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ORIGINAL PAPER

Influence of body mass index on revision rates after primary total knee arthroplasty

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Abstract
Purpose Studies demonstrate that revision rates after primary total knee arthroplasty (TKA) tend to be higher in obese patients. However, the existence of a body mass index (BMI) threshold remains unexplored.
Methods We conducted a prospective cohort study of 2442 primary TKAs in 2035 patients (69.1 % women; mean age 72 years; mean follow-up 93 months, range 38–203). We evaluated the influence of BMI in five categories on all-cause revision after TKA using incidence rates (IR), hazard ratios (HR), and Kaplan–Meier survival analysis. Adjustment for baseline imbalances was performed using Cox regression analysis.
Results Over the study period, 71 revisions occurred. Revision rates were 3.2 cases/1000 patient-years for patients of normal weight, 3.4/1000 for overweight patients and 3.0/1000 for patients classified as obese class I. At BMI≥35, a significant increase in revision was noted. Comparing BMI≥35 vs. < 35, there were 6.4 vs. 3.2 /1000. Crude HR was 2.0 [95 % confidence interval (CI) 1.2–3.3, p=0.009], and the adjusted HR was 2.1 (95 % CI 1.2–3.6, p=0.008).
Conclusion All-cause revision rates after primary TKA doubled in patients with a BMI of 35 but were similar in those with a BMI <35.

Keywords Total knee arthroplasty (TKA) · Body mass index (BMI) · Revision · Threshold · Obesity

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Introduction

The prevalence of obesity has almost doubled over the last 30 years, and more than half a billion people worldwide are obese [1]. Obesity is recognised as a main risk factor for knee osteoarthritis [2, 3]. Consequently, the number of obese patients undergoing total knee arthroplasty (TKA) is disproportionately high [4, 5], with about 50 % being obese, and this proportion is expected to increase in the coming years [6]. Previous studies demonstrate that obese patients achieve good pain reduction and functional outcome following TKA [7–10]. Nonetheless, higher complication and revision rates have been reported in this group [8–23]. Existing literature is most often restricted to a comparison above and below a BMI of 30, which might be low [24]. The assessment of a threshold above which revision rates increase, evaluating all World Health Organization (WHO) classes of obesity [25], has not been performed so far. Determining a threshold is important to avoid unnecessary concerns for patients and surgeons by labelling all obese patients as being at high risk" for revision and in an extreme case even denial of care [24]. It is also important in order to provide an efficient cut-off for peri-operative treatment optimisation (e.g. medication dosage [26, 27], weight loss and surveillance recommendations), to facilitate outcome comparison and optimise case-mix adjustment between studies and registries and also to improve outcome prediction and shared decision making.

Our objective was to identify a BMI cut-off value above which the all-cause revision rate after primary TKA increases while taking into account baseline differences of patient characteristics and comorbidities.

Materials and methods

Study design, population and data collection

Since April 1998, all patients undergoing TKA at our institution were enrolled in a prospective hospital-based cohort. Approval for the registry was obtained from the local Ethical Committee. We included all PFC Sigma primary TKAs operated upon between April 1998 and December 2011. Information concerning baseline characteristics and the surgical intervention was documented by the operating surgeon. Information about comorbidities was retrieved from the anaesthesia record and patient discharge summary. The treatment of any major complication (including deep infections, periprosthetic fractures, re-operations and revisions) is systematically recorded in our registry. For this study, revisions performed until 28 February 2015 were assessed.

Our institution is a tertiary hospital, and the only public hospital in this canton (a member state of the Swiss Confederation). Patients residing in the canton are treated at the canton's hospital in case there is any complication, as the public health insurance reimbursement law during the study period required patients to be treated in their state of residence. Information on change of residency and death was obtained from the canton's population registry.

Exposure

The exposure of interest was BMI at the time of operation. First, we evaluated BMI in five categories according to the WHO classification [25], as follows: normal weight (BMI <25 kg/m^2), overweight (BMI 25–29.9 kg/m^2), obese class I (BMI 30–34.9 kg/m^2), obese class II (BMI 35–39.9 kg/m^2) and obese class III (BMI ≥40 kg/m^2). The final analysis was performed with only two BMI categories above and below the identified BMI cutoff.

Outcomes

Outcome of interest was all-cause revision after TKA, defined as a partial or total change of implants for any reason. It was further specified into aseptic loosening, deep infection and other causes (pain, knee instability, periprosthetic fracture, implant malposition).

Co-variates

The following patient- and operation-related variables were assessed at the time of surgery and used to perform adjusted analysis: sex; age at operation; American Society of Anaesthesiology (ASA) score [28, 29]; diabetes; hypertension; aetiology of osteoarthritis (primary vs. secondary); statin use; smoking status; surgeon's experience (experienced surgeons defined as having performed >50 cases); component size difference (femoral = > or < tibial size).

Implant- and technique-related information

A total of 2442 primary TKAs in 2035 patients were assessed. The PFC Sigma (DePuy–Synthes, Warsaw, IN, USA) was the only implant considered for analysis. Other implants were excluded in order to avoid implant-related bias. Only posterior-stabilised components were used. A mobile bearing was used in 114 (4.7 %) cases. Both femoral and tibial components were anchored with hand-mixed gentamicin-loaded bone cement. Patellar resurfacing was performed in 2255 (93.3 %) cases. The preferred approach was medial parapatellar, used in 2428 (99.4 %); lateral parapatellar was used in 14 (0.6 %) cases. Operations were performed either by, or under the supervision, of experienced surgeons in 1527 (62.5 %) cases. Cefuroxime (1.5 g IV) was used for antibiotic prophylaxis in all patients, except in case of allergy or body methicillin-resistant *Staphlycoccus aureus* (MRSA) carriage, where a single dose of vancomycin (1 g IV) was administered.

Statistical analysis

First, to compare covariates across the five BMI categories, we used the analysis of variance (ANOVA) linear contrast analysis method for continuous variables, and the linear-by-linear association test (ordinal chi-square) for categorical variables. Then we measured the incidence rates (IR) and their 95 % confidence intervals (CI) in five BMI categories calculated using the quadratic approximation to the Poisson log likelihood for the log-rate parameter as implemented in Stata®. We calculated person-time for being at risk for revision by the length of the interval between the date of surgery for primary TKA and the date of either revision, death, leaving the area of residency or end of follow-up (28 February 2015). A Kaplan–Meier survival analysis according to the two (below and above the identified threshold) and five BMI categories with endpoint all-cause revision was performed, and the log-rank test was reported. We then calculated IR and hazard ratios (HR) according to the two BMI categories. Adjusted HRs were obtained using Cox regression analysis. We adjusted for the covariates mentioned above. Proportionality of hazards assumptions was assessed on log-minus-log plots of the cumulative incidence. Finally, a sensitivity analysis was done repeating the crude and adjusted analyses according to the two BMI categories by including only the first TKA of each patient that was recorded in the registry. P values≤0.05 (all two-tailed) were considered significant. Statistical analysis was performed using

SPSS® 22 (IBM Corporation, Armonk, NY, USA) and Stata® 13 (StataCorp, College Station, TX, USA).

Results

Of the 2476 TKAs corresponding to the inclusion criteria, weight and/or height information was missing in 34 (1.4 %), leaving 2442 TKAs in 2035 patients for inclusion. Mean age at surgery was 72 years [standard deviation (SD) ±9.0], and 69.1 % of TKAs was performed in women. The mean follow-up was 93 months (SD ±45, median 88, range 38–203). Sixty-seven cases (2.7 %) were lost to follow-up after a median of 33 months (range 2–134); 398 (16.3 %) patients died a median of 63 months (range 0–175) after surgery. Four hundred and ninety-three (20.2 %) TKAs were performed in patients of normal weight, 904 (37.0 %) in overweight patients, 638 (26.1 %) in obese class I, 289 (11.9 %) in obese class II and 118 (4.8 %) in obese class III. Baseline characteristics were compared using five BMI categories (Table 1). Increasing BMI was significantly associated with a higher proportion of women, decreasing age, more comorbidities (including diabetes and hypertension), statin use, more frequent primary osteoarthritis (OA) and bilateral disease and, although less often, previous knee surgery. No differences were seen for smoking status, component size or surgeon's experience.

Over the study period, there were 71 revisions: 12 in patients of normal weight, 24 in overweight, 15 in obese class I, 15 in obese class II and five in obese class III. Crude incidence rates did not substantially differ between patients who were normal weight (3.2 cases/1000 person-years), overweight (3.4 cases/1000 person-years, lowest revision rate) and obese class I (3.0 cases/1000 person-years), but increased to 6.7 cases/1000 person-years in obese class II and 5.7 cases/1000 person-years in obese class III (Table 2). BMI≥35 (obese class II and higher) was associated with a two-times-higher revision rate (crude HR 2.0, 95 % CI 1.2–3.3, p=0.009) compared with a BMI<35. The effect was almost unchanged after adjustment for co-variates (adjusted HR 2.1, 95 % CI 1.2–3.6, p=0.008) (Table 3). In the adjusted model, none of the HRs associated with these co-variates played a statistically significant role (all p values>0.05). In regards to causes of revision: in the BMI group≥35, eight TKAs were revised for aseptic loosening, ten for deep infection and two for other causes. In the C< 35 grouop, 17 were revised for aseptic loosening, 16 for deep infection and 17 for other causes.

We repeated the analyses using only the first primary TKA recorded in the registry, and results were comparable (Table 3). Kaplan–Meier survival analyses showed that: (1) graphically, survival did not appear to be different between normal weight, overweight and obese class I patients (Fig. 1), and (2) the group with BMI≥35 had a significantly lower survival rate (log rank test p=0.008). At five years, survivorship (BMI≥35 vs. < 35) was 96.4 % (95 % CI 94.0–97.9) vs. 98.3 % (95 % CI 97.6–98.7) and at ten years 93.7 % (95 % CI 90.0–96.1) vs. 97.2 % (95 % CI 96.2–97.9) (Fig. 2).

Discussion

We observed a clear threshold for all-cause revision at a BMI > 35 kg/m^2, resulting in a two times higher incidence rate compared with those below the threshold. Our results can help to target treatment optimisation to the group most in need and avoid labelling patients at high risk" when, in fact, they are not [24]. Considering all obese patients at increased risk for revision, as suggested [30], or only those with a BMI > 35, substantially decreased the proportion of patients concerned (from 43 % to 17 %) in our study.

A number of studies have addressed the role of BMI on TKA revision [7–15, 17, 19, 30–33]. However, comparison is hampered by restriction of BMI categories and differences in BMI categorisation and follow-up times. Vazquez-Vela et al. [31] demonstrated that age<60 years, BMI≥30 and male sex were associated with lower TKA survival. Bordini et al. [19], in a cohort of 9735 TKAs divided into four BMI categories and followed on average for three years, found differences in revision rates. Moreover, in a meta-analysis published in 2012, Kerkhoffs et al. [30] studied the occurrence of complications, including revision, after TKA. Nearly 2300 patients with a minimum follow-up of five years were combined in the analysis regarding revision. The odds ratio (OR) in patients with a BMI≥30 for revision was 1.8 (95 % CI 1.2–2.8). Revision was also evaluated as a secondary outcome in studies addressing the clinical results of TKA [7–15, 17, 32]. However, they were limited by a small sample size. Some authors [13, 17] reported more frequent complications and a higher revision rate in patients with BMI≥40. Others of similar design were not conclusive [7–12, 14, 15, 32]. Some authors suggested revision rates increased with increasing BMI [8, 23]. A large study by Culliford et al. [23] evaluated BMI as a continuous variable and reported a 2.6 % increase in the subhazard of revision by one unit (kg/m^2) increase in BMI. Moreover, they assessed the effect of BMI on revision in five BMI categories, including three categories < 30 and two > 30 (BMI 30–39.9 and BMI ≥ 40). They found a significant increase in the subhazard for revision among those with BMI ≥ 40 and a trend towards a higher revision subhazard in those with BMI 30–39.9, compared with BMI 18.5–24.9. However, no information was given regarding BMI category 35–39.9. A study by Abdel et al. [33] analysed the impact of five BMI categories on aseptic loosening of the tibial component; they, also, found that patients with a BMI≥35 kg/m^2 were more likely to undergo revision due to aseptic tibial failure (HR=1.9; p<0.05).

Table 1 Baseline characteristics according to five body mass index (BMI) categories

	BMI<25 kg/m^2 [n=493 (20.2 %)]	BMI 25–29.9 kg/m^2 n=904 (37.0 %)	BMI 30–34.9 kg/m^2 n=638 (26.1 %)	BMI 35–39.9 kg/m^2 n=289 (11.9 %)	BMI≥40 kg/m^2 n=118 (4.8 %)	*P* value for linear trend
Sex (%)						0.003[1]
Women	349 (70.8)	590 (65.3)	435 (68.2)	211 (73.0)	103 (87.3)	
Men	144 (29.2)	314 (34.7)	203 (31.8)	78 (27.0)	15 (12.7)	
Age at operation (years), mean (SD)	73.7 (±10.8)	73.5 (±8.4)	71.6 (±8.3)	69.6±(8.4)	67.2 (±6.7)	<0.001[2]
BMI (kg/m^2), mean (SD)	22.7 (±1.9)	27.6 (±1.5)	32.2 (±1.4)	36.9 (±1.4)	44.3 (±4.1)	<0.001[2]
Weight (kg), mean (SD)	62.0 (±8.8)	75.1 (±9.1)	86.2 (±10.8)	97.2 (±11.6)	110.0 (±12.8)	<0.001[2]
Height (cm), mean (SD)	165 (±9)	165 (±9)	163 (±10)	162 (±9)	158 (±8)	<0.001[2]
ASA score[3] (%)						<0.001[1]
1–2	372 (75.6)	664 (73.9)	435 (68.4)	168 (58.5)	54 (45.8)	
3–4	120 (24.4)	234 (26.1)	201 (31.6)	119 (41.5)	64 (54.2)	
Total bilateral TKA (%)	142 (28.8)	300 (33.2)	219 (34.3)	116 (40.2)	52 (44.1)	<0.001[1]
Diabetes (%)	42 (8.5)	107 (11.8)	130 (20.4)	63 (21.8)	30 (25.4)	<0.001[1]
Hypertension (%)[4]	49 (55.1)	88 (64.7)	79 (69.3)	38 (76.0)	17 (81.0)	<0.001[1]
Ever smokers (%)[5]	114 (23.8)	180 (20.6)	138 (22.2)	67 (23.6)	24 (21.4)	0.985[1]
Statin users (%)	70 (14.2)	181 (20.1)	164 (25.7)	60 (20.8)	27 (22.9)	0.001[1]
Aetiology for osteoarthritis (%)						
Primary	362 (75.3)	725 (82.2)	528 (84.1)	254 (88.5)	108 (93.1)	<0.001[1,6]
Postmensis.	50 (10.4)	71 (8.1)	50 (8.0)	19 (6.6)	6 (5.2)	
Aseptic necrosis	12 (2.5)	18 (2.0)	14 (2.2)	3 (1.1)	1 (0.9)	
Inflammatory arthritis[7]	11 (2.3)	10 (1.1)	3 (0.5)	0 (0.0)	0 (0.0)	
Other causes[8]	46 (9.6)	58 (6.6)	33 (5.3)	11 (3.8)	1 (0.9)	
Previous knee surgery (%)	78 (15.8)	114 (12.6)	77 (12.1)	26 (9.0)	9 (7.6)	0.002[1,9]
Meniscectomy	44 (55.7)	71 (61.7)	38 (49.4)	19 (73.1)	5 (55.6)	
Osteosynthesis	14 (17.7)	11 (9.6)	6 (7.8)	2 (7.7)	1 (11.1)	
Osteotomy	10 (12.7)	27 (23.5)	17 (22.1)	4 (15.4)	2 (22.2)	
Multiple surgeries	5 (6.3)	2 (1.7)	9 (11.7)	0 (0.0)	0 (0.0)	
Ligamentoplasty	1 (1.3)	3 (2.6)	6 (7.8)	1 (3.9)	0 (0.0)	
Others	5 (6.3)	1 (0.9)	1 (1.3)	0 (0.0)	1 (11.1)	
Experienced surgeon	313 (63.5)	581 (64.3)	383 (60.0)	176 (60.9)	74 (62.7)	0.256[1]
Component size (%)						0.798[1]
Femoral = tibial	275 (55.8)	500 (55.3)	364 (57.0)	158 (54.7)	57 (48.3)	
Femoral > tibial	193 (39.1)	360 (39.8)	241 (37.8)	115 (39.8)	53 (44.9)	
Femoral < tibial	25 (5.1)	44 (4.9)	33 (5.2)	16 (5.5)	8 (6.8)	

[1] Linear trend for categorical variables assessed using the linear-by-linear association test (ordinal chi-square)

[2] Linear trend for continuous variables assessed using the analysis of variance (ANOVA) linear contrast analysis method

[3] American Society of Anaesthesiologists (ASA) score missing in 11 cases (0.5 %)

[4] Hypertension information was not recorded before 2010; information was available for 410 of 429 cases and missing for 19 (4.4 %)

[5] Tobacco consumption was missing in 70 cases (2.9 %)

[6] Linear trend of primary osteoarthritis vs. all other aetiologies across BMI categories

[7] Inflammatory arthritis includes a total of 18 cases of rheumatoid arthritis among other inflammatory arthritis

[8] Other causes include 148 cases of posttraumatic arthritis and 11 of postinfectious arthritis, among others

[9] Linear trends for all categories of previous knee surgeries not evaluated due to low number of events

Our work revealed no substantial change between normal weight, overweight and obese class I, but we found a doubling of revision rates with obese class II and higher, suggesting BMI≥35 kg/m^2 as a useful threshold value. The lowest

Table 2 All-cause revision rates according to five body mass index (BMI) categories

	BMI<25 kg/m^2 n=493 (20.2 %)	BMI 25–29.9 kg/m^2 n=904 (37.0 %)	BMI 30–34.9 kg/m^2 n=638 (26.1 %)	BMI 35–39.9 kg/m^2 n=289 (11.8 %)	BMI≥40 kg/m^2 n=118 (4.8 %)
Cases	12	24	15	15	5
Person-years	3740	6981	5027	2231	883
Incidence rate (cases/1000 person-years), (95 % CI)	3.2 (1.8–5.6)	3.4 (2.3–5.1)	3.0 (1.8–4.9)	6.7 (4.1–11.2)	5.7 (2.4–13.6)

CI confidence interval

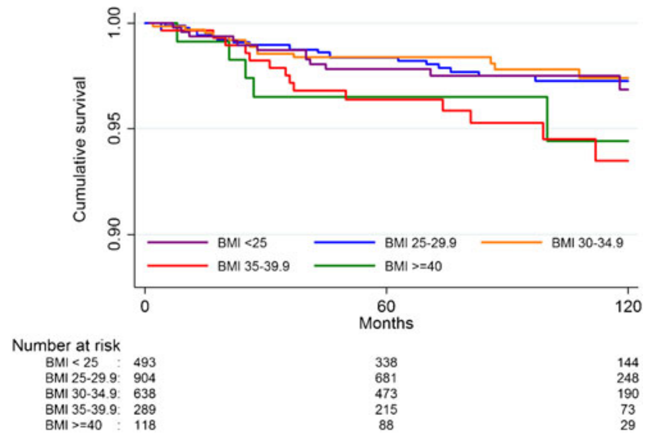

Fig. 1 Kaplan–Meier survival curve with endpoint all-cause revision comparing five body mass index (BMI) categories. Cases at risk are reported at the *bottom*

revision rate was observed in the overweight category, consistent with previous findings for osteolysis after primary total hip arthroplasty [34]. In accordance with previous studies, we found that the difference in revision rates remained small among BMI categories in the first years but increased at later follow-up [8, 12].

Higher BMI has been associated with increased load across the bone–cement interface, therefore potentially favouring aseptic loosening [7, 12, 31]. Since activity levels tend to be lower in obese patients [35, 36], other authors assumed that increased mechanical stress was counterbalanced by lower demand on the TKA components [7, 8, 10, 37]. Moreover, Estes et al. [38] reported that the incidence of limb malalignment was more frequent in patients with a BMI≥35, most likely due to poorer surgical exposure and less prominent bony landmarks, which interfere with positioning of the cutting guides. Ritter et al. [39] demonstrated that limb malalignment (±2.5° from neutral mechanical axis) was associated with higher rates of aseptic loosening. Furthermore, increased revision rate is also due to the obesity-related higher incidence of infection, especially acknowledged in obese class II and III patients [16, 40]. Taken together, increased mechanical stress, more frequent limb malalignment and higher incidence of infection may all contribute to the higher revision rate in patients with BMI≥35.

There are several limitations to our study. First, some patients may have had a revision performed in another hospital without this information being reported to us. However, due to the local health care structure, presumably only few revisions would have been missed. Second, we had no direct measures of patient activity levels, which is known to influence the risk of revisions due to aseptic loosening. We did, however, adjust for age, sex, and ASA score, which have been shown to correlate well with patient activity [41]. Third, information on postoperative limb alignment (mechanical axis), also related to revision for aseptic loosening, was not systematically available. Residual confounding due to this and other unmeasured factors cannot be ruled out. Fourth, the number of TKAs in BMI category≥40 was limited. However, this did not preclude

Table 3 All-cause revision rates according to two body mass index (BMI) categories

	All TKAs		Only first TKA	
	BMI<35 n=1984 (83.3 %)	BMI≥35 n=407 (16.7 %)	BMI<35 n=1710 (84.0 %)	BMI≥35 n=325 (16.0 %)
Cases	51	20	46	17
Person-years	15,748	3115	13,384	2544
Incidence rate (cases/1000 person-years), (95 % CI)	3.2 (2.5–4.3)	6.4 (4.1–10.0)	3.4 (2.6–4.6)	6.7 (4.2–10.8)
Crude HR (95 % CI)	2.0 (1.2–3.3, p=0.009)		2.4 (1.1–3.4, p=0.018)	
Adjusted HR (95 % CI)	2.1 (1.2–3.6, p=0.008)		2.5 (1.2–3.8, p=0.013)	

CI confidence interval, *HR* hazard ratio, *TKA* total knee arthroplasty, *BMI* body mass index

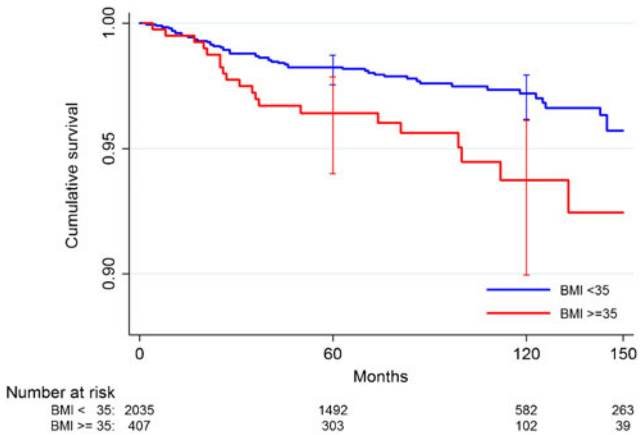

Fig. 2 Kaplan–Meier survival curve with endpoint all-cause revision comparing body mass index (BMI)<35 vs. ≥ 35. Cases at risk are reported at the *bottom* ; 95 % confidence intervals (CIs) are represented at five and ten years; they overlap at five years but not at ten years

detecting the threshold at BMI 35, and rates were close to those of BMI category 35–39.9. Fifth, the only implant type considered was—the PFC Sigma; the observed threshold might be different for other implant types. Sixth, validation of the threshold in an external cohort is necessary.

In conclusion, after primary TKA, a two-times higher rates of all-cause revision was found in patients with a BMI≥35 compared with those with a BMI<35. Importantly, no substantial difference in revision rates was seen between obese class I, overweight and normal-weight patients. Identifying a BMI threshold for the possibility of increase revision is essential in order to optimise the care of obese patients and to direct improvement efforts to those most in need, as well as to facilitate outcome comparison and improve case-mix adjustment between studies and registries.

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Compliance with ethical standards

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Conflict of interest No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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