A commentary by Kanu Okike, MD, MPH, is linked to the online version of this article at jbjs.org.

Total Hip Arthroplasty Versus Hemiarthroplasty for Displaced Femoral Neck Fracture

A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Background: Hip fractures are a leading cause of disability worldwide, with displaced femoral neck fractures being of particular concern. A recent meta-analysis reported that total hip arthroplasty (THA) was superior to hemiarthroplasty (HA) in terms of reoperations, but inferior in terms of dislocations. However, publication of 4 additional randomized controlled trials that enrolled nearly 1,780 additional patients merits an updated meta-analysis.

Methods: We conducted a literature search of 4 databases to identify randomized controlled trials comparing THA and HA in patients with displaced femoral neck fractures. For patient-reported outcomes, the minimally important difference informed calculation of risk differences. We performed a subgroup analysis to address the possible impact of risk of bias and performed meta-regression to assess the possible impact of duration of follow-up.

Results: Sixteen studies that enrolled 3,084 patients randomized to undergo THA (n = 1,521) or HA (n = 1,563) proved eligible. There were no significant differences between the 2 groups in terms of the revision rate at up to 5 years of follow-up or functional outcome at up to 3 years. Health-related quality of life was superior in the THA group (mean difference [MD] = 0.05, 95% confidence interval [CI] = 0.02 to 0.07, minimally important difference, 0.145). There was no significant difference between the groups in terms of dislocation or periprosthetic fracture incidence. Operative time was significantly shorter in the HA group (MD = 22 minutes, 95% CI = 9 to 35 minutes). Analyses addressing risk of bias and length of follow-up did not reveal subgroup differences. Certainty of evidence for all outcomes was rated as moderate.

Conclusions: The best evidence showed, with moderate certainty, that HA and THA likely result in similar revision rate, function, mortality, periprosthetic fracture, and dislocation at up to 5 years, with a small, possibly unimportant benefit in health-related quality of life with THA. More specifically, the improvements are well below established cutoffs for clinical importance. Almost half of all patients were from a single large randomized controlled trial, although the results were consistent across the studies. In addition, HA likely results in a clinically unimportant reduction in operative time.

Level of Evidence: Therapeutic Level I. See Instructions for Authors for a complete description of levels of evidence.

Hip fractures are a leading cause of disability worldwide, with >300,000 hip fractures annually in the United States alone[1]. These injuries are associated with massive individual and societal costs[2]: the estimated annual cost of hip fractures is over $10 billion in the United States[3]. Given the scale of this problem, it is important that the most efficacious and cost-effective treatment modalities be identified and used globally.

Displaced femoral neck fractures, 1 of the 2 main types of hip fractures, are particularly concerning as they pose a threat to the blood supply of the femoral head. The femoral head is supplied in retrograde fashion by the medial femoral circumflex artery in adults, and is at risk of osteonecrosis with any displaced fracture through the femoral neck[4]. In displaced femoral neck fractures (Garden III or IV), total hip arthroplasty

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(THA) or hemiarthroplasty (HA) is preferred over fracture fixation because of the higher risk of surgical complications[5].

A recent meta-analysis of randomized controlled trials (RCTs) concluded that THA was superior to HA in terms of reoperations, albeit with a higher dislocation rate[6]. More recently, however, a large multicenter RCT that randomized 1,495 patients with displaced femoral neck fractures to THA or HA reported no significant difference in revision or dislocation rates[7], and 3 further RCTs have been published since the most recent meta-analysis[8-10].

Given the addition of 1,780 randomized patients, we performed an updated systematic review and meta-analysis of RCTs comparing THA and HA for displaced femoral neck fractures with respect to mortality, revision surgery rate, function, and quality of life.

Materials and Methods

This systematic review was registered a priori with PROSPERO (CRD42020147485). The review was conducted according to the Cochrane Handbook for Systematic Reviews of Interventions[11] and reported according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines[12].

Eligibility Criteria

Eligible studies were RCTs that compared THA and HA for displaced femoral neck fractures, included patients with a mean age of >50 years, and were available as full text in English. When publications included overlapping reports of a single trial, we included results from the report with the most recent follow-up unless the loss to follow-up was ≥5% higher in the follow-up study than in the earlier report.

Information Sources

The literature search, performed on November 25, 2019, included results since the inception of MEDLINE, Embase, the Web of Science, and the Cochrane Central Register of Controlled Trials. The search strategy was developed in consultation with a health sciences librarian (see Appendix 1).

Study Selection

After removal of duplicates, 2 independent reviewers screened the titles, abstracts, and full texts; full texts were obtained if either reviewer judged the study potentially eligible. At the full-text review stage, the reviewers discussed discrepancies until they reached a consensus. At each stage, reviewer agreement was assessed by calculating the Cohen kappa (κ) statistic, which was categorized a priori according to previous literature[13].

Data Collection

A collaborative online spreadsheet (Google Sheets), piloted by 2 reviewers prior to starting, facilitated data extraction. Reviewers performed data extraction in duplicate and compared results for verification.

Reviewers recorded details regarding study design, methodology, patient demographics, prosthetic device, surgical approach, and surgeon experience. Revision rate, function, health-related quality of life (HRQoL), mortality, number of dislocations, periprosthetic fracture, and operative time constituted the outcomes of interest.

Risk of Bias in Individual Studies

Risk of bias was assessed, using a modified version of the Cochrane Risk of Bias instrument (version 1.0)[14], for each individual study as well as for each outcome. Using criteria established a priori, studies were classified as having low risk of bias if they had no more than 1 domain at high risk of bias.

Summary Measures and Synthesis of Results

Demographic data and follow-up duration are summarized across studies as the pooled mean, weighted by sample size, and the standard deviation (SD). Comparisons of dichotomous data are reported as the odds ratio (OR) and 95% confidence interval (CI), and comparisons of functional and HRQoL outcomes are reported as the mean difference (MD) and 95% CI and as the risk difference (RD), defined as the difference in the proportion achieving the minimally important difference (MID), and 95% CI. Data at the latest available time point were used in the analysis. As suggested by the Cochrane Handbook, a predefined algorithm or an imputed SD was used to estimate the SD if a study did not report the SD[11].

For function and HRQoL scores, conversion into the most familiar instrument for each outcome (the Harris hip score [HHS] for function, and the EuroQol-5 Dimensions [EQ-5D] index for HRQoL) preceded calculation of MDs according to previously established methods[15-17]. This method is 1 of the preferred options for combining continuous outcomes, and allows for comparison with the MID[18]. The analysis used established methods to obtain an RD for the proportion of patients in each group who reached or surpassed the MID[15,19]. The RD analysis was based on a random-effects inverse-variance model with a DerSimonian-Laird estimator for τ^2. The Jackson method was used to estimate the CI for τ and τ^2. For all meta-analyses, the chi-square test and the I^2 statistic provided estimates of heterogeneity.

Additional Analyses

A subgroup analysis, performed using a random-effects model (random intercepts, fixed slopes), addressed duration of follow-up, with a meta-regression of follow-up as a continuous variable versus revision rate and functional outcomes. In addition, we conducted a subgroup analysis for studies at high and low risk of bias. PROMID (Patient Reported Outcome Minimal Important Difference), a comprehensive evidence-based catalog of available published MIDs for patient-reported outcome measures, provided MIDs for functional and HRQoL outcomes[20].

The certainty of evidence for each outcome was rated using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) framework[11]. Each outcome was assessed for publication bias by creation of funnel plots and assessment of symmetry and outliers beyond the 95% CI lines. Data analyses were performed using RevMan (Review Manager) version 5.3 (The Cochrane Collaboration)[21] and R (R Foundation for Statistical Computing)[22].

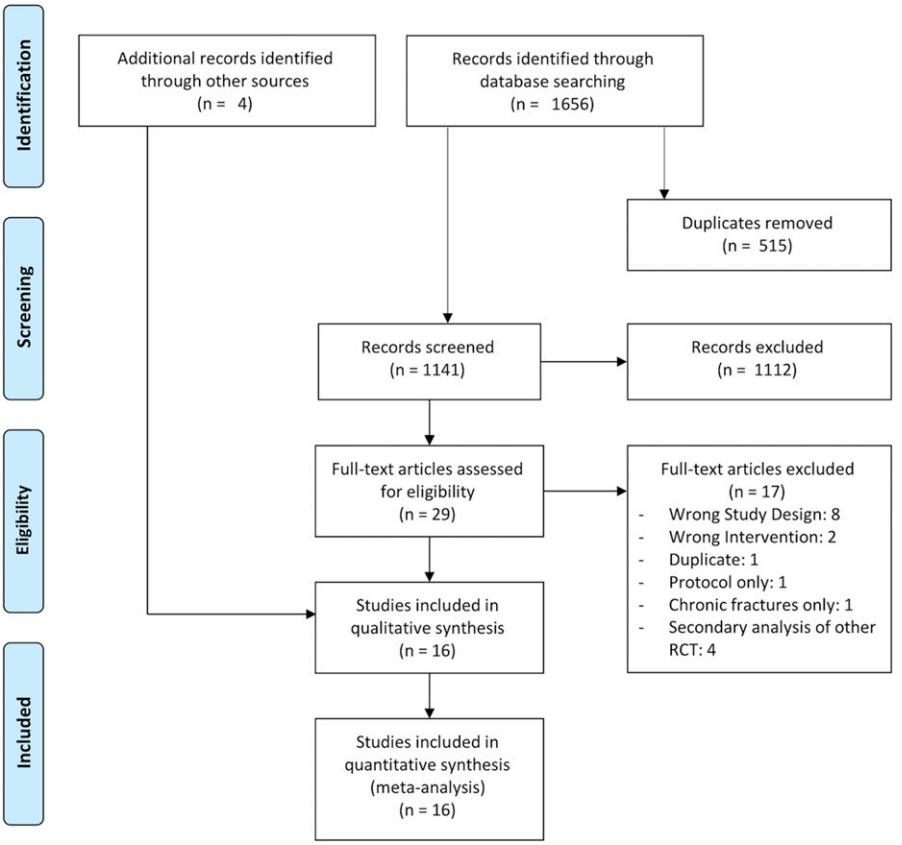

Fig. 1
PRISMA flow diagram.

Results

Study Selection

The original search strategy yielded 1,656 results, from which 515 duplicates were removed, resulting in 1,141 unique records. Four studies were excluded as they were long-term follow-ups of other included RCTs with very high loss to follow-up[23-26]. Four additional studies were located by manual searching and screening of references. Ultimately, 16 unique RCTs proved eligible[7-10,27-38] (Fig. 1). There was strong interreviewer agreement at the title and abstract stage ($\kappa = 0.83$, 95% CI = 0.71 to 0.95) and full-text stage ($\kappa = 0.84$, 95% CI = 0.64 to 1.0).

Study Characteristics

The 16 eligible RCTs enrolled 3,084 patients with a displaced femoral neck fracture to undergo THA (1,521) or HA (1,563); these numbers omit those in 1 study that did not report the numbers allocated to each group. Table I details the characteristics of the included studies.

Risk of Bias in Individual Studies

Twelve of the 16 studies had at least 1 domain at high risk of bias. Blinding of outcome assessors to the allocated intervention was the domain most frequently rated as a source of bias, with 10 studies at high risk, 4 studies probably at risk, and only 2 studies at low risk of bias (see Appendix 2).

Synthesis of Results

Duration of Follow-up

The meta-regression did not reveal any significant effect of duration of follow-up on either functional outcome ($p = 0.93$) or revision rate (0.72). Thus, the latest available follow-up provided data for analysis.

Revision Surgery

Twelve studies (n = 2,590) reported on the risk of revision at 1 to 5 years postoperatively[7-10,27,30,32,33,35-38]. THA and HA had similar rates of revision (OR = 0.89, 95% CI = 0.66 to 1.20, $p = 0.44$), with no heterogeneity ($I^2 = 0\%$) (Fig. 2). The GRADE certainty of evidence was rated as moderate for revision surgery, being rated down 1 level due to imprecision given the wide CI (Table II). Appendix 3 summarizes the risk-of-bias assessment specific to revision surgery. Given that 1 of the included trials included closed reduction in the definition of revisions, a sensitivity analysis was performed with the removal of closed reductions from the analysis. The results remained non-significant (OR = 0.75, 95% CI = 0.51 to 1.10, $I^2 = 4\%$, $p = 0.14$).

Functional Outcomes

Six studies (n = 1,022) reported on the functional outcome at 1 to 3 years of follow-up with sufficient information to inform the pooled analysis[7,10,27,31,37,38]. One study used the Hip Rating

TABLE I Characteristics of Included Studies

Study	Country	Sample Size	Female *(%)*	Mean Age *(yr)*
Baker[33] (2006)	U.K.	81	79	75
Bhandari[7] (2019)	Multicenter	1,495	70	79
Blomfeldt[34] (2007)	Sweden	120	84	81
Cadossi[35] (2013)	Italy	96	75	83
Chammout[10] (2019)	Sweden	120	75	86
Dorr[36] (1986)	U.S.A.	89	65	69
Iorio[8] (2019)	Italy	60	58	83
Keating[37] (2006)	Scotland	138	77	75
Macaulay[38] (2008)	U.S.A.	40	53	79
Mouzopoulos[27] (2008)*	Greece	129	78	74
Parker[9] (2019)	U.K.	105	81	77
Ren[28] (2017)	China	100	45	70
Sharma[29] (2016)	India	80	55	76
Skinner[30] (1989)*	U.K.	278	90	81
Sonaje[31] (2018)	India	42	68	66
van den Bekerom[32] (2010)	Netherlands	252	81	81

*The study had 3 arms, 1 of which was internal fixation. That arm is reflected in the total sample size shown here, but patients in the internal fixation arm were excluded from all analyses in this review.

Questionnaire[37], 2 studies reported the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[7,38], and 3 studies reported the HHS[10,27,31]. The pooled estimate favored THA but the CI included the possibility of a very small benefit for HA (MD = 3.06, 95% CI = −0.37 to 6.49) (Fig. 3). The best MID estimate for the HHS was determined to be 8 points, and

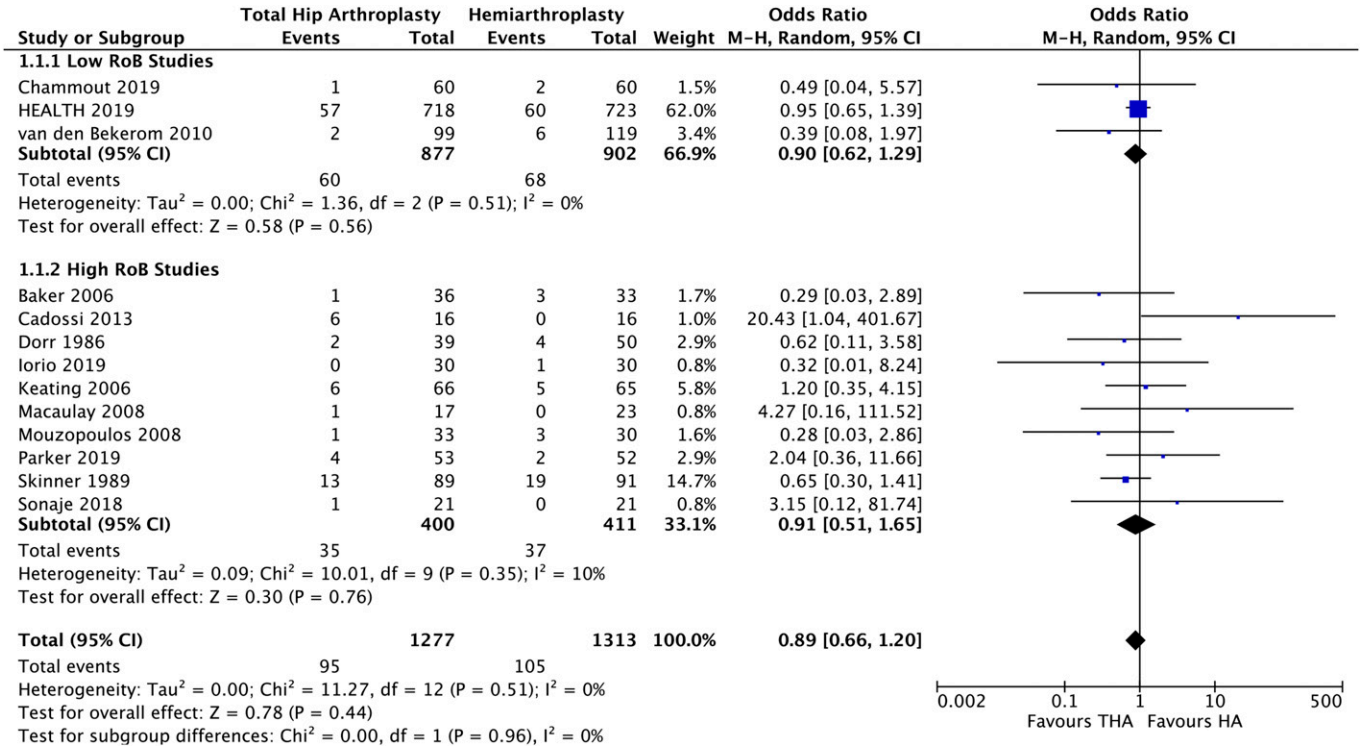

Fig. 2

Forest plot of revision surgery. MH = Mantel-Haenszel, and RoB = risk of bias.

TABLE II GRADE Evidence Profile*

Outcome	Follow-up Range (mo)	Studies (Patients)	Certainty Assessment					Effect, THA vs. HA (95% CI)		Certainty of Evidence	Summary
			Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias				
Revision surgery	12-60	13 (2,590)	No serious limitation	No serious limitation	No serious limitation	Some limitation†	No serious limitation	OR: 0.89 (0.66 to 1.20)	8 fewer per 1,000 (26 fewer to 14 more)	Moderate	THA likely results in little to no difference in revision surgery compared with HA
Functional outcomes (HHS units)	12-36	6 (1,022)	No serious limitation	No serious limitation	No serious limitation	Some limitation‡	No serious limitation	RD: 8.0% greater (4% less to 20% greater) probability of reaching MID	MD (HHS)§: 3.06 (−0.37 to 6.49)	Moderate	THA likely results in little to no difference in function compared with HA
HRQoL (EQ-5D units)	12-36	5 (1,164)	No serious limitation	No serious limitation	No serious limitation	Some limitation‡	No serious limitation	RD: 8.5% greater (0.4% less to 17.3% greater) probability of reaching MID	MD (EQ-5D)#: 0.05 (0.02 to 0.07)	Moderate	THA likely improves HRQoL slightly compared with HA, although MD is less than MID
Mortality	12-60	11 (2,522)	No serious limitation	No serious limitation	No serious limitation	Serious limitation†	No serious limitation	OR: 0.98 (0.79 to 1.22)	3 fewer per 1,000 (27 fewer to 27 more)	Moderate	THA likely results in little to no difference in mortality compared with HA
Dislocation	12-60	12 (2,427)	No serious limitation	No serious limitation	No serious limitation	Serious limitation†	No serious limitation	OR: 1.40 (0.51 to 3.84)	11 more per 1,000 (14 fewer to 75 more)	Moderate	THA likely results in little to no difference in risk of dislocation compared with HA
Periprosthetic fracture	12-36	7 (1,953)	No serious limitation	No serious limitation	No serious limitation	Serious limitation†	No serious limitation	OR: 1.14 (0.73 to 1.78)	5 more per 1,000 (10 fewer to 28 more)	Moderate	THA likely results in little to no difference in periprosthetic fracture compared with HA
Operative time		7 (605)	No serious limitation	Serious limitation**	No serious limitation	No serious limitation	No serious limitation	Weighted mean for HA: 68.2 min	MD (min): 21.7 (8.7 to 34.8)	Moderate	HA likely results in a reduction in operative time compared with THA

*THA = total hip arthroplasty, HA = hemiarthroplasty, CI = confidence interval, OR = odds ratio, RD = risk difference, MD = mean difference, HHS = Harris hip score, HRQoL = health-related quality of life, EQ-5D = EuroQol-5 Dimensions, and MID = minimally important difference. †Rated down due to differing conclusions at extremes of CIs. ‡Rated down due to wide CI around RD. §MID for HHS: 8 points. #MID for EQ-5D: 0.145. **Rated down due to high heterogeneity.

the RD calculation revealed that patients in the THA group had an 8.0% higher (95% CI = 3.6% lower to 19.6% higher) probability of having an outcome that exceeded the MID threshold. The GRADE certainty of evidence was rated as moderate for functional outcomes, being rated down 1 level for imprecision given the wide CI around the RD estimate (Table II). Appendix 4 contains a risk-of-bias assessment specific to functional outcome.

HRQoL

Six studies reported on the HRQoL outcome at 1 to 3 years of follow-up[7,10,27,33,37,38]. Three studies used the EQ-5D[7,10,37], 2 used the Short Form-36 (SF-36)[33,38], and 1 used the Barthel Index[27]. One study did not provide the SD or enough other information to allow estimation of the SD. The pooled analysis of the remaining 5 studies[7,10,28-30] (n = 1,164) revealed a significant benefit in favor of THA, although the effect size was small (MD = 0.05, 95% CI = 0.02 to 0.07, p = 0.001) (Fig. 4). The best MID estimate for the EQ-5D was determined to be 0.145, and the RD calculation revealed that patients in the THA group had an 8.5% higher probability of having an outcome that exceeded the MID threshold. The GRADE certainty of evidence was rated as moderate for HRQoL, being rated down 1 level for imprecision given the wide CI around the RD estimate (Table II). Appendix 5 contains a risk-of-bias assessment specific to HRQoL.

Mortality

Eleven studies (n = 2,522) reported on mortality at 1 to 5 years of follow-up[7-10,27,30,32-35,38]. The pooled estimate for THA compared with HA revealed an OR of 0.98 (95% CI = 0.79 to 1.22, p = 0.87), with no heterogeneity (I^2 = 0%, Appendix 6). The GRADE certainty of evidence was rated as moderate for mortality,

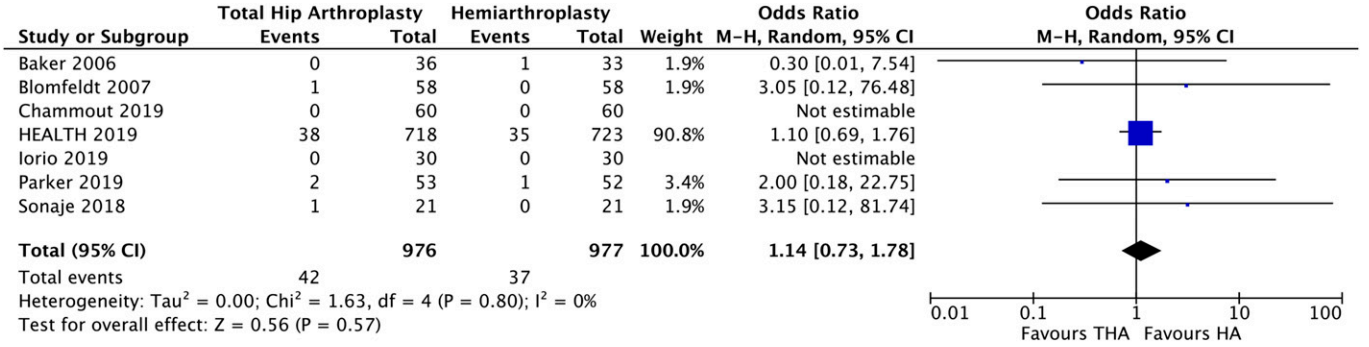

Fig. 3

Forest plot of functional outcomes. IV = inverse variance.

being rated down 1 level due to imprecision (Table II). Appendix 7 contains a risk-of-bias assessment specific to mortality.

Dislocation

Twelve studies (n = 2,427) reported on the dislocation rate at 1 to 5 years of follow-up[7-10,29,31-34,36-38]. The CI around the pooled estimate included a reduction of almost 50% with THA and an almost quadrupling of the rate with THA (OR = 1.40, 95% CI = 0.51 to 3.84, p = 0.52), with moderate heterogeneity (I^2 = 56%, Appendix 8). The GRADE certainty of evidence was rated as moderate for dislocation, being rated down 1 level due to concern regarding imprecision (Table II). Appendix 9 contains a risk-of-bias assessment specific to dislocation.

Periprosthetic Fracture

Seven studies (n = 1,953) reported periprosthetic fracture data at 1 to 3 years of follow-up[7-10,31,33,34]. The pooled estimate of the OR for THA compared with HA was 1.14 (95% CI = 0.73 to 1.78, p = 0.57), with minimal heterogeneity (I^2 = 0%, Appendix 10). The GRADE certainty of evidence was rated as moderate for periprosthetic fracture, being rated down 1 level due to imprecision (Table II). Appendix 11 contains a risk-of-bias assessment specific to periprosthetic fracture.

Operative Time

Seven studies reported on operative time (n = 605)[8-10,28,31,37,38], with 5 studies finding a significant benefit in favor of HA[8,10,28,31,37]. The pooled analysis comparing THA with HA found a mean difference of 21.7 minutes (95% CI = 8.7 to 34.8 minutes, p = 0.001), with high heterogeneity (I^2 = 97%, Appendix 12). Given that the upper boundary of this CI (35 minutes) was shorter than the shortest reported mean operative time for any operation in the included studies (48 minutes), we concluded that, even in the best-case scenario, the shorter operative time associated with HA would not allow for the addition of 1 extra case of similar length and was thus unimportant. The GRADE certainty of evidence was rated as moderate for operative time, being rated down 1 level for inconsistency given the high level of heterogeneity (Table II). Appendix 13 contains a risk-of-bias assessment specific to operative time.

Subgroup Analysis

The 3 studies that met our predefined criteria for low risk of bias accounted for 60% of the total sample size (1,836 of 3,071)[7,10,32]. The subgroup analysis did not affect the conclusions for revision surgery, mortality, or dislocation (Fig. 2 and Appendices 6 and 8, respectively).

Discussion

This systematic review and meta-analysis, which incorporates all available RCT evidence, demonstrates results that are consistent across the large body of the evidence to date[7]. Based on the findings of this review, it is likely (moderate-certainty evidence) that there is no clinically important difference between HA and THA in terms of revision rate at up to 5 years of follow-up or function, dislocation, periprosthetic fracture, or mortality at up to 3 years. There is likely a small difference in HRQoL favoring THA and a small difference in operative time favoring HA that may, or may not, be important.

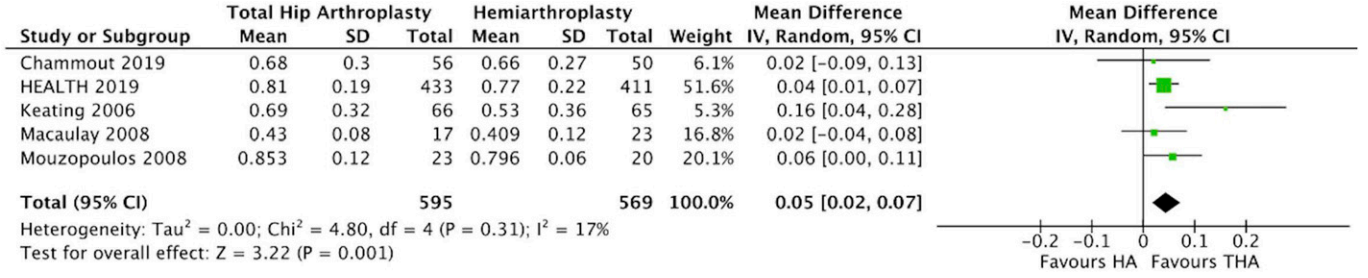

Fig. 4

Forest plot of health-related quality of life, presented as EQ-5D index values. IV = inverse variance.

Duration of follow-up did not appear to influence the revision rate or functional outcome.

With regard to patients' daily function, the point estimate for functional outcome, assessed in terms of the HHS, favored THA. The CI, however, overlapped no effect, and the estimated effect was less than the MID of 8 for the HHS. The results, therefore, provide scant support for the use of THA in ambulatory patients in order to achieve a benefit in function in the short to medium-term. The pooled estimate did reveal a significant but small benefit in favor of THA with regard to HRQoL; the effect on the EQ-5D of 0.05, less than a third of the MID of 0.145. Taking into account possible differences in effect across patients suggests that the best estimate of the proportion of patients who achieve a benefit from the choice of THA in terms of HRQoL equal to at least the MID is 8.5%.

It will be interesting to assess whether the publication of a recent large RCT, along with the present systematic review and meta-analysis, will have any impact on practice patterns. A study using the Medicare administrative database found that there was relatively little change in the management of femoral neck fractures (including nondisplaced fractures) between 1991 and 2008, with the majority (>60%) already being treated with HA[39]. Another, more recent study found similarly consistent rates of HA across time, although with small but significant increases in THA utilization[40]. It will be important to assess practice patterns over the coming years to determine if the weight of evidence has any impact on actual practice patterns.

The strengths of this study include the prospective protocol design and registration, explicit eligibility criteria, a comprehensive search of the relevant literature, assessment of eligibility and risk of bias in duplicate, and exploration of possible subgroup effects related to risk of bias and duration of follow-up. In addition, we conducted sophisticated analyses of patient-reported outcomes that made optimal use of available evidence and related the results to the MIDs while also looking at the proportion of patients who might obtain an important benefit.

The limitations of this study include the limited data for assessment of functional and HRQoL outcomes, as well as the limited availability of long-term follow-up studies. However, given the high mortality rate associated with hip fractures, the long-term studies that do exist have very high attrition rates. The high rate of loss to follow-up in long-term studies leads to high risk of bias, and thus assessing long-term complications is not appropriate when >30% of the patients in the initial study population are not available for follow-up[23-26].

Future Directions

A cost-utility analysis based on evidence from this meta-analysis would likely provide important additional evidence. At this point, given that we have moderate-quality evidence for the key outcomes and that differences, if present, are likely to be small or very small, further study of this question may be a poor use of limited research resources. There may, however, be a role for comparing these 2 interventions specifically in a younger, more active population with longer-term follow-up.

Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJS/G49). ■

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