Risk Factors for Infection After Knee Arthroplasty

A Register-Based Analysis of 43,149 Cases

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Background: Clinical studies have revealed a number of important risk factors for postoperative infection following total knee arthroplasty. Because of the small numbers of cases in those studies, there is a risk of obtaining false-negative results in statistical analyses. The purpose of the present study was to determine the risk factors for infection following primary and revision knee replacement in a large register-based series.

Methods: A total of 43,149 primary and revision knee arthroplasties, registered in the Finnish Arthroplasty Register, were followed for a median of three years. The Finnish Arthroplasty Register and the Finnish Hospital Discharge Register were searched for surgical interventions that were performed for the treatment of deep postoperative infections. Cox regression analysis with any reoperation performed for the treatment of infection as the end point was performed to determine the risk factors for this adverse outcome.

Results: Three hundred and eighty-seven reoperations were performed because of infection. Both partial and complete revision total knee arthroplasty increased the risk of infection as compared with the risk following primary knee replacement. Male patients, patients with seropositive rheumatoid arthritis or with a previous fracture around the knee, and patients with constrained and hinged prostheses had increased rates of infection after primary arthroplasty. Wound-related complications increased the risk of deep infection. The rate of septic failure was lower after unicondylar than after total condylar primary knee arthroplasty, but the difference was not significant. The combination of parenteral antibiotic prophylaxis and prosthetic fixation with antibiotic-impregnated cement protected against septic failure, especially after revision knee arthroplasty. Following revision total knee arthroplasty, diagnosis and prosthesis type had no effect, but previous revision for the treatment of infection and wound-healing problems predisposed to repeat revision for the treatment of infection.

Conclusions: There was an increased risk of deep postoperative infection in male patients and in patients with rheumatoid arthritis or a fracture around the knee as the underlying diagnosis for knee replacement. The results of the present study suggest that the infection rate is similar after partial revision and complete revision total knee arthroplasties. Combining intravenous antibiotic prophylaxis with antibiotic-impregnated cement seems advisable in revision arthroplasty.

Level of Evidence: Prognostic Level II. See Instructions to Authors for a complete description of levels of evidence.

A number of risk factors for deep postoperative infection after knee arthroplasty have been found in clinical case-control and cohort studies[1-3]. Clinical data allow in-depth analysis of a variety of patient-related factors and, for example, diabetes mellitus, rheumatoid arthritis, and other comorbidities as measured with the American Society of Anesthesiologists score carry an increased probability of septic complications[1-4]. Although they provide detailed patient-level data, various surgery-related and provider-related factors often cannot be reliably studied in clinical investigations because of the limited number of surgeons, techniques, and prosthesis types. Additionally, because of the contemporary low infection rates, there is a risk of obtaining false-negative results in statistical analyses.

Even though local and national arthroplasty register data have been used to study factors associated with the survival of primary and revision knee replacements[5-8], to the best of our knowledge, there have been no recent studies involving arthroplasty register-based data that have evaluated the risk factors

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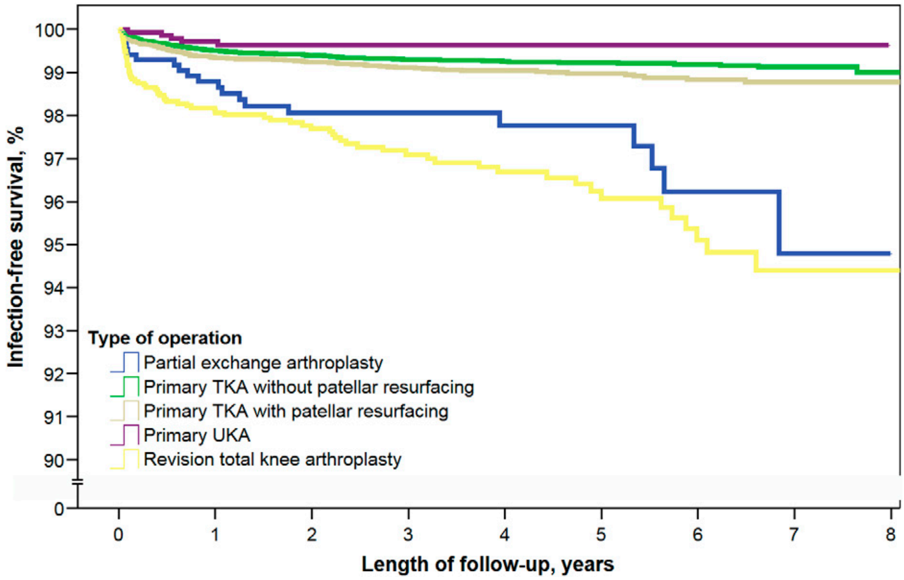

Fig. 1

Kaplan-Meier curves illustrating crude prosthetic survival, with reoperation for the treatment of infection as the end point, after primary unicondylar knee arthroplasty (UKA), total knee arthroplasty (TKA), partial revision arthroplasty, and revision total knee arthroplasty.

for infection. Previous operations on the involved knee are associated with an increased infection rate[1,2], but we are aware of no reports on factors affecting the risk of infection after revision knee replacement.

The purpose of the present study was to determine the risk factors for infection following primary and revision knee replacement in a large series of knee arthroplasties from the Finnish Arthroplasty Register.

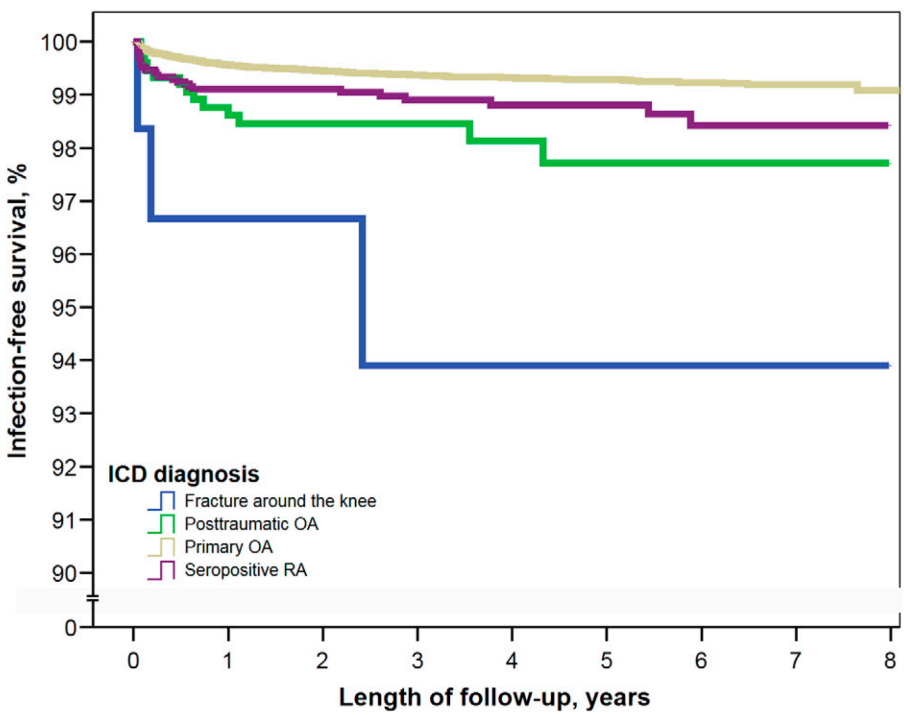

Fig. 2

Kaplan-Meier curves illustrating crude prosthetic survival, with reoperation for the treatment of infection as the end point, after primary knee replacement performed for selected diagnoses. ICD = International Classification of Diseases, Tenth Revision; OA = osteoarthritis; and RA = rheumatoid arthritis.

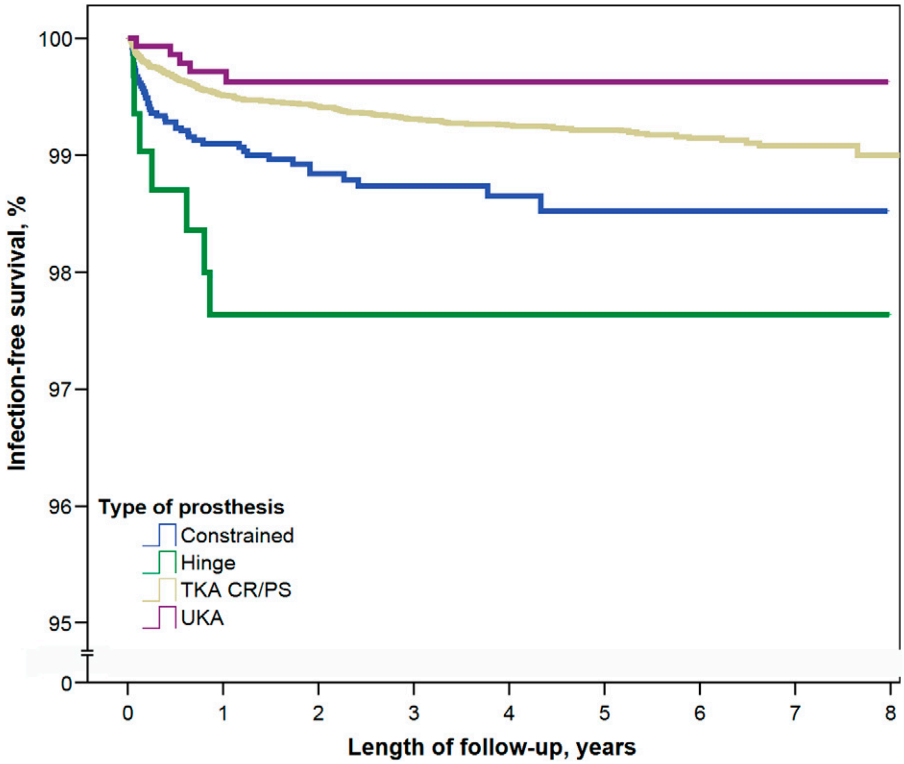

Fig. 3

Kaplan-Meier curves illustrating crude prosthetic survival, with reoperation for the treatment of infection as the end point, after primary knee replacement performed with different types of prostheses. TKA = total knee arthroplasty; CR/PS = cruciate-retaining or cruciate-substituting; and UKA = unicondylar knee arthroplasty.

Materials and Methods

All primary and revision knee arthroplasties (including isolated patellar resurfacing procedures and exchanges of a part of a knee prosthesis) that were performed in Finland from January 1997 to June 2004 and registered in the Finnish Arthroplasty Register were included in the study. The first-stage procedures of staged exchange arthroplasties (that is, resection arthroplasties) and operations for which the type of procedure was not registered were excluded. Each knee was followed until the end of 2004, resulting in a minimum duration of follow-up of six months. The data of the Finnish Arthroplasty Register are based on mandatory reporting on all joint replacement operations performed in Finland; the register has good coverage, but its data have not yet been scientifically validated[9,10]. For the present study, the Finnish Arthroplasty Register data were supplemented by data on hospitalization, collected from the Finnish Hospital Discharge Register.

Reoperations

Reoperations performed for the treatment of infection were ascertained by combining data from the Finnish Arthroplasty Register and the Finnish Hospital Discharge Register. The technique for using such a combination of two registers to detect reoperations has been described and discussed elsewhere[10]. In the Finnish Arthroplasty Register data, any reoperation performed for the treatment of infection was considered to be evidence of a deep knee infection. In the Finnish Hospital Discharge Register, the surgical procedure code[11] indicating débridement, removal of the prosthesis, change or addition of any prosthesis component, any revision arthroplasty, arthrodesis, or amputation, together with an ICD-10 (International Classification of Diseases, Tenth Revision) diagnosis code suggestive of infection, were required to indicate a septic end point event. All other reoperations were considered to have been performed for reasons other than infection. If two or more reoperations were recorded for an index operation, the one occurring first was included for analysis. If the operatively treated side was unknown and both knees of a patient were being followed, both were excluded from further follow-up.

Statistical Analyses

All data were analyzed with the knee as the statistical unit of analysis, and primary and revision procedures were analyzed separately. The proportion of knees that had a reoperation because of infection to the total number of operatively treated joints (the infection rate) is described for different subgroups, with the 95% confidence intervals calculated according to the method of Wilson[12]. For continuous variables, the median and the range are reported. Comparisons of explanatory variables between different operation types were performed with use of

TABLE I Demographic Data and Operation Setting, Stratified According to Type of Operation

	Primary Arthroplasty (N = 40,135)	Revision Total Knee Arthroplasty (N = 2166)	Partial Revision Arthroplasty* (N = 848)	P Value
Median age (range) *(yr)*	71 (14 to 96)	72 (17 to 91)	71 (27 to 94)	<0.001
Age group†				<0.001
<65 years	10,155 (25.3%)	510 (23.5%)	209 (24.6%)	
65 to 75 years	19,497 (48.6%)	993 (45.8%)	401 (47.3%)	
>75 years	10,483 (26.1%)	663 (30.6%)	238 (28.1%)	
Sex†				0.379
Female	28,985 (72.2%)	1587 (73.3%)	601 (70.9%)	
Male	11,150 (27.8%)	579 (26.7%)	247 (29.1%)	
Diagnosis†				0.050
Primary osteoarthritis	35,298 (87.9%)	1876 (86.6%)	748 (88.2%)	
Secondary osteoarthritis	1077 (2.7%)	46 (2.1%)	21 (2.5%)	
Rheumatoid arthritis	3040 (7.6%)	185 (8.5%)	65 (7.7%)	
Other arthritis	392 (1.0%)	31 (1.4%)	7 (0.8%)	
Other	328 (0.8%)	28 (1.3%)	7 (0.8%)	
Operating hospital†				<0.001
University hospital	8327 (20.7%)	877 (40.5%)	203 (23.9%)	
Central hospital	13,467 (33.6%)	590 (27.2%)	213 (25.1%)	
Regional hospital	13,515 (33.7%)	258 (11.9%)	238 (28.1%)	
Other	4826 (12.0%)	441 (20.4%)	194 (22.9%)	

*Including secondary patellar resurfacing and isolated exchange of the tibial insert or of either femoral or tibial component alone. †The values are given as the number of knees, with the percentage in parentheses.

the chi-square test or the Fisher test for categorical variables and with use of the Kruskal-Wallis test for continuous variables.

Cox regression analysis with reoperation for the treatment of infection as the end point was used for the analysis of risk factors. Besides reoperation for the treatment of infection, follow-up was considered to have ended at death, any reoperation performed for a reason other than infection, and, for the remaining patients, on December 31, 2004.

The effect of each explanatory variable on the rate of reoperations for the treatment of infection was tested in a univariate model. To ensure that the proportional hazards assumption was not violated, each Cox-predicted survival curve for the type of operation, diagnosis, prosthesis constraint, and the type of antibiotic prophylaxis was plotted on a corresponding Kaplan-Meier survival curve (Figs. 1 through 4), and the congruity of predicted and observed survival curves was graphically assessed. Except for the later years of follow-up in several subgroups within the revision arthroplasty group (patients with other illness, a cementless prosthesis, no antibiotic prophylaxis, or antibiotic cement only), the predicted and observed curves were found to be equal, demonstrating that the Cox model adequately followed the observed survival.

In addition to the univariate analysis, each variable was tested in the Cox model with adjustment for age, sex, and diagnosis as recommended by Robertsson et al.[7]. Additionally, the type (constraint) of the implanted prosthesis (unicondylar, cruciate-retaining or cruciate-substituting total condylar, constrained total condylar, or hinged knee prosthesis) was included as a proxy for the severity of joint destruction in the adjusted analyses because it had been found in an earlier study to affect prosthetic survival[3]. Hazard ratios along with 95% confidence intervals calculated with the adjusted Cox model are reported. Finally, all variables with a significant ($p < 0.05$) association with infection in the adjusted analysis were entered into the adjusted forward stepwise Cox model to analyze their relative importance.

The level of significance was set at $p < 0.05$. For sensitivity analysis, the adjusted analyses were performed with the inclusion of only the reoperations that were registered in the Finnish Arthroplasty Register.

Source of Funding

External funding from independent nonprofit organizations was received for this study. None of the funding sources played any role in the preparation or performance of this study.

Results

The Finnish Arthroplasty Register provided data on 43,149 operations. The procedures included 40,135 primary total knee arthroplasties (93.0%), 2166 revision total knee arthroplasties (5.0%), and 848 partial revision arthroplasties (including 618 secondary patellar resurfacing procedures, 198 isolated exchanges of a tibial insert, and thirty-two revisions of either the femoral or tibial component alone) (Table I). Cor-

TABLE II Risk Factors for Reoperation Because of Infection After Primary and Revision Knee Arthroplasty, According to Cox Regression Model Adjusted for Sex, Age, Diagnosis, and Type (Constraint) of Implanted Prosthesis*

	Primary Knee Arthroplasty			Revision Total Knee Arthroplasty†		
	No. of Knees	No. of Reoperations for Infection per 100 Knees	Adjusted Hazard Ratio (95% Confidence Interval)	No. of Knees	No. of Reoperations for Infection per 100 Knees	Adjusted Hazard Ratio (95% Confidence Interval)
Age group						
<65 years	10,155	0.83	1	510	3.14	1
65 to 75 years	19,497	0.73	0.97 (0.74 to 1.28)	993	3.73	1.25 (0.69 to 2.25)
>75 years	10,483	0.69	0.97 (0.70 to 1.34)	663	2.41	0.93 (0.46 to 1.89)
Sex						
Female	28,985	0.66	1	1587	2.46	1
Male	11,150	0.97	**1.54 (1.21 to 1.96)**	579	5.18	**2.23 (1.38 to 3.62)**
Diagnosis						
Primary osteoarthritis	35,298	0.66	1	1876	3.23	1
Secondary osteoarthritis	1077	1.58	**1.86 (1.12 to 3.11)**	46	0	—
Rheumatoid arthritis	3040	1.32	**1.86 (1.31 to 2.63)**	185	3.24	1.01 (0.44 to 2.34)
Other arthritis	392	1.28	1.77 (0.73 to 4.30)	31	3.22	1.03 (0.14 to 7.40)
Other illness	328	0.92	0.93 (0.29 to 3.04)	28	3.57	1.05 (0.15 to 7.62)
Type of implanted prosthesis						
Unicondylar	1425	0.35	0.59 (0.24 to 1.43)	4	0	—
Cruciate-retaining/ posteriorly stabilized	34,456	0.70	1	574	2.44	1
Constrained	3938	1.17	**1.74 (1.27 to 2.40)**	1167	3.60	1.75 (0.95 to 3.21)
Hinged	316	2.22	**2.93 (1.34 to 6.40)**	421	3.09	1.54 (0.72 to 3.28)
Patellar component						
Not implanted	27,882	0.67	1	1211	3.88	1
Implanted	12,253	0.91	1.18 (0.93 to 1.50)	955	2.30	**0.50 (0.30 to 0.83)**
Fixation method						
Cemented	37,142	0.72	1	1922	2.43	1
Hybrid	2051	0.93	1.26 (0.79 to 2.01)	215	1.59	1.66 (0.69 to 4.01)
Cementless	942	1.17	1.51 (0.82 to 2.79)	29	6.90	3.01 (0.70 to 12.90)
Same-day contralateral arthroplasty						
No	36,905	0.76	1	2145	3.22	1
Yes	3230	0.56	0.68 (0.42 to 1.10)	21	0	—
Bone grafts						
None	39,412	0.74	1	1786	3.36	1
Any	723	0.83	0.83 (0.37 to 1.88)	380	2.37	0.61 (0.30 to 1.24)
Intravenous antibiotic prophylaxis						
Any	39,468	0.74	1	2100	3.10	1
None	667	0.60	0.77 (0.29 to 2.06)	66	6.06	2.15 (0.77 to 5.99)
Antibiotic cement‡						
Any	33,411	0.69	1	1940	2.78	1
None	5782	1.00	**1.35 (1.01 to 1.81)**	197	6.60	**2.10 (1.14 to 3.88)**
Antibiotic prophylaxis						
None	174	0	—	22	9.09	3.42 (0.81 to 14.50)
Intravenous only	6550	1.05	**1.42 (1.08 to 1.88)**	204	6.37	**2.12 (1.14 to 3.92)**
Cement only	493	0.81	1.13 (0.42 to 3.04)	44	4.55	1.85 (0.45 to 7.65)
Combined	32,918	0.68	1	1896	2.74	1

TABLE II ***(Continued)***

	Primary Knee Arthroplasty			Revision Total Knee Arthroplasty†		
	No. of Knees	No. of Reoperations for Infection per 100 Knees	Adjusted Hazard Ratio (95% Confidence Interval)	No. of Knees	No. of Reoperations for Infection per 100 Knees	Adjusted Hazard Ratio (95% Confidence Interval)
Postoperative complications						
None	39,706	0.70	1	2136	3.04	1
Any	429	4.90	**7.08 (4.53 to 11.06)**	30	13.33	**5.80 (2.09 to 16.15)**
Type of operating hospital						
University hospital	8327	1.01	1	877	3.31	1
Central hospital	13,467	0.66	0.77 (0.56 to 1.05)	590	4.24	1.40 (0.81 to 2.40)
District hospital	13,515	0.72	0.88 (0.64 to 1.19)	258	1.16	0.41 (0.12 to 1.34)
Other	4826	0.58	0.62 (0.40 to 0.95)	441	2.72	0.87 (0.44 to 1.70)
Time since previous arthroplasty§	NA		NA			
<2 years				1621	4.63	**1.74 (1.06 to 2.86)**
>2 years				540	2.71	1
Reason for revision#	NA		NA			
Loosening				528	2.46	1
Infection				291	8.25	**2.98 (1.49 to 5.95)**
Luxation				81	3.70	1.76 (0.49 to 6.27)
Malposition				258	1.16	0.47 (0.13 to 1.67)
Fracture of bone				68	0	—
Fracture of prosthesis				110	3.64	1.47 (0.48 to 4.53)
Other reason				552	1.99	0.84 (0.37 to 1.87)
Patellar complication				59	1.69	0.65 (0.08 to 4.94)

*Significant results ($p < 0.05$) are marked in bold. NA = not applicable. †Partial revision arthroplasties are excluded. ‡Cementless knee prostheses were excluded. §Data available for 2161 knees. #Data available for 1947 knees.

responding hospitalization data in the Hospital Discharge Register could be matched to Finnish Arthroplasty Register data in 95.7% of the cases.

Table I describes the detailed demographic data on the study population. Operative and perioperative details are presented in the Appendix. Same-day arthroplasty of the contralateral knee was performed in 7.6% of all cases. A patellar component was implanted in association with 30.5% and 44.1% of the primary and revision arthroplasties, respectively. Antibiotic-impregnated cement was used for the fixation of at least one prosthetic component in 84% of the knees. With few exceptions, all patients received antibiotic prophylaxis, for which intravenous cefuroxime was most often used.

The populations of patients undergoing primary and revision arthroplasties were essentially similar with respect to age, sex, and diagnosis, although some qualitatively small but significant differences were observed (Table I) (see Appendix).

Reoperations

In total, 387 reoperations for the treatment of infection (0.90%; 95% confidence interval, 0.81% to 0.99%) were registered during the follow-up period (average, 3.1 years; range, zero to 8.6 years), and 262 (68%) of them were performed within one year after the index procedure.

Partial revision arthroplasties (adjusted hazard ratio, 3.4; 95% confidence interval, 2.2 to 5.5) and revision total knee arthroplasties (adjusted hazard ratio, 4.7; 95% confidence interval, 3.6 to 6.3) were associated with significantly higher risks of septic failure in comparison with primary knee replacement without patellar resurfacing (Fig. 1).

Risk Factors for Infection

Table II presents the results of the adjusted analyses for primary and revision knee arthroplasties. The results of the univariate analyses and the proportions of the knees that had a reoperation because of infection are presented in the Appendix.

Sex, diagnosis, the type of prosthesis, the use of antibiotic cement for prosthetic fixation, and postoperative complications were found to be the strongest factors that showed a significant association with postoperative infection following primary knee replacement in the adjusted analyses (Table II). With regard to revision arthroplasties, the strongest determi-

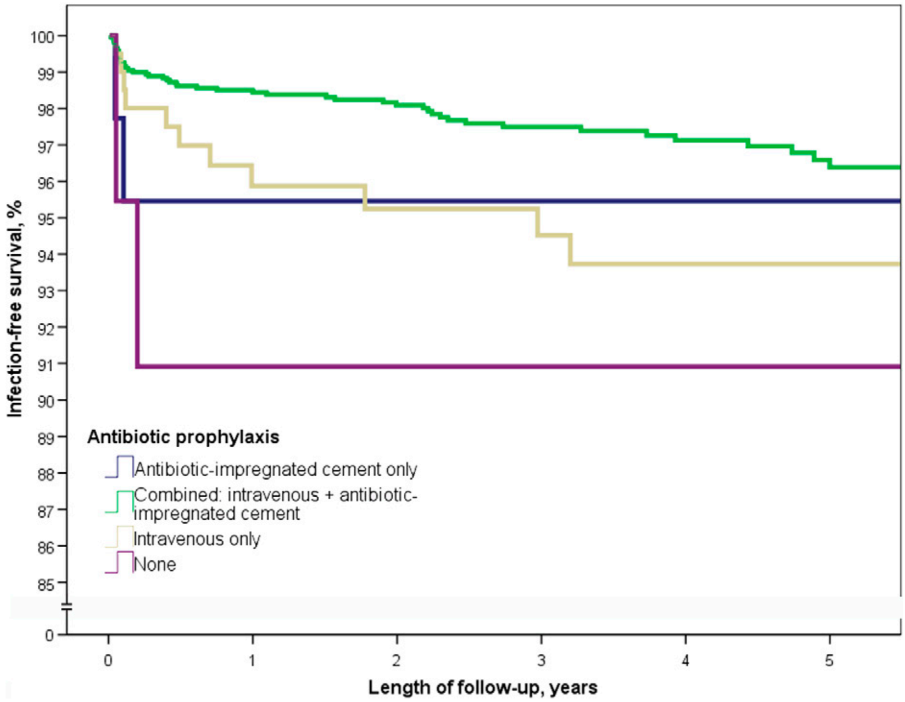

Fig. 4

Kaplan-Meier curves illustrating crude prosthetic survival, with reoperation for the treatment of infection as the end point, after revision total knee replacement performed with different types of antibiotic prophylaxis and without antibiotic prophylaxis.

nants of subsequent repeat revision because of infection were sex, the use of antibiotic cement for prosthetic fixation, postoperative complications, and the reason for revision (infection).

Patient-Related Factors

Male patients had a higher overall risk of reoperation for infection (hazard ratio, 1.6; 95% confidence interval, 1.3 to 2.0) as compared with female patients after both primary and revision knee replacement. The difference was independent of age and also was seen in the subgroup of patients with primary osteoarthritis (data not shown).

There was an increased rate of reoperations because of infection following primary arthroplasties performed for the treatment of arthritic diseases other than primary osteoarthritis (see Appendix). The ICD-10 diagnoses that were associated with an increased risk of reoperations for the treatment of infection, as compared with the diagnosis of primary osteoarthritis, were posttraumatic osteoarthritis (hazard ratio, 2.4; 95% confidence interval, 1.3 to 4.2), unspecified osteoarthritis (ICD code M17.9) (hazard ratio, 2.7; 95% confidence interval, 1.3 to 5.4), seropositive rheumatoid arthritis (hazard ratio, 1.7; 95% confidence interval, 1.1 to 2.6), and fracture around the knee (hazard ratio, 6.3; 95% confidence interval, 2.0 to 20.0). After one year, the number of septic failures in patients with rheumatoid arthritis did not differ significantly from that in patients with primary osteoarthritis (hazard ratio, 1.3; 95% confidence interval, 0.6 to 3.0) (Fig. 2).

Type of Prosthesis

In general, there was a trend showing an increased rate of infections in association with constrained and hinged prostheses in comparison with nonconstrained total knee prostheses (Fig. 3), but in the adjusted analyses the trend was significant only for primary arthroplasties (Table II). Although the rate of infections was the lowest after primary unicondylar knee arthroplasty, unicondylar prostheses did not survive significantly better than nonconstrained total condylar prostheses did in the subgroup of knees with primary osteoarthritis (hazard ratio, 0.6; 95% confidence interval, 0.2 to 1.5).

Antibiotic Prophylaxis

After primary knee arthroplasty, fewer infections were seen when antibiotics were administered both intravenously and impregnated in the cement used for prosthetic fixation (combined antibiotic prophylaxis) than were seen when either method of administration was used alone (Table II). The lack of use of antibiotic-impregnated cement (hazard ratio, 1.42; 95% confidence interval, 1.08 to 1.88) had a more dramatic effect than did the lack of use of intravenous antibiotics (hazard ratio, 1.13; 95% confidence interval, 0.42 to 3.04) in comparison with the use of combined antibiotic prophylaxis. This finding also was seen after revision arthroplasty (corresponding hazard ratios, 2.12 [95% confidence interval, 1.14 to 3.92] and 1.85 [95% confidence interval, 0.45 to 7.65]). Despite clear differences between different types of antibiotic prophylaxis in terms of the infection rates after revision knee arthroplasty (Fig. 4), a significant difference was observed only in the comparison between intravenous antibiotics only and combined antibiotic prophylaxis (Table II).

Postoperative Complications

The occurrence of any postoperative complication reported to the Finnish Arthroplasty Register (n = 486 complications in 459 knees) was associated with an increased risk of reoperation for the treatment of infection (hazard ratio, 7.2; 95% confidence interval, 4.8 to 10.8) in comparison with uncomplicated cases. The highest rates of reoperation for the treatment of infection were related to anesthetic complications (11.8% [two of seventeen]; 95% confidence interval, 3.3% to 34.3%), wound infection (21.9% [fourteen of sixty-four]; 95% confidence interval, 13.5% to 33.4%), wound hematoma (13.9% [five of thirty-six]; 95% confidence interval, 6.1% to 28.7%), and wound necrosis (14.3% [seven of forty-nine]; 95% confidence interval, 7.1% to 26.7%). In uncomplicated cases, infection resulted in reoperation in 0.82% (95% confidence interval, 0.74% to 0.91%) of cases.

Revision Arthroplasties

There were more reoperations for the treatment of infection after revision arthroplasties performed within two years after the preceding operation (hazard ratio, 1.7; 95% confidence interval, 1.1 to 2.9) than after revisions performed later. Infection accounted for 33% of these early revisions ($p < 0.001$ for the differences in the reasons for revision between early and late revisions) and was strongly associated with the risk of repeat revision for the treatment of infection (hazard ratio, 3.0; 95% confidence interval, 1.5 to 6.0). Other reasons for revision were not associated with reoperation for the treatment of infection.

Discussion

The most important findings in the present study concern the effect of diagnosis, constraint of the implanted prosthesis, the type of antibiotic prophylaxis, and wound-healing complications on postoperative infections. Although male sex also was associated with an increased rate of reoperations for the treatment of infection, the conflicting results of earlier studies[3,4,7,13] suggest that sex differences likely function as a proxy for some risk factors that could not be further explored with the present data.

Seropositive rheumatoid arthritis has been associated with an inferior outcome and infection after knee arthroplasty[1,2,14,15]. However, even more infections were seen in the relatively small group of younger patients having knee replacements because of secondary or, in particular, posttraumatic osteoarthritis. A hypothetical explanation might be the effect of previous procedures[2].

The higher rate of infection when a knee replacement is performed to treat a fracture is in accordance with the increased risk of infection when a hip replacement is performed to treat a hip fracture[16]. The reasons underlying this association are likely multifactorial and are related to both patient characteristics and the complex nature of the operation. Lack of preoperative conditioning of the teeth and skin and treatment of possible infection foci, which is routine in elective joint arthroplasty, also may have contributed to the increased infection rate.

It has been suggested that age, sex, and diagnosis should be included as covariates in analyses of the outcome of arthroplasty[7]. As more infections occur in association with an increase in prosthetic constraint, prosthesis type was included to characterize the severity of arthritic joint destruction. This method provided a viable explanation for the differences in the infection rates between different types of hospitals.

It has been suggested that fewer infections occur after unicondylar than total condylar knee replacement[6,7,14]. Surprisingly, in the present series, the infection rate (although lower after unicondylar knee arthroplasty) did not differ significantly between unicondylar and nonconstrained condylar knee prostheses in the adjusted analysis despite the typically lesser tissue damage associated with unicondylar prostheses (Fig. 3). Because of the low number of infections, however, there was not enough statistical power for appropriate comparison. With longer follow-up, considerably more infections have been reported to occur in the total knee arthroplasty group, resulting in a more than threefold difference between tricompartmental and unicondylar arthroplasty by ten years[6]. We believe that the choice between these two prosthesis types should be based on concerns other than the infection rate.

In recent years, antibiotic-impregnated cement has become a standard in Nordic countries for use in primary arthroplasty[17], although the scientific background for its use is uncertain[18,19]. According to the present study, the rate of reoperations for the treatment of infection was lowest when a combination of intravenous antibiotic prophylaxis and prosthesis fixation with antibiotic-impregnated cement was used. These results are comparable with those in a series of 22,170 primary total hip replacements from the Norwegian Arthroplasty Register[17].

Although some experimental studies have suggested that the concentration of antibiotic released from cement is subinhibitory[20], the present study—together with an earlier large register-based study[20]—supports the opinion that the initial burst of antibiotics released is sufficient to prevent the formation of bacterial biofilm on the implanted prosthesis and hence to prevent a postoperative infection. Prosthetic fixation with antibiotic-impregnated cement seems to be of particular value in the revision setting. Nevertheless, there is evidence to support the efficacy of the combined regime as compared with intravenous prophylaxis only for the prevention of deep postoperative infection after primary knee arthroplasty in patients with risk factors for infection (diabetes)[21] and after operations performed in suboptimal conditions[22].

Revision arthroplasty carries an increased risk of infection[1,2,15,23], but, to our knowledge, factors associated with later infection after revision knee replacement have not been investigated previously. Even though >2000 revision arthroplasties were included in the present study, only sex, the type of antibiotic prophylaxis, and the reason for revision emerged with a clear association with subsequent septic failure. Surprisingly, diagnosis and age were not associated with an increase in the infection rate. This finding concurs with those of earlier reports on the outcome of revision knee replacement[8,24] but may also be related to surgeons refraining from performing repeat revisions for elderly or medically compromised patients.

Consistent with the results of earlier studies[25-29], the high rate of early septic failures following partial revisions in the present study indicates that these operations cannot be considered minor. The reasons for the need for surgery should be carefully evaluated to rule out a possible underlying low-grade infection.

The use of register-based materials, unfortunately, is not without limitations. No microbiological data or clinical data on the infection are recorded, and cases of infection cannot therefore be confirmed. Then, if the primary outcome is based on data concerning surgical interventions, infections that were treated conservatively are discarded. Additionally, coding of complications in administrative registers, such as the Finnish Hospital Discharge Register in our case, with the appropriate ICD diagnosis codes is infrequent[10]. Therefore, the overall infection rate seen in the register materials is lower than that seen in clinical series and infection-surveillance programs[3,4,30]. On the other hand, the cases considered to be infections in the present study were very likely true infections. The infections that have remained undetected are probably distributed randomly within different patient subgroups and therefore do not cause any systematic bias in the results. However, the case numbers were low in some patient subgroups despite comprehensive follow-up and extensive materials, achieved by combining data from two national Finnish registries. The reader should therefore keep the probability of false-negative results in mind when considering the results of the present study.

Appendix

eA Tables showing operative and perioperative variables and the results of the univariate analyses are available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on "Supplementary Material") and on our quarterly CD/DVD (call our subscription department, at 781-449-9780, to order the CD or DVD). ■

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