All measurements were performed using centricity Enterprise Web (v8.0.1400.511; GE Healthcare, Chicago, IL, USA). Radiological parameters for aseptic loosening were circumferential radiolucency at the bone–cement interface surrounding the prosthesis stem completely, prosthesis subsidence and changes in the position of the stem or cement [23,24]. Coronal alignment was evaluated by measuring HKA in standing long leg anterior-posterior X-ray images. Knee alignment was considered in varus for HKAs of <177°, in valgus for >183°, and in neutral for 180° ± 3° [25].

2.6. Statistics

All data were analyzed using GraphPad Prism 7 software (GraphPad Software, San Diego, CA, USA) and Excel (v16.30; Microsoft Corporation, Redmond, WS, USA). Kaplan–Meier curves were used to plot the probability of prosthesis survival. All data are presented as a mean ± one standard deviation. Statistical analysis was performed using one-way analysis of variance. Log-rank test, unpaired Student's *t*-test for samples of unequal variances, and chi-squared test were used to test for statistical significance ($p < 0.05$). When applicable, p values are listed.

3. Results

3.1. Prosthesis Survival

Kaplan–Meier curves showed continuously increasing probability for overall prosthesis failure, for recurrent PJI and for aseptic loosening over time (Figure 2). While overall prosthesis survival probability was 96.4% after one year, it was found to be 69.1% after 7.5 years (Figure 2A). Comparably, risk of aseptic loosening and recurrent PJI increased from 0.9% to 16.8% and from 2.7% to 16.9%, respectively (Figure 2B,C).

Notably, women were significantly more at risk for developing aseptic loosening after revision arthroplasty (Figure 2B): the risk of aseptic loosening was 22.3% for females compared to 9.8% for males. Men were slightly more at risk for recurrent PJI (Figure 2C). Overall prosthesis survival was slightly lower for women (Figure 2A).

3.2. Patient Characteristics

To identify potential causes for the significantly increased risk for aseptic loosening after revision arthroplasty in females, we analyzed the characteristics of our study population in detail (Table 1). Of the 109 patients analyzed in this study, 49 were male and 60 were female. Overall, mean age was 69.1 ± 10.3 years and average follow-up time was 39.3 ± 24.5 months (minimum 6 and maximum 88 months). On average, patients had 3.5 ± 3.0 prior surgeries on the affected knee. Almost all patients suffered from more than one comorbidity (>96%) reflected by CCI (4.3 ± 2.5) and ASA scores (ASA2: 43.1% of patients; ASA3: 48.6% of patients). Overall, our patient cohort did not show gender-dependent characteristics in any of the analyzed parameters: No significant differences were found in average age, follow-up time, number of prior surgeries, BMI, or CCI between male and female patients. Additionally, while higher ASA scores correlated with increased risk for recurrent PJI and aseptic loosening, no significant difference between men and women was found. Of note, male patients suffering from recurrent PJI were significantly younger than their female counterparts. Besides this, no gender-dependent differences were found for any of the prosthesis outcome groups.

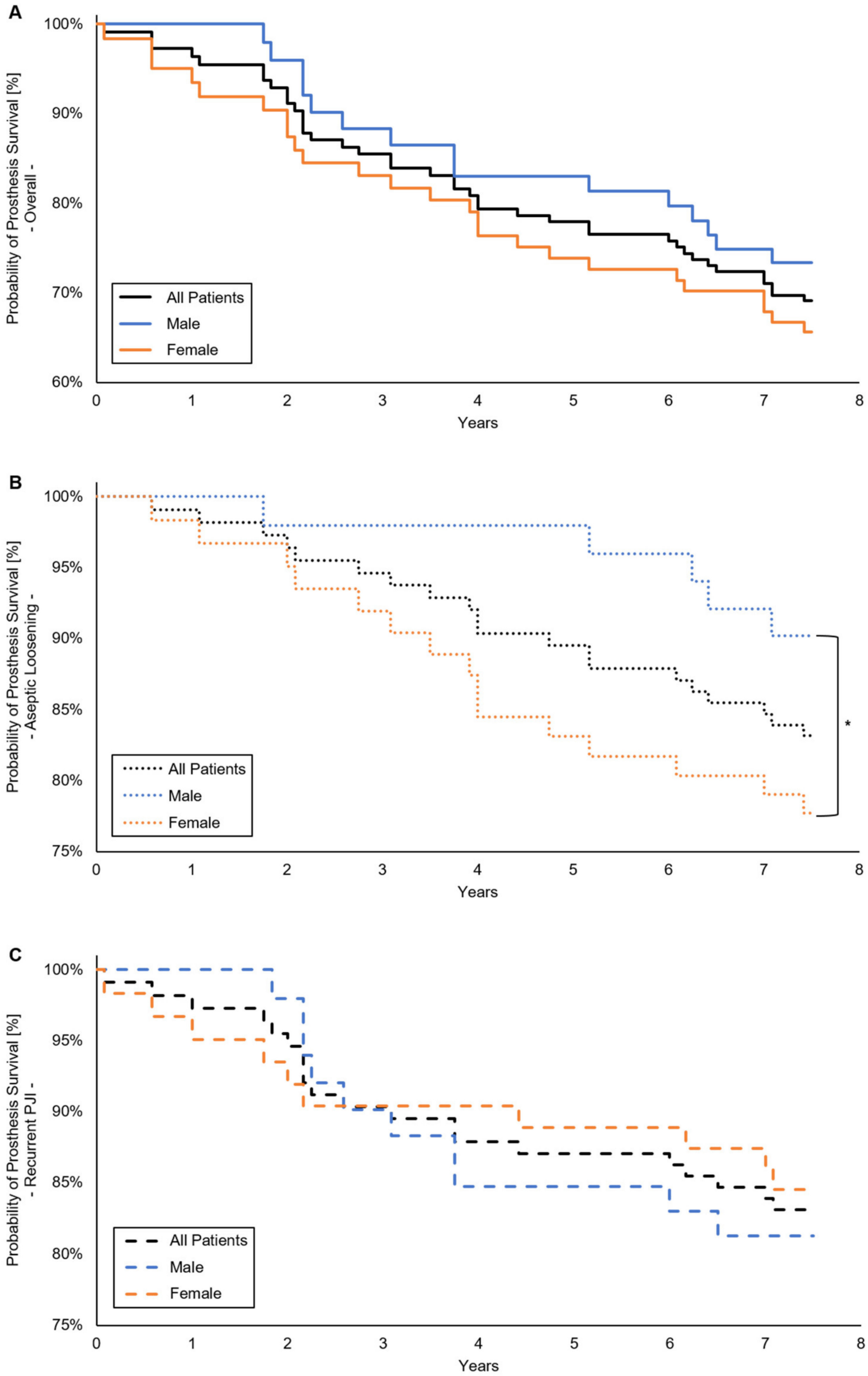

Figure 2. Prosthesis survival probabilities. (**A**) Overall prosthesis survival probability. Risk for prosthesis failure continuously increased over time for all patients (black line). After 7.5 years, the prosthesis survival probability was 73% for male patients (blue line) and 66% for female patients (orange line). No significant differences in overall prosthesis survival probability were found in between genders. (**B**) Probability of aseptic loosening. Risk for aseptic loosening continuously increased over time for all patients (black line). The probability of aseptic loosening was significantly higher for male patients (blue line) compared with female patients (orange line; * $p = 0.039$). The risk for prosthesis failure continuously increased over time for all patients (black line). (**C**) Probability of recurrent PJI. The risk for recurrent PJI continuously increased over time for all patients (black line). Male patients (blue line) were slightly more at risk for recurrent PJI. However, no significant differences in risk for recurrent PJI were found in between male and female patients (orange line).

Table 1. Patient characteristics.

Descriptive	All Outcomes				Prosthesis Survival			Aseptic Loosening			Recurrent PJI		
	All Patients	**Male**	**Female**	***p* Value**	**Male**	**Female**	***p* Value**	**Male**	**Female**	***p* Value**	**Male**	**Female**	***p* Value**
Count [number]	109	49	60	-	32	35	-	7	15	-	12	10	-
Age [years]	69.1 ± 10.3	68.2 ± 10.0	69.9 ± 10.5	0.401	69.0 ± 11.1	69.1 ± 11.3	0.969	66.8 ± 6.7	68.7 ± 10.0	0.872	**67.1 ± 7.2**	**74.2 ± 5.7**	**0.025**
Follow-Up Time [months]	39.3 ± 24.5	37.3 ± 24.4	41.0 ± 24.5	0.362	32.0 ± 23.8	40.9 ± 23.5	0.135	56.7 ± 23.3	45.7 ± 23.1	0.266	40.6 ± 17.9	38.4 ± 30.4	0.844
>1 Comorbidity	96.3% (105)	93.9% (46)	98.3% (59)	-	93.8% (30)	97.1% (34)	-	100.0% (7)	100.0% (15)	-	91.7% (11)	100.0% (10)	-
Number of Prior Surgeries on Affected Knee [Count]	3.5 ± 3.0	3.5 ± 3.5	3.5 ± 3.5	0.935	3.1 ± 2.0	3.5 ± 4.3	0.692	4.7 ± 2.0	4.3 ± 3.7	0.655	4.3 ± 2.1	2.6 ± 1.9	0.082
Clinical Scores													
BMI	31.3 ± 6.9	30.2 ± 5.7	32.2 ± 7.7	0.141	29.7 ± 5.6	32.8 ± 8.2	0.080	30.5 ± 4.4	30.8 ± 7.5	0.115	32.3 ± 6.6	31.9 ± 5.0	0.903
CCI	4.3 ± 2.5	4.4 ± 2.6	4.3 ± 2.3	0.943	4.5 ± 2.9	4.1 ± 2.3	0.550	3.7 ± 2.2	4.5 ± 2.4	0.807	4.6 ± 1.8	5.0 ± 2.4	0.660
ASA1 [%] (No. of Patients)	8.3% (9)	12.2% (6)	5.0% (3)	0.190	12.5% (4)	5.7% (2)	0.285	0.0% (0)	0.0% (0)	-	16.7% (2)	10.0% (1)	0.450
ASA2 [%] (No. of Patients)	43.1% (47)	42.9% (21)	43.3% (26)	0.970	46.9% (15)	60.0% (21)	0.692	28.6% (2)	26.7% (4)	0.567	33.3% (4)	10.0% (1)	0.115
ASA3 [%] (No. of Patients)	48.6% (53)	44.9% (22)	51.7% (31)	0.614	40.6% (13)	34.3% (12)	0.479	71.4% (5)	73.3% (11)	0.270	50.0% (6)	80.0% (8)	0.875

3.3. Microbiology

For both male and female patients, *Staphylococci* comprised more than 60% of all cases, with coagulase-negative *Staphylococci* being the most commonly found pathogen (Figure 3). In >50% of all cases, only one pathogen was detected. Approximately 20% of all patients had a polymicrobial or culture-negative PJI, respectively. Gender-dependent differences in pathogen spectrum were assessed as a conceivable cause for an increased risk of aseptic loosening in females. However, no significant difference was found between genders overall (Figure 3) or depending on long-term outcome (Supplemental Table S1).

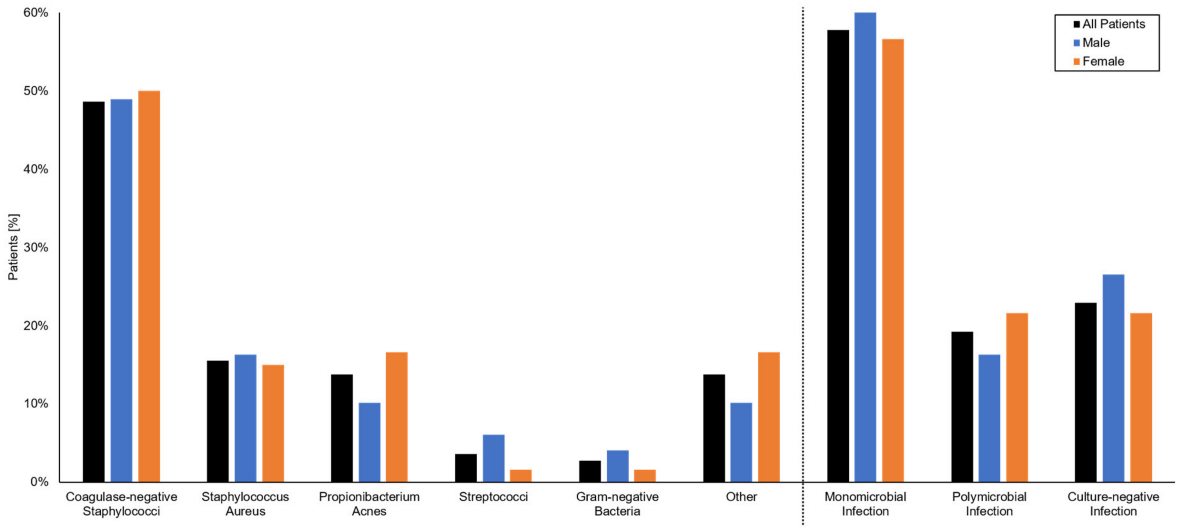

Figure 3. Pathogens at the time of PJI. Coagulase-negative staphylococci were the most common cause of PJI. Most patients were diagnosed with a monomicrobial infection. No significant differences in between male (blue) and female patients (orange) were found in terms of causative pathogen or number of pathogens detected.

3.4. Laboratory and Pathology

Pre-operative joint aspirate, bloodwork and pathology of intraoperative biopsies were screened for differences in male versus female patients. In joint aspirates, average total cell number was 20,293.7 ± 32,438.2 cells/nL (median: 2774.5 cells/nL); average PMN cell number was 18,397.7 ± 29,955.0 cells/nL (median: 1608.5 cells/nL); and average percentage of PMN was 64.7% ± 26.9% (median: 70.7%). CRP was found to be elevated in patients with PJI prior to prosthesis removal (average: 39.8 ± 59.2 mg/L). While cell numbers and CRP levels varied greatly inter-individually, no significant differences between male and female cases were found (Supplemental Table S2). Additionally, we did not observe significant gender-dependent differences while taking long-term outcome prosthesis survival, recurrent PJI or aseptic loosening into account for any of the analyzed parameters (Supplemental Table S2). Similarly, there were no differences for female patients compared to male patients in histopathological classification of the intraoperatively acquired tissue specimens (Supplemental Table S2).

3.5. Treatment

Length of hospital stay for implant removal (19.6 ± 13.4 days) and reimplantation (17.9 ± 17.3) were similar (Table 2). Average total length of stay did not differ significantly between genders and was 35.7 ± 19.3 days for males and 34.8.5 ± 23.1 days for females. Length of hospital stay and the interval between implant removal and reimplantation were decided individually for each case, resulting in large inter-individual differences. In most cases, two-stage exchange revision arthroplasty was performed (males: 81.6%; females: 86.7%). In the remainder of cases, multiple-stage exchange surgery was indicated. No significant gender-dependent differences in type and manufacturer of the prostheses used at reimplantation were perceived. On average, male patients underwent 0.9 ± 1.3 and female patients 0.7 ± 1.0 additional revision surgeries. Antibiotic treatment regimen was chosen based on bacterial susceptibility and in consultation with our department for microbiology and infectiology. For the majority of patients, ampicillin/sulbactam (79.6% of male patients versus 66.7% of female patients) was administered as an initial empiric treatment, and a combination of rifampicin with at least one additional antibiotic (for male and female patients ≥75%) as a targeted therapy. There were no significant differences regarding the evaluated treatment parameters between male and female patients.

3.6. Coronal Alignment

HKA was assessed radiologically to determine postoperative coronal alignment. On average, HKA was 179.5 ± 3.2° for men and 179.7 ± 3.7° for women. Overall, knees of patients diagnosed with aseptic loosening (27.3%) and recurrent PJI (28.6%) were more often in varus and only rarely in valgus (Figure 4A). However, no correlation of long-term outcome with non-neutral alignment was evident.

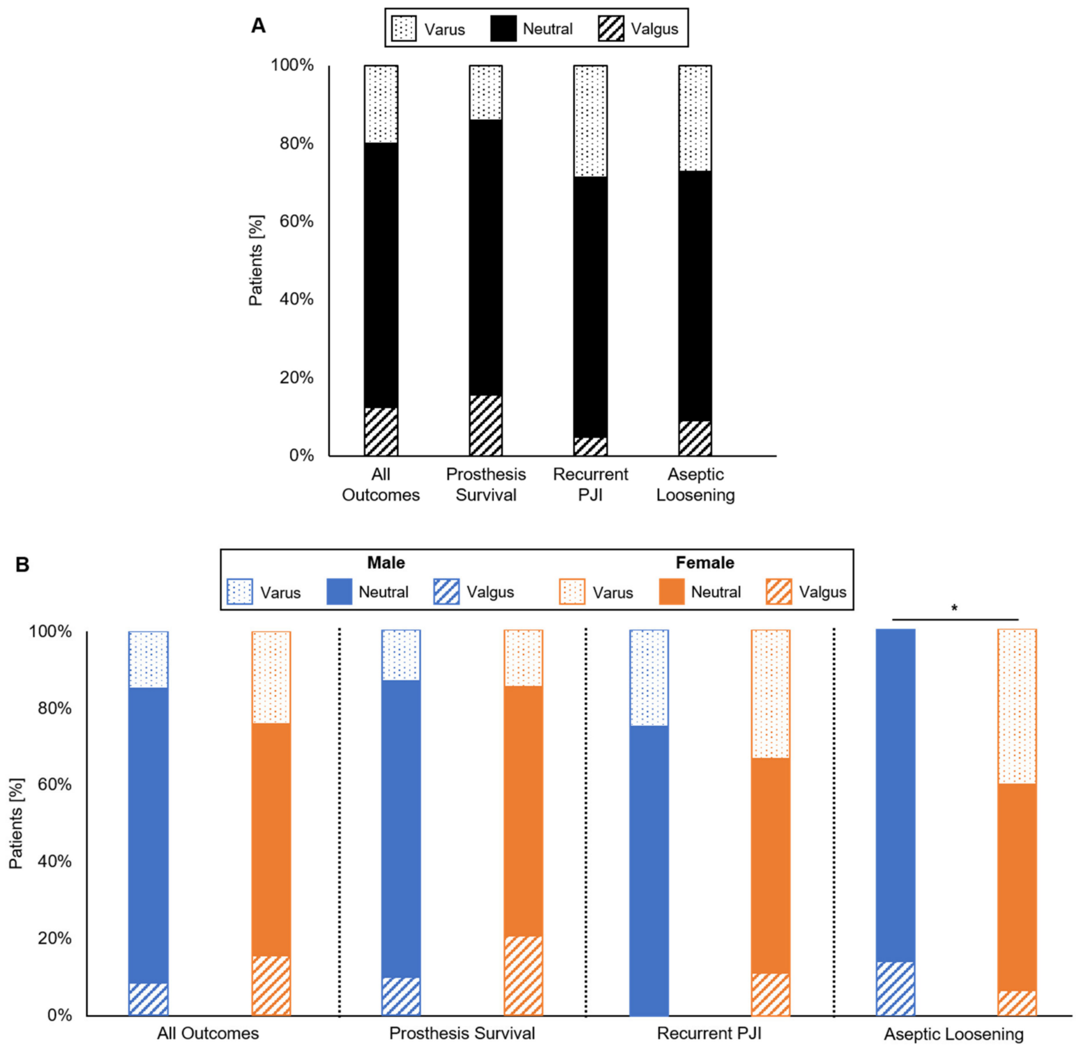

Figure 4. Knee alignment. (**A**) Postoperative coronal alignment was more often in varus in patients with prosthesis failure. However, the number of patients with neutral alignment was similar in all outcome groups. (**B**) Coronal alignment of female patients (orange) was more common in both valgus and varus compared to male patients (blue). However, a significant gender-dependent difference was only found in patients diagnosed with aseptic loosening: knees of female patients suffering from aseptic loosening after revision surgery were significantly more often in varus (* p = 0.016).

Table 2. Hospital stay and surgical treatment parameters.

Descriptive	All Outcomes				Prosthesis Survival			Aseptic Loosening			Recurrent PJI		
	All Patients	**Male**	**Female**	***p* Value**	**Male**	**Female**	***p* Value**	**Male**	**Female**	***p* Value**	**Male**	**Female**	***p* Value**
Length [Days]													
Stay for Prosthesis Removal	19.4 ± 13.5	20.7 ± 16.7	18.3 ± 10.0	0.365	21.8 ± 19.6	19.0 ± 12.3	0.502	19.8 ± 18.4	16.7 ± 10.8	0.338	17.1 ± 4.1	18.0 ± 3.3	0.655
Interval between Surgeries	70.9 ± 51.5	73.2 ± 63.1	69.0 ± 39.6	0.678	71.2 ± 70.0	66.7 ± 38.5	0.745	87.1 ± 68.1	57.5 ± 34.4	0.368	67.5 ± 34.9	94.7 ± 51.9	0.178
Stay for Prosthesis Reimplantation	18.0 ± 17.3	17.1 ± 11.5	18.8 ± 21.0	0.553	16.7 ± 11.9	17.3 ± 13.1	0.840	19.0 ± 11.1	14.6 ± 11.4	0.806	18.5 ± 12.4	31.4 ± 44.5	0.321
Stay total	33.8 ± 15.9	35.7 ± 19.3	32.3 ± 12.1	0.841	35.0 ± 20.9	34.3 ± 13.6	0.880	38.7 ± 20.3	29.1 ± 12.6	0.419	36.4 ± 13.9	29.6 ± 8.2	0.568
Number of Revision Surgeries on Affected Knee [Count]	0.8 ± 1.1	0.9 ± 0.9	0.7 ± 0.7	0.580	0.2 ± 0.5	0.3 ± 0.6	0.644	1.7 ± 0.9	1.1 ± 0.7	0.846	2.3 ± 1.4	1.8 ± 1.6	0.441
Surgical Strategy [%] (No. of Patients)													
Two-stage Exchange	84.4% (92)	81.6% (40)	86.7% (52)	0.776	78.1% (25)	85.7% (30)	0.732	85.7% (6)	93.3% (14)	0.860	91.7% (11)	80.0% (8)	0.769
Multiple-stage Exchange	15.6% (17)	18.4% (9)	13.3% (8)	0.508	21.9% (7)	14.3% (5)	0.463	14.3% (1)	6.7% (1)	0.580	8.3% (1)	20.0% (2)	0.461

In our study population, women were more often affected by non-neutral alignment (24.5% varus, 18.4% valgus) than men (14.3% varus, 8.2% valgus; Figure 4B). Knees of female patients diagnosed with aseptic loosening were significantly more often in varus. In contrast, no significant gender-dependent differences were found for patients with no long-term complication or recurrent PJI after revision arthroplasty.

4. Discussion

In this report, we retrospectively studied the influence of patients' gender on the risk for the long-term complications aseptic loosening and recurrent PJI after PJI-dependent revision arthroplasty. Additionally, we investigated potential gender-related differences in clinical presentation, risk factors and the treatment provided. While overall prosthesis failure rates and risk of recurrent PJI did not differ among genders, long-term risk of aseptic loosening was significantly elevated in female patients. Postoperatively, female knees that later showed signs of aseptic loosening were significantly more in varus. Besides coronal alignment, no gender-dependent differences in clinical presentation at the time of PJI or in treatment were evident.

Gender-dependent differences in knee joint anatomy and in prevalence and progression of orthopedic diseases, such as osteoarthritis of the knee, are widely acknowledged [26–28]. When conservative treatment fails, TKA is one of the most commonly used surgical options for the treatment of knee osteoarthritis [29]. Despite the aforementioned differences in anatomy and osteoarthritis, clinical outcome and long-term prosthesis failure rates do not differ after primary TKA [30–32]. After revision arthroplasty, prosthesis failure rates have been shown to be significantly increased [9,10]. While postoperative pain and functional scores displayed no gender-dependent differences regarding PJI-dependent revision arthroplasty [33], there is paucity of data on long-term prosthesis survival. Our findings demonstrate a significantly increased risk for aseptic loosening in female and a statistical trend for increased risk of recurrent PJI in male patients. In contrast, overall prosthesis failure rates did not differ among genders.

This study had several limitations, including differences in the type of revision TKA implant used and the short follow-up time in few cases. Additionally, while partial prosthesis loosening may be clinically relevant, only patients with circumferential radiolucency surrounding the prosthesis stem completely were diagnosed with aseptic loosening. Patients were diagnosed using X-ray imaging. However, previous reports suggested that the number of patients with aseptic loosening after primary TKA may in fact be underestimated using this imaging technique [34]. Conversely, in some patients loosening may not be aseptic but instead due to an occult infection [35,36].

The pathomechanisms responsible for development of aseptic loosening are subject to an ongoing debate [37,38]. In this study, we found that patient-specific risk factors, clinical and paraclinical parameters and treatments received did not differ among genders. We thus concluded that these parameters are unlikely to be the cause of increased risk for aseptic loosening in females. For the development of aseptic loosening, several studies demonstrated the role of wear particles, altered biological bone properties and osteoimmunological pathways [39–43]. The observed gender-dependent differences in long-term outcome in our study support these theories surrounding the role of bone metabolism in the development of aseptic loosening, as gender-related variances in bone metabolism have been illustrated previously [44]. Previous research suggested these differences in healthy bone to be due to sex hormones impacting the expression of bone turnover regulator osteoprotegerin and receptor activator of nuclear factor κ B ligand [45,46]. However, gender-dependent differences in post-surgical bone metabolism and alterations in osteoimmunological pathways after PJI remain unknown. Additionally, age has been shown to impact the bone remodeling capacity [47]. In our study, average patient age was almost 70 years. While little is known about the post-PJI bone metabolism, it has to be speculated that increasing age might accentuate gender-dependent differences both in bone metabolism and osteoimmunological capacity.

The importance of neutral coronal alignment after primary knee arthroplasty has been extensively studied [48–50]. Conversely, Morgan et al. reported that coronal alignment has no impact on development of aseptic loosening after revision TKA [51]. In contrast, we found postoperative coronal alignment to be significantly more in varus for women, which later developed aseptic prosthesis loosening. It can be speculated that the mechanical properties of stemmed rotating-hinge or full-hinged prostheses increase shear forces and subsequently mechanical stress on the bone structure. In this respect, shifted coronal alignment and the subsequently increased mechanical forces would accentuate the metabolic and structural properties of the bone that lead to aseptic loosening. Additionally, larger bone defects due to previous revision surgeries may result in suboptimal fixation and a subsequent increase in sheer forces on the bone. In such cases involving extended bone loss, cones and sleeves allowing stable metaphyseal prosthetic fixation can reduce shear forces and thus potentially decrease prosthetic failure rates [52]. In healthy individuals, female knees tend to be more in valgus [15,16]. Potential surgical overcorrection during primary and revision TKA and the resulting musculoskeletal imbalance have to be debated as factors for the elevated risk for aseptic loosening in females. While previous studies did not find any evidence for short or long-term advantages in gender-dependent designs for primary TKA [17,18], our data suggest that further research on a female design for PJI-dependent revision prostheses might be warranted.

5. Conclusions

Female patients displayed a significantly increased risk for aseptic loosening after PJI-dependent revision TKA. No differences in clinical and paraclinical parameters or treatment explaining the differences in outcome were found. These observations also have implications for future investigations. Studies researching alterations in bone homeostasis and osteoimmunological pathways will have to consider a gender bias. Future research developing new targeted therapies and treatment strategies is needed.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/osteology1020010/s1.

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