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

Results From the Danish Knee Arthroplasty Registry

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– Results from the Danish Knee Arthroplasty Registry

21 Abstract

22 **Background:** High tibial osteotomy (HTO) is a joint preserving treatment of unicompartmental

23 osteoarthritis in the knee. In cases with insufficient or deteriorating clinical results patients may

24 undergo a total knee arthroplasty (TKA). The influence of prior HTO on TKA survival is debated.

25 **Methods:** We conducted a population-based registry study comparing 1,044 primary TKA in

26 patients with prior HTO to 63,763 de novo TKA inserted from 1997 to 2015. Implant survival was

27 estimated by Kaplan Meier analysis with revision of any kind as endpoint. Patient- and surgery

28 characteristics, including choice of implant design, were compared and their influence on TKA

29 survival was estimated by Cox regression. Finally, indications of revision were compared between

30 the groups.

31 **Results:** TKA following HTO had an inferior survival with a 10-year estimated survival of 91%

32 compared to 94% for de novo TKA, corresponding to a crude hazard ratio (HR) of 1.73 (p<0.001).

33 However, after adjustment for differences in sex and age this risk diminished (HR=1.19, p=0.09).

34 The choice of implant constraint was similar between the groups and in both groups posterior

35 stabilized TKA (PS-TKA) was associated with inferior survival with an adjusted hazard ratio of

36 1.46 (p=0.03) in post-HTO TKA when compared to cruciate retaining TKA.

37 **Conclusion:** TKA following HTO had a crude inferior survival when compared to TKA without

38 prior surgery of any kind. The inferior survival was explainable by patient characteristics, defined

39 by male sex and lower age, rather than the prior HTO. However, when the prior HTO resulted in the

40 use of PS-TKA the survival decreased.

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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).

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

80 stabilized (PS), constrained condylar (CCK), hinged (Hinged), and undefined when the components

81 were unknown.

82 From the DKR, we retrieved data on all TKAs inserted due to primary OA from 1st of January 1997

83 till 31st of December 2015 in knees previously treated solely with high tibial osteotomy (HTO).

84 Registrations in the DKR do not allow for distinction between closed or open wedge HTO thus both

85 procedures were included in this group. The validity of the reported HTO was reviewed by auditing

86 patient records of a sample of all HTOs converted to TKA, performed at our local hospital (n=134).

87 Of these 128 (96%) were confirmed with prior HTO, in 3 (2%) cases we were unable to retrieve the

88 patient record but confirmed the diagnosis by crosschecking in the Danish National Patient Registry

89 [22] and in 3 (2%) cases we could not confirm the HTO. As controls, we retrieved all de novo TKA

90 from the same period, inserted due to primary OA in patients without registered prior knee surgery

91 of any kind. We considered each knee as an individual observation thus patients treated bilaterally

92 with TKA, within the study period, contributed with two individual observations. Recent studies have

93 addressed the potential problems with bilateral observations and reported these as negligible in large

94 epidemiological arthroplasty studies concerning revisions [23,24].

95

96 *Statistics*

97 Kaplan Meier analysis was used to estimate survival and these estimations were compared by Log

98 Rank test. We considered revision of any kind as endpoint and censored unrevised patients by the

99 first coming event of death, emigration or end of study by the 31st of December 2015. Cox regression

100 was used to compare the risk of revision between the groups with de novo TKA as reference and with

101 successive adjustment for patient characteristics that both differed statistically and were of clinical

102 interest. The assumption of proportional hazards was tested by Schönfeld residual test [25] and was

103 not violated for the chosen co-variates (p>0.1, for all comparisons) except age. In long term

104 arthroplasties studies, as this, the hazard related to age varies over time thus violating the assumption

105 of proportional hazards (p<0.001 in this study). Therefore, we chose to include age as a time-varying

106 co-variate in the cox regression analysis. Furthermore, death could arguably be a collateral risk in

107 long term arthroplasties studies due to the long follow up in an elderly population [26]. Therefore,

108 we additionally analyzed the hazard ratio by competing risk regression based on Fine-Gray's

109 proportional sub hazards model with death as a competing risk [27]. We found a slightly increased

110 crude hazard ratio when calculated by competing risk regression (1.85 vs. 1.73) with a similar level

111 of significance (p<0.001 for both analyses). The difference is explainable by a higher age in the de

112 novo group with increased risk of experiencing the competing event. In this paper, we present the

113 more widely used Cox regression as the difference was small and the results from Cox regression is

114 more usable for orthopaedic surgeons informing patients [28]. Categorical variables were compared

115 by chi square test if n≥5 and by Fischer's exact test if n<5, and Wilcoxon Rank sum test was used to

116 compared cumulative variables. A 95% confidence interval (CI) was chosen and p<0.05 was

117 considered as significant. Standard deviations (SD) were clustered at a hospital-level to shield against

118 inter-hospital variations such as traditions in decision making. All analyses were conducted in

119 STATA 15.

120

121 Ethics and funding:

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

149 difference when tested by log rank test (p=0.14) or Cox regression (p>0.27, for all comparisons) thus

150 adjustment for time periods as confounding variable was omitted.

151 TKA following HTO had an inferior estimated survival as depicted in figure 1 (p<0.001) with an

152 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

153 (CI: 0.98-0.99) and 0.94 (CI: 0.94-0.95) in de novo TKA. The difference corresponded to a significant

154 crude hazard ratio (HR) for revision of 1.73 (CI: 1.40-2.15, p<0.001) in TKA following HTO.

155 However, the significant hazard ratio decreased after adjustment for the difference in sex (HR=1.69,

156 CI: 1.36-2.09, p<0.001) and the significance vanished after adjustment for age as a time varying co-

157 variate (HR=1.19, CI: 0.97-1.45, p=0.09). Older age (per year) had a baseline inferior risk of revision

158 (HR= 0.97, CI: 0.97-0.98, p<0.001) and for each year the patient got older, the baseline risk decreased

159 additionally with 0.01 (CI: 0-0.01, p<0.001).

160
161 *Revisions*
162
163 The distribution of revision indications did not differ significantly between the groups (p=0.59) as

164 shown in table 4. However, instability and wear occurred more frequent (22.5% vs 17% and 7.25%

165 vs 4%, respectively) in our group of patients with previous HTO. Aseptic loosening was the most

166 frequent indication in both groups but occurred more frequent patients with de novo TKA (27% vs

167 22.5%) whereas infection was more evenly distributed between the groups (24% in de novo TKA and

168 22% in TKA following HTO).

169

170 *Type of implant*

171 In the HTO group, cruciate retaining TKA (CR-TKA) were used in 80% (n=829) and posterior

172 stabilized TKA (PS-TKA) in 15% (n=150). The remaining 5% (n=65) were mainly undefined. A

173 similar distribution was present for de novo TKA with 81% (n=51,866) CR-TKA, 14% (n=8,657)

174 PS-TKA and 5% (n=3,240) mainly undefined. Although the difference between groups was statically

175 significant (p<0.001), we consider it without clinical relevance. Since PS-TKA and CR-TKA

176 dominated both groups, we compared the survival of PS-TKA to CR-TKA.

177 Overall, the survival of both PS-TKA and CR-TKA was unchanged (p>0.17) during the three time

178 periods (1997-2003, 2004-2009, 2010-2015) thus adjustment for time periods was omitted. The mean

179 follow up were clinically comparable between the two types of implants (PS-TKA: 6.66 years vs CR-

180 TKA: 6.50 years, p<0.001).

181 In post-HTO TKA, there was no difference in age (PS-TKA: 63 vs CR-TKA: 62, p=0.68) or duration

182 of index surgery (PS-TKA: 91 minutes vs CR-TKA: 87 minutes, p=0.11). However, other

183 characteristics differed both statistically and clinically between the two implants. In PS-TKA, females

184 were more frequent (60% vs 40%, p<0.001), the average weight was slightly lower (83 kg vs 85 kg,

185 p=0.03) and the distribution in Charnley class differed slightly (p=0.04) with a higher proportion of

186 patients in class C in PS-TKA (8% vs 3%). Altogether, 12% (n=18) of the PS-TKA were revised

187 compared to 9% (n=75) of the CR-TKA thus PS-TKA was associated with an increased crude hazard

188 ratio for revision of 1.45 (CI: 1.05-2.01, p=0.02). The increased hazard was unaffected by successive

189 adjustment for the differences in sex, weight and Charnley class with a final adjusted hazard ratio of

190 1.46 (CI: 1.05-2.03, p=0.03). Noteworthy, the need for additional components (11% vs 1%, p<0.001)

191 and perioperative complications (4% vs 1%, p=0.01) were more pronounce in PS-TKA indicating a

192 more complicated procedure. Instability was the leading cause of revision in PS-TKA (28%)

193 compared to infection in CR-TKA (24%). However, the overall distribution of indications did not

194 differ between the two implants (p=0.63).

195 In de novo TKA, age, sex, weight, Charnley class and procedure time did not differed clinically

196 between PS-TKA and CR-TKA. Revision occurred more frequent in PS-TKA (7%, n=586) when

197 compared to CR-TKA (4%, n=2,155) corresponding to a crude hazard ratio of 1.60 (CI: 1.24-2.07,

198 p<0.001). The need for component supplementation was slightly more pronounced in PS-TKA (2%

199   vs 0.5%, p<0.001) whereas the frequency of perioperative complications was similar (1% vs 0.5%,

200   p=0.08). Indications for revisions differed significantly in de novo TKA (p<0.001) even though

201   aseptic loosening (PS-TKA: 29% vs CR-TKA: 26%) and infection (PS-TKA: 24% vs CR-TKA: 25%)

202   were the most frequent indication of revision in both group. Instability occurred more frequent in CR-

203   TKA (19%) than in PS-TKA (11%) as opposed to the tendency in post-HTO TKA.

204 Discussion
205
206 The data from the DKR revealed an inferior crude survival of TKA inserted after HTO. Preoperative

207 characteristics differed between the groups with an increased proportion of men (57% vs 35%) and

208 lower age (62 years vs 70 years) in post-HTO TKA. These factors have previously been shown to

209 increase the risk of revision [29–31] and, in this study, the increased hazard ratio for revision

210 disappeared after adjustment for sex and age with age being the determining factor. In addition,

211 differences in perioperative characteristics indicated a more complicated index surgery when TKA

212 followed HTO with an increased procedure time (88 minutes vs 71 minutes), need for component

213 supplementation (3% vs 1%) and perioperative complications (2% vs 0.5%). As these characteristics

214 were determined by the knee condition following HTO and presumably led to increased operative

215 complexity, we did not adjust for these in our Cox regression. The Cox regression suggests that age

216 and sex carried the risk of revision, and not the prior HTO. However, from the data, it is not possible

217 to determine if age and sex carried the risk of revision alone or they were characterizing a group of

218 patients sharing other risks such as high physical activity and/or expectations which might lead to an

219 undesired result from both the HTO and the TKA [32].

220 This study complements recent studies with opposing results from the other Nordic arthroplasty

221 registries [15–17]. The results oppose studies from Sweden and Finland which have reported an

222 inferior survival of TKA following HTO with an adjusted hazard ratio ranging from 1.4-1.7 [15,16],

223 but are in concordance with results from the Norwegian registry reporting a similar survival for both

224 groups with an insignificant adjusted HR of 0.97 [17].

225 Post-HTO TKA were revised more frequent than de novo TKA (9.5% vs 4.5%) but overall there was

226 no significant difference in the distribution of indications for revision in this study. However, an

227 interesting tendency was present as both revisions due to instability (22.5% vs 17%) and wear (7.25%

228 vs 4%) occurred more often in TKA following HTO. The tendency of increased implant wear might

229 be related to the increased follow up or associated with potential undefined characteristics, such as

230 increased physical activity, in patients treated with TKA following HTO. The higher frequency of

231 instability could be related to the complexity of the index surgery depicted in the prolonged duration

232 of index surgery, threefold increase in component supplementation and fourfold increase in

233 perioperative complications. Both the increased incidence of instability and the increased complexity

234 of index surgery could be explained by the altered knee anatomy after HTO-surgery described

235 elsewhere [33,34]. A similar complexity and increased proportion of instability have been described

236 for TKA inserted in knees with previous fractures [35] thus implying meticulously balancing of the

237 knee and choice implants as key components of post-HTO knee arthroplasty surgery as well [32].

238 The current study also investigated the survival among different implants inserted in knees with

239 previous HTO. We found that posterior stabilized TKA (PS-TKA) had approximately 1.5 times

240 increased risk of revision when compared to cruciate retaining TKA (CR-TKA). This risk sustained

241 after adjustment for pre-operative difference between the groups. PS-TKA might be chosen in

242 challenging cases which is supported by the increase in component supplementation (11% vs 1%),

243 perioperative complications (4% vs 1%) and the trend towards increased revisions due to instability

244 (28% vs 24%). In de novo TKA, PS-implants had a similar increased risk of revision (HR of 1.64)

245 when compared to CR-TKA. The need for additional components was slightly increased in PS-TKA

246 (2% vs 0.5%) however not as pronounced as in post-HTO TKA. In addition, perioperative

247 complications did not differ between the implants in de novo TKA and revision due to instability was

248 not more pronounced in de novo PS-TKA. Thus, even though PS-TKA was associated with inferior

249 survival in both groups, PS-TKA following HTO seemed to be a more complicated procedure than

250 de novo PS-TKA. However, it is not possible to conclude if the increased risk of revision was a result

251 of the implant itself or confounded by the surgical conditions and/or surgeon preference. These results

252 challenge former studies conducted on smaller cohorts which concluded a similar outcome [13,14]

253   for PS-TKA when compared to CR-TKA in post-HTO TKA but supports a recent study from the

254   Australian Knee Arthroplasty Registry reporting an increased HR for revision of PS-TKA compared

255   to CR-TKA[36]. The increased risk of revision observed with PS-TKA combined with the higher

256   incidence of revision due to instability might encourage surgeons to consider the need for a more

257   constrained solution when planning primary TKA in challenging post-HTO knees. However, more

258   studies are needed to elucidate this relationship.

259

260   The study has some limitations to address. Firstly, information and selection bias might be present in

261   registry studies and, currently, the number of misclassifications is unknown in the DKR. However,

262   our validation study supports the reliability of the DKR concerning HTO. Secondly, the pooling of

263   open and closed wedge osteotomies might disguise individual challenges such as patella baja

264   following closed wedge osteotomy [8]. However, a recent study found no difference in the outcome

265   of TKA following lateral closed wedge or medial open wedge osteotomy [37]. Thirdly, the time from

266   HTO to TKA was not retriable and might be a confounding variable as patients with early HTO failure

267   might be a younger subgroup with a complex HTO thus affecting the TKA survival. Fourthly, even

268   though Charnley class is associated with the outcome of arthroplasties [20] it does not provide

269   information about medical comorbidities, such as diabetes, affecting implant survival [38,39] and the

270   age difference in this study might have resulted in an uneven distribution of medical comorbidities.

271   Fifthly, almost one third of the patients contributed with bilateral observation in this study. This is a

272   higher proportion than previously reported not to bias the result of epidemiological studies [23]. To

273   evaluate the influence of including bilateral observation we repeated analyses including only the first

274   TKA in each patient and found similar results (data not shown) supporting that ignoring bilateral

275   observation did not bias this study. Finally, this study solely analyzed differences in survival leaving

276   differences in the clinical outcome between TKA following HTO and de novo TKA unknown.

.

277   In summary, this national registry-based long-term study shows a crude inferior survival of TKA in

278   knees with prior high tibial osteotomy when compared to de novo TKA. However, after adjustment

279   for male sex and younger age post-HTO TKA had similar survival as de novo TKA. In addition, we

280   found that posterior stabilized TKA was associated with inferior survival in post-HTO TKA when

281   compared to cruciate retaining TKA. We conclude that HTO alone does not alter the survival of a

282   subsequent TKA and surgeons should not desist HTO due to concerns for increased risk of later TKA-

283   revisions. However, post-HTO TKA is more complicated and if posterior stabilized TKA is needed

284   the risk of revision seems to increase.

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.

294   *Figure 1*

295
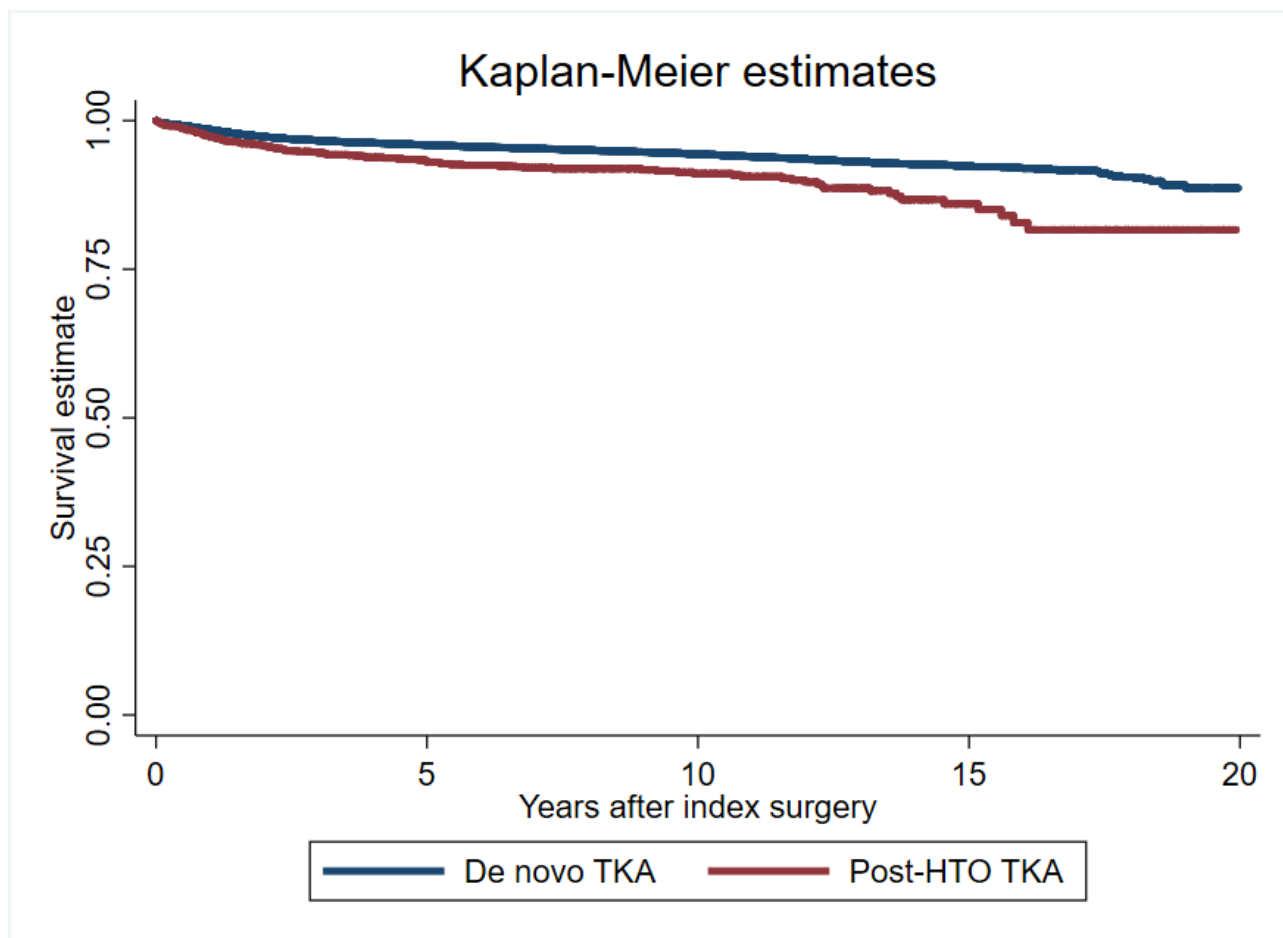
Figure 1: Kaplan-Meier survival estimate for post-HTO TKA when compared to de novo TKA (p<0.001). In patients with TKA following HTO the estimated 1-, 5- and 10-year survivals were 0.97 with a 95% confidence interval (CI) of 0.96-0.98, 0.93 (CI: 0.91-0.94) and 0.91 (CI: 0.89-0.93), respectively. Accordingly, 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.

301

302 *Table 4*

303

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%)*

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

References

[1] Murphy L, Schwartz TA, Helmick CG, Renner JB, Tudor G, Koch G, et al. Lifetime risk of symptomatic knee osteoarthritis. Arthritis Care Res 2008;59:1207–13. doi:10.1002/art.24021.

[2] Hoy D, Cross M, Smith E, Nolte S, Ackerman I, Fransen M, et al. The global burden of hip and knee osteoarthritis: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis 2014;73:1323–30. doi:10.1136/annrheumdis-2013-204763.

[3] Trieb K, Grohs J, Hanslik-Schnabel B, Stulnig T, Panotopoulos J, Wanivenhaus A. Age predicts outcome of high-tibial osteotomy. Knee Surgery, Sport Traumatol Arthrosc 2006;14:149–52. doi:10.1007/s00167-005-0638-5.

[4] Niinimaki TT, Eskelinen A, Mann BS, Junnila M, Ohtonen P, Leppilahti J. Survivorship of high tibial osteotomy in the treatment of osteoarthritis of the knee: Finnish registry-based study of 3195 knees. J Bone Joint Surg Br 2012;94:1517–21. doi:10.1302/0301-620X.94B11.29601.

[5] Sabzevari S, Ebrahimpour A, Khalilipour Roudi M, Kachooei AR. High Tibial Osteotomy: A Systematic Review and Current Concept. Arch Bone Jt Surg 2016;204:204–12.

[6] Bae DK, Song SJ, Yoon KH. Total knee arthroplasty following closed wedge high tibial osteotomy. Int Orthop 2010;34:283–7. doi:10.1007/s00264-009-0749-6.

[7] Kim H-J, Kim Y-G, Min S-G, Kyung H-S. Total knee arthroplasty conversion after open-wedge high tibial osteotomy: A report of three cases. Knee 2016;23:1164–7. doi:10.1016/j.knee.2016.06.010.

[8] Windsor RE, Insall JN, Vince KG. Technical considerations of total knee arthroplasty after proximal tibial osteotomy. J Bone Joint Surg Am 1988;70:547–55.

[9] Meding JB, Keating EM, Ritter MA, Faris PM. Total knee arthroplasty after high tibial osteotomy. A comparison study in patients who had bilateral total knee replacement. J Bone Joint Surg Am 2000;82:1252–9.

[10] van Raaij TM, Bakker W, Reijman M, Verhaar JA. The effect of high tibial osteotomy on the results of total knee arthroplasty: a matched case control study. BMC Musculoskelet Disord 2007;8:74. doi:10.1186/1471-2474-8-74.

[11] Farfalli LA, Farfalli GL, Aponte-Tinao LA. Complications in total knee arthroplasty after high tibial osteotomy. Orthopedics 2012;35:e464-8. doi:10.3928/01477447-20120327-21.

[12] Parvizi J, Hanssen AD, Spangehl MJ. Total knee arthroplasty following proximal tibial osteotomy: risk factors for failure. J Bone Joint Surg Am 2004;86–A:474–9.

[13] Akasaki Y, Matsuda S, Miura H, Okazaki K, Moro-Oka TA, Mizu-Uchi H, et al. Total knee arthroplasty following failed high tibial osteotomy: Mid-term comparison of posterior cruciate-retaining versus posterior stabilized prosthesis. Knee Surgery, Sport Traumatol Arthrosc 2009;17:795–9. doi:10.1007/s00167-009-0790-4.

[14] Chen JY, Lo NN, Chong HC, Pang HN, Tay DKJ, Chin PL, et al. Cruciate retaining versus posterior stabilized total knee arthroplasty after previous high tibial osteotomy. Knee Surgery, Sport Traumatol Arthrosc 2015;23:3607–13. doi:10.1007/s00167-014-3259-z.

[15] Robertsson O, W-Dahl A. The Risk of Revision After TKA Is Affected by Previous HTO or UKA. Clin Orthop Relat Res 2015;473:90–3. doi:10.1007/s11999-014-3712-9.

[16] Niinimäki T, Eskelinen A, Ohtonen P. Total knee arthroplasty after high tibial osteotomy : a registry - based case – control study of 1 , 036 knees 2014:73–7. doi:10.1007/s00402-013-1897-0.

[17] Badawy M, Fenstad AM, Indrekvam K, Havelin LI, Furnes O. The risk of revision in total knee arthroplasty is not affected by previous high tibial osteotomy A 15-year follow-up of 32

353		, 476 total knee arthroplasties in the Norwegian 2015;86:734–9.
354		doi:10.3109/17453674.2015.1060402.
355	[18]	Pedersen AB, Mehnert F, Odgaard A, Schroder HM. Existing data sources for clinical
356		epidemiology: The Danish Knee Arthroplasty Register. Clin Epidemiol 2012;4:125–35.
357		doi:10.2147/clep.s30050.
358	[19]	Dansk Knæalloplastiske Register. DKR Årsrapport 2016 2016.
359	[20]	Bjorgul K, Novicoff WM, Saleh KJ. Evaluating comorbidities in total hip and knee
360		arthroplasty: available instruments. J Orthop Traumatol 2010;11:203–9. doi:10.1007/s10195-
361		010-0115-x.
362	[21]	Schmidt M, Pedersen L, Sorensen HT. The Danish Civil Registration System as a tool in
363		epidemiology. Eur J Epidemiol 2014;29:541–9. doi:10.1007/s10654-014-9930-3.
364	[22]	Mason K, Thygesen LC, Stenager E, Brønnum-Hansen H, Koch-Henriksen N. Evaluating the
365		use and limitations of the Danish National Patient Register in register-based research using
366		an example of multiple sclerosis. Acta Neurol Scand 2012;125:213–7. doi:10.1111/j.1600-
367		0404.2011.01558.x.
368	[23]	Robertsson O, Ranstam J. No bias of ignored bilaterality when analysing the revision risk of
369		knee prostheses : Analysis of a population based sample of 44 , 590 patients with 55 , 298
370		knee prostheses from the national Swedish 2003;4:1–4.
371	[24]	Na YG, Kang YG, Chang MJ, Chang CB, Kim TK. Must bilaterality be considered in
372		statistical analyses of total knee arthroplasty? Clin Orthop Relat Res 2013;471:1970–81.
373		doi:10.1007/s11999-013-2810-4.
374	[25]	Ranstam J, Karrholm J, Pulkkinen P, Makela K, Espehaug B, Pedersen AB, et al. Statistical
375		analysis of arthroplasty data. II. Guidelines. Acta Orthop 2011;82:258–67.
376		doi:10.3109/17453674.2011.588863.
377	[26]	Gillam MH, Ryan P, Graves SE, Miller LN, de Steiger RN, Salter a. Competing risks
378		survival analysis applied to data from the Australian Orthopaedic Association National Joint
379		Replacement Registry. Acta Orthop 2010;81:548–55. doi:10.3109/17453674.2010.524594.
380	[27]	Fine JP, Gray RJ. A Proportional Hazards Model for the Subdistribution of a Competing
381		Risk. J Am Stat Assoc 1999;94:496–509. doi:10.1080/01621459.1999.10474144.
382	[28]	Ranstam J, Robertsson O. The Cox model is better than the Fine and Gray model when
383		estimating relative revision risks from arthroplasty register data. Acta Orthop 2017;3674:1–3.
384		doi:10.1080/17453674.2017.1361130.
385	[29]	Blum M a, Singh J a, Lee G-C, Richardson D, Chen W, Ibrahim S a. Patient race and
386		surgical outcomes after total knee arthroplasty: An analysis of a large regional database.
387		Arthritis Care Res (Hoboken) 2013;65:414–20. doi:10.1002/acr.21834.
388	[30]	Rand JA, Trousdale RT, Ilstrup DM, Ws, Harmsen W. Factors affecting the durability of
389		primary total knee prostheses. J Bone Jt Surg Am 2003;85–A:259–65.
390	[31]	Julin J, Jämsen E, Puolakka T, Konttinen YT, Moilanen T. Younger age increases the risk of
391		early prosthesis failure following primary total knee replacement for osteoarthritis. A follow-
392		up study of 32,019 total knee replacements in the Finnish Arthroplasty Register. Acta Orthop
393		2010;81:413–9. doi:10.3109/17453674.2010.501747.
394	[32]	Lombardi A V., Berend KR, Adams JB. Why knee replacements fail in 2013: Patient,
395		surgeon, or implant? Bone Jt J 2014;96B:101–4. doi:10.1302/0301-620X.96B11.34350.
396	[33]	Whitehead TS, Willits K, Bryant D, Giffin JR, Fowler PJ. Impact of Medial Opening or
397		Lateral Closing Tibial Osteotomy on Bone Resection and Posterior Cruciate Ligament
398		Integrity During Knee Arthroplasty. J Arthroplasty 2009;24:979–89.
399		doi:10.1016/j.arth.2008.05.004.
400	[34]	Erak S, Naudie D, MacDonald SJ, McCalden RW, Rorabeck CH, Bourne RB. Total knee

401   arthroplasty following medial opening wedge tibial osteotomy. Technical issues early clinical
402   radiological results. Knee 2011;18:499–504. doi:10.1016/j.knee.2010.11.002.
403 [35] El-Galaly A, Haldrup S, Pedersen AB, Kappel A, Jensen MU, Nielsen PT. Increased risk of
404   early and medium-term revision after post-fracture total knee arthroplasty: Results from the
405   Danish Knee Arthroplasty Register. Acta Orthop 2017;3674:1–6.
406   doi:10.1080/17453674.2017.1290479.
407 [36] Vertullo CJ, Orth F, Lewis PL, Orth F, Lorimer M, Graves SE. The Effect on Long-Term
408   Survivorship of Surgeon 2017:1129–39.
409 [37] Preston S, Howard J, Naudie D, Somerville L, McAuley J. Total knee arthroplasty after high
410   tibial osteotomy: No differences between medial and lateral osteotomy approaches knee. Clin
411   Orthop Relat Res 2014;472:105–10. doi:10.1007/s11999-013-3040-5.
412 [38] Yang K, Yeo SJ, Lee BP, Lo NN. Total knee arthroplasty in diabetic patients: a study of 109
413   consecutive cases. J Arthroplasty 2001;16:102–6. doi:10.1054/arth.2001.19159.
414 [39] Bolognesi MP, Marchant Jr. MH, Viens NA, Cook C, Pietrobon R, Vail TP. The impact of
415   diabetes on perioperative patient outcomes after total hip and total knee arthroplasty in the
416   United States. J Arthroplast 2008;23:92–8. doi:10.1016/j.arth.2008.05.012.
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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**

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