Prior High Tibial Osteotomy Does Not Affect the Survival of Total Knee Arthroplasties

Results From the Danish Knee Arthroplasty Registry

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Keywords: Total Knee Arthroplasty, Survival, High Tibial Osteotomy, Revision, Osteoarthritis

Abstract

Background: High tibial osteotomy (HTO) is a joint preserving treatment of unicompartmental osteoarthritis in the knee. In cases with insufficient or deteriorating clinical results patients may undergo a total knee arthroplasty (TKA). The influence of prior HTO on TKA survival is debated.

Methods: We conducted a population-based registry study comparing 1,044 primary TKA in patients with prior HTO to 63,763 de novo TKA inserted from 1997 to 2015. Implant survival was estimated by Kaplan Meier analysis with revision of any kind as endpoint. Patient- and surgery characteristics, including choice of implant design, were compared and their influence on TKA survival was estimated by Cox regression. Finally, indications of revision were compared between the groups.

Results: TKA following HTO had an inferior survival with a 10-year estimated survival of 91% compared to 94% for de novo TKA, corresponding to a crude hazard ratio (HR) of 1.73 ($p<0.001$). However, after adjustment for differences in sex and age this risk diminished (HR=1.19, $p=0.09$). The choice of implant constraint was similar between the groups and in both groups posterior stabilized TKA (PS-TKA) was associated with inferior survival with an adjusted hazard ratio of 1.46 ($p=0.03$) in post-HTO TKA when compared to cruciate retaining TKA.

Conclusion: TKA following HTO had a crude inferior survival when compared to TKA without prior surgery of any kind. The inferior survival was explainable by patient characteristics, defined by male sex and lower age, rather than the prior HTO. However, when the prior HTO resulted in the use of PS-TKA the survival decreased.

Introduction

45% of the people in the western world are estimated to develop symptomatic primary knee osteoarthritis (OA) during their lifetime [1] making OA a major cause of disability [2]. Unicompartmental OA can be treated with high tibial osteotomy (HTO) [3] in order to postpone or maybe avoid subsequent arthroplasty surgery [4]. HTO is most commonly conducted either as medial open wedge or lateral closed wedge procedure to treat medial OA. Of these, closed wedge is the classical procedure while open wedge has become more common in the recent years [5]. The clinical results from HTO might deteriorate over time and 33% are later treated with a total knee arthroplasty (TKA) [4]. These conversion TKA are complicated by scar tissue, altered knee mechanics and retained surgical hardware [6–8]. It may therefore be hypothesized that prior HTO leads to an inferior survival of conversion TKA and that the altered knee mechanics might result in the need of more constrained implants. There is a current dispute about the impact of previous HTO on the survival of subsequent TKA as well as the optimal choice of constraint [9–14], and recent epidemiological studies from Nordic knee arthroplasty registries report conflicting survival estimates [15–17]. Therefore, the purpose of this study was to analyze the survival of TKA inserted in knees previously treated with HTO based on data from the Danish Knee Arthroplasty Registry (DKR).

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Methods

Study population

The study was based on registrations from the Danish Knee Arthroplasty Registry (DKR) which has been collecting data prospectively on knee arthroplasties performed in Denmark (population of 5.7 mill.) since the registry was initiated the 1st of January 1997. Recently, the DKR was reported suitable for epidemiological studies [18] and the registry completeness has increased from 88% in 2010 to 99% in 2015 [19]. The DKR records patient characteristics such as age, gender, weight, previous knee surgeries, as well as details about the surgeries including procedure time and perioperative complications (fractures, rupture of the patella ligament etc), and details regarding components, including level of constraint and supplementation defined as stem, augments or cones. Comorbidity is recorded using the Charnley classification which has been associated with the outcome of arthroplasties [20], and is sorted in class A (patients with unilateral arthritis), B1 (patients with bilateral arthritis), B2 (patients with opposite knee treated with arthroplasty) and C (patients with other conditions limiting their active daily living). In addition, the DKR is linked with the Danish Civil Registration System which has been collecting information on Danish citizens since its origin in 1968 and, among other data points, contains vital status [21].

The DKR defines revision as exchange, addition or removal of any component in an existing arthroplasty. Indications for revision are classified as aseptic loosening, pain, instability, infection, polyethylene failure, secondary insertion of patella component, progression of arthritis and others (including periprosthetic fractures, soft tissue injury and stiffness) and have the possibility of reporting multiple indications for a single revision. We created a clinical hierarchy to rank the indications for revision (Table 1) and thereby only considered the most important indication for each revision. TKAs were grouped according to level of constraint in cruciate retaining (CR), posterior stabilized (PS), constrained condylar (CCK), hinged (Hinged), and undefined when the components were unknown.

From the DKR, we retrieved data on all TKAs inserted due to primary OA from 1st of January 1997 till 31st of December 2015 in knees previously treated solely with high tibial osteotomy (HTO). Registrations in the DKR do not allow for distinction between closed or open wedge HTO thus both procedures were included in this group. The validity of the reported HTO was reviewed by auditing patient records of a sample of all HTOs converted to TKA, performed at our local hospital (n=134). Of these 128 (96%) were confirmed with prior HTO, in 3 (2%) cases we were unable to retrieve the patient record but confirmed the diagnosis by crosschecking in the Danish National Patient Registry [22] and in 3 (2%) cases we could not confirm the HTO. As controls, we retrieved all de novo TKA from the same period, inserted due to primary OA in patients without registered prior knee surgery of any kind. We considered each knee as an individual observation thus patients treated bilaterally with TKA, within the study period, contributed with two individual observations. Recent studies have addressed the potential problems with bilateral observations and reported these as negligible in large epidemiological arthroplasty studies concerning revisions [23,24].

Statistics

Kaplan Meier analysis was used to estimate survival and these estimations were compared by Log Rank test. We considered revision of any kind as endpoint and censored unrevised patients by the first coming event of death, emigration or end of study by the 31st of December 2015. Cox regression was used to compare the risk of revision between the groups with de novo TKA as reference and with successive adjustment for patient characteristics that both differed statistically and were of clinical interest. The assumption of proportional hazards was tested by Schönfeld residual test [25] and was not violated for the chosen co-variates ($p>0.1$, for all comparisons) except age. In long term arthroplasties studies, as this, the hazard related to age varies over time thus violating the assumption of proportional hazards ($p<0.001$ in this study). Therefore, we chose to include age as a time-varying co-variate in the cox regression analysis. Furthermore, death could arguably be a collateral risk in long term arthroplasties studies due to the long follow up in an elderly population [26]. Therefore, we additionally analyzed the hazard ratio by competing risk regression based on Fine-Gray's proportional sub hazards model with death as a competing risk [27]. We found a slightly increased crude hazard ratio when calculated by competing risk regression (1.85 vs. 1.73) with a similar level of significance ($p<0.001$ for both analyses). The difference is explainable by a higher age in the de novo group with increased risk of experiencing the competing event. In this paper, we present the more widely used Cox regression as the difference was small and the results from Cox regression is more usable for orthopaedic surgeons informing patients [28]. Categorical variables were compared by chi square test if $n \geq 5$ and by Fischer's exact test if $n<5$, and Wilcoxon Rank sum test was used to compared cumulative variables. A 95% confidence interval (CI) was chosen and $p<0.05$ was considered as significant. Standard deviations (SD) were clustered at a hospital-level to shield against inter-hospital variations such as traditions in decision making. All analyses were conducted in STATA 15.

Ethics and funding:

The study was approved by the Danish Data Protection Agency (entry no. 2008-58-0028) and the authors did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Results:

Study Population

In total 65,127 TKA were retrieved from the DKR. We excluded incorrect registrations (HTO: n=5, de novo: n=315) and estimated missing values in weight, duration of index surgery and Charnley class by multiple imputation. An overview of excluded and missing values is presented in table 2 (see appendix). 64,807 TKA were included in the final analyses and of these 1,044 were TKA following HTO and 63,763 were de novo TKA. In total 12,130 patients contributed with bilateral TKA and of these 72 had bilateral post-HTO TKA, 232 had post-HTO TKA in one knee and de novo TKA in the other, and 11,826 had bilateral de novo TKA.

Patient and surgery characteristics

Patient and surgery characteristics differed on key variables between TKA following HTO and de novo TKA (table 3). The proportion of males was significantly higher in the HTO group (57% vs 35%, $p<0.001$), the average age was 8 years lower in patients with previous HTO (62 years vs 70 years, $p<0.001$) and there was a longer follow up in this group (8.55 years vs 6.58 years, $p<0.001$). On average, the surgical procedure was 17 minutes longer in patients with previous HTO (88 minutes vs 71 minutes, $p<0.001$), and both perioperative complications (2% vs 0.5%, $p<0.001$) and component supplementation (3% vs 1%, $p<0.001$) were more pronounced in this group. Statistically, the distribution in Charnley class and the preoperative weight differed significantly but these differences were small and not of clinical interest.

Survival

To evaluate potential improvement in the survival of TKAs during the last decades we compared the survival of TKA from 3 different time periods (1997-2003, 2004-2009, 2010-2015). No significate

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difference when tested by log rank test ($p=0.14$) or Cox regression ($p>0.27$, for all comparisons) thus adjustment for time periods as confounding variable was omitted.

TKA following HTO had an inferior estimated survival as depicted in figure 1 ($p<0.001$) with an estimated 1- and 10-year survival of 0.97 (CI: 0.96-0.98) and 0.91 (CI: 0.89-0.93) compared to 0.98 (CI: 0.98-0.99) and 0.94 (CI: 0.94-0.95) in de novo TKA. The difference corresponded to a significant crude hazard ratio (HR) for revision of 1.73 (CI: 1.40-2.15, $p<0.001$) in TKA following HTO. However, the significant hazard ratio decreased after adjustment for the difference in sex (HR=1.69, CI: 1.36-2.09, $p<0.001$) and the significance vanished after adjustment for age as a time varying co-variate (HR=1.19, CI: 0.97-1.45, $p=0.09$). Older age (per year) had a baseline inferior risk of revision (HR= 0.97, CI: 0.97-0.98, $p<0.001$) and for each year the patient got older, the baseline risk decreased additionally with 0.01 (CI: 0-0.01, $p<0.001$).

Revisions

The distribution of revision indications did not differ significantly between the groups ($p=0.59$) as shown in table 4. However, instability and wear occurred more frequent (22.5% vs 17% and 7.25% vs 4%, respectively) in our group of patients with previous HTO. Aseptic loosening was the most frequent indication in both groups but occurred more frequent patients with de novo TKA (27% vs 22.5%) whereas infection was more evenly distributed between the groups (24% in de novo TKA and 22% in TKA following HTO).

Type of implant

In the HTO group, cruciate retaining TKA (CR-TKA) were used in 80% (n=829) and posterior stabilized TKA (PS-TKA) in 15% (n=150). The remaining 5% (n=65) were mainly undefined. A similar distribution was present for de novo TKA with 81% (n=51,866) CR-TKA, 14% (n=8,657) PS-TKA and 5% (n=3,240) mainly undefined. Although the difference between groups was statically significant ($p<0.001$), we consider it without clinical relevance. Since PS-TKA and CR-TKA dominated both groups, we compared the survival of PS-TKA to CR-TKA.

Overall, the survival of both PS-TKA and CR-TKA was unchanged ($p>0.17$) during the three time periods (1997-2003, 2004-2009, 2010-2015) thus adjustment for time periods was omitted. The mean follow up were clinically comparable between the two types of implants (PS-TKA: 6.66 years vs CR-TKA: 6.50 years, $p<0.001$).

In post-HTO TKA, there was no difference in age (PS-TKA: 63 vs CR-TKA: 62, p=0.68) or duration of index surgery (PS-TKA: 91 minutes vs CR-TKA: 87 minutes, p=0.11). However, other characteristics differed both statistically and clinically between the two implants. In PS-TKA, females were more frequent (60% vs 40%, $p<0.001$), the average weight was slightly lower (83 kg vs 85 kg, p=0.03) and the distribution in Charnley class differed slightly (p=0.04) with a higher proportion of patients in class C in PS-TKA (8% vs 3%). Altogether, 12% (n=18) of the PS-TKA were revised compared to 9% (n=75) of the CR-TKA thus PS-TKA was associated with an increased crude hazard ratio for revision of 1.45 (CI: 1.05-2.01, p=0.02). The increased hazard was unaffected by successive adjustment for the differences in sex, weight and Charnley class with a final adjusted hazard ratio of 1.46 (CI: 1.05-2.03, p=0.03). Noteworthy, the need for additional components (11% vs 1%, $p<0.001$) and perioperative complications (4% vs 1%, p=0.01) were more pronounce in PS-TKA indicating a more complicated procedure. Instability was the leading cause of revision in PS-TKA (28%) compared to infection in CR-TKA (24%). However, the overall distribution of indications did not differ between the two implants (p=0.63).

In de novo TKA, age, sex, weight, Charnley class and procedure time did not differed clinically between PS-TKA and CR-TKA. Revision occurred more frequent in PS-TKA (7%, n=586) when compared to CR-TKA (4%, n=2,155) corresponding to a crude hazard ratio of 1.60 (CI: 1.24-2.07, $p<0.001$). The need for component supplementation was slightly more pronounced in PS-TKA (2%

vs 0.5%, p<0.001) whereas the frequency of perioperative complications was similar (1% vs 0.5%, p=0.08). Indications for revisions differed significantly in de novo TKA (p<0.001) even though aseptic loosening (PS-TKA: 29% vs CR-TKA: 26%) and infection (PS-TKA: 24% vs CR-TKA: 25%) were the most frequent indication of revision in both group. Instability occurred more frequent in CR-TKA (19%) than in PS-TKA (11%) as opposed to the tendency in post-HTO TKA.

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Discussion

The data from the DKR revealed an inferior crude survival of TKA inserted after HTO. Preoperative characteristics differed between the groups with an increased proportion of men (57% vs 35%) and lower age (62 years vs 70 years) in post-HTO TKA. These factors have previously been shown to increase the risk of revision [29–31] and, in this study, the increased hazard ratio for revision disappeared after adjustment for sex and age with age being the determining factor. In addition, differences in perioperative characteristics indicated a more complicated index surgery when TKA followed HTO with an increased procedure time (88 minutes vs 71 minutes), need for component supplementation (3% vs 1%) and perioperative complications (2% vs 0.5%). As these characteristics were determined by the knee condition following HTO and presumably led to increased operative complexity, we did not adjust for these in our Cox regression. The Cox regression suggests that age and sex carried the risk of revision, and not the prior HTO. However, from the data, it is not possible to determine if age and sex carried the risk of revision alone or they were characterizing a group of patients sharing other risks such as high physical activity and/or expectations which might lead to an undesired result from both the HTO and the TKA [32].

This study complements recent studies with opposing results from the other Nordic arthroplasty registries [15–17]. The results oppose studies from Sweden and Finland which have reported an inferior survival of TKA following HTO with an adjusted hazard ratio ranging from 1.4-1.7 [15,16], but are in concordance with results from the Norwegian registry reporting a similar survival for both groups with an insignificant adjusted HR of 0.97 [17].

Post-HTO TKA were revised more frequent than de novo TKA (9.5% vs 4.5%) but overall there was no significant difference in the distribution of indications for revision in this study. However, an interesting tendency was present as both revisions due to instability (22.5% vs 17%) and wear (7.25% vs 4%) occurred more often in TKA following HTO. The tendency of increased implant wear might be related to the increased follow up or associated with potential undefined characteristics, such as increased physical activity, in patients treated with TKA following HTO. The higher frequency of instability could be related to the complexity of the index surgery depicted in the prolonged duration of index surgery, threefold increase in component supplementation and fourfold increase in perioperative complications. Both the increased incidence of instability and the increased complexity of index surgery could be explained by the altered knee anatomy after HTO-surgery described elsewhere [33,34]. A similar complexity and increased proportion of instability have been described for TKA inserted in knees with previous fractures [35] thus implying meticulously balancing of the knee and choice implants as key components of post-HTO knee arthroplasty surgery as well [32].

The current study also investigated the survival among different implants inserted in knees with previous HTO. We found that posterior stabilized TKA (PS-TKA) had approximately 1.5 times increased risk of revision when compared to cruciate retaining TKA (CR-TKA). This risk sustained after adjustment for pre-operative difference between the groups. PS-TKA might be chosen in challenging cases which is supported by the increase in component supplementation (11% vs 1%), perioperative complications (4% vs 1%) and the trend towards increased revisions due to instability (28% vs 24%). In de novo TKA, PS-implants had a similar increased risk of revision (HR of 1.64) when compared to CR-TKA. The need for additional components was slightly increased in PS-TKA (2% vs 0.5%) however not as pronounced as in post-HTO TKA. In addition, perioperative complications did not differ between the implants in de novo TKA and revision due to instability was not more pronounced in de novo PS-TKA. Thus, even though PS-TKA was associated with inferior survival in both groups, PS-TKA following HTO seemed to be a more complicated procedure than de novo PS-TKA. However, it is not possible to conclude if the increased risk of revision was a result of the implant itself or confounded by the surgical conditions and/or surgeon preference. These results challenge former studies conducted on smaller cohorts which concluded a similar outcome [13,14]

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for PS-TKA when compared to CR-TKA in post-HTO TKA but supports a recent study from the Australian Knee Arthroplasty Registry reporting an increased HR for revision of PS-TKA compared to CR-TKA[36]. The increased risk of revision observed with PS-TKA combined with the higher incidence of revision due to instability might encourage surgeons to consider the need for a more constrained solution when planning primary TKA in challenging post-HTO knees. However, more studies are needed to elucidate this relationship.

The study has some limitations to address. Firstly, information and selection bias might be present in registry studies and, currently, the number of misclassifications is unknown in the DKR. However, our validation study supports the reliability of the DKR concerning HTO. Secondly, the pooling of open and closed wedge osteotomies might disguise individual challenges such as patella baja following closed wedge osteotomy [8]. However, a recent study found no difference in the outcome of TKA following lateral closed wedge or medial open wedge osteotomy [37]. Thirdly, the time from HTO to TKA was not retriable and might be a confounding variable as patients with early HTO failure might be a younger subgroup with a complex HTO thus affecting the TKA survival. Fourthly, even though Charnley class is associated with the outcome of arthroplasties [20] it does not provide information about medical comorbidities, such as diabetes, affecting implant survival [38,39] and the age difference in this study might have resulted in an uneven distribution of medical comorbidities. Fifthly, almost one third of the patients contributed with bilateral observation in this study. This is a higher proportion than previously reported not to bias the result of epidemiological studies [23]. To evaluate the influence of including bilateral observation we repeated analyses including only the first TKA in each patient and found similar results (data not shown) supporting that ignoring bilateral observation did not bias this study. Finally, this study solely analyzed differences in survival leaving differences in the clinical outcome between TKA following HTO and de novo TKA unknown.

In summary, this national registry-based long-term study shows a crude inferior survival of TKA in knees with prior high tibial osteotomy when compared to de novo TKA. However, after adjustment for male sex and younger age post-HTO TKA had similar survival as de novo TKA. In addition, we found that posterior stabilized TKA was associated with inferior survival in post-HTO TKA when compared to cruciate retaining TKA. We conclude that HTO alone does not alter the survival of a subsequent TKA and surgeons should not desist HTO due to concerns for increased risk of later TKA-revisions. However, post-HTO TKA is more complicated and if posterior stabilized TKA is needed the risk of revision seems to increase.

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Table 1

	Indication	Definition
1.	Infection	Confirmed or suspected infection
2.	Aseptic loosening	Aseptic implant loosening
3.	Wear	Polyethylene failure
4.	Instability	Surgeon or patient reported instability
5.	Secondary Patella	Secondary insertion of patella component
6.	Pain	Patient reported pain
7.	Others	Periprosthetic fractures, soft tissue injury, stiffness, etc.
8.	Undefined	Revisions without registered indications

Table 1: Hierarchy of indications for revision. Clinically most important from top to bottom.

Table 3:

	Post-HTO TKA	De novo TKA
Observations	1,044	63,763
Revisions	98 (9.5 %)***	2,933 (4.5 %)***
Mean Follow up (years)	8.55***	6.58***
Patient characteristics:		
Sex		
Male	596 (57%)***	22.621 (35%)***
Female	448 (43%)***	41.142 (65%)***
Mean age (years)	62 (SD:9.5) ***	70 (SD: 9) ***
Mean weight (Kg)	85 (SD: 20) **	84 (SD: 19) **
Charnley Class		
A	399 (38%)**	22.474 (35%)**
B1	386 (37%)**	22.356 (35%)**
B2	215 (21%)**	15.360 (24%)**
C	44 (4%)**	3.573 (6%)**
Surgery characteristics:		
TKA		
Cruciate retaining	829 (80%)***	51,866 (81%)***
Posterior stabilized	150 (15%)***	8,657 (14%)***
Hinged constrained	5 (0%)***	41 (0%)***
Non-hinged constrained	4 (0%)***	215 (0%)***
Undefined	56 (5%)***	2,984 (5%)***
Mean procedure time (minutes)	88 (SD: 28) ***	71 (SD: 22) ***
Perioperative complications	18 (2%)***	403 (0.5%)***
Component supplementation	32 (3%)***	646 (1%)***

Table 3: Patients and surgery characteristics sorted in TKA following high tibial osteotomy (HTO) and de novo TKA. Asterisks indicates level of significance (*≤0.05, **<0.01, ***<0.001). SD: standard derivations.

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Figure 1

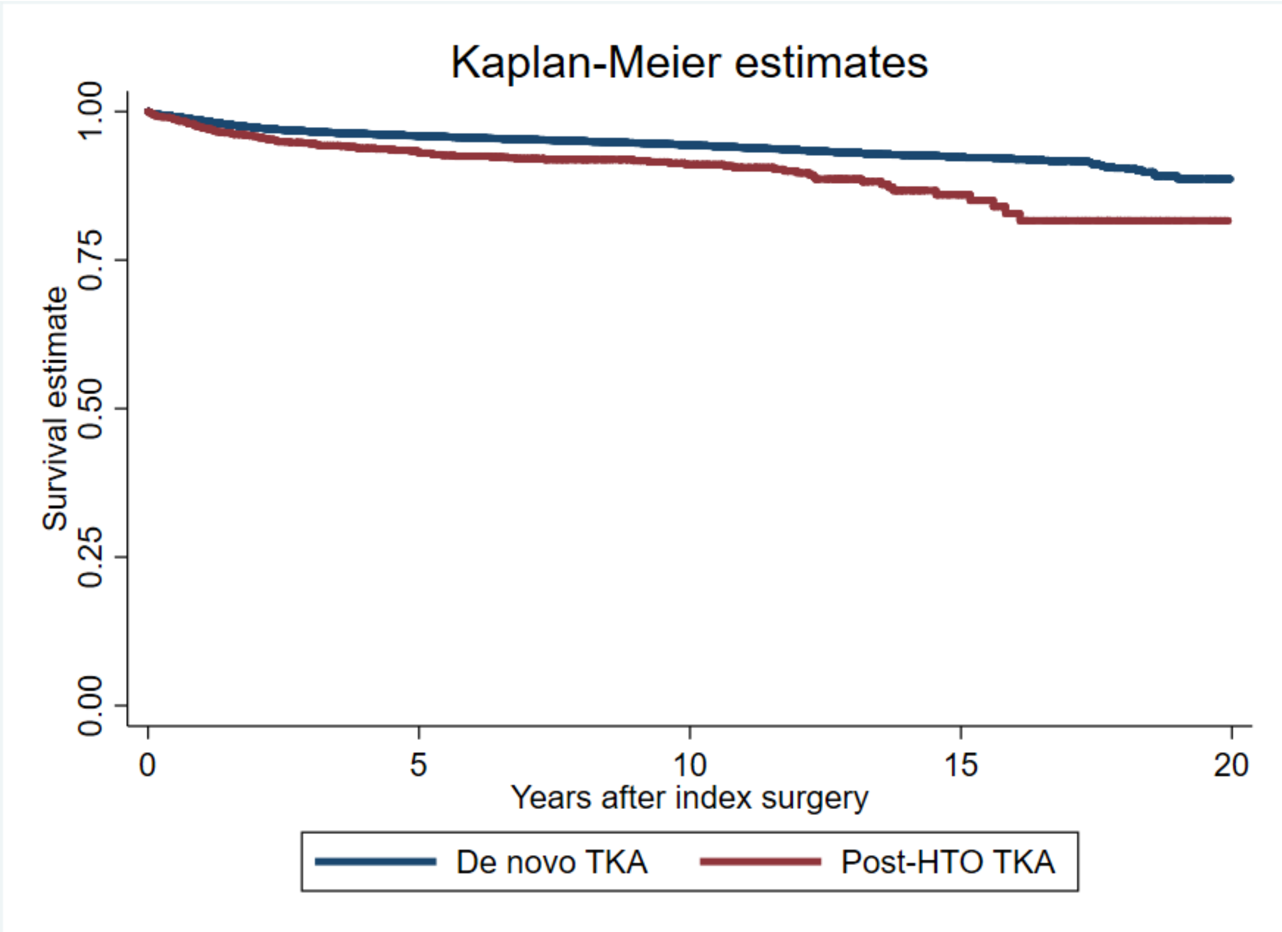

Figure 1: Kaplan-Meier survival estimate for post-HTO TKA when compared to de novo TKA ($p<0.001$). In patients with TKA following HTO the estimated 1-, 5- and 10-year survivals were 0.97 with a 95% confidence interval (CI) of 0.96-0.98, 0.93 (CI: 0.91-0.94) and 0.91 (CI: 0.89-0.93), respectively. Accordingly, the estimated 1-, 5- and 10-year survivals were 0.98 (CI: 0.98-0.99), 0.96 (CI: 0.96-0.96) and 0.94 (CI: 0.94-0.95) for de novo TKA.

Table 4

Indications	**Post-HTO TKA**	**De novo TKA**
Aseptic loosening	22 (22.5%)	796 (27.0%)
Infection	21 (22.0%)	707 (24.0%)
Instability	22 (22.5%)	498 (17.0%)
Pain	7 (7.25%)	221 (7.5%)
Secondary insertion of patella component	7 (7.25%)	250 (8.5%)
Wear	7 (7.25%)	117 (4.0%)
Unknown	4 (4.0%)	98 (3.5%)
Others	8(8.25%)	246 (8.5%)
Total	*98 (100%)*	*2,933 (100%)*

Table 4: Indications of revision sorted in post-HTO TKA and de novo TKAs. P=0.59 tested by Fishers Exact test

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Appendix

Table 2:

	TKA following HTO	de novo TKA	Total
TKA before exclusion	**1,049**	**64,078**	**65,127**
Excluded:			
Revision before index surgery	0	74	74
Missing side	0	14	14
Unicompartment Arthroplasty	5	193	198
Second stage of two staged revision	0	34	34
Included TKA	**1,044**	**63,763**	**64,807**
Missing Weight	35	1,876	1,911
Missing duration of index surgery	0	141	141
Missing Charnley class	7	158	165
Imputed variables	**42**	**2,175**	**2,217**

Table 2: Observations with missing or imputated values. Patients with revision before index surgery, unicompartment arthroplasties, missing side or second stage of two stage-revision were excluded. Missing observations in weight, duration of index surgery and Charnley class were estimated by multiple imputation by either predictive mean matching or ordered logistic regression.