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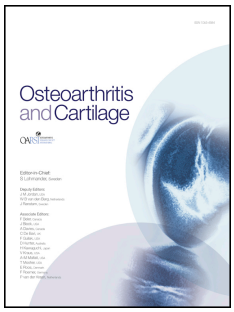

Tibial plateau fractures are associated with a long-lasting increased risk of total knee arthroplasty a matched cohort study of 7,950 tibial plateau fractures

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Tibial plateau fractures are associated with a long-lasting increased risk of total knee arthroplasty

a matched cohort study of 7,950 tibial plateau fractures

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Objective: This study aims to investigate the risk of total knee replacement (TKR) following tibia plateau fractures. Secondary the study aims to investigate the risk of knee arthroscopy following tibial plateau fractures.

Method: The study was designed as a matched cohort study. All patients who sustained a tibial plateau fracture in Denmark between January 1, 1996, and December 31, 2000, were included and followed until December 31, 2015. For each patient with a tibial plateau fracture, 10 matched citizens without a tibial plateau fracture were included as a reference group.

Results: 7,950 patients sustained a tibial plateau fracture in Denmark during the study period. The median age of patients was 52.6 (IQR: 32.4-71.5) years. The mean observational period was 13.9 years. 5.7% were treated with a TKR (N=452), and 2.0% of patients from the reference group were treated with a TKR (N=1,623). Patients with a tibial plateau fracture had a 3.5 (95%CI: 3.1-3.9) times higher hazard ratio (HR) compared to patients from the reference group. 7.6% of patients with a tibial plateau fracture were treated with a secondary knee arthroscopy (N=603) and 2.0% of patients from the reference group were treated with a knee arthroscopy (N=1,565). Patients with a

tibial plateau fracture presented with a 5.0 (95%CI: 4.5-5.6)) times higher hazard ratio compared to patients in the reference group.

Conclusions: Tibial plateau fractures are associated with a 3.5 times increased risk of TKR compared with an age- and gender-matched reference group with a mean follow-up of 13.9 years.

Running title: Increased risk of TKR following tibial plateau fractures

Keywords: tibial plateau fracture; total knee replacement; knee arthroplasty, knee arthroscopy; long-term follow-up

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The manuscript including related data, figures, and tables has not been submitted or is not simultaneously being submitted elsewhere, and no portion of the data has been or will be published in proceedings or transactions of meetings or symposium volumes.

All authors have made substantial contributions to all of the following: (1) the conception and design of the study, acquisition of data, analysis, and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

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Conclusions: Tibial plateau fractures are associated with a 3.5 times increased risk of TKR compared with an age- and gender-matched reference group with a mean follow-up of 13.9 years.

INTRODUCTION

Fractures of the tibial plateau are reported with an incidence of 10.3/100,000/year[1]. Surgical treatment of displaced tibial plateau fractures has become the treatment of choice[2]. The surgical procedure is challenging due to the majority of patients presenting with multi-fragmented bones in combination with cartilage damage and intra-articular soft tissue lesions[3].

A common and well-known complication following tibial plateau fractures is an increased risk of post-traumatic knee osteoarthritis[2,4–8]. The incidence of knee osteoarthritis following tibial plateau fractures has been reported between 13% and 83%, indicating a wide range in severity of osteoarthritis and follow-up time[2,6,9–19]. Increasing fracture comminution, comorbidity, and patients age are commonly reported to increase the risk of early onset of post-traumatic knee osteoarthritis[7].

Total knee replacement as a salvage procedure in the treatment of patients with end-stage knee osteoarthritis is widely accepted[8]. Treatment with TKR following tibial plateau fractures has been less reported and with different frequencies[2,7,18,20]. However, most studies available included only small patient groups and/or short follow-up periods. Recently, a study by Wasserstein et al.[7] with a 10-year follow-up period reporting on 8,426 tibial plateau fractures suggests a 5.3 times increase in the likelihood of TKR compared to a matched reference group, corresponding to 7.3% of patients in the 10-year period. However, only adult patients treated by open reduction internal fixation (ORIF) were included, excluding young patients and patients managed by conservative means or external fixation.

Intra-articular soft tissue lesions and restrictions in knee joint motion following tibial plateau fractures are commonly reported[21–23]. Secondary treatment with knee arthroscopy is indicated for some patients[24]. However, the incidence of secondary knee arthroscopy following tibial plateau fractures has not been previously reported.

The primary question is: What is the national risk of TKR following tibia plateau fractures regardless of treatment modalities compared to an age- and gender-matched reference group without a prior tibial plateau fracture?

The secondary questions were to investigate the incidence of secondary knee arthroscopy following a tibial plateau fracture and compare this to an age- and gender-matched reference group without a prior tibial plateau fracture. A further secondary question was to compare the time to TKR and secondary arthroscopy following a tibial plateau fracture compared to that of the age- and gender-matched reference group.

PATIENTS AND METHODS

Study design

The study was designed as a matched cohort study. Prospectively obtained registry data including all citizens of Denmark were used.

All patients who sustained a tibial plateau fracture in Denmark between January 1, 1996, and December 31, 2000, were included and followed until December 31, 2015, regarding treatment with TKR and/or secondary knee arthroscopy.

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Secondary knee arthroscopy was defined as all knee arthroscopy procedures performed at least 30 days after the primary operation. Arthroscopic procedures performed during primary operative treatment of the tibial plateau fracture were excluded from this analysis.

Danish law requires that all patient contacts with hospital and outpatient clinics in Denmark are registered in the Danish National Patient Register[25]. Hospital identification, date and time of activity, and the patient's municipality (among other characteristics) are registered. A civil registration number (CPR) is given to all residents of Denmark and registered in the Civil Registration System, and information on emigration and death is recorded in this registry[26]. This enables researchers to have a complete and valid registration of all health-related issues on an individual level in the entire Danish population[27].

The Danish Data Protection Agency approved the study (J. nr. 2008-58-0028, Id: 2016-176). A full study protocol and study analysis plan was published online before the start of the study[28]. The reporting of the study complies with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement[29].

Study population and data

The group of patients with a tibial plateau fracture was identified through a retrospective review in the Danish National Patient Register. All Danish citizens registered with a tibial plateau fracture between January 1, 1996, and December 31, 2000, were included. Information regarding gender and age at the time of fracture was registered. Patients with prior tibial plateau fractures and TKR were excluded from

the study. All patients were followed with regard to surgery with TKR and/or secondary arthroscopic surgery of the knees throughout the observational period.

The matched reference group consisted of individuals identified from the Civil Registration System matched to the tibial plateau patient group on age and gender. For each patient with a tibial plateau fracture, 10 matched citizens were included.

Both groups were censored in case of emigration from the country or at the end of follow-up. Death was considered a competing event as was receiving a TKR when considering secondary knee arthroscopy as the outcome.

The primary outcome was treatment with a TKR. The secondary outcome was treatment with secondary knee arthroscopy.

Statistical methods

The risk of experiencing a TKR was assessed using cumulative incidence proportions which were calculated using the Aalen-Johansen estimator[30].

The effect of tibial plateau fracture on the incidence of TKR was performed using a Cox proportional hazards regression model comparing the group of patients with tibial plateau fractures and the matched reference group. The effect estimate was reported as a hazard ratio with a corresponding 95% confidence interval to estimate the incidence rate ratio. Results from the crude analysis without adjustments were reported. Furthermore, we repeated the analysis stratified by age groups (0-50, 51+)

and gender. To investigate the assumption of proportional hazards, the follow-up time is divided into five-year periods.

Additional analyses were performed to investigate the effect of tibial plateau fracture on the secondary outcome (secondary knee arthroscopy) following the same methods as for the main analysis except that TKR, in addition to death, was considered a competing event for secondary arthroscopy.

All analyses were performed using Stata statistical software (StataCorp LP), and the significance level for analyses (α) was set to 0.05.

RESULTS

A total of 7,950 patients sustained a tibial plateau fracture in Denmark during the study period. The matched reference group consists of 79,300 citizens. Only 13 patients with a tibial plateau fracture were matched by age and gender with less than 9 citizens from the reference group (0.16%).

The median age of patients was 52.6 (IQR: 32.4-71.5) years. The gender distribution was 56.4% women and 43.6% men. The mean observational period was 13.9 years.

Primary outcome

The analysis showed that 5.7% of patients with a tibial plateau fracture were treated with a TKR (N=452) and that 2.0% of patients from the reference group were treated with a TKR (N=1623) during the observational period. The distribution of arthroplasties procedures for both groups is presented in Table 1.

Patients with a tibial plateau fracture had a 3.5 (95%CI: 3.1-3.9) times higher hazard ratio (HR) compared to patients from the reference group. The effect was highest during the first five years after the fracture (HR: 8.6 (95%CI: 7.1-10.3)) (Table 2). The cumulative incidence of TKR during the entire observational period expressed for the two groups is shown in Figure 1. The figure shows a significantly increased risk of TKR in patients with a tibial plateau fracture compared to patients from the reference group throughout the observational period.

Analyses of age and gender difference on TKR

Both men and women presented with a significantly increased incidence of TKR in patients with a tibial plateau fracture compared with the reference group. Compared to men, women presented with an increased incidence of TKR throughout the observational period. The incidence of TKR for women showed a substantial increase during the first five years compared to men. The age group above 50 years presented with a substantially increased risk of TKR compared to the age group below 50 years. (Supplemental figure 1-4).

Secondary outcomes—secondary knee arthroscopy

The analysis showed that 7.6% of patients with a tibial plateau fracture were treated with a secondary knee arthroscopy (N=603) and 2.0% of patients from the reference group were treated with a knee arthroscopy (N=1,565). The distribution of knee arthroscopy procedures in both groups is presented in Table 3.

Patients with a tibial plateau fracture presented with a 5.0 (95%CI: 4.5-5.6)) times higher hazard ratio compared to patients in the reference group. As for TKR, the

effect was highest during the first five years after the tibial plateau fracture. (HR: 9.7 (95%CI: 8.5-11.0)) (Table 4).

The cumulative incidence of secondary knee arthroscopy throughout the observational period is shown in Figure 2. The figure shows a significantly increased risk of secondary knee arthroscopy within the first five years following the tibial plateau fracture compared to the reference group. After the first five years, patients with a tibial plateau fracture and the reference group presented with almost equal risk of receiving a TKR.

The analyses of age and gender differences in the incidence of knee arthroscopy show that men presented with increased risk during the first five years compared to women, with almost equal risk of receiving a knee arthroscopy past five years. The analysis of age differences showed that the age group below 50 years of age presented with considerably increased risk compared to the age group above 50 years of age. (Supplemental Figure 5-8).

DISCUSSION

This large-scale matched cohort study based on high-quality data showed that patients following a tibial plateau fracture increase the likelihood of TKR 3.5 times and knee arthroscopy 5.0 times. By a mean of 13.9 years follow-up, 5.7% of patients were treated with a TKR, and 7.9% with knee arthroscopy. The incidence of TKR and knee arthroscopy was highest during the first five years following the tibial plateau fracture. These findings indicated a long-lasting elevated risk of knee pain and decreased knee function in patients following a tibial plateau fracture.

The association between tibial plateaus fracture and TKR have been discussed extensively in the literature. However, most available studies are limited by small samples, short follow-up periods, and methodological quality. Recently, a study by Wasserstein et al.[7] with a 10-year follow-up period reported a 5.3 times increase in the likelihood of TKR, corresponding to 7.3% of patients treated with a TKR. The difference between the two studies may be explained by the present study including patients managed by all treatment modalities (ORIF, conservative means, and external fixation) in contrast to the study by Wasserstein et al., including only patients treated by ORIF. By including non-operative tibial plateau fractures in the present study, we included a cohort of patients who most likely had lower energy and less severe fractures compared to the Wasserstein[7] study, which is likely the major reason for the observed differences. Moreover, the increased risk of TKR in the study by Wasserstein may be partly explained by younger age. Moreover, conservative treatment of tibial plateau fracture may be more likely in older patients with a higher degree of comorbidity and decreased physical performance. Unfortunately, the present study did not include data on comorbidity and distribution between treatment modalities, which is an interesting research question for further studies. The need for long observational periods to investigate the increased risk of TKR following a tibial plateau fracture is evident as the 15-20 year hazard ratio is 1.86, indication a continually increased risk and hence the need for long follow-up periods.

This study showed that patients following a tibial plateau fracture presented with an increased likelihood of TKR throughout life. However, end-stage osteoarthritis and treatment with TKR are rare. In the present study, 5.7% of patients were treated with

TKR by a mean of 13.9 years follow-up. Investigating the association between a tibial plateau fracture and subsequent treatment with TKR is challenging due to the rarity and the long-term follow-up needed to capture the development of end-stage osteoarthritis. To the author's knowledge, the present study presented the largest cohort and longest follow-up of patients following a tibial plateau fracture.

Although the incidence of knee arthroscopy in patients with knee osteoarthritis is decreasing, the operative procedure is still common before treatment with TKR[31]. Moreover, intra-articular soft tissue lesions and restrictions in knee joint motion following a fracture of the tibial plateau are common, which may lead to secondary knee arthroscopy in some patients. The present study showed that patients with a previous tibial plateau fracture had a five times higher incidence of a knee arthroscopy compared to the matched control group. During the first five years after the fracture, the likelihood of knee arthroscopy was increased almost 10 times. The subgroup analyses showed that especially younger men were treated with knee arthroscopy. In the authors opinion, younger patients are much more likely to be offered knee arthroscopy for continued knee pain following a tibial plateau fracture in an effort to preserve the knee joint and are less likely to be offered knee replacement. The converse is true for older patients. A single non-matched cohort study by Mehin et al.[6] supported these findings, reporting that 16% of patients (N=311) following a tibial plateau fracture at 10 years follow-up had an elective operative procedure (arthroscopic procedure or intra-articular injection). This study suggested that many patients experience knee pain and decreased knee function, especially in the first years following a tibial plateau fracture. However, this study did not include clinical information regarding the underlying causes leading to arthroscopic surgery and the

outcomes following the procedures. Further research is needed to address specific indications and outcomes of secondary knee arthroscopy in patients with a prior tibial plateau fracture.

Nevertheless, the present study included the entire Danish population of patients with tibial plateau fractures and compared this to a 10-fold non-exposed age- and gender-matched control group; some important limitations may be addressed. Information regarding laterality of tibial plateau fracture, TKR, and secondary arthroscopy is missing as side-specific information was not mandatory in the Danish National Patient Register. This is a limitation, and as a result, the ipsilateral risk of TKR and arthroscopy is likely higher than the risk estimates reported in the present study. Moreover, clinical information regarding comorbidity, fracture severity, treatment methods, and outcomes is not available from the register. It is likely that such clinical factors may affect secondary treatment with TKR and knee arthroscopy in subgroups[7]. Finally, shortcomings related to health registers may be addressed. Since 1978, reporting to the Danish National Patient Register was required by Danish national law. Moreover, the allocation of payment to health care providers is partly based on this reporting. However, a small private activity, especially regarding arthroscopy, might have eluded the registry until mandatory registration by private hospitals was introduced in 2003. Although this might have had some effect on the crude incidence of surgery, this effect would have been present in both groups.

In conclusion, tibial plateau fractures are associated with a 3.5 times increased risk of total knee replacement and a 5.0 times increased risk of secondary knee arthroscopy

compared with an age- and gender-matched reference group with a mean follow-up of 13.9 years.

Author contributions

Larsen, Elsoe and Johansen contributed all to the conception and design of this work. Larsen, Elsoe and Johansen contributed to analysis and interpretation of the data. Johansen contributed the data analysis. All authors were involved in drafting the article or revising it critically for important intellectual content, and granted final approval of the manuscript.

Conflict of interest

The authors declared no conflicts of interest.

Source of founding

None

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Legends:

Table 1— The distribution of arthroplastie procedures for patients with a tibial plateau fracture and patients from the matched reference group.

Table 2— Cox proportional hazards regression model of TKR comparing patients with a tibial plateau fracture with the matched reference group.

Table 3— The distribution of secondary knee arthroscopy procedures for patients with a tibial plateau fracture and patients from the matched reference group.

Table 4— Cox proportional hazards regression model of secondary knee arthroscopy comparing patients with a tibial plateau fracture with the matched reference group.

Figure 1—Cumulative incidence of TKR
Legends: -- tibial plateau fracture group, -- reference group

Figure 2– Cumulative incidence of arthroscopy
Legends: -- tibial plateau fracture group, -- reference group

Supplemental figures:

Figure 1—Cumulative incidence of TKR, Women
Legends: -- tibial plateau fracture group, -- reference group

Figure 2—Cumulative incidence of TKR, Men
Legends: -- tibial plateau fracture group, -- reference group

Figure 3—Cumulative incidence of TKR, below 50 years of age
Legends: -- tibial plateau fracture group, -- reference group

Figure 4—Cumulative incidence of TKR, above 50 years of age
Legends: -- tibial plateau fracture group, -- reference group

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Figure 5—Cumulative incidence of arthroscopy, Women

Legends: -- tibial plateau fracture group, -- reference group

Figure 6—Cumulative incidence of arthroscopy, Men

Legends: -- tibial plateau fracture group, -- reference group

Figure 7—Cumulative incidence of arthroscopy, below 50 years of age

Legends: -- tibial plateau fracture group, -- reference group

Figure 8—Cumulative incidence of arthroscopy, above 50 years of age

Legends: -- tibial plateau fracture group, -- reference group

Table 1—Cox proportional hazards regression model of TKR and knee arthroscopy comparing patients 0-50 years with a tibial plateau fracture with the matched reference group.

Table 2—Cox proportional hazards regression model of TKR and knee arthroscopy comparing patients 50+ years with a tibial plateau fracture with the matched reference group.

Table 3—Cox proportional hazards regression model of TKR and knee arthroscopy comparing men with a tibial plateau fracture with the matched reference group.

Table 4—Cox proportional hazards regression model of TKR and knee arthroscopy comparing women with a tibial plateau fracture with the matched reference group.

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Table 1:

	Tibial plateau fractures		Reference group	
Procedure:				
Cemented TKR	335	74%	1160	71%
Hybrid TKR	48	11%	246	15%
Uncemented TKR	43	10%	90	6%
Medial arthroplasty	5	1%	66	4%
Other	21	5%	61	4%
Total arthroscopies	452	100%	1623	100%

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Table 2:

Follow-up time	N at beginning of interva	# events in interva	HR (95% CI)
0-5 years	87248	509	8.55 [7.12 - 10.27]
5-10 years	74510	588	2.41 [1.92 - 3.02]
10-15 years	65279	659	2.15 [1.72 - 2.70]
15-20 years	57484	318	1.86 [1.31 - 2.66]
0-20 years	87248	2074	3.50 [3.14 - 3.91]

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Table 3:

	Tibial plateau fractures				Reference group			
	Knee Arthroplasty		No Knee Arthroplasty		Knee Arthroplasty		No Knee Arthroplasty	
Diagnostic arthroscopy	75	61%	458	65%	167	62%	1381	63%
Synovectomia	16	13%	96	14%	26	10%	243	11%
Miniscal resection	17	14%	81	12%	57	21%	424	19%
Cartilage resection	7	6%	33	5%	12	4%	95	4%
Other	8	7%	33	5%	6	2%	43	2%
Total arthroscopies	123	100%	701	100%	268	100%	2186	100%
One arthroscopy	71	76%	353	69%	97	57%	739	53%
> 1 arthroscopy	23	24%	156	31%	74	43%	655	47%
Total	94	100%	509	100%	171	100%	1394	100%
Total	603				1565			

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Table 4:

Follow-up time	N at beginning of interva	# events in interva	HR (95% CI)
0-5 years	86927	936	9.66 [8.45 - 11.03]
5-10 years	73347	482	1.87 [1.43 - 2.44]
10-15 years	63743	322	1.63 [1.15 - 2.31]
15-20 years	55779	91	1.05 [0.48 - 2.30]
0-20 years	86927	1831	5.02 [4.52 - 5.57]

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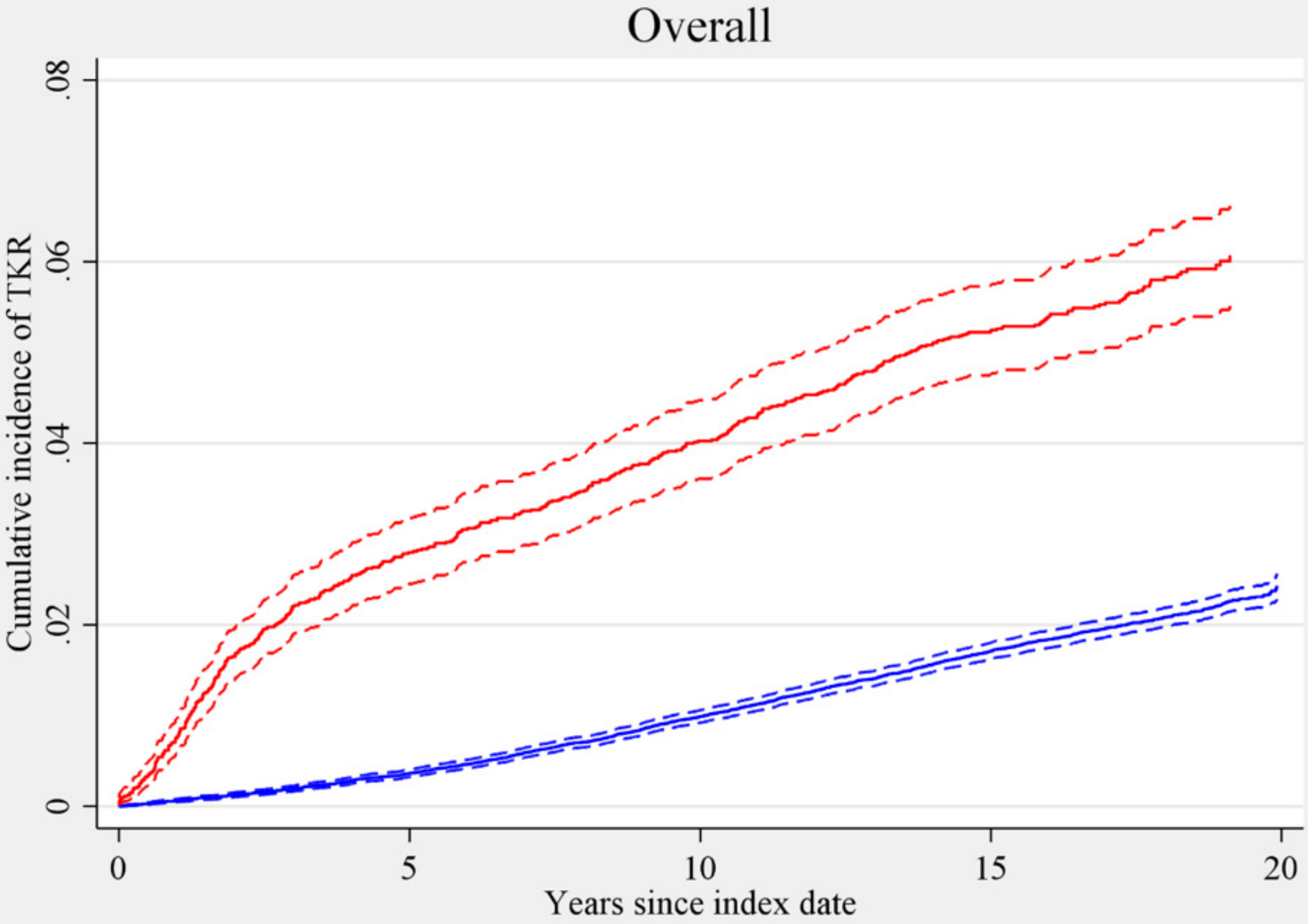
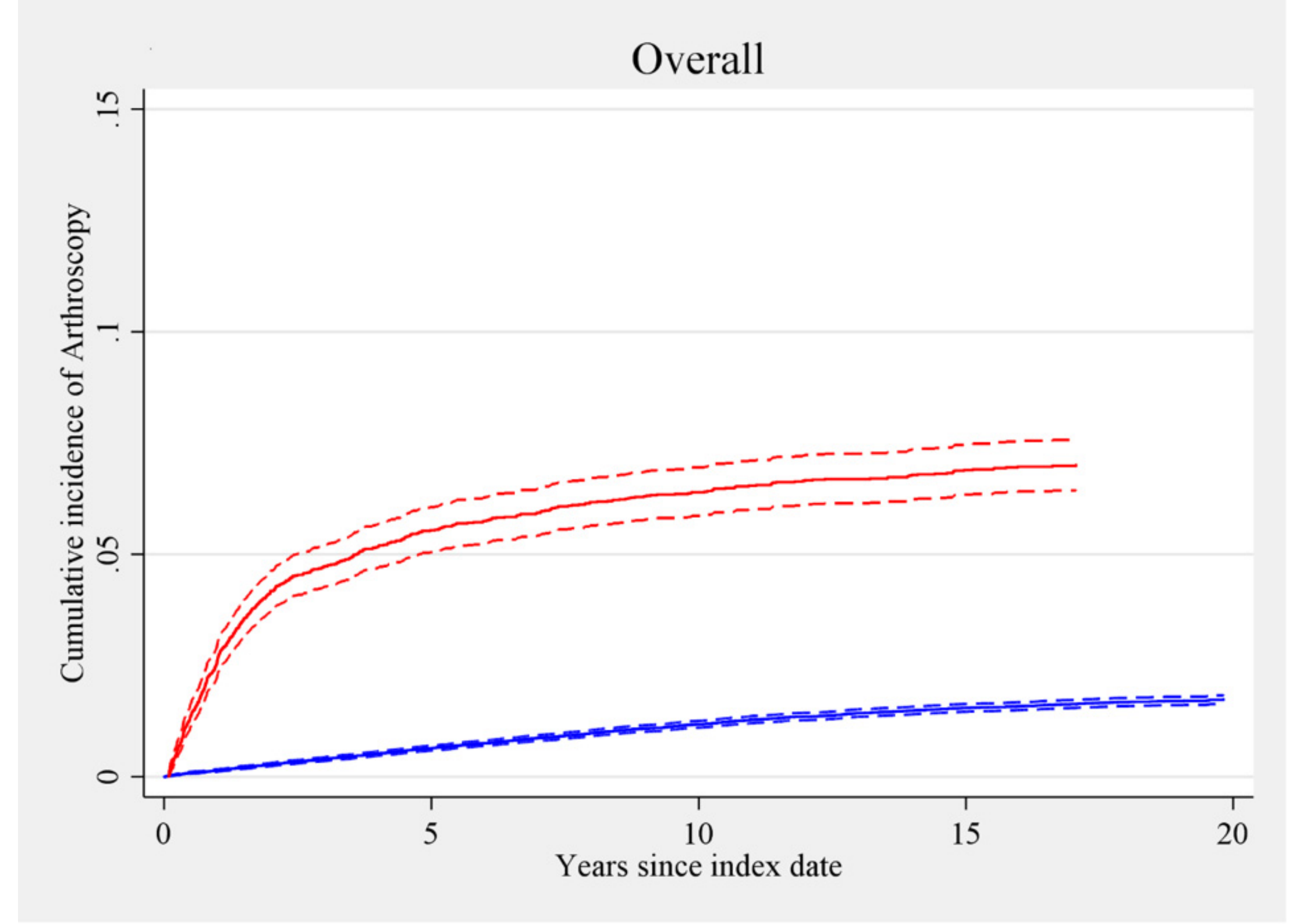

Overall
Cumulative incidence of TKR
0
.02
.04
.06
.08
0
5
10
15
20
Years since index date


Overall
Cumulative incidence of Arthroscopy
0
.05
.1
.15
0
5
10
15
20
Years since index date