The association of body mass index with long term revision rates and 90-day mortality rates following primary total hip replacements: Findings from "The National Joint Registry of England, Wales, Northern Ireland and the Isle of Man"

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Abstract

Background

The influence of obesity on outcome following total hip replacement (THR) is unclear. Restriction to THR on the basis of body mass index (BMI) has been suggested. The purpose of this study was to assess the influence of BMI on the risk of revision and 90-day mortality.

Methods

This study is a population-based longitudinal cohort study of the National Joint Registry (NJR). Using data recorded from April 2003 to December 2015, linked to Office for National Statistics data, we ascertained revision and 90-day mortality rates following primary THR by BMI category. The probability of revision was estimated using Kaplan-Meier methods. Associations between BMI, revision and mortality were explored using adjusted Cox proportional hazards regression models.

Results

We investigated revision and 90-day mortality in 415,598 and 413,741 operations, respectively. Each dataset accounts for approximately 58% of the total number of recorded operations in the NJR. 38% of patients were obese. At 10 years, obese class III patients had the highest cumulative probability of revision (6.7%;95%CI:5.5,8.2), twice that of the underweight group (3.3%;95%CI:2.2,4.9). When adjusted for age, gender, ASA grade, year of operation, indication and type of operation and compared to normal BMI, significantly higher hazard ratios for revision were observed in obese class I (1.14;95%CI:1.07,1.22;$p<0.0001$), II (1.30;95%CI:1.19,1.40;$p<0.0001$) and III (1.43;95%CI:1.27,1.61;$p<0.0001$) patients.

Underweight patients had a substantially higher 90-day mortality (1.17%;95%CI:0.9,1.6) than normal. The hazard ratio of 90-day mortality was significantly higher in underweight (2.09;95%CI:1.51,2.89;$p<0.0001$) and significantly lower in overweight

(0.70;95%CI:0.61,0.81;p<0.0001), obese class I (0.69;95%CI:0.59,0.81;p<0.0001), and II (0.79;95%CI:0.63,0.98;p=0.049) patients.

Conclusions

Although revision rates in the long term following THR are higher in obese patients, the rates remained acceptable by contemporary standards and are balanced by a lower risk of 90-day mortality.

Level of Evidence: Level II

Introduction

The outcome of total hip replacement (THR) is assessed by various metrics[1]; including revision[2,3] and increases in mortality above background population rates[4].

The prevalence of obesity (body mass index (BMI) $\geq$30 kg.m^{-2}) in the United States of America (USA) increased from 12% in 1991[5] to 38% in 2014[6] and in the United-Kingdom (UK) from 15% in 1993 to 27% in 2015[7]. Obesity is associated with an increased risk of developing osteoarthritis (OA) [8] and undergoing THR[9].

Several studies have investigated the effect of BMI on revision risk; however these studies do not all agree. Studies of primary care databases and national registries from the UK and New Zealand ranging from 5,357 to 63,162 patients have shown variable associations between increased BMI and the risk of revision[10-12]. Other large cohorts and regional registry studies ranging from 1,421 to 27,571 patients have shown no significant association between BMI and revision[13-16].

Studies of BMI and mortality at 30-days, 90-days have shown mixed results. Four registry studies in the USA[17-20] and a single center study in the UK[21] (n=2,000 to 432,841), showed no significant association. Registry studies based in Denmark and the UK (n=34,000 and 410,000) have shown a protective effect of being overweight on 30- and 90-day mortality[4,22]. One small Finnish study showed a protective effect of increasing BMI on mortality risk[23].

The association between obesity, measured by BMI, with revision and mortality following THR is unclear. This is a contentious issue in settings such as the NHS[24-26] and the USA[27] due to the proposed restriction of THR according to BMI, although there is currently no restriction by the NHS[28]. Using data from the National Joint Registry for England, Wales Northern Ireland and the Isle of Man (NJR), we aim to investigate the association between BMI, the risk of revision surgery up to 11-years and risk of 90-day mortality.

Materials and Methods

Data was prospectively collected by the NJR in England and Wales from April 1, 2003 to December 31, 2015. Data was mandatorily collected in the private sector from inception, and in the public sector from 2011. A recent national audit of data entered into the NJR in 2014 and 2015 estimated data capture of 95% for primary THA and 91% for revision THA. Date of death was provided by the Office for National Statistics.

BMI was recorded for the first time in April, 2004 with version 2 of the NJR Minimum Data Set (MDS) data collection form, data collected before that date were therefore excluded. In revision analyses, procedures were also excluded for the following reasons: 1) implausible (<10kg/m^2 or >60 kg/m^2) or missing BMIs; 2) missing age, gender, NHS number; 3) unspecified hip replacement type, operation indication, or bearing type; 4) patients receiving THR due to trauma. In mortality analyses, for patients undergoing same-day bilateral procedures, one of the two procedures was randomly excluded (figure 1).

The primary exposure was obesity defined using the BMI, classified according to World Health Organisation criteria: underweight (**10-**18.5 kg/m^2); normal (19-24 kg/m^2); overweight (25-29 kg/m^2); obese class I (30-34 kg/m^2); obese class II (35-39 kg/m^2); and obese class III (40**-60** kg/m^2). The primary outcomes were revision following primary THR and mortality within 90-days. Patients had a potential maximum 11.75 years follow-up. Confounding variables included; age at primary (grouped [<55], [55-59], [60-64], [65-69], [70- 74], [75-79], [≥80] years); gender; American Society of Anesthesiologists (ASA) physical status classification (grouped [P1], [P2], [P3], [P4-P5]); year of primary THR ([2004- 2006], [2007-2009], [2010-2012], [2013-2015]; type of THR and fixation (cemented, uncemented, hybrid, reverse hybrid and resurfacing) and operation indication (OA, OA and other reason/(s) or other reason/(s)).

Following application of the above criteria, the exposure and confounders had no missing values.

To describe continuous variables we used medians and interquartile ranges (IQR), and for categorical variables frequencies and percentages.

Kaplan-Meier failure estimates were plotted to describe revision up to 11.75-years and mortality up to 90-days. Time zero was considered the date of the operation, patients exited after the first failure was observed, patients were censored upon death and administratively censored on December 31, 2015. Where the numbers at risk in subgroups fell below 100 beyond 10-years follow-up, the 10-year results are presented to provide reasonable estimates of the 95% confidence intervals (CI). Log-rank tests were used to compare groups.

The association between BMI, revision and mortality were explored using Cox 'proportional hazards' regression models. Multivariable analyses were used to investigate the effect of confounding. Models investigating revision were sequentially adjusted: Revision Model (RM)1 univariate model; RM2 adjusted for age and gender; RM3 further adjusted for ASA and year of primary operation; RM4 further adjusted for fixation type and indication for operation. Models investigating mortality were sequentially adjusted: Mortality Model (MM)1 univariate model; MM2 adjusted for age and gender; MM3 uses baseline stratification by the reason for operation to allow for non-proportionality; MM4 further adjusted for ASA and year of primary operation.

Hazard rate ratios (HR), 95% CIs and p-values are reported. Proportional hazard assumptions were investigated graphically using log-log plot of the survival function.

Analyses were performed with Stata 14.2 (Stata Statistical Software: v.14. College Station, TX: StataCorp LP).

Sensitivity analyses

Two models were fitted to investigate the interaction between BMI and age in revision (RM5) and mortality (MM5). Likelihood ratio tests were used to detect significance.

All analyses were repeated using a competing risk framework, the cumulative incidence function instead of 1-KM, and a Fine-Gray model instead of Cox models. In addition, cubic splines models were fitted and compared with the Cox models.

Missing Data

We compared demographic characteristics of procedures of complete and incomplete BMI to investigate the potential for systematic biases, and restricted analyses to data collected after 2007 where BMIs were more complete.

Source of Funding

***** Blinded by JBJS *****

Results

From April 1, 2003 to December 31, 2015, 796,636 primary hip replacements were recorded[2]. Following the exclusion criteria, 415,598 and 413,741 procedures were available to investigate revision and 90-day mortality respectively (figure 1), with a maximum follow up of 11.75-years. Each cohort accounted for approximately 58% of the total number of operations (table 1); cases with BMI available are representative of the whole cohort, the only disparity being in the year of primary, which is accounted for in our modelling.

Descriptive statistics were extracted using the revision dataset (n=415,598). 59% of THRs were performed in females. Males were slightly younger than females (table 2). 62% of patients receiving THA were non-obese (BMI <30 kg/m^2), and the majority of obese patients (BMI ≥30 kg/m^2) were class I. Females were more prevalent in every BMI category (table 3). Low ASA grades were more frequent in underweight, normal and overweight patients, while higher ASA grades were similar. The type of hip replacement did not vary depending on the BMI.

Figure 2 illustrates the cumulative probability of revision surgery. Increasing levels of obesity were associated with an increased probability of revision (table 4). Patients classified as obese class III had a 6.7% (95%CI:5.5,8.2) probability of revision at 10 years after THR compared to 3.3% (95%CI:2.2,4.9) for underweight patients (figure 3).

Figure 4 illustrates the probability of 90-day mortality; a log-rank test indicated a significant difference between BMI categories, $p<0.0001$. 90-day mortality was very low for patients in all groups (table 5). Underweight patients had a substantially higher probability of 90-day mortality (1.2% 95%CI:0.9,1.6) compared to other groups (figure 5).

Table 6 presents the Cox 'proportional hazards' regression analysis for revision. RM4 shows that obese class I, II and III patients are 14%, 30% and 43% respectively more likely to undergo revision than normal BMI patients (table 6). No significant difference was found between the hazard ratios of the other BMI classes, while there was a trend showing that underweight patients were 16% less likely, and overweight patients no more likely, to undergo revision than normal BMI patients (table 6).

Table 7 presents the association between BMI and mortality. MM1 to 4 indicate strong evidence that underweight patients have higher and overweight or obese class I have lower 90-day mortality rates, compared to normal BMI patients. MM4 shows that the mortality rate of underweight patients is 109% greater than normal BMI patients. Patients classified as either overweight or obese class I are approximately 30% less likely to die within 90-days of surgery, while obese classes II and III are 21% and 27% respectively less likely to die compared with a normal BMI (table 7). Proportional hazards assumptions were satisfied for all the models.

A greater proportion of underweight patients were revised for periprosthetic fracture and adverse soft tissue reaction to particulate debris than patients in higher BMI classes. Obese class III patients were more likely to be revised for infection (table 8). None of these effect sizes is large enough to account for the overall patterns observed.

Sensitivity analyses

Likelihood ratio tests demonstrated that there was no interaction between BMI and age for either revision or mortality. Analyses performed using a competing risks framework did not alter the interpretation of any of the analyses reported (table 9, figure 6). Also, cubic spline models suggested the same outcomes (figures 7-8). Exclusion of operations before 2007 gave the same results as the main analysis (appendix tables 1-4).

Discussion

Our results demonstrate that long-term revision rates following primary THR are similar for normal and overweight individuals, but they are higher for obese class I, II and III (BMI≥30 kg/m^2) patients. Despite this, the revision rates of obese class III patients remain acceptable by contemporary standards, exceeding the level required for a 10A rating by the Orthopaedic Data Evaluation Panel in the UK[29]. The lowest revision rates were observed in the underweight group but the numbers were small, and may be a chance observation. We observed a higher risk of 90-day mortality in underweight patients with rates twice as high as normal BMI patients. The rates in overweight and obese class I and II patients were significantly lower than normal BMI individuals. Lower mortality rates were observed in obese class III, but again the numbers were small.

There is little research of the influence of BMI on the long-term revision risk following primary THR. Previous studies have used small cohorts and grouped BMI rather than using the WHO classification[10-16]. Analyses have been restricted to particular implants[11,14], considered BMI as a continuous variable[10] or only offered short-term follow-up[10-12,16]. Contrary to our findings, a number of studies have found no association between BMI and revision[14,15]. These include a single-centre study of 3,290 patients showing no association between obesity and revision risk at a minimum follow-up of 2-years[16]; the only association seen was between morbid obesity and the risk of infection. Although we observed a higher proportion of obese class III patients revised for infection, this difference was not sufficient to account for the overall patterns observed. A regional registry study of 27,571 THRs found no difference in revision rates according to BMI, but did show a weight of greater than 80 kilograms was predictive of revision[13]. This finding, limited to men for one indication for revision, is of limited generalisability. In a larger study of 63,132 THRs, a 66% higher rate of revision in morbidly obese compared to those with normal weight was observed, higher than the difference observed in our study[10]. A previous study based on a cohort of 5,357 patients in the NJR at a maximum follow-up of 2-years found higher revision rates in the different categories of overweight and obese patients but none of these findings were significant[12]. In a larger NJR analysis of 17,166 patients receiving one type of THR for whom BMI data were available, a higher rate of revision was observed when patients with a BMI of >30 kg/m^2 were compared to patients with a lower BMI[11].

Our group has previously observed a protective effect of being overweight when the risk of mortality following primary THR is considered[4]. In the current study, we observed a significantly lower risk of mortality in overweight and obese class I and II patients but no significant difference between obese class III patients and those with normal BMI. The highest rates of mortality were observed in the underweight group. This protective effect of increasing BMI was also seen in a single centre study of 756 primary THRs, although non-standard groupings were used and the findings were not significant[23]. Data from the Danish registries demonstrated significantly higher mortality in underweight and normal BMI patients compared to overweight patients and suggested a BMI of 27-28 kg/m^2 was associated with the lowest risk of mortality[22]. In contrast with these findings and our own study, analysis of USA registers and a single center study of 1,744 patients in the UK observed no significant association between BMI and the risk of mortality[17-21].

The "obesity paradox", whereby being overweight or obese offers a protective effect against adverse outcomes or mortality, has been observed in cardiac[30,31], oncology[32] and surgical fields[33]. There is a risk of bias when considering the influence of BMI on outcomes such as mortality, the risk of collider bias through mediators such as diabetes does not explain the observation, and alternative causative explanations require further investigation[34]. Although those that are underweight may have comorbidities or other illnesses to explain their low BMI, the population considered is screened for fitness to undergo surgery, the "healthy patient selection effect", and therefore we do not believe illness in the underweight group explains the higher mortality, particularly as our models adjust for ASA grade. Smoking is a potential confounding factor that has been identified in patients with cardiovascular disease that may at least partially explain the observed mortality patterns and requires further investigation[35].

The current study has significant strengths. 1) This is the largest cohort we are aware of with complete BMI data analysed to date. 2) Patients were not restricted by demographic or prosthesis, for example, all patients that had a resurfacing hip replacement were included as they could have conceivably received a THR. 3) Follow up time for revision was substantially longer than currently reported, and is informative for obese patients with respect to the longevity of THR. 4) Consistent with our previous work, mortality was restricted to 90 days following surgery, at which point the risk returns to baseline[4].

The study does have limitations. The outcomes are limited to revision and mortality. These are commonly used criteria when assessing the outcome following THR but other outcomes such as pain[36] and function measured by PROMS, or adverse events[37] may be important. We did not adjust for co-morbidities, for example coronary heart disease or diabetes, due to lack of available data. However, the risk of inducing bias, as co-morbidities may lie on the causal pathway between BMI and the outcome of interest, by such a strategy mitigates this limitation[38]. BMI is measured on a single occasion prior to surgery, we were therefore not able to investigate effect of BMI trajectories on revision. Due to the relatively short mortality window (90 days), we do not believe BMI is likely to change appreciably in this short interval. BMI completeness prior to 2007 is poor and patients with BMI in excess of 60 kg/m^2 were excluded. However, we assume the reason for missingness is unrelated to the outcomes of interest, and under the Missing At Random statistical assumption[39], therefore unbiased results will be obtained. Sensitivity analyses restricting data to post 2007 illustrates results are unchanged. Our analysis is based on observational data and attributing causation is difficult.

We have analysed data from a large and generalisable prospective national cohort and demonstrated that the current trend towards the restriction of access to THR on the basis of BMI is not justified when the outcomes of revision and mortality are considered. Whilst surgeons, patients and other stakeholders need to be aware of the individual risk profiles associated with BMI and interventions such as THR, in order to make fully informed decisions, we have shown that the revision and mortality rates are acceptable by contemporary standards. We found no evidence to suggest that access to THR should be restricted on the basis of BMI for patients with a BMI between 10 and 60 kg/m^2.

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Figure Legends

Figure 1. Flow diagram of patient selection to investigate revision and mortality. THR for Trauma included the following indications included on different versions of the NJR Minimum Dataset forms: acute-neck of femur, fractured neck of femur, failed hemiarthroplasty, chronic trauma, failed internal fixation, unspecified previous hip trauma or other hip trauma.

Figure 2. Cumulative probability of revision up to 11-years after primary THR. The number at risk shown at 0, 3, 5, 7, 10 and 11 years following primary THR. Cumulative probabilities have been multiplied by 100, shown in percentages (%).

Figure 3. Cumulative probability of revision with 95% C.I. up to 11-years after the primary THR, by BMI classification. Cumulative probabilities have been multiplied by 100, shown in percentages (%).

Figure 4. Cumulative probability of death up to 90-days after primary THR. The number at risk shown at 0, 30, 60 and 90 days. Cumulative probabilities have been multiplied by 100, shown in percentages (%).

Figure 5. Cumulative probability of death with 95% C.I. up to 90 days after the primary THR, by BMI classification. Cumulative probabilities have been multiplied by 100, shown in percentages (%).

Figure 6. Cumulative incidence function of revision up to 11-years after primary THR. Adjusting for the competing risk of death separately for each BMI classification. 415,598 primary THR were included in the analysis.

Figure 7. Revision hazard ratio with BMI for RM4 and cubic spline model with 95% C.I. The cubic spline model adjusts for the same confounders as RM4.

Figure 8. Mortality hazard ratio with BMI for RM4 and cubic spline model with 95% C.I. The cubic spline model adjusts for the same confounders as MM4.