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Effectiveness and safety of cemented and uncemented hemiarthroplasty for the treatment of intracapsular hip fractures: a systematic review and meta-analysis of randomised controlled trials

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Abstract

Aims: We conducted a systematic review and meta-analysis to compare mortality, morbidity and functional outcomes of cemented versus uncemented hemiarthroplasty (HA) for the treatment of intracapsular hip fractures, analysing contemporary and non-contemporary prostheses separately.

Methods: PubMed, Medline, EMBASE, CINAHL and Cochrane Library were searched to 02/Feb/2020 for randomised controlled trials (RCTs) comparing the primary outcome, mortality and secondary outcomes: function, quality of life, reoperation, post-operative complications, peri-operative outcomes, pain and hospital stay. Relative risks (RRs) and mean differences (with 95% confidence intervals, CIs) were used as summary association measures.

Results: 18 articles corresponding to 16 non-overlapping RCTs comprised 2,819 intracapsular hip fractures. Comparing contemporary cemented vs. uncemented HA, RRs (95% CIs) for mortality were 1.32 (0.44-3.99) perioperatively, 1.01 (0.48-2.10) at 30 days and 0.90 (0.71-1.15) at 1 year. Contemporary cemented HA reduced intraoperative and postoperative periprosthetic fracture risk. There were no differences in the risk of other complications, function, pain, and quality of life. Except for increases in duration of surgery and overall anaesthesia for contemporary cemented HA: mean differences (95% CIs) of 6.67 (2.65, 10.68) and 4.90 (2.02, 7.78) minutes respectively, there were no differences in perioperative outcomes. Morbidity and mortality outcomes were not different between non-contemporary cemented and uncemented HA.

Conclusions: There are no differences in mortality risk when comparing contemporary cemented with uncemented HA for the management of intracapsular hip fractures. Contemporary cemented HA is associated with a substantially lower risk of intraoperative and periprosthetic fractures.

Keywords cemented; uncemented; hemiarthroplasty; hip fracture; mortality; complication; systematic review, meta-analysis

Clinical relevance of paper

- In patients treated for an intracapsular hip fracture, contemporary cemented hemiarthroplasty does not increase the risk of mortality perioperatively, at 30 days or 1 year when compared to uncemented hemiarthroplasty.
- Cemented hemiarthroplasty does increase the duration of surgery and overall duration of anaesthesia in comparison to uncemented hemiarthroplasty but there are no differences in other outcomes of interest such as complications, function, pain, and quality of life.

Introduction

Globally, hip fractures are expected to rise from 1.66 million in 1990 to an estimated 6.26 million per year in 2050¹ with 76,000 hip fractures occurring annually in the UK.² They are associated with significant mortality and disability, constituting a major public health problem and in 2017, hip fractures cost the National Health Service (NHS) £1 billion, 1% of its budget.³

60% of hip fractures are intracapsular of which over 80% are displaced.³ Surgical management of displaced intracapsular hip fractures commonly involves hemiarthroplasty (HA) or total hip replacement (THR),⁴ with HA recommended in the elderly, cognitively impaired and less mobile population.⁵ Variations within treatments for HA include surgical approach, prosthesis head and type and stem fixation. Whether stem fixation affects complication rates differentially following HA is controversial, due to inconsistent findings from randomised controlled trials (RCTs).

Previous reviews have shown cemented HA to be associated with longer operation times and fewer implant-related complications.⁶⁻¹⁰ Some reviews have shown equivalent pain outcomes,⁸ blood loss,^{6,8} and risk of general complications⁶⁻⁸ but others have shown less residual pain^{6,7,11} but greater blood loss with cemented HA¹² and more complications with uncemented HA.⁹ Previous reviews are limited by, first, inclusion of old studies of non-contemporary prostheses. Second, the majority were based on pooled analysis of very few trials, reducing power to make effective comparisons. Third, inappropriate pooling of the results of RCTs and observational studies. Fourth, few outcomes were considered. Finally, several new trials which utilize newer (contemporary) implants have been published since the last relevant review.

Given the persisting uncertainties, we aimed to assess the comparative effectiveness and safety of contemporary cemented and uncemented HA for the treatment of intracapsular hip fractures using an updated systematic review and meta-analysis which included all relevant RCTs published to date. In a subsidiary analysis, we also compared outcomes between non-contemporary cemented and uncemented HA.

Methods

Data sources and search strategy

We conducted this review using PRISMA and MOOSE guidelines^{13,14} (**Supplementary Materials 1-2**). The protocol was pre-defined and registered (PROSPERO: CRD42016047785). PubMed, Medline, Embase, CINAHL, Web of Science and Cochrane Library were searched from inception to 02 February 2020 by combining relevant MeSH search terms and key words related to the population (e.g., “hip fracture”, “femoral neck fracture”) and intervention (e.g., “hemiarthroplasty”, “cemented”, “uncemented”) (MEDLINE search strategy: **Supplementary Material 3**). Searches were restricted to human studies with no language restrictions. Initial screening of all retrieved titles and abstracts was performed by one reviewer (NNK), followed by full text acquisition and detailed evaluation, performed by two independent reviewers (NNK and SKK). Reference lists of relevant review articles and included studies were manually assessed to identify additional papers.

Eligibility criteria

Eligible studies were RCTs that: (i) recruited adult patients with a non-pathological (not primary or metastatic malignant lesions) intracapsular hip fracture; (ii) compared cemented with uncemented fixation of HA (or vice versa); and (ii) reported the primary outcome of mortality (peri-operative, 30 day and 1 year) or any of the secondary outcomes –measures of function or quality of life [Harris Hip Score (HHS), Physical Activities of Daily Living (PADL), Instrumental Activities of Daily Living (IADL), Short Musculoskeletal Function Assessment Questionnaire (SMFA), Timed-Up-and-Go (TUG), SF-12, EQ-5D], revision, reoperation, post-operative complications [pneumonia, thromboembolic events (deep vein thrombosis (DVT) and/or pulmonary embolism (PE), cardiovascular (CV) complications, deep or superficial infection, fracture, dislocation, urinary tract infection, cardiac arrest and haematoma], peri-operative details (e.g. duration of surgery and anaesthesia, blood loss, blood transfusion), pain and length of hospital stay.

Implant definition

Implant stems were classified as contemporary or non-contemporary based on a pragmatic approach using details of implants used for elective THR published in the National Joint Registry (NJR). Implant stems were

classified as contemporary if they were implanted as part of an elective THR construct and recorded in the NJR in 2018.¹⁵

Data extraction and quality assessment

One reviewer (NNK) extracted information from eligible RCTs into a standardised data collection spreadsheet. A second (SKK) and third reviewer (ED) independently checked extracted data with that in the original papers. The first author's name, year of publication, country and geographical location, baseline year of recruitment, mean or median age, type of surgical treatment and characteristics, sample size, operation details, duration of follow-up and outcome data were extracted. When the same study was described in multiple publications, the most comprehensive paper was used, or non-overlapping data was extracted. Bias was assessed with the Cochrane Collaboration's risk of bias tool.

Statistical analyses

Summary measures were presented as mean differences (95% confidence intervals, CIs) for continuous outcomes and relative risks (RRs) (95% CIs) for binary outcomes. Hazard ratios and odds ratios were assumed to approximate the same measure of RR following Cornfield's rare disease assumption.¹⁶ Relative risks were calculated from the extracted raw counts. For data reported as medians, ranges, and 95% CIs, means and standard deviations were calculated.¹⁷ Random-effects models were used to combine RRs to minimize the effect of heterogeneity.¹⁸ Where appropriate, fixed effects models were used in parallel analyses. Heterogeneity was assessed using the Cochrane χ^2 statistic and the I^2 statistic.¹⁹ Publication bias was evaluated through funnel plots and Egger's regression symmetry tests.²⁰ The statistical analyses employed STATA release 16 (Stata Corp, College Station, Texas, USA).

Results

Study identification and selection

The search strategy and manual screening identified 9,127 potentially eligible articles. Following initial screening of abstracts, there remained 135 articles for full text evaluation. Following detailed evaluation, 117 articles were excluded because (i) exposure was not relevant (n=8); (ii) based on reviews and letters (n=22); (iii) no appropriate control group (n=11); (iv) population not relevant (n=1); (v) duplicates of included studies (n=6); (vi) outcomes not relevant (n=6); (vii) full texts not obtainable (n=11); (viii) were not RCTs (n=52). Eighteen articles corresponding to 16 non-overlapping RCTs were included (**Figure 1**).²¹⁻³⁸ Two articles were based on follow-up data of previous trials and three were based on published abstracts.

Study characteristics and quality

Publication dates ranged 1982-2020 (**Table 1**). The 16 RCTs included 2,819 intracapsular hip fractures. Thirteen were conducted in Europe (Croatia, Denmark, Italy, Netherlands, Norway, Sweden, UK), 2 in North America (USA) and 1 in Oceania (New Zealand). The average baseline age of participants ranged from 69.0 to 85.2 years; the weighted mean was 82.8 years. The average follow-up ranged from 1 to 5 years, with a weighted mean of 1.8 years.

One trial demonstrated a high risk of bias within two domains (random sequencing and allocation concealment), the other 15 trials had unclear to low risk of bias. 5 trials had a high risk of bias in blinding of participants and personnel. 2 trials had high risk of bias in blinding of outcome assessment. All trials had an unclear or low risk of bias in incomplete outcome data, selective reporting and other bias (**Supplementary Material 4**).

Contemporary comparison

Mortality: In pooled analysis of five studies, the RR (95% CI) of mortality at 1 year comparing contemporary cemented vs. contemporary cemented HA was 0.90 (0.71-1.15) (**Figure 2**) with no evidence of significant study heterogeneity ($I^2=13\%$; 95% CI: 0-82%; $p=0.33$). Perioperatively the RRs for mortality were 1.32 (0.44-3.99) in 4 studies and 1.01 (0.48-2.10) at 30 days in 3 studies (**Figure 2**).

Other complications: In pooled analysis of 5 studies, the RR (95% CI) of any complications was 0.74 (0.51-1.06) (**Figure 3**). There was evidence of substantial heterogeneity ($I^2=74\%$; 95% CI: 35-90%; $p=0.004$). The corresponding RRs for infection (deep and superficial; 5 studies) were 0.76 (0.40-1.46), for re-operation (5 studies) 0.73 (0.36-1.48), for dislocation (3 studies) 1.03 (0.37-2.84) and revision to THR (2 studies) 0.48 (0.15-1.51) with no evidence of heterogeneity. Contemporary cemented HA was associated with a reduced risk of periprosthetic fractures: RRs of 0.27 (0.13-0.57) for intraoperative fracture and 0.19 (0.07-0.50) for postoperative fracture. The corresponding RR for cardiovascular complications in pooled analysis of 5 studies was 1.13 (0.58-2.21), with no differences in risk of DVT or PE based on findings from a single study (**Supplementary Material 6**).

Measures of function: Comparing contemporary cemented vs. contemporary uncemented HA, there was no difference in the risk of living in their own home postoperatively (3 studies); RR of 1.06 (0.91-1.24) (**Supplementary Material 9**). Single reports showed no significant differences in the risk of walking independently, assisted living, discharge to a rehabilitation facility, or ambulation assistance (**Supplementary Material 9**). There was no difference in HHS (2 studies); mean difference of 1.11 (-2.20, 4.42). There were no differences in other continuous measures of function; however, contemporary cemented HA was associated with a decrease in SMFA dysfunction and bother scores and better recovery of mobility in single reports (**Supplementary Material 10**).

Measures of pain: Comparing contemporary cemented vs. contemporary uncemented HA, results from single reports showed no differences in the risk of not needing pain medication and residual (at least 6 weeks after operation) pain (**Supplementary Material 9**) or HHS pain subscore (**Supplementary Material 13**).

Quality of life: Comparing contemporary cemented vs. contemporary uncemented HA, results from single reports showed no differences in quality of life scores (**Supplementary Material 13**).

Perioperative outcomes: There was no difference in the risk of receiving a blood transfusion between contemporary cemented and contemporary uncemented HA (3 studies): RR of 0.93 (0.74-1.17) (**Supplementary Material 14**). Duration of surgery was increased for contemporary cemented HA [mean difference of 6.67 (2.65-10.68) min] (**Figure 4**) and overall duration of anaesthesia (2 studies): mean difference of 4.90 (2.02, 7.78) min (**Supplementary Material 17**). There were no significant differences in blood loss or hospital stay: mean differences of 5.28 (-23.00, 33.57) ml and -0.64 (-2.25, 0.96) days respectively (**Supplementary Materials 15-16**).

Non-contemporary comparison

Mortality and other complications: Comparing non-contemporary cemented vs. non-contemporary uncemented HA, RRs of mortality perioperatively (2 studies) and at 1 year (5 studies) were 1.22 (0.34-4.37) and 0.87 (0.71-1.08) respectively (**Supplementary Material 5**). A single report showed lower risk of intraoperative fractures with non-contemporary cemented HA but no differences for other complications (**Supplementary Materials 7-8**).

Measures of function: A single report showed a decreased risk of ambulation assistance for non-contemporary cemented HA but there were no differences in the risk of living in their own home postoperatively (2 studies) or assisted living (2 studies) (**Supplementary Material 11**). Results from single reports showed an increase in HHS, there were no differences in total functional score (**Supplementary Material 12**).

Measures of pain: There was no difference in residual pain, RR of 0.76 (0.46-1.23) (4 studies: **Supplementary Material 11**) for the non-contemporary comparison. Results from a single reports showed an increased risk of not needing pain medication and a significant decrease in residual pain for non-contemporary cemented HA; mean difference of -0.40 (-0.65, -0.15). (**Supplementary Material 11**).

Perioperative outcomes: There was an increased duration of surgery for non-contemporary cemented HA [mean difference of 9.30 (5.98, 12.62) min] (4 studies; **Supplementary Material 18**) and an increase in

overall duration of anaesthesia (**Supplementary Material 20**). There was no difference in hospital stay in pooled analysis of 4 studies [mean difference of 13.04 (-15.54, 41.62) days] (**Supplementary Material 19**). There was no difference in the amount of blood transfused: mean difference of 0.12 (-0.04, 0.27) units (2 studies; **Supplementary Material 20**) and in one study, no difference in blood loss.

Discussion

Main findings

We conducted an updated meta-analysis based on all RCTs conducted to date and a comprehensive list of outcomes to evaluate the effectiveness and safety of contemporary cemented HA compared with contemporary uncemented HA for the treatment of intracapsular hip fractures. There were no differences in mortality risk perioperatively up to 1 year postoperatively. Contemporary cemented HA reduced the risk of intraoperative (RR of 0.27 (95% CI: 0.13-0.57) and postoperative periprosthetic fractures (RR of 0.19 (95% CI: 0.07-0.50), however, it increased the durations of surgery (mean difference 6.67 (2.65-10.68) min) and overall duration of anaesthesia (mean difference of 4.90 (2.02, 7.78) min). Contemporary cemented HA appeared to improve post-operative function, but these findings were based on findings from single trials, otherwise there were no significant differences demonstrated for complications and most measures of function, pain and quality of life. In the secondary analysis of non-contemporary cemented and uncemented HA, morbidity and mortality outcomes were not different.

Comparison with previous work

Unlike previous reviews, we have compared outcomes separately for contemporary and non-contemporary implants and reported new findings. The majority of previous reviews in this area evaluated mortality at one-year or at undefined time points,^{7,8,10,11} whereas our review evaluated multiple time points (peri-operative, 30-day, 1 year). The finding of longer operative time associated with cemented HA is consistent with previous reviews,^{6-8,10,12} as are no significant differences in complications such as infection and dislocation.^{6,10} In a 2019 review based on 4 RCTs and 6 observational studies, lower pooled reoperation and revision rates for cemented HA were reported.¹¹ In our study, based on more RCTs, we showed no significant differences. New findings include no significant differences in vascular complications (e.g. adverse cardiovascular outcomes) and thromboembolic events. We reported on a more comprehensive panel of measures of function, pain and quality of life than any previous review.

Possible explanations for findings

It has been suggested that cemented HA may increase the risk of mortality due to higher incidence of cardiopulmonary complications (e.g., hypoxaemia, PE, hypotension etc),³⁹ but our findings indicate otherwise. The increased surgical and overall duration of anaesthesia associated with cemented HA is attributed to the time spent on femoral preparation and cementing, with better functional recovery attributed to better primary stability, reduced aseptic loosening, pain and enhanced ambulation.⁴⁰ The increased risk of periprosthetic fractures associated with uncemented stems has been reported to result from fracture during femoral broaching, stem insertion or failure of osseointegration.

Implications of findings

For the majority of measures of effectiveness and safety, outcomes for contemporary prostheses appear to be equivalent. However, contemporary cemented HA reduced the risk of both intraoperative and postoperative periprosthetic fractures, a significant source of morbidity due to increased surgical time, high morbidity revision or fixation procedures, exposure to anaesthesia and risk of neurovascular damage.⁴¹ Contemporary cemented HA improved some measures of function, but only in single studies. There have been concerns that cement insertion could cause an increased risk of cardiovascular complications;^{39,42} however, we did not find evidence of this. Contemporary cemented HA was associated with increased operating time and overall duration of anaesthesia; lower operative and anaesthetic times could result in an overall cost savings of 18.6% for uncemented HA.⁴³ Uncemented prostheses are reported to be cheaper,^{9,44} but this typically assumes non-contemporary designs are used. Similarly, non-contemporary cemented implants are reported to be cheaper than their contemporary counterparts and there is some evidence reporting equivalent health related quality of life for the Thompson's prosthesis.⁴⁵

Taking the overall evidence together, it appears cemented HA may be more advantageous in terms of clinical effectiveness and safety but a formal cost effectiveness study has not been performed. A health economic analysis comparing contemporary cemented with contemporary uncemented hemiarthroplasty in hip fracture is anticipated when the WHITE 5 trial reports its findings.^{46,47}

Strengths and limitations

The current review has several strengths in comparison to the most recent review.¹⁰ We compared outcomes separately for contemporary and non-contemporary implants, taking into account the evolving nature of implant designs and surgical procedures. There was enhanced power to evaluate associations given the inclusion of additional RCTs. We reported on a comprehensive list of outcomes, employing appropriate meta-analytic approaches, including harmonisation of data to a consistent comparison to ensure pooling, sensitivity analyses to ensure robustness of the results, and quantification of heterogeneity. Finally, there was very little evidence of heterogeneity between contributing studies for the majority of outcomes evaluated. There were a number of inherent limitations: (i) several different measures of pain, function and quality of life were used in different reports; (ii) a number of included trials had a high risk of bias in at least one domain; and (iii) limited number of studies (<10) for the majority of outcomes precluded assessment of effect modification and small study bias.

Conclusion

There are no differences in mortality risk when comparing contemporary cemented with uncemented HA for the management of intracapsular hip fractures. Contemporary cemented HA is associated with a substantially lower risk of intraoperative and periprosthetic fractures but is associated with increased durations of surgery and anaesthesia. We found no evidence of a difference in morbidity and mortality outcomes between non-contemporary cemented and uncemented HA.

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Figure Legends

Figure 1. PRISMA flow diagram

RCT, randomised controlled trial

Figure 2. Risk of mortality at specific time-points comparing contemporary cemented versus contemporary uncemented hemiarthroplasty

CI, confidence interval (bars); RR, relative risk

Figure 3. Risk of complications comparing contemporary cemented versus contemporary uncemented hemiarthroplasty

CI, confidence interval (bars); RR, relative risk

Figure 4. Contemporary cemented versus contemporary uncemented hemiarthroplasty and duration of surgery

CI, confidence interval (bars)