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Peer reviewed version

Link to published version (if available):
10.1016/S1473-3099(19)30419-0

Link to publication record in Explore Bristol Research

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Mortality and adverse joint outcomes following septic arthritis of the native knee: a longitudinal cohort study of patients undergoing treatment with arthroscopic washout

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Word count:

3454

ABSTRACT

BACKGROUND

The short and long-term consequences of septic arthritis are uncertain. The purpose of this study was to determine the risk of mortality and adverse joint outcomes following septic arthritis of the native knee.

METHODS

A retrospective cohort study of patients undergoing knee washout for septic arthritis, without prior knee surgery, was performed utilising the national hospital database for England over twenty-years. The rate of mortality within 90-days, and the 1-year and long-term rate of adverse joint outcomes (arthrodesis, amputation, arthroplasty), was determined. The mortality rate for patients with a primary admitting diagnosis of septic arthritis (ICD-10; M00) was compared to cases where this was a secondary diagnosis.

FINDINGS

12132 patients were included (mean age 56.6 years; SD 24.9; 36% [4307/12132] female). Of the 10195 (84%) cases with septic arthritis as the primary admitting diagnosis, the 90-day mortality rate was 7.05% (719/10195; 95% CI 6.56-7.57) rising to 22.69% (418/1842; 95% CI 20.80-24.68) for patients aged over 79-years. Secondary septic arthritis was associated with adjusted odds for mortality of 2.10 (odds ratio; 95% CI 1.79-2.46; p<0.001). The 1-year rate of arthrodesis was 0.13% (15/11393; 95% CI 0.07-0.22), amputation 0.40% (46/11393; 95% CI 0.30-0.54), and arthroplasty 1.33% (152/11393; 95% CI 1.13-1.56). Within 15-years, 8.76% (159/1816; 95% CI 7.50-10.15) underwent arthroplasty, corresponding to an annual risk of 6.14 times (risk ratio; 95% CI 4.95-7.62; p<0.001) that of the general population.

INTERPRETATION

The consequences of septic knee arthritis (in a cohort of patients undergoing arthroscopic knee washout) are serious, with a 7% risk of mortality within 90-days, greater than 1% risk of adverse joint outcomes within 1-year, and 9% risk of knee arthroplasty within 15-years. These findings highlight the potentially devastating outcomes associated with sepsis from musculoskeletal joint infection.

FUNDING

National Institute for Health Research (NIHR), UK

RESEARCH IN CONTEXT

Evidence before this study

A new search of Medline and Embase and Cochrane was performed to update that of a previous systematic review (("pyogenic" OR "septic" OR "infectious") AND "arthritis"; title, 01/01/2008 to 12/11/2018). Seventeen articles (from 2519 deduplicated results) reported more than 100 cases of suspected or proven septic arthritis in adults. No study was joint specific and most studies included patients with small joint infection, prior surgery or joint arthroplasty, and outcomes were reported at inconsistent periods of follow up. Several studies were limited to either older age-groups, patients with rheumatoid arthritis, a minority ethnic group, or reported results in less developed healthcare settings. The largest epidemiological study (40,433 care episodes) identified episodes of care for patients with a diagnosis code of septic arthritis (non-specific for joint) from United States emergency care admissions and reported mortality based on inpatient discharge destination. This study reported the lowest mortality rate of 0.77% (311/40433; 95% CI 0.69 to 0.86; 1 study). Combined with the other studies, the overall mortality rate in all study patients was 1.56% (804/51527; 95% CI 1.46 to 1.67; 17 studies), but rates exceeding 5% were reported in 13 studies and exceeding 10% in 5 studies. A poor joint outcome (functional or arthroplasty) was reported in 9.00% of cases (97/1078; 95% CI 7.36 to 10.87; 6 studies) but this was inconsistently defined. There is therefore considerable uncertainty around these outcomes. No cohort has been limited to the most commonly affected joint, the knee, or excluded patients with prior knee surgery such are total joint arthroplasty which is likely to change outcomes. The rates of objective, native joint, adverse outcomes, as defined by arthrodesis, amputation, or arthroplasty, are particularly poorly defined.

Added value of this study

This study of 12,132 patients was limited to patients undergoing arthroscopic washout of the knee joint for a diagnosis of septic arthritis. Patients with a history of prior knee surgery were excluded. This study reports a higher rate of mortality (8.94% at 90-days; 1084/12132; 95% CI 8.43-9.46) than previously reported studies which had highly heterogenous inclusion criteria. In comparison to patients with a primary admitting diagnosis of septic arthritis, patients where this was a secondary diagnosis had significantly greater odds of mortality (odds ratio 2.10; 95% CI 1.79 to 2.46; p<0.001) and older patients also had greater odds of mortality (odds ratio 1.38 per 5-years; 95% CI 1.34 to 1.42; p<0.001). A reduction in the rate of mortality was observed over the twenty-year study period (odds ratio 0.89 per 5-years; 95% CI 0.83 to 0.96; p=0.002). Objective, joint specific, adverse outcomes (arthrodesis, amputation, arthroplasty) are reported at 1-year (0.13%, 0.40%, 1.33% respectively). The long-term, mortality-adjusted, rate of joint survival (not undergoing knee arthroplasty) is reported for the first time. The odds of mortality and hazard of arthroplasty are reported, stratified by patient factors including age, sex, comorbidity, deprivation, diabetes, ethnicity, and prior joint disease.

Implications of all the available evidence

These findings confirm that septic arthritis of the knee (in a cohort of patients undergoing arthroscopic knee washout) is associated with a high rate of mortality and morbidity. The rate of mortality is considerably higher than reported in many other studies that included small joint infections alongside septic arthritis of large joints such as the knee. In the long-term, 8.76% (159/1816; 95% CI 7.50-10.15) patients underwent arthroplasty within 15-years, corresponding to an annual risk that was 6.14 times (risk ratio; 95% CI 4.95 to 7.62; p<0.001) that of the general population. These findings will be informative to patients and clinicians and should drive further work to improve the short- and long-term outcomes of patients presenting with this serious medical diagnosis.

INTRODUCTION

Septic arthritis is an uncommon condition but has been considered a medical emergency due to potential life and limb threatening consequences.[1,2] Rates of mortality as high as 10-15%,[3–8] osteomyelitis in 8%,[8] and a subjective poor outcome in 20-30% of cases have been reported.[3,6,8–10] The true rate of adverse outcomes has remained uncertain as previous studies have had a number of limitations, such as heterogenous inclusion criteria and inconsistent reporting of outcomes. No study has been joint specific and most studies included patients with small joint infection, prior surgery or joint arthroplasty, and outcomes were reported at inconsistent periods of follow up. Several studies were limited to either older age-groups, patients with rheumatoid arthritis, a minority ethnic group, or reported results in less developed healthcare settings. The knee is the joint most commonly affected by septic arthritis,[6,8] but no study has been limited to, or focused on, patients with septic arthritis of the knee and the true rate of mortality and long-term adverse joint outcomes in these patients is unknown.

The purpose of this study was to determine the short- and long-term consequences of septic arthritis of the knee joint in patients without a history of prior knee surgery. A cohort of patients undergoing arthroscopic knee washout for septic arthritis was identified over a twenty-year period. The rate of mortality within 90-days and rate of adverse joint outcomes in the short- and long-term was determined with stratification by patient-factors including age, sex, prior comorbidity or joint disease, deprivation, ethnicity, and according to whether septic arthritis of the knee was the primary admitting diagnosis or a secondary diagnosis.

METHODS

Data source

We performed a longitudinal cohort study utilising the national healthcare records for England, UK. Data was provided by NHS Digital (application DARS-NIC-68703). These data, the national Hospital Episode Statistics (HES), contain a record of all episodes of care delivered by NHS hospitals in England.[11] Records are submitted prospectively by hospitals to claim for reimbursement of care provided, including surgical procedures. HES includes episodes of care delivered in treatment centres (including those in the independent sector) but funded by the NHS, episodes of care in England where patients are resident outside of England, and privately funded patients treated within NHS England hospitals. Data recorded includes patient age, sex, location of residence, primary and secondary diagnoses, procedures performed, and mortality data (deaths occurring either in hospital or in the community) from the Office for National Statistics (ONS).

Participants and exposure

All patients undergoing arthroscopic knee washout with a corresponding diagnosis of septic arthritis between 1 April 1997 and 31 March 2017 were eligible for inclusion. All HES records for these patients were extracted after identification using the recorded Classification of Surgical Operations and Procedures (OPCS-4) procedure code (W852) and ICD-10 diagnosis code for pyogenic arthritis (M00).[12] Patients with a history of prior knee surgery to the same knee were excluded.

Outcomes

The primary outcome was mortality within 90-days. The primary outcome was compared for patients where septic arthritis was the primary admission diagnosis (ICD-10 M00) and for patients where this was a secondary diagnosis. The secondary outcomes were early and late adverse joint outcomes. Early adverse joint outcomes were defined as joint arthrodesis (fusion), amputation, or arthroplasty within 1-year. The long-term rate of arthroplasty in the same knee was compared to the estimated rate of arthroplasty in the national population (without a recorded history of septic arthritis in this cohort). Surgical outcomes were matched by knee laterality (side). Temporal trends in the rate of washout for septic arthritis over the twenty-year period were also analysed.

Statistical analysis

Demographic data were summarised with descriptive statistics. The age- and sex-standardised temporal trends in the population rate of arthroscopic washout for septic arthritis was calculated using census data from the ONS with 95% confidence intervals reported according to the methodology of the Association of Public Health Observatories (APHO).[13] The absolute rates of 90-day mortality and 1-year adverse joint outcomes were reported as proportions with corresponding 95% confidence intervals (CI). Factors

associated with the odds of mortality within 90-days were calculated by logistic regression modelling, adjusting for primary versus secondary diagnosis, age group, sex, index of multiple deprivation (quintile derived from regional factors in England including average income, employment, education, housing, and crime; 1=least deprived area, 5=most deprived), ethnicity, modified Charlson comorbidity index (derived with maximum 5-year diagnosis code lookback period), prior osteoarthritis or rheumatoid osteoarthritis, diabetes, year of treatment, rurality, and ethnicity.[14–17]

Long-term rates of knee arthroplasty were calculated as proportions of the cohort at 5-, 10-, or 15- years follow-up respectively. In addition, a mortality adjusted Kaplan-Meier survival analysis (survival was defined as not undergoing knee arthroplasty) was performed, stratified by patient age group. A Cox proportional-hazards model was used to calculate the unadjusted hazard for knee arthroplasty over time by each of the variables described above for the odds of mortality and adjusted including all these variables.

The relative risk (risk ratio) of knee arthroplasty in comparison to the general population (without a history of joint washout for septic arthritis) was estimated for the year 2016-17. Nationally, all patients undergoing knee arthroplasty in 2016-17 were identified and the number of these patients with a recorded history of previous septic knee washout (in the prior years of HES data) versus those without this history made up the numerator for each respective population. The population denominators were the number of patients with a history of septic arthritis that had not undergone a knee arthroplasty prior to 2016-17 and the ONS mid-year population estimates less the septic arthritis population, respectively.

Stata v15.1 (StataCorp, College Station, Texas, USA) was used to perform all analyses. All confidence intervals are reported at the 95% level with corresponding p-values where appropriate for the analyses.

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

RESULTS

Between April 1, 1997 and March 31, 2017, 15323 cases of arthroscopic knee washout for septic arthritis were identified of which 12132 procedures (12132 patients) were included (Figure 1).

Demographics and trends

The demographics of the cohort are summarised in Table 1. The mean age of the full cohort was 56.6 years (SD 24.9) and 35.5% (4307/12132) were female; for 10195 patients (84%; /12132), septic arthritis was the primary admission diagnosis.

There was a greater proportion from the most deprived quintile of the population (2871/12132; 23.66%; 95% CI 22.9 to 24.4) than expected for the whole population (p<0.001). 15.92% (1932/12132) of the cohort had a prior diagnosis of osteoarthritis and 6.28% (762/12132) rheumatoid arthritis. Just over half the cohort had no recorded comorbidities prior to treatment (6435/12132; 53.04%) and 15.90% (1929/12132) a diagnosis of diabetes. The median length of hospital stay was 13 days (interquartile range 6 to 26).

There was a 44% increase in the rate of knee washout for septic arthritis over the twenty-year study period from 0.9/100,000 (95% CI 0.8 to 0.9) in 1997/97 to 1.3/100,000 (95% CI 1.2 to 1.4) in 2016/17. Over the study period, the age standardised intervention rate was 1.7/100,000 (95% CI 1.6 to 1.7) for men and 0.8/100,000 (95% CI 0.8 to 0.8) for women.

Mortality within 90-days

The 90-day mortality rate for the whole cohort was 8.94% (1084/12132; 95% CI 8.43 to 9.46). For patients with a primary diagnosis of septic arthritis the mortality rate was 7.05% (719/10195; 95% CI 6.56 to 7.57) and for those with a secondary diagnosis of septic arthritis, the mortality rate was 18.84% (365/1937; 95% CI 17.12 to 20.66).

In patients aged 40-59-years, the 90-day mortality rate was 1.84% (42/2284; 95% CI 1.33 to 2.48) in primary septic arthritis and 8.81% (31/352; 95% CI 6.06 to 12.27) in secondary cases. In those aged 60-79-years the mortality rate was 7.39% (251/3396; 95% CI 6.53 to 8.32) in primary cases and 18.87% (140/742; 95% CI 16.11 to 21.87) in secondary cases. In those aged over 79-years, the mortality rate was 22.69% (418/1842; 95% CI 20.80 to 24.68) in primary cases and 37.25% (190/510; 95% CI 33.05 to 41.61) in secondary cases (Table 1).

Overall, a secondary diagnosis of septic arthritis was associated with 2.10 times greater adjusted odds of mortality (95% CI 1.79 to 2.46; p<0.001) (Table 2). The odds of mortality fell over the twenty-year study

period (adjusted odds ratio [OR] 0.89 per 5-years; 95% CI 0.83 to 0.96; p=0.002) (Table 2). The increased rate of mortality in older age groups corresponded to an odds ratio of 1.38 per 5-years of age (95% CI 1.34 to 1.42; p<0.001). The odds of mortality were greater with increasing comorbidity index (OR 1.34 per 5-units Charlson index; 95% CI 1.30 to 1.39; p<0.001) and, independently (excluding Charlson index from the model), with diabetes (OR 1.54; 95% CI 1.31 to 1.81; p<0.001). Lower odds of mortality were observed in patients with a diagnosis of osteoarthritis (OR 0.72; 95% CI 0.60 to 0.87; p=0.001). There was not, however, any association with sex, deprivation, rurality, or ethnicity (Table 2).

Adverse joint outcomes within 1-year
Of patients with at least 1-year of follow-up (n=11393), the rate of knee arthrodesis within 1-year was 0.13% (15/11393; 95% CI 0.07 to 0.22), amputation 0.40% (46/11,393; 95% CI 0.30 to 0.54), and arthroplasty 1.33% (152/11393; 95% CI 1.13 to 1.56). These outcomes were observed at a similar rate across the cohort as summarised in Table 3.

Long-term knee arthroplasty
Of patients with the corresponding minimum period of follow-up, 5.62% (403/7170; 95% CI 5.10 to 6.18) underwent arthroplasty within 5-years, 6.68% (289/4326; 95% CI 5.95 to 7.47) within 10-years, and 8.76% (159/1816; 95% CI 7.50 to 10.15) within 15-years. The mortality-adjusted joint survival curve (not undergoing knee arthroplasty) by age-group, over 15-years, is shown in Figure 2. There was a greater hazard for arthroplasty in patients with a history of osteoarthritis (hazard ratio [HR] 2.50; 95% CI 2.09 to 3.00; p<0.001) and rheumatoid arthritis (HR 3.73; 95% CI 2.92 to 4.75; p<0.001) respectively, but lower in patients with a greater comorbidity index (HR 0.78 per 5-years; 95% CI 0.73 to 0.84; p<0.001) or, independently (excluding Charlson index from the model), diabetes (HR 0.77; 95% CI 0.61 to 0.98; p=0.032) (Table 4).

The absolute and relative annual risk of knee arthroplasty in the population of patients with a history of septic arthritis in comparison to that estimated for the general population (with no recorded history of septic arthritis) is summarised in Table 5. The absolute annual risk of arthroplasty for patients over the age of 30-years with a history of septic arthritis was 1.29% (95% CI 1.03 to 1.60) in comparison to 0.21% (95% CI 0.21 to 0.21) for the general population. The annual risk, in 2016-17, for patients over the age of 30-years with a recorded history of knee washout for septic arthritis (in the preceding 20-years) was 6.14 times that of the general population estimate (risk ratio [RR]; 95% CI 4.95 to 7.62; p<0.001); rising to 27.25 times (RR; 95% CI 13.01 to 57.09; p<0.001) at a younger age (40-49-years) (Table 5).

DISCUSSION

Principal findings

The consequences of septic knee arthritis are serious, with a 7% rate of mortality within 90-days, greater than 1% risk of adverse joint outcomes within 1-year, and 9% risk of knee arthroplasty within 15-years. The odds of mortality were double when septic arthritis was a secondary diagnosis for a hospital admission. These findings confirm septic arthritis of the knee to be a medical emergency with potentially severe consequences. Older patients and patients with medical comorbidities were at greatest risk of mortality, although the risk of mortality has fallen slightly over time.

Comparison with other studies

The incidence of suspected or proven, any joint, septic arthritis has been estimated at approximately 4-10/100,000 patient-years.[2,7,18] In 2016/17, the intervention rate for septic arthritis of the knee in our study was 1.3/100,000 patient-years. The lower rate is likely to reflect the fact that only the knee joint was considered although it may also partly reflect the high specificity of our approach to case identification. Previous studies have indicated a higher rate of septic arthritis in patients in disadvantaged groups.[19,20] We observed similar findings, with the more deprived quintile of the English population being over-represented in the cohort at 24%. Patients with rheumatoid or skin disease have been shown to have a greater incidence of septic arthritis.[2,8,20,21] Consistent with this, the proportion of our study cohort with a diagnosis of rheumatoid arthritis was 6%, in comparison to the expected population prevalence for rheumatoid arthritis of 0.5-1.0%.[8,20,21] Diabetes was also associated with septic arthritis in our cohort. The proportion of the cohort with diabetes was 16% in comparison to a population prevalence of approximately 5% in the United Kingdom.[22]

Few studies have previously reported adverse outcomes associated with septic arthritis. Rates of mortality as high as 10-15% have been reported in some studies,[6,8,20] but a lower rate of 2.7% was reported in a nationwide study in Iceland, and 0.77% in a study of emergency care admissions in the United States.[18,23] The rate of mortality in our study was between these estimates at 7.05% for patients with a primary admitting diagnosis of septic arthritis but rising to 18.84% in secondary diagnosis cases (16% of cohort). Overall, the adjusted odds of mortality in our cohort fell over the study period. A similar reduction in mortality over time has been observed for patients undergoing elective orthopaedic procedures.[24,25] In the present cohort, the fall in mortality may reflect a similar general improvement in healthcare, and outcomes could also have been influenced, in part, by initiatives such as the international "Surviving Sepsis" campaign and guidelines first published in 2004.[26,27]

Older age and pre-existing joint disease have previously been shown to be poor prognostic factors for both joint outcome, mortality, and quality of life after an episode of septic arthritis in a small series of patients.[6] This may be due to lower functional reserve in these individuals. A greater odds of mortality was observed in patients with diabetes in the present cohort, as has been reported by other studies of surgical outcomes.[28] The largest age group in our study cohort was the 60-79-year age group and the 90-day mortality in the primary septic arthritis cohort in this age group was 7.39%, in comparison to 0.061% in the same period of time following arthroscopic partial meniscectomy, and 0.233% for the general population.[25] A diagnosis of osteoarthritis was also found to be associated with mortality in our cohort. In the unadjusted model, osteoarthritis was associated with increased odds of mortality, as has been previously observed for all cause and disease specific longer term mortality rates in other cohorts.[29,30] In previous series, this effect has been observed to be driven by higher rates of cardiac events, especially in those with a history of prior cardiovascular disease and osteoarthritis.[29,30] In our cohort, the association was reversed after adjusting for age and comorbidity, but the reason for this unexpected observation is unclear. This could be a selection effect and, as the severity of the osteoarthritis is not recorded, one possibility is that this observation could be due to the presence of a healthier and more active age-matched patient group within the cohort being more likely to have a diagnosis of early osteoarthritis without other comorbidities, but the true reason for this finding is unknown.

Long-term rates of osteoarthritis and knee replacement have been poorly defined but permanent loss of function has been reported by some studies in more than a quarter of septic arthritis patients.[7,31–33] In one series, arthrodesis, amputation, or joint arthroplasty was reported in up to 23% (27/116) of cases within two-years of septic arthritis.[6] In another small study of patients developing septic arthritis after anterior cruciate ligament reconstruction, however, no evidence of progressive osteoarthritis was reported at 1 to 11 years.[34] In our study cohort, the rate of adverse joint outcomes was just over 1% at one-year, and by 15-years, 8.76% of patients had undergone knee arthroplasty. Patients with a pre-existing diagnosis of osteoarthritis or rheumatoid arthritis were at higher risk of undergoing subsequent arthroplasty, as would be expected. Patients with a greater comorbidity index were at lower risk of subsequent arthroplasty and this could be a result of patients with more comorbidities being less likely to either seek, or be able to access, arthroplasty.[35]

Importantly, the annual rate of arthroplasty in patients with a history of knee washout for septic arthritis was six times greater than that of the general population without this history. There was also evidence of accelerated progression of osteoarthritis as evidenced by the rate of knee arthroplasty at a younger age being increased by up to twenty-seven times the annual rate of the general population for patients aged 40-49-years.

Strengths and limitations

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This is the largest cohort of septic arthritis patients that has been reported, thereby increasing the precision and clinical importance of our findings. It is more comprehensive than all previous studies, reporting rates of 90-day mortality and long-term rates of joint-loss, and comparing mortality outcomes for those with a primary admitting diagnosis of septic arthritis with those where this was secondary diagnosis. There are, however, some limitations. Our cohort only included operatively managed patients, undergoing arthroscopic washout; patients managed non-operatively, for example by serial aspirations and antibiotics, or with open washout were not included. Patients with suspected septic arthritis but a negative synovial aspirate are also highly likely to be underrepresented in our cohort, as these individuals will be less likely to undergo surgical treatment. The outcomes reported in this study cannot, therefore, be generalised to these patients or others managed with a non-operative treatment strategy. In some previous observational studies, patients undergoing operative management of septic arthritis had a worse outcome than those managed non-operatively, but without randomised clinical evidence there is high likelihood of confounding by indication.[8,36] In several studies, arthroscopic washout has been reported to have comparable results to both open washout and needle arthrocentesis.[2,36–39] In one small cohort study in children, however, arthroscopic washout was found to be superior to open washout in clearing infection after the first treatment.[40]

Patients with a prior history of knee surgery were excluded from our cohort. Approximately 1% of joint infections in children and 33-42% in adults are iatrogenic.[7,18] The intention of this exclusion criterion was to create a more homogenous cohort with native knee joint septic osteoarthritis, undergoing arthroscopic washout, but it should be noted that our findings cannot be generalised to patients developing infection following previous surgery. Although patients had not undergone prior knee surgery, it is still possible that some of the infections were iatrogenic from, for example, intra-articular injections. In a cohort reported in Iceland, up to 18% of septic arthritis cases were detected following a history of joint injection, although other studies have reported lower rates between 2% and 6%.[7,18,20]

Although our study was able to stratify analyses by a range of patient factors including demographics, pre-existing medical and joint conditions, primary or secondary diagnosis, and regional deprivation, there are a number of unmeasured and potentially confounding factors that might increase or decrease risks. These include the duration of symptoms before diagnosis, the initiation and type of antibiotic therapy provided, serum inflammatory markers and microbiological findings. Other unmeasured patient factors include body mass index, smoking status, and medication history. Our study also relies on accurate data coding within the Hospital Episode Statistics database. The study cohort was identified by the procedure undertaken with a corresponding diagnosis of pyogenic arthritis. Previously, the Charlson comorbidity index as calculated from HES diagnosis fields, and records of serious vascular complications, have both been shown to correlate strongly with primary care records.[41,42] The procedure and diagnosis code used for this cohort has not, however, been specifically validated, and laboratory verification was not available.

CONCLUSION

In this study, septic arthritis (in a cohort of patients undergoing arthroscopic knee washout) was associated with a 7% rate of mortality within 90-days and a greater than 1% rate of adverse joint outcomes within 1-year. Patients with a secondary diagnosis of septic arthritis were at considerably greater risk of mortality than those where this was the primary admission diagnosis. Within 15-years, 9% of patients underwent knee arthroplasty corresponding to approximately six times the annual rate of arthroplasty in the general population. A fall in the odds of mortality over the twenty-year study period was observed which may reflect improved treatment of patients with sepsis. Nevertheless, our findings indicate that septic arthritis is associated with a high rate of mortality and morbidity even after joint washout, highlighting the potentially devastating consequences of musculoskeletal joint infection and the need for an immediate and appropriately intensive level of care.

Details of contributors

SA: concept, methodology, analysis, writing and editing paper, guarantor.

AA: methodology, editing paper.

AJ: methodology, analysis, editing paper.

DB: concept, editing paper.

AP: concept, methodology, editing paper.

Transparency declaration

The lead author (SA) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and registered) have been explained.

Competing interests

Funding

Ethical approval

Not required.

Data sharing

No additional data available.

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TABLES

TABLE 1:

Demographics and 90-day Mortality for Patients with Septic Arthritis as the Primary Admission Diagnosis (ICD-10 M00) versus a Secondary Diagnosis

	Primary Admission Diagnosis				Secondary Admission Diagnosis			
	Demographics		90-day Mortality		Demographics		90-day Mortality	
	n	%	n	%	n	%	n	%
Total	10,195	100	719	7.05% (6.56, 7.57)	1,937	100	365	18.84% (17.12, 20.66)
Sex								
Male	6,603	64.77	426	6.45% (5.87, 7.07)	1,222	63.09	210	17.18% (15.11, 19.42)
Female	3,592	35.23	293	8.16% (7.28, 9.10)	715	36.91	155	21.68% (18.71, 24.88)
Age Group								
< 20	1,110	10.89	1	0.09% (0.00, 0.50)	128	6.61	1	0.78% (0.02, 4.28)
20 - 39	1,563	15.33	7	0.45% (0.18, 0.92)	205	10.58	3	1.46% (0.30, 4.22)
40 - 59	2,284	22.4	42	1.84% (1.33, 2.48)	352	18.17	31	8.81% (6.06, 12.27)
60 - 79	3,396	33.31	251	7.39% (6.53, 8.32)	742	38.31	140	18.87% (16.11, 21.87)
80 +	1,842	18.07	418	22.69% (20.80, 24.68)	510	26.33	190	37.25% (33.05, 41.61)
Charlson comorbidity index								
0	5,753	56.43	124	2.16% (1.80, 2.56)	682	35.21	42	6.16% (4.47, 8.23)
1 - 15	3,134	30.74	257	8.20% (7.26, 9.22)	729	37.64	127	17.42% (14.74, 20.37)
16 - 30	985	9.66	224	22.74% (20.16, 25.49)	367	18.95	127	34.60% (29.74, 39.72)
31 - 50	323	3.17	114	35.29% (30.08, 40.78)	159	8.21	69	43.40% (35.57, 51.48)
Prior joint disease								
No	7,984	78.31	517	6.48% (5.95, 7.04)	1,454	75.06	263	18.09% (16.14, 20.16)
Osteoarthritis	1,592	15.62	138	8.67% (7.33, 10.16)	340	17.55	74	21.76% (17.49, 26.53)
Rheumatoid arthritis	619	6.07	64	10.34% (8.05, 13.01)	143	7.38	28	19.58% (13.42, 27.04)
Diabetes								
No	8,696	85.3	524	6.03% (5.53, 6.55)	1,507	77.8	263	17.45% (15.57, 19.46)
Yes	1,499	14.7	195	13.01% (11.35, 14.82)	430	22.2	102	23.72% (19.78, 28.03)
Index of multiple deprivation (quintile)								
1 = least deprived	1,731	17.52	139	8.03% (6.79, 9.41)	325	17.1	68	20.92% (16.63, 25.76)
2	1,841	18.63	129	7.01% (5.88, 8.27)	364	19.15	80	21.98% (17.83, 26.59)
3	1,955	19.79	152	7.77% (6.63, 9.05)	371	19.52	79	21.29% (17.24, 25.82)
4	1,931	19.54	153	7.92% (6.76, 9.22)	392	20.62	61	15.56% (12.12, 19.54)
5 = most deprived	2,422	24.51	138	5.70% (4.81, 6.70)	449	23.62	75	16.70% (13.37, 20.48)
Missing	315				36			
Rurality								
Urban	7,911	79.72	556	7.03% (6.47, 7.61)	1,517	79.47	272	17.93% (16.03, 19.95)
Rural	2,012	20.28	161	8.00% (6.85, 9.27)	392	20.53	92	23.47% (19.36, 27.98)
Missing	272				28			
Ethnicity								
White	8,805	91.59	627	7.12% (6.59, 7.68)	1,673	90.58	322	19.25% (17.38, 21.22)
Mixed	68	0.71	1	1.47% (0.04, 7.92)	15	0.81	2	13.33% (1.66, 40.46)
Asian	396	4.12	15	3.79% (2.14, 6.17)	86	4.66	13	15.12% (8.30, 24.46)
Black	258	2.68	9	3.49% (1.61, 6.52)	60	3.25	3	5.00% (1.04, 13.92)
Other	87	0.90	3	3.45% (0.72, 9.75)	13	0.7	2	15.38% (1.92, 45.45)
Missing	581				90			

TABLE 2:
Odds ratios for mortality (within 90 days of surgery)

	Unadjusted Odds Mortality (90 day)		Adjusted* Odds Mortality (90 day)		
	OR	95% CI	OR	95% CI	p-value
Primary versus Secondary Diagnosis (M00)					
Primary	1.00	1.00	1.00	1.00	
Secondary	3.06	2.67, 3.51	2.10	1.79, 2.46	<0.001
Sex					
Male	1.00	1.00	1.00	1.00	
Female	1.31	1.16, 1.49	0.87	0.75, 1.01	0.076
Age (per five years) ‡					
Age	1.45	1.41, 1.49	1.38	1.34, 1.42	<0.001
Year of treatment (per five years)					
Year	1.08	1.02, 1.15	0.89	0.83, 0.96	0.002
Charlson comorbidity index (per five units) ‡					
Charlson index	1.52	1.48, 1.56	1.34	1.30, 1.39	<0.001
Prior joint disease					
No	1.00	1.00	1.00	1.00	
Knee osteoarthritis	1.37	1.17, 1.61	0.72	0.60, 0.87	0.001
Rheumatoid arthritis	1.52	1.21, 1.92	0.90	0.68, 1.18	0.437
Index of multiple deprivation (quintile)					
1 = least	1.00	1.00	1.00	1.00	0.336
2	0.94	0.76, 1.15	0.89	0.70, 1.13	0.872
3	0.98	0.81, 1.20	1.02	0.81, 1.28	0.689
4	0.91	0.74, 1.11	1.05	0.83, 1.33	0.172
5 = most	0.72	0.59, 0.87	1.18	0.93, 1.51	0.336
Rurality					
Urban	1.00	1.00	1.00	1.00	
Rural	1.22	1.05, 1.42	1.12	0.93, 1.34	0.227
Ethnicity					
White	1.00	1.00	1.00	1.00	
Mixed	0.38	0.12, 1.19	1.03	0.28, 3.75	0.961
Asian	0.62	0.42, 0.91	1.03	0.67, 1.59	0.875
Black	0.39	0.22, 0.70	0.77	0.41, 1.45	0.417
Other	0.53	0.21, 1.30	1.91	0.71, 5.18	0.201
Diabetes ‡					
No	1.00	1.00	1.00	1.00	
Yes	2.18	1.89, 2.51	1.54	1.31, 1.81	<0.001

*adjusted by all variables in the table except diabetes (see below ‡); OR = odds ratio; CI = confidence interval; TKA = total or partial knee arthroplasty; ‡ Diabetes is included within the Charlson comorbidity index and therefore these colinear variables were not included together in the model. The main model reported in this table included the Charlson comorbidity index. The secondary adjusted model for diabetes included all the variables in the table except the Charlson comorbidity index: to show the association of the outcome with diabetes, independent from the other comorbidities recorded in the Charlson index.

TABLE 3:

One-year adverse operative outcomes in all patients with at least one-year of follow-up (n=11,393)

	1-year Arthrodesis			1-year Amputation			1-year Arthroplasty		
	n	Outcome	% (95% CI)	n	Outcome	% (95% CI)	n	Outcome	% (95% CI)
Total	**11,393**	**15**	**0.13% (0.07, 0.22)**	**11,393**	**46**	**0.40% (0.30, 0.54)**	**11,393**	**152**	**1.33% (1.13, 1.56)**
Male	7,333	10	0.14% (0.07, 0.25)	7,333	34	0.46% (0.32, 0.65)	7,333	97	1.32% (1.07, 1.61)
Female	4,060	5	0.12% (0.04, 0.29)	4,060	12	0.30% (0.15, 0.52)	4,060	55	1.35% (1.02, 1.76)
Age group (years)									
< 20	1,175	0	0.00% (0.00, 0.31)	1,175	0	0.00% (0.00, 0.31)	1,175	0	0.00% (0.00, 0.31)
20 - 39	1,682	1	0.06% (0.00, 0.33)	1,682	2	0.12% (0.01, 0.43)	1,682	1	0.06% (0.00, 0.33)
40 - 59	2,456	3	0.12% (0.03, 0.36)	2,456	10	0.41% (0.20, 0.75)	2,456	33	1.34% (0.93, 1.88)
60 - 79	3,897	8	0.21% (0.09, 0.40)	3,897	28	0.72% (0.48, 1.04)	3,897	105	2.69% (2.21, 3.25)
80 +	2,183	3	0.14% (0.03, 0.40)	2,183	6	0.27% (0.10, 0.60)	2,183	13	0.60% (0.32, 1.02)
Modified Charlson comorbidity index									
0	6,125	9	0.15% (0.07, 0.28)	6,125	5	0.08% (0.03, 0.19)	6,125	86	1.40% (1.12, 1.73)
1 - 15	3,584	3	0.08% (0.02, 0.24)	3,584	23	0.64% (0.41, 0.96)	3,584	60	1.67% (1.28, 2.15)
16 - 30	1,254	3	0.24% (0.05, 0.70)	1,254	13	1.04% (0.55, 1.77)	1,254	5	0.40% (0.13, 0.93)
31 - 50	430	0	0.00% (0.00, 0.85)	430	5	1.16% (0.38, 2.69)	430	1	0.23% (0.01, 1.29)
Prior joint disease									
No	8,934	10	0.11% (0.05, 0.21)	8,934	37	0.41% (0.29, 0.57)	8,934	77	0.86% (0.68, 1.08)
Knee osteoarthritis	1,904	5	0.26% (0.09, 0.61)	1,904	7	0.37% (0.15, 0.76)	1,904	62	3.26% (2.51, 4.16)
Rheumatoid arthritis	716	0	0.00% (0.00, 0.51)	716	2	0.28% (0.03, 1.01)	716	22	3.07% (1.94, 4.62)
Diabetes									
No	9,615	12	0.12% (0.06, 0.22)	9,615	24	0.25% (0.16, 0.37)	9,615	130	1.35% (1.13, 1.60)
Yes	1,778	3	0.17% (0.03, 0.49)	1,778	22	1.24% (0.78, 1.87)	1,778	22	1.24% (0.78, 1.87)
Index of multiple deprivation (quintiles)									
1 = least deprived	1,946	4	0.21% (0.06, 0.53)	1,946	5	0.26% (0.08, 0.60)	1,946	30	1.54% (1.04, 2.19)
2	2,074	2	0.10% (0.01, 0.35)	2,074	10	0.48% (0.23, 0.88)	2,074	30	1.45% (0.98, 2.06)
3	2,168	4	0.18% (0.05, 0.47)	2,168	9	0.42% (0.19, 0.79)	2,168	41	1.89% (1.36, 2.56)
4	2,187	1	0.05% (0.00, 0.25)	2,187	5	0.23% (0.07, 0.53)	2,187	33	1.51% (1.04, 2.11)
5 = most deprived	2,706	3	0.11% (0.02, 0.32)	2,706	17	0.63% (0.37, 1.00)	2,706	18	0.67% (0.39, 1.05)
Missing									
Rurality									
Urban	8,891	10	0.11% (0.05, 0.21)	8,891	36	0.40% (0.28, 0.56)	8,891	102	1.15% (0.94, 1.39)
Rural	2,238	4	0.18% (0.05, 0.46)	2,238	10	0.45% (0.21, 0.82)	2,238	50	2.23% (1.66, 2.93)
Missing									
Ethnicity									
White	9,838	15	0.15% (0.09, 0.25)	9,838	45	0.46% (0.33, 0.61)	9,838	145	1.47% (1.25, 1.73)
Mixed	74	0	0.00% (0.00, 4.86)	74	1	1.35% (0.03, 7.30)	74	0	0.00% (0.00, 4.86)
Asian	440	0	0.00% (0.00, 0.83)	440	0	0.00% (0.00, 0.83)	440	2	0.45% (0.06, 1.63)
Black	296	0	0.00% (0.00, 1.24)	296	0	0.00% (0.00, 1.24)	296	2	0.68% (0.08, 2.42)
Other	90	0	0.00% (0.00, 4.02)	90	0	0.00% (0.00, 4.02)	90	1	1.11% (0.03, 6.04)
Missing									

CI = confidence interval

TABLE 4:

Hazard ratios (subsequent TKA within maximum of 20 years)

	Unadjusted Risk Subsequent TKA		Adjusted* Risk Subsequent TKA		
	HR	95% CI	HR	95% CI	p-value
Sex					
Male	1.00	1.00	1.00	1.00	
Female	1.50	1.29, 1.75	1.12	0.96, 1.32	0.145
Age (per five years) ‡					
Age	1.15	1.13, 1.17	1.12	1.10, 1.15	<0.001
Year of treatment (per five years)					
Year	1.13	1.04, 1.22	1.04	0.95, 1.13	0.390
Charlson comorbidity index (per five units) ‡					
Charlson index	0.98	0.93, 1.04	0.78	0.73, 0.84	<0.001
Prior joint disease					
No	1.00	1.00	1.00	1.00	
Knee osteoarthritis	3.72	3.13, 4.41	2.50	2.09, 3.00	<0.001
Rheumatoid arthritis	3.94	3.14, 4.95	3.73	2.92, 4.75	<0.001
Index of multiple deprivation (quintile)					
1 = least	1.00	1.00	1.00	1.00	
2	1.03	0.81, 1.31	0.99	0.78, 1.26	0.936
3	1.16	0.92, 1.46	1.16	0.92, 1.47	0.216
4	0.98	0.77, 1.25	1.09	0.85, 1.39	0.500
5 = most	0.61	0.47, 0.78	0.80	0.61, 1.04	0.093
Rurality					
Urban	1.00	1.00	1.00	1.00	
Rural	1.50	1.26, 1.78	1.18	0.98, 1.41	0.079
Ethnicity					
White	1.00	1.00	1.00	1.00	
Mixed	0.93	0.39, 2.25	1.58	0.65, 3.84	0.309
Asian	0.46	0.28, 0.77	0.61	0.36, 1.04	0.072
Black	0.26	0.11, 0.57	0.39	0.17, 0.87	0.022
Other	0.16	0.02, 1.12	0.29	0.04, 2.05	0.215
Diabetes ‡					
No	1.00	1.00	1.00	1.00	
Yes	1.04	0.83, 1.31	0.77	0.61, 0.98	0.032

adjusted by all variables in the table except diabetes (see below ‡); HR = hazard ratio; CI = confidence interval; TKA = total or partial knee arthroplasty; ‡ Diabetes is included within the Charlson comorbidity index and therefore these colinear variables were not included together in the model. The main model reported in this table included the Charlson comorbidity index. The secondary adjusted model for diabetes included all the variables in the table except the Charlson comorbidity index: to show the association of the outcome with diabetes, independent from the other comorbidities recorded in the Charlson index.
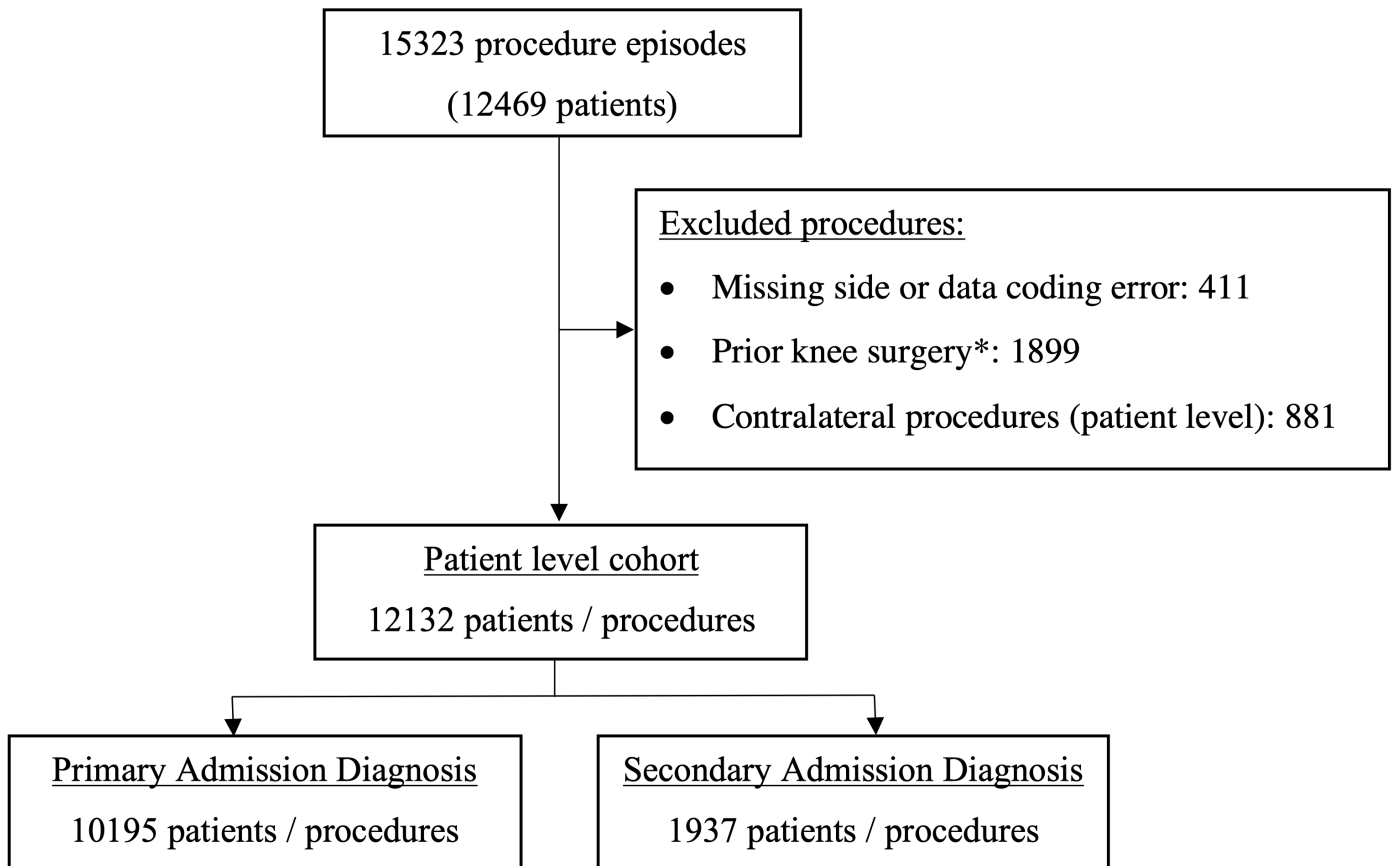
TABLE 5:

Rates and relative risk of undergoing TKA with a history of previous septic knee washout (within prior 20 years) versus the general population (without a recorded history of previous septic knee washout) by age in 2016-17

| Age in 2016-17 (years) | Prior septic knee | | Without prior septic knee | | Relative Risk of Arthroplasty (Annual) | | |
	Annual Rate TKA /100k	95% CI	Annual Rate TKA /100k	95% CI	RR	95% CI	p-value
30 - 39	0.00 (0.00%)	0.00, 499.95 (0.00%, 0.50%)	2.07 (0.00%)	1.75, 2.42 (0.00%, 0.00%)	-	-	-
40 - 49	693.07 (0.69%)	279.09, 1422.74 (0.28%, 1.42%)	25.27 (0.03%)	24.13, 26.44 (0.02%, 0.03%)	27.25	13.01, 57.09	<0.001
50 - 59	1620.59 (1.62%)	946.81, 2582.08 (0.95%, 2.58%)	151.22 (0.15%)	148.40, 154.09 (0.15%, 0.15%)	10.56	6.59, 16.93	<0.001
60 - 69	2154.40 (2.15%)	1385.12, 3188.70 (1.39%, 3.19%)	413.67 (0.41%)	408.46, 418.93 (0.41%, 0.42%)	5.12	3.45, 7.61	<0.001
70 +	1399.18 (1.40%)	970.86, 1949.77 (0.97%, 1.95%)	534.92 (0.53%)	529.28, 540.61 (0.53%, 0.54%)	2.59	1.86, 3.62	<0.001
Overall (30 +)	1293.58 (1.29%)	1030.11, 1603.16 (1.03%, 1.60%)	208.30 (0.21%)	206.78, 209.84 (0.21%, 0.21%)	6.14	4.95, 7.62	<0.001

*TKA = total or partial knee arthroplasty; CI = confidence interval; RR = risk ratio.*

FIGURES

FIGURE 1: Flow chart illustrating extraction of patient level cohort


```
                    ┌─────────────────────────────┐
                    │   15323 procedure episodes  │
                    │      (12469 patients)       │
                    └─────────────────────────────┘
```

Excluded procedures:

- Missing side or data coding error: 411
- Prior knee surgery*: 1899
- Contralateral procedures (patient level): 881

Patient level cohort

12132 patients / procedures

Primary Admission Diagnosis

10195 patients / procedures

Secondary Admission Diagnosis

1937 patients / procedures

open or arthroscopic knee surgery (including knee arthroscopy or knee arthroplasty).

FIGURE 2: Survival curve (not undergoing knee arthroplasty), by age group †
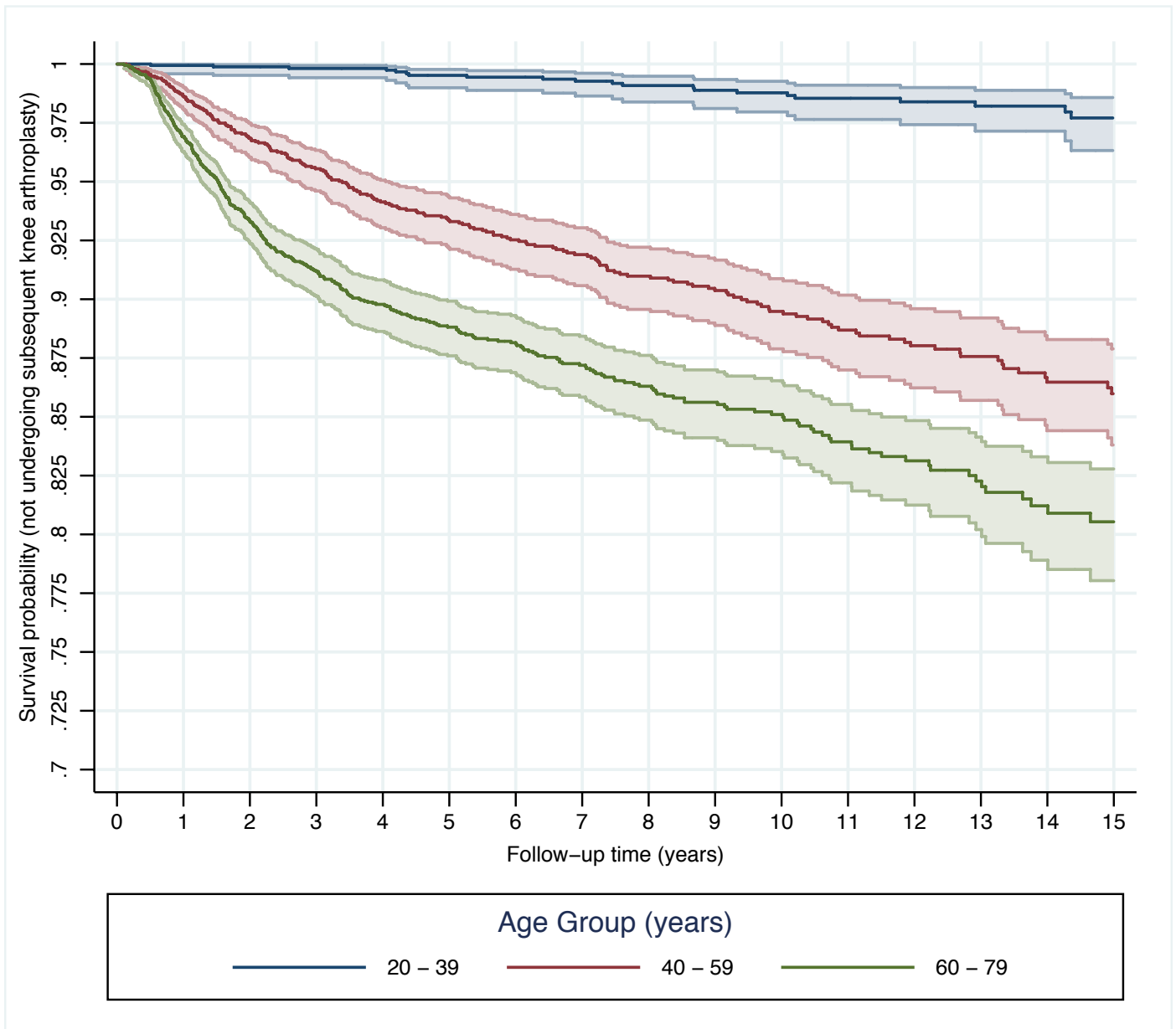
† Age groups < 20 years and 80+ years suppressed due to small numbers