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Body Mass Index Is Associated With All-cause Mortality After THA and TKA

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Abstract

Background Both obesity and underweight are associated with a higher risk of mortality in adulthood, but the association between mortality after arthroplasty and extreme ranges of body mass index (BMI) have not been evaluated beyond the first year.

Questions/purposes The purpose of this study was to investigate the association between BMI and all-cause mortality after TKA and THA.

Methods Data from two arthroplasty registries, the St Vincent's Melbourne Arthroplasty (SMART) Registry from Australia and the Kaiser Permanente Total Joint Replacement Registry (KPTJRR) from the United States, were used to identify patients aged ≥ 18 years undergoing elective TKAs and THAs between January 1, 2002, and December 31, 2013. Same-day bilateral THA and hemiarthroplasties were excluded. All-cause mortality was recorded from the day of surgery to the end of the study (December 31, 2013). Data capture was complete for the SMART Registry. No patients were lost to followup in the KPTJRR cohort and 2959 (5%) THAs and 5251 (5%) TKAs had missing data. Cox proportional hazard regression was used to estimate the all-cause mortality associated with six BMI categories: underweight (< 18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2), obese class I (30.0-34.9 kg/m^2), obese class II (35.0-39.9 kg/m^2), and obese class III (> 40 kg/m^2). For TKA, the SMART cohort had a median followup of 5 years (range, 0-12 years) and the KPTJRR cohort had a median followup of 4 years (range, 0-12 years). For THA, the SMART cohort had a median followup of 5 years (range, 0-12 years) and the KPTJRR cohort had a median followup of 4 years (range, 0-12 years).

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Each author certifies that his or her institution approved the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research.
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Results In both the Australian and US cohorts, being underweight (Australia: hazard ratio [HR], 3.72; 95% confidence interval [CI], 1.94-7.08; $p < 0.001$ and United States: HR, 1.88; 95% CI, 1.33-2.64; $p < 0.001$) was associated with higher all-cause mortality after TKA, whereas obese class I (Australia: HR, 0.66; 95% CI, 0.47-0.92; $p = 0.015$; United States: HR, 0.71; 95% CI, 0.66-0.78; $p < 0.001$) or obese class II (Australia: HR, 0.54; 95% CI, 0.35-0.82; $p = 0.004$; United States: HR, 0.73; 95% CI, 0.66-0.81; $p < 0.001$) was associated with lower mortality when compared with normal-weight patients. In the US cohort, being overweight was also associated with a lower risk of mortality (HR, 0.76; 95% CI, 0.71-0.82; $p < 0.001$). In the US cohort, being underweight had a higher risk of mortality after THA (HR, 2.09; 95% CI, 1.65-2.64; $p < 0.001$), whereas those overweight (HR, 0.73; 95% CI, 0.67-0.80; $p < 0.001$), obese class I (HR, 0.68; 95% CI, 0.62-0.75; $p < 0.001$), or obese class II (HR, 0.71; 95% CI, 0.62-0.81; $p < 0.001$) were at a lower risk of mortality after THA when compared with normal-weight patients. In patients undergoing THA in the Australian cohort, we observed no association between BMI and risk of death.

Conclusions We found that even severe obesity is not associated with a higher risk of death after arthroplasty. Patients should be informed of this when considering surgery. Clinicians should be cautious when considering total joint arthroplasty in underweight patients without first considering their nutritional status.

Level of Evidence Level III, therapeutic study.

Introduction

The association between obesity and risk of complications after elective total joint arthroplasty (TJA) is clear. Numerous studies confirm a greater risk of medical, surgical, and wound complications after TJA in individuals with obesity or severe obesity than for those whose body mass index (BMI) is within the normal range [25-27, 42, 44]. Less is known about the risks of surgery for the minority of underweight patients undergoing TJA, although increased risk of complications has been documented in this group for other major surgical procedures [43]. Although the financial [6] and functional burden of a high BMI in TJA has been demonstrated [2, 13], little is known about the association between BMI and mortality after surgery.

Studies using registry data sets have reported the paradox of a lower risk of all-cause mortality between 30 days and 1 year after TJA in overweight versus normal-weight patients as well as a higher risk for underweight patients [18, 40]. The results for obese groups, however, are more variable with some reporting an association between severe obesity and higher risk of all-cause mortality 1 year after TJA [40] and others showing no association between obesity and mortality within the first 90 days [18]. Population-level data also suggest that being overweight confers a lower risk of all-cause mortality relative to those who are normal weight, whereas being underweight or severely obese, a higher risk of mortality is demonstrated [14]. The inherent limitations in population-level studies and registry reports are notable and include a large number of missing values [18] and underrepresentation [40] or misrepresentation of subgroups [35]. Furthermore, we could find no evidence of an association between BMI and all-cause mortality after TJA beyond 1 year. Understanding BMI-mortality associations after TJA allows providers to evaluate current practices and to identify patient groups who might benefit from nutritional intervention before surgery.

The purpose of this study, therefore, was to examine, in the context of two large, independent arthroplasty registries on different continents, the association between longer term all-cause mortality and underweight, overweight, and obese patient groups undergoing TJA.

Materials and Methods

A retrospective study using data from the Kaiser Permanente Total Joint Replacement Registry (KPTJRR) and the St Vincent's Melbourne Arthroplasty Outcomes (SMART) Registry was conducted. The KPTJRR covers the largest integrated healthcare system in the United States [31]. Data collection procedures, coverage, participation rate, and data and tools available from the KPTJRR have already been published [31-33]. Briefly, the KPTJRR was implemented in 2001 and covers all joint arthroplasties performed in the Kaiser Permanente membership population of > 10.6 million patients [19] in seven geographic US regions (ie, Southern California, Northern California, Northwest, Hawaii, Colorado, Georgia, and Mid-Atlantic). The Kaiser Permanente membership population has been shown to be mostly sociodemographically representative of the larger geographic areas it covers [20, 21]. The registry reported a > 95% voluntary participation rate in 2011 [33].

The SMART Registry is a clinical registry in Australia that captures information from surgeons performing joint arthroplasty at one major metropolitan hospital. Data collection procedures, outcome measures, and participation rates have been previously described [13] and participants are demographically representative of the Australian patient population [5]. Registry data collection started in 1998 and > 11,000 procedures are now registered with 800 new yearly registrations. The Registry has complete capture of all pre- and postoperative encounters and achieves 98% followup of patient-reported outcome measures at 1 year [10, 11].

Adult (aged ≥ 18 years old) patients undergoing primary TKA and THA for any elective indication for surgery registered between January 1, 2002, and December 31, 2013, were included in the sample. Patients who underwent same-day bilateral THA or patients who underwent hemiarthroplasty were not included.

The final KPTJRR TKA cohort (n = 109,333) included arthroplasty procedures from 51 hospitals and 450 surgeons and the final SMART TKA cohort (n = 3,453) included arthroplasty procedures from one hospital and 26 surgeons. The median age of the KPTJRR cohort was 67 years (interquartile range [IQR], 61-74) and 62% were women, whereas the median age of the SMART cohort was 71 years (IQR, 64-77) and 66% were women (Table 1).

Table 1. TKA and THA study samples by registry

Variable	Measure	TKA		THA	
		KPTJRR Number (%)	SMART Number (%)	KPTJRR Number (%)	SMART Number (%)
Total sample		109,333	3435	57,049	2950
Age (years), continuous	Mean (SD)	67 (9.4)	70 (8.7)	66 (11)	67.6 (11)
	Median (IQR)	67 (61-74)	71 (64-77)	66 (58-74)	69 (61-75)
Age group (years)	< 50	2961 (3)	52 (2)	4461 (8)	188 (6)
	50-59	19,464 (18))	340 (10)	11,953 (21)	389 (13)
	60-69	40,892 (37)	1123 (33)	18,587 (33)	965 (33)
	70-79	35,000 (32)	1455 (42)	15,684 (28)	1067 (36)
	≥ 80	11,016 (10)	465 (14)	6364 (11)	341 (12)
Gender*	Female	67,955 (62)	2233 (65)	32,812 (58)	1742 (59)
	Male	41,378 (38)	1202 (35)	24,236 (43)	1208 (41)
Race	Asian	6171 (6)	x	2047 (4)	x
	Black	9123 (8)	x	4530 (8)	x
	Hispanic	14,996 (14)	x	4213 (7)	x
	Other/multi	1534 (1)	x	717 (1)	x
	Unknown	3191 (3)	x	1933 (3)	x
	White	74,318 (68)	x	43,609 (76)	x
Australian-born	Yes	x	1641 (48)	x	1686 (57)
	No	x	1794 (52)	x	1264 (43)
Diagnosis	Osteoarthritis	106,678 (98)	3215 (94)	52,874 (93)	2538 (86)
	Osteonecrosis	393 (.4)	10 (.3)	3237 (6)	173 (6)
	Posttraumatic arthritis	1141 (1)	x	443 (1)	x
	Rheumatoid arthritis	1943 (2)	210 (6)	954 (2)	144 (5)
	Other	914 (1)	x	342 (1)	95 (3)
ASA category	Missing	2862 (3)	x	1633 (3)	0 (0)
	1 and 2	64,067 (59)	2012 (59)	35,277 (62)	1811 (61)
	≥ 3	42,404 (39)	1423 (41)	20,139 (35)	1139 (39)
Bilateral (same day)		9097 (8)	0 (0.0)	0 (0)	0 (0)
Diabetes		29,433 (27)	681 (20)	10,711 (19)	358 (12)
Current smoker	Current smoker	x	220 (6)	x	372 (13)
BMI (kg/m^2), continuous	Mean (SD)	31.5 (6.0)	32.7 (6.2)	29.0 (5.8)	29.8 (5.8)
	Median (IQR)	30.8 (27.1-35.1)	32.0 (28.3-36.5)	28.6 (25.1-32.6)	29.1 (25.7- 33.2)
BMI group (kg/m^2)	Underweight (< 18.5)	265 (0.2)	3 (0.1)	466 (1)	26 (1)
	Normal (18.5-24)	12,958 (12)	303 (9)	12,652 (22)	574 (20)
	Overweight (25-29)	34,039 (31)	908 (26)	20,076 (35)	1014 (34)
	Obese class I (30-34)	32,160 (29)	1085 (32)	13,733 (24)	813 (28)
	Obese class II (35-39)	18,069 (17)	697 (20)	6206 (11)	355 (12)
	Obese class III (≥ 40)	9383 (9)	439 (13)	2547 (5)	168 (6)
	Missing	2459 (2)	0 (0)	1369 (2)	0 (0)

*Missing (gender KP THA n = 1).
KPTJRR = Kaiser Permanente Total Joint Replacement Registry; SMART = St Vincent's Melbourne Arthroplasty Outcomes Registry; ASA = American Society of Anesthesiologists; BMI = body mass index; IQR = interquartile range.

There was a higher proportion of obese (class I-III) patients in the SMART Registry cohort (65%) than in the KPTJRR (55%). The KPTJRR cohort had a median followup of 4 years (IQR, 1.8-6.6; range, 0-12 years). The SMART cohort had a median followup of 5 years (IQR, 2.5-7.6; range, 0-12 years). No patients were lost to followup in either cohort.

The final KPTJRR THA cohort (n = 57,049) included arthroplasty procedures from 51 hospitals and 379 surgeons and the final SMART THA cohort (n = 2950) included arthroplasty procedures from one hospital and 26 surgeons. In the KPTJRR cohort, the median age was 66 years (IQR, 58-74) and 58% were women (Table 1). In the SMART cohort, the median age was 69 years (IQR, 61-75) and 59% were women. There was a higher proportion of obese patients (class I-III) in the SMART cohort (45%) than in the KPTJRR cohort (40%) (Table 1). The median followup in the KPTJRR cohort was 4 years (IQR, 1.9-6.9; range, 0-12 years). The median followup in the SMART cohort was 5 years (IQR, 2.4-7.6; range, 0-12 years). No cases were lost to followup in either cohort.

The main exposure of interest was BMI. The World Health Organization definitions were used to group patients according to their intraoperative BMI as follows: underweight (< 18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2), obese class I (30.0-34.9 kg/m^2), obese class II (35.0-39.9 kg/m^2), and obese class III (≥ 40 kg/m^2). BMI was captured by the KPTJRR using Kaiser Permanente integrated healthcare system electronic medical records. The body and height measures closest in date to the patient's surgery were used for the BMI calculation. In the SMART Registry, BMI was obtained from the anesthetist's chart on the day of surgery.

The outcome of interest was all-cause mortality from the day of surgery to the end of the study followup (December 31, 2013). Kaiser Permanente analytical data sets were made available postrelease of their 2014 report and the current study was subsequently started in late 2015. The KPTJRR captured mortality from the electronic medical records of people who are Kaiser Permanente members and the enrollment/membership roll of the institution yearly when analytical data sets for the KPTJRR are prepared. The Kaiser Permanente enrollment/membership files are validated against the US Social Security Administration periodically. The exact date of death is captured.

The SMART Registry captured mortality data from the hospital medical records on an ongoing basis. In addition, on an annual basis, death data are verified using data obtained from the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) on all TJAs performed at the hospital. The AOANJRR link their data with the National Death Index (NDI), which is a Commonwealth database that contains records of deaths registered in Australia since 1980. The NDI draws this information from the Registrars of Births, Deaths and Marriages in each jurisdiction, the National Coronial Information System, and the Australian Bureau of Statistics. Exact date of death is captured.

Covariates of interest were baseline demographic and patient characteristics including age (per 10-year increment), sex, race (in the Kaiser Permanente registry specifically), Australian-born (in the SMART Registry specifically), American Society of Anesthesiologists (ASA) Physical Status Classification [28], year of operation (per 1-year increment), surgical indication (osteoarthritis, rheumatoid arthritis, osteonecrosis, posttraumatic arthritis, and other), and comorbidities. These data were obtained from the patient's medical record for entry into the Registries. In addition, in the SMART Registry, smoking status, socioeconomic status (SES) using the fAustralian Bureau of Statistics SES index for area scores (1-10) [9], and rurality using the geographic accessibility index (ARIA+) [12] were covariates of interest. In both SMART and KPTJRR, diabetes was evaluated as a confounder.

Statistical Analysis

All analyses were conducted independently for each registry and by THA and TKA cohorts and pooling of registry data was not performed. Our intent was to present the results of both cohorts separately so that local-level data (either United States or Australia) could be used by clinicians to inform their decision-making around TJA. Each study cohort was described using frequencies, proportions, means, SDs, medians, and IQRs. Followup was defined as the difference between the joint replacement surgery date and the date of death or the end date of the study period. Survival analyses were performed using Kaplan-Meier curves and Cox proportional hazard models to assess risk of death by each weight group with normal weight being the reference category. All variables associated with mortality ($p < 0.2$) were included in the final models as possible confounders. ASA Physical Status Classification scores were collapsed a priori (1 and 2 versus ≥3). Post hoc analysis using ASA levels 1 to 4 (ASA 5 was grouped with 4 because there were < 10 cases) revealed minimal differences (data not shown) and therefore the original analyses are presented. Effect modification by age group and gender was also investigated. Proportionality assumptions for survival by obesity level were verified testing the interaction of the obesity variable with time and visually assessed using log(-log[survival]) versus log of survival time graphs. To account for potential lack of independence among the observations, the model was adjusted for surgeon clustering [22]. We used a fixed effect-only model and used robust standard errors (to adjust for the nesting of surgical cases within surgeons). Arthroplasty procedures with missing data (KPTJRR TKA cohort: 2459 [5%] and KPTJRR THA cohort: 1369 [5%]) were excluded from the final KPTJRR models. Sensitivity analyses that also handled missing data with multiple imputations were conducted (similar results found, data not shown). Hazard ratios (HRs), 95% confidence intervals (CIs), and Wald chi square p values are provided by registry and cohort. Data were analyzed using SAS Version 9.2 software (SAS Institute, Cary, NC, USA) with $\alpha = 0.05$ as the statistical threshold for significance.

This study was approved by the Southern California Kaiser Permanente institutional review board (#5488) and the Human Research Ethics Committee of St Vincent's Hospital Melbourne (HREC-A 100/14).

Results

Association Between BMI and Death After TKA

After adjusting for age, gender, year of operation, indication for surgery, ASA category, race (KPTJRR only), Australian-born (SMART Registry only), bilateral surgery (KPTJRR only), and diabetes, the risk of mortality after TKA was higher in both the KPTJRR (HR, 1.88; 95% CI, 1.33-2.64; p < 0.001) and SMART cohorts (HR, 3.72; 95% CI, 1.94-7.08; p < 0.001) for patients who were underweight at the time of their surgery compared with normal-weight patients. Compared with normal-weight patients, those who were obese class I (KPTJRR: HR, 0.71; 95% CI, 0.66-0.78; p < 0.001; SMART: HR, 0.66; 95% CI, 0.47-0.92; p = 0.015) or obese class II (KPTJRR: HR, 0.73; 95% CI, 0.66-0.81; p < 0.001; SMART: HR, 0.54; 95% CI, 0.35-0.82; p = 0.004) had a lower risk of mortality. Furthermore, in the KPTJRR TKA cohort, being overweight was also associated with a lower risk of mortality (HR, 0.76; 95% CI, 0.71-0.82; p < 0.001), whereas in the SMART cohort, there was no difference in the risk of mortality for overweight patients (HR, 0.79; 95% CI, 0.57-1.09; p = 0.146). No differences in the risk of mortality between the most severe level of obesity identified in our study (class III) compared with normal-weight patients were observed in either the KPTJRR (HR, 0.91; 95% CI, 0.80-1.04; p = 0.181) or the SMART (HR, 0.73; 95% CI, 0.46-1.16; p = 0.186) cohort (Table 2). No interactions (effect modification) by age groups and gender were observed (data not shown). The crude cumulative mortality rate at 5 years (Appendix, Supplemental Digital Content 1) and overall survival analyses (Fig. 1A-B) demonstrated a linear pattern between BMI group and risk of death with mortality rates highest in underweight patients and lowest in obese patient groups.

Association Between BMI and Death After THA

After adjusting for age, gender, year of operation, indication for surgery, ASA category, race (KPTJRR only), Australian-born (SMART Registry only), and diabetes, in the KPTJRR cohort, patients who were underweight had a higher risk of mortality (HR, 2.09; 95% CI, 1.65-2.64; p < 0.001) than normal-weight patients and those who were overweight (HR, 0.73; 95% CI, 0.67-0.80; p < 0.001), obese class I (HR, 0.68; 95% CI, 0.62-0.75; p < 0.001), or obese class II (HR, 0.71; 95% CI, 0.62-0.81; p < 0.001) were at a lower risk of mortality. For the SMART cohort, there was no difference in the risk of mortality for underweight (HR, 1.89; 0.76-4.71; p = 0.170) overweight (HR, 0.84; 95% CI, 0.63-1.12; p = 0.226), obese class I (HR, 0.86; 95% CI, 0.63-1.17; p = 0.332), and obese class II (HR, 0.77; 95% CI, 0.49-1.22; p = 0.265) patients compared with normal-weight patients. No differences in the risk of mortality between the most severe levels of obesity identified in our study (class III) compared with normal-weight patients were observed in either the KPTJRR (HR, 0.91; 95% CI, 0.75-1.12; p = 0.379) or the SMART (HR, 0.68; 95% CI, 0.35-1.33; p = 0.260) cohort (Table 2). No interactions (such as effect modification) by age groups and gender were observed (data not shown). The crude cumulative mortality rate at 5 years (Appendix 1) and overall survival analyses (Fig. 2A-B) demonstrated a linear pattern between BMI group and risk of death with mortality rates highest in underweight patients and lowest in obese patient groups.

Discussion

TJA is one of the most commonly performed surgical procedures in the developed world with an estimated 7 million Americans living with a hip or knee arthroplasty in 2010 [23]. For the majority of Organization for Economic Cooperation and Development countries, there have been increases in both TKA and THA in the previous 10 years with the strongest growth in TJA occurring in the younger population and in countries with the highest prevalence of obesity [29, 30]. Surgeons may make decisions about whether to offer elective TJA to patients based on whether they are obese or not because there is a perception that they have an increased surgical risk [16, 25-27]. Conversely, little attention is given to underweight patients, despite the increased risk of morbidity after major surgical procedures documented in this group [43]. Because both being underweight or obese are associated with increased risk of surgical morbidity, it would seem logical that BMI would also be associated with mortality risk after TJA. However, the evidence to date is variable with some suggesting

Table 2. Age and fully adjusted hazard ratios of mortality by intraoperative BMI levels after TKA and THA by registry

TKA	Intraoperative obesity level (BMI range; kg/m^2)	KPTJRR Age-adjusted HR (95% CI)	KPTJRR p value	KPTJRR Adjusted HR (95% CI)*	KPTJRR p value	SMART Age-adjusted HR (95% CI)	SMART p value	SMART Adjusted HR (95% CI)†	SMART p value
	Normal (20-24), reference	1.0		1.0		1.0		1.0	
	Underweight (< 18.5)	2.13 (1.54-2.92)	< 0.001	1.88 (1.33-2.64)	< 0.001	4.73 (0.65, 34.21)	0.124	3.72 (1.94-7.08)	< 0.001
	Overweight (25-29)	0.66 (0.61-0.71)	< 0.001	0.76 (0.71-0.82)	< 0.001	0.80 (0.59, 1.07)	0.133	0.79 (0.57, 1.09)	0.146
	Obese class I (30-34)	0.50 (0.47-0.55)	< 0.001	0.71 (0.66-0.78)	< 0.001	0.64 (0.47, 0.88)	0.006	0.66 (0.47-0.92)	0.015
	Obese class II (35-39)	0.43 (0.40-0.47)	< 0.001	0.73 (0.66-0.81)	< 0.001	0.58 (0.40, 0.85)	0.005	0.54 (0.35-0.82)	0.004
	Obese class III (≥ 40)	0.44 (0.39-0.49)	< 0.001	0.91 (0.80-1.04)	0.181	0.84 (0.56, 1.27)	0.410	0.73 (0.46-1.16)	0.186

THA	Intraoperative obesity level (BMI range; kg/m^2)	KPTJRR Age-adjusted HR (95% CI)	KPTJRR p value	KPTJRR Adjusted HR (95% CI)*	KPTJRR p value	SMART Age-adjusted HR (95% CI)	SMART p value	SMART Adjusted HR (95% CI)†	SMART p value
	Normal (20-24), reference	1.0		1.0		1.0		1.0	
	Underweight (< 18.5)	2.20 (1.74-2.80)	< 0.001	2.09 (1.65-2.64)	< 0.001	2.36 (0.97-5.77)	0.059	1.89 (0.76-4.71)	0.170
	Overweight (25-29)	0.67 (0.61-0.73)	< 0.001	0.73 (0.67-0.80)	< 0.001	0.82 (0.62-1.10)	0.186	0.84 (0.63-1.12)	0.226
	Obese class I (30-34)	0.56 (0.52-0.62)	< 0.001	0.68 (0.62-0.75)	< 0.001	0.95 (0.70-1.30)	0.765	0.86 (0.63-1.17)	0.332
	Obese class II (35-39)	0.51 (0.45-0.57)	< 0.001	0.71 (0.62-0.81)	< 0.001	0.87 (0.55-1.37)	0.549	0.77 (0.49-1.22)	0.265
	Obese class III (≥ 40)	0.60 (0.50-0.71)	< 0.001	0.91 (0.75-1.12)	0.379	0.94 (0.49-1.80)	0.849	0.68 (0.35-1.33)	0.260

*Adjusted for age, race, year of operation, gender, diabetes, bilateral, primary diagnoses, and ASA category.
†adjusted for age, Australian-born, year of operation, gender, diabetes, primary diagnoses, and ASA category.
BMI = body mass index; HR = hazard ratio; CI = confidence interval; KPTJRR = Kaiser Permanente Total Joint Replacement Registry; SMART = St Vincent's Melbourne Arthroplasty Outcomes Registry; ASA = American Society of Anesthesiologists.

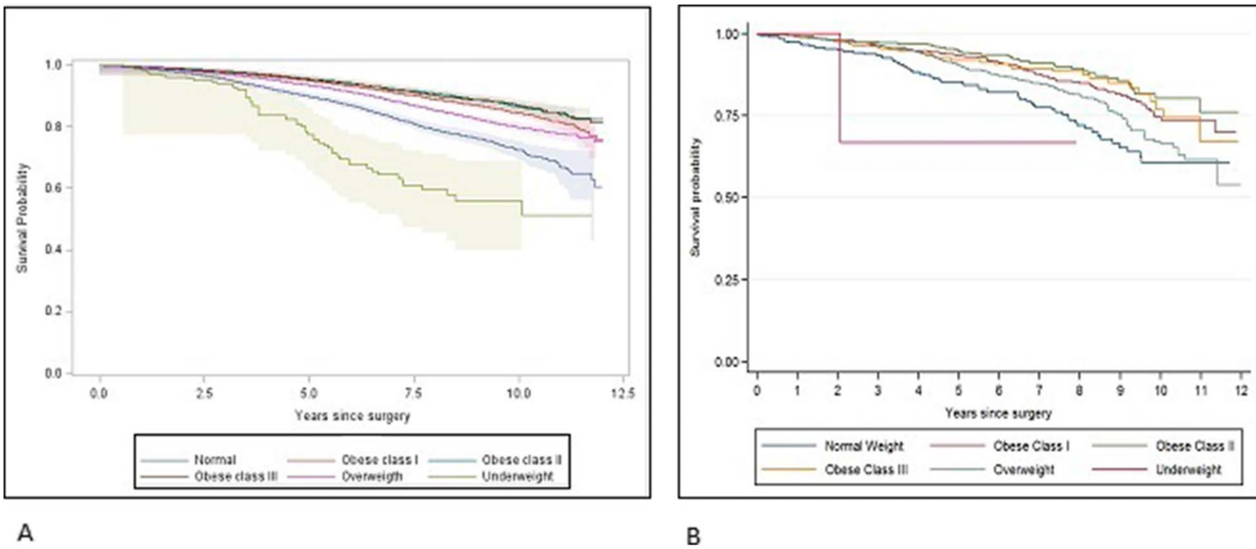

Fig. 1 A-B The Kaplan-Meier survival curves for TKA by intraoperative BMI groups demonstrate that the survival probability was lowest for underweight patients and highest for obese patient groups in both the KPTJRR (**A**) and SMART Registry (**B**) cohorts.

a paradoxic association between BMI and mortality in the first 30 days to 1 year after TJA, whereas others have demonstrated an increased risk of death associated with severe obesity but not with other BMI categories within the first year [18, 40]. We could find no studies examining BMI and risk of mortality after TJA beyond this early time period and therefore sought to fill this gap by examining the association between BMI and all-cause mortality beyond 1 year in patients undergoing TJA. This study had two important findings; first, being underweight was associated with a higher risk of all-cause mortality for both hip and knee arthroplasty and, second, a reduced risk of mortality in patients who are overweight, obese, and severely obese, which calls into question withholding arthroplasty from patients based on obesity alone.

This study has limitations, most notably the data represent a snapshot in time in terms of measuring BMI. We do not know the patterns of weight loss or gain in our cohort before nor subsequent to their TJA; therefore, it remains unclear what impact this might have had on mortality after surgery. Although current research indicates that for the majority, weight remains stable or increases after TJA [7, 8], there is evidence to suggest that the impact of obesity on mortality is dependent on the length of time an individual is obese [34].

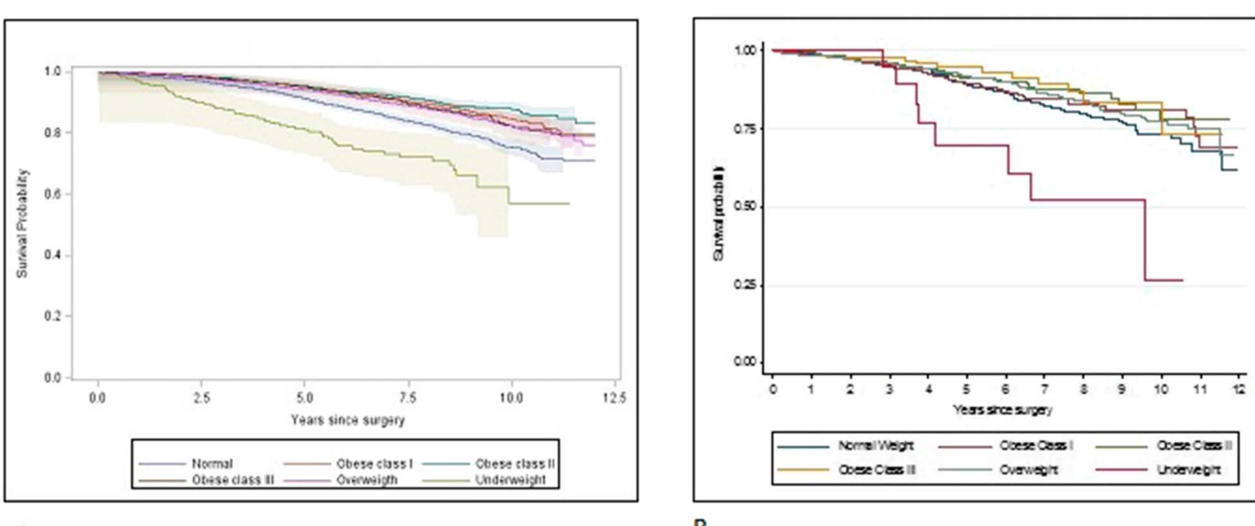

Fig. 2 A-B The Kaplan-Meier survival curves for THA by intraoperative BMI groups demonstrate that the survival probability was lowest for underweight patients and highest for obese patient groups in both the KPTJRR (**A**) and SMART Registry (**B**) cohorts.

Obesity that occurs in early adulthood may confer a different mortality risk than if occurring later in life. Furthermore, we did not have data on cause-specific mortality and therefore were unable to investigate associations between obesity and reasons for death.

Followup for some patients was quite short with the end date of both surgery and mortality followup being December 31, 2013, and this may also be considered a limitation. However, because both of our cohorts were longitudinally followed with varying surveillance periods, we conducted survival analyses, which account for the varying followup of the cohort. Using survival analysis, we have provided descriptive information on the survival of our cohort by reporting time-specific survival estimates. This means that short-term events do not bias the estimates because they are for the specific periods presented. Furthermore, excluding people with the shorter followup in such a study design would bias the survival estimates (excluding those who died within the first couple of years).

Collider stratification bias, an unmeasured confounding induced by selection bias, may also explain our contrary-to-expected finding. Collider stratification bias has been described [24] as a noncausal association induced between an exposure (like obesity) and an outcome (such as mortality) that can arise when analyzing data from only one highly restricted subgroup (eg, TJA) of people. However, we believe this provides at best a partial explanation. Although collider bias has been put forth as a common explanation for the obesity paradox, a recent study testing this supposition using counterfactual causal analysis in a range of scenarios found that the effect of collider bias was small relative to the causal relationships between variables. The authors concluded that collider bias was unlikely to be the main explanation for a reverse direction of an association to a true causal relationship and that alternative explanations of the obesity paradox should be explored [39].

Assessment for potential confounding was limited to available covariates in the two registries and, in that regard, neither reliable smoking data nor SES were available in KPTJRR. However, both smoking and SES data were available in SMART with no association observed between either variable on unadjusted analyses. Surprisingly, a recent systematic review [38] cited only one study examining risk of mortality after TJA among smokers, demonstrating an increased risk in the first 60 days after THA [37]. A greater mortality rate in smokers after TKA in the longer term has also been demonstrated [4]. In contrast, despite one study demonstrating a higher risk of adverse events after TJA in the socioeconomically disadvantaged, no association with mortality was observed in the short term [1].

Another limitation in our analyses arises from the very small number of arthroplasty procedures in the SMART Registry underweight group and, as such, the results for this subgroup may be unreliable. Therefore, no inferences about mortality and underweight patients should be drawn from the results of the SMART Registry data alone. The Kaiser Permanente Registry, however, had adequate representation of underweight patients, from which we could make a more robust assessment.

Many studies have suggested patients who are obese have a higher risk of medical complications [16, 25-27]. One would imagine, therefore, that obesity may infer a higher risk of death, but we found otherwise. Patients who were overweight and obese (class I and II) had a lower risk of mortality compared with normal-weight patients in this study. This finding has been reported in several patient populations, including those with coronary heart disease and heart failure [3]. Although an explanation for this relationship remains elusive, in chronic heart disease, it has been postulated that both central obesity and body fat percentage provide more accurate markers of mortality risk than BMI [15]. Conversely, patient selection bias may exist whereby only the healthiest of the patients who are obese are referred for major surgical procedures [41].

Most notably, we also observed that being underweight was associated with higher mortality. A higher risk of mortality in underweight patients undergoing TJA has been reported in the first 30 days to 1 year post-TJA [40]. Our findings extend beyond the first year and are consistent with the suggestion that higher long-term mortality among underweight patients may occur as a result of a condition known as sarcopenia [36]. In patients with hip osteoarthritis, reduced mobility at baseline assessment has been shown to predict lower survival at 14 years followup [17]. However, further studies will be required to determine whether these factors are associated with mortality risk in patients undergoing TJA.

Many studies have suggested patients who are obese undergoing TJA have a higher risk of medical complications, but despite those, we did not find a higher risk of death; in fact, we found the opposite. TJA results in substantial improvements in quality of life for many and despite a higher risk of complications, withholding surgery on the basis of obesity alone may not be justified in light of our findings. Conversely, clinicians should be cautious when considering TJA in underweight patients without first considering their nutritional status. Randomized controlled trials may be warranted to examine the role of nutritional interventions in reducing morbidity and mortality risk for underweight patients considering TJA.

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References

1. Agabiti N, Picciotto S, Cesaroni G, Bisanti L, Forastiere F, Onorati R, Pacelli B, Pandolfi P, Russo A, Spadea T, Perucci CA;

Italian Study Group on Inequalities in Health Care. The influence of socioeconomic status on utilization and outcomes of elective total hip replacement: a multicity population-based longitudinal study. *Int J Qual Health Care.* 2007;19:37–44.
2. Balasubramaniam U, Dowsey M, Ma F, Dunin A, Choong P. Functional and clinical outcomes following anterior hip replacement: a 5-year comparative study versus posterior approach. *ANZ J Surg.* 2016;86:589–593.
3. Berstock JR, Beswick AD, Lenguerrand E, Whitehouse MR, Blom AW. Mortality after total hip replacement surgery: a systematic review. *Bone Joint Res.* 2014;3:175–182.
4. Clement ND, Jenkins PJ, Brenkel IJ, Walmsley P. Predictors of mortality after total knee replacement: a ten-year survivorship analysis. *J Bone Joint Surg Br.* 2012;94:200–204.
5. Dixon T, Urquhart DM, Berry P, Bhatia K, Wang Y, Graves S, Cicuttini FM. Variation in rates of hip and knee joint replacement in Australia based on socio-economic status, geographical locality, birthplace and indigenous status. *ANZ J Surg.* 2011;81: 26–31.
6. Dowsey MM, Liew D, Choong PF. Economic burden of obesity in primary total knee arthroplasty. *Arthritis Care Res (Hoboken).* 2011;63:1375–1381.
7. Dowsey MM, Liew D, Stoney JD, Choong PF. The impact of obesity on weight change and outcomes at 12 months in patients undergoing total hip arthroplasty. *Med J Aust.* 2010;193:17–21.
8. Dowsey MM, Liew D, Stoney JD, Choong PF. The impact of preoperative obesity on weight change and outcome in total knee replacement: a prospective study of 529 consecutive patients. *J Bone Joint Surg Br.* 2010;92:513–520.
9. Dowsey MM, Nikpour M, Choong PF. Outcomes following large joint arthroplasty: does socio-economic status matter? *BMC Musculoskelet Disord.* 2014;15:148.
10. Dowsey MM, Nikpour M, Dieppe P, Choong PF. Associations between pre-operative radiographic changes and outcomes after total knee joint replacement for osteoarthritis. *Osteoarthritis Cartilage.* 2012;20:1095–1102.
11. Dowsey MM, Nikpour M, Dieppe P, Choong PF. Associations between pre-operative radiographic osteoarthritis severity and pain and function after total hip replacement: radiographic OA severity predicts function after THR. *Clin Rheumatol.* 2016;35:183–189.
12. Dowsey MM, Petterwood J, Lisik JP, Gunn J, Choong PF. Prospective analysis of rural-urban differences in demographic patterns and outcomes following total joint replacement. *Aust J Rural Health.* 2014;22:241–248.
13. Dowsey MM, Smith AJ, Choong PF. Latent class growth analysis predicts long term pain and function trajectories in total knee arthroplasty: a study of 689 patients. *Osteoarthritis Cartilage.* 2015;23:2141–2149.
14. Flegal KM, Kit BK, Orpana H, Graubard BI. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. *JAMA.* 2013;309:71–82.
15. Goel K, Lopez-Jimenez F, De Schutter A, Coutinho T, Lavie CJ. Obesity paradox in different populations: evidence and controversies. *Future Cardiol.* 2014;10:81–91.
16. Guss D, Bhattacharyya T. Perioperative management of the obese orthopaedic patient. *J Am Acad Orthop Surg.* 2006;14: 425–432.
17. Hawker GA, Croxford R, Bierman AS, Harvey PJ, Ravi B, Stanaitis I, Lipscombe LL. All-cause mortality and serious cardiovascular events in people with hip and knee osteoarthritis: a population based cohort study. *PLoS One.* 2014;9:e91286.
18. Hunt LP, Ben-Shlomo Y, Clark EM, Dieppe P, Judge A, MacGregor AJ, Tobias JH, Vernon K, Blom AW; National Joint Registry for England, Wales, and Northern Ireland. 90-day mortality after 409,096 total hip replacements for osteoarthritis, from the National Joint Registry for England and Wales: a retrospective analysis. *Lancet.* 2013;382:1097–1104.
19. Kaiser Permanente. Fast Facts about Kaiser Permanente. 2016. Available at: https://share.kaiserpermanente.org/article/fast-facts-about-kaiser-permanente/. Accessed October 5, 2016.
20. Karter AJ, Ferrara A, Liu JY, Moffet HH, Ackerson LM, Selby JV. Ethnic disparities in diabetic complications in an insured population. *JAMA.* 2002;287:2519–2527.
21. Koebnick C, Langer-Gould AM, Gould MK, Chao CR, Iyer RL, Smith N, Chen W, Jacobsen SJ. Sociodemographic characteristics of members of a large, integrated health care system: comparison with US Census Bureau data. *Perm J.* 2012;16: 37–41.
22. Lin DY, Wei LJ. The robust inference for the Cox proportional hazards model. *J Am Stat Assoc.* 1989;84:1074–1078.
23. Maradit Kremers H, Larson DR, Crowson CS, Kremers WK, Washington RE, Steiner CA, Jiranek WA, Berry DJ. Prevalence of total hip and knee replacement in the United States. *J Bone Joint Surg Am.* 2015;97:1386–1397.
24. Mayeda ER, Glymour MM. The obesity paradox in survival after cancer diagnosis: tools for evaluation of potential bias. *Cancer Epidemiol Biomarkers Prev.* 2017;26:17–20.
25. Murgatroyd SE, Frampton CM, Wright MS. The effect of body mass index on outcome in total hip arthroplasty: early analysis from the New Zealand Joint Registry. *J Arthroplasty.* 2014;29: 1884–1888.
26. Namba RS, Inacio MC, Paxton EW. Risk factors associated with surgical site infection in 30,491 primary total hip replacements. *J Bone Joint Surg Br.* 2012;94:1330–1338.
27. Namba RS, Inacio MC, Paxton EW. Risk factors associated with deep surgical site infections after primary total knee arthroplasty: an analysis of 56,216 knees. *J Bone Joint Surg Am.* 2013;95:775–782.
28. Owens WD, Felts JA, Spitznagel EL Jr. ASA physical status classifications: a study of consistency of ratings. *Anesthesiology.* 1978;49:239–243.
29. Pabinger C, Geissler A. Utilization rates of hip arthroplasty in OECD countries. *Osteoarthritis Cartilage.* 2014;22:734–741.
30. Pabinger C, Lothaller H, Geissler A. Utilization rates of knee-arthroplasty in OECD countries. *Osteoarthritis Cartilage.* 2015; 23:1664–1673.
31. Paxton EW, Inacio MC, Khatod M, Yue EJ, Namba RS. Kaiser Permanente National Total Joint Replacement Registry: aligning operations with information technology. *Clin Orthop Relat Res.* 2010;468:2646–2663.
32. Paxton EW, Inacio MCS, Kiley ML. The Kaiser Permanente implant registries: effect on patient safety, quality improvement, cost effectiveness, and research opportunities. *Perm J.* 2012;16:33–40.
33. Paxton EW, Kiley ML, Love R, Barber TC, Funahashi TT, Inacio MC. Kaiser Permanente implant registries benefit patient safety, quality improvement, cost-effectiveness. *Jt Comm J Qual Patient Saf.* 2013;39:246–252.
34. Peeters A, Barendregt JJ, Willekens F, Mackenbach JP, Al Mamun A, Bonneux L; NEDCOM, the Netherlands Epidemiology and Demography Compression of Morbidity Research Group. Obesity in adulthood and its consequences for life expectancy: a life-table analysis. *Ann Intern Med.* 2003;138:24–32.
35. Ramos-Esquivel A. Overweight, obesity, and all-cause mortality. *JAMA.* 2013;309:1680.
36. Romero-Corral A, Montori VM, Somers VK, Korinek J, Thomas RJ, Allison TG, Mookadam F, Lopez-Jimenez F. Association of

bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. *Lancet.* 2006;368:666–678.
37. Sadr Azodi O, Bellocco R, Eriksson K, Adami J. The impact of tobacco use and body mass index on the length of stay in hospital and the risk of post-operative complications among patients undergoing total hip replacement. *J Bone Joint Surg Br.* 2006;88:1316–1320.
38. Singh JA. Smoking and outcomes after knee and hip arthroplasty: a systematic review. *J Rheumatol.* 2011;38:1824–1834.
39. Sperrin M, Candlish J, Badrick E, Renehan A, Buchan I. Collider bias is only a partial explanation for the obesity paradox. *Epidemiology.* 2016;27:525–530.
40. Thornqvist C, Gislason GH, Kober L, Jensen PF, Torp-Pedersen C, Andersson C. Body mass index and risk of perioperative cardiovascular adverse events and mortality in 34,744 Danish patients undergoing hip or knee replacement. *Acta Orthop.* 2014;85:456–462.
41. Tjeertes EK, Hoeks SE, Beks SB, Valentijn TM, Hoofwijk AG, Stolker RJ. Obesity–a risk factor for postoperative complications in general surgery? *BMC Anesthesiol.* 2015;15:112.
42. Wallace G, Judge A, Prieto-Alhambra D, de Vries F, Arden NK, Cooper C. The effect of body mass index on the risk of post-operative complications during the 6 months following total hip replacement or total knee replacement surgery. *Osteoarthritis Cartilage.* 2014;22:918–927.
43. Windsor JA. Underweight patients and the risks of major surgery. *World J Surg.* 1993;17:165–172.
44. Yuan K, Chen HL. Obesity and surgical site infections risk in orthopedics: a meta-analysis. *Int J Surg.* 2013;11:383–388.