

A systematic review and meta-analysis comparing arthroplasty and internal fixation in the treatment of elderly displaced femoral neck fractures

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Abstract

Background: Currently, there are 2 mainstream treatments for displaced femoral neck fracture, including internal fixation and arthroplasty. However, there are still some controversial problems as to which treatment should be primarily chosen.

Methods: The relevant studies comparing arthroplasty with internal fixation were searched in the databases of PubMed, Embase, and Cochrane Library. Finally, 31 relevant randomized controlled trials were included in this meta-analysis. The quality of studies was evaluated and meta-analyses were performed using RevMan 5.3 software. We also assessed the heterogeneity among studies and publication bias via the I-squared index and forest plots.

Results: There was no significant difference between arthroplasty and internal fixation groups in patient mortality at both short-term and long-term points. However, patients treated with arthroplasty showed significantly lowered risks of reoperation both at short-term (5.6% vs 31.5%; relative risks (RR) = 0.19; 95% CI, 0.13–0.28; $P < .00001$) and long-term follow-up (9.5% vs 45.9%; RR = 0.23; 95% CI, 0.17–0.33; $P < .00001$). Similarly, arthroplasty-treated patients demonstrated a significant decrease in the risk of postoperation complications at short-term (10.3% vs 34.4%; RR = 0.37, 95% CI, 0.24–0.57; $P < .00001$) and long-term follow-up (11.7% vs 42.5%; RR = 0.30, 95% CI, 0.16–0.57; $P < .0002$). Besides, patients in the arthroplasty group were associated with better alleviation of pain postoperation (18.3% vs 31.1%; RR = 0.50, 95% CI, 0.33–0.78; $P = .002$).

In trial sequence analyses, all cumulative Z curves except that of mortality crossed the trial sequential monitoring boundaries and conventional boundaries, and required information size has been reached.

Conclusions: Arthroplasty leads to a lower rate of reoperation, a reduced risk of complications, and a better alleviation of postoperation pain both at short-term and long-term follow-up. Most importantly, and according to trial sequence analyses, more than enough evidence has been achieved that arthroplasty does show better outcomes than internal fixation in terms of reoperation rate, complications, and postoperation pain.

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

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JD, GW, and JL should be considered co-first authors as they contributed equally to this paper.

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1. Introduction

With the growing number of the geriatric population and traffic accidents, patients with femoral neck fractures have been on the rise in the last 2 decades or 3.^[1] Every year, about 1,600,000 individuals worldwide suffer from this kind of fracture and this number will continue to rise to 6.26 million by 2050.^[2,3] Moreover, femoral neck fractures are usually characterized by the high incidence of nonunion and femoral head necrosis, which, therefore, result in a sharp increase in the morbidity and disability rate.^[4]

Although there is a wide range of treatments that are currently available for those patients with displaced femoral neck fractures, arthroplasty (AR), including total hip arthroplasty (THA) and hemiarthroplasty (HA), and internal fixation (IF) are still the 2 primary alternatives. As for those young patients with good bone quality and good health, treatment of reduction with IF would be strongly recommended in most cases. However, for the elderly patients, the best option is still far from definite, so both AR and IF have been widely used in the treatment of displaced neck fractures.^[5] On the one hand, AR is currently becoming increasingly popular amongst orthopaedists for its significantly lower incidence of reoperation rate and rapid functional

recovery.^[6,7] Nevertheless, AR, which involves extensive soft tissue dissection, also leads to prosthetic loosening,^[8,9] dislocation,^[10] and infection.^[11] On the other hand, IF with screws and plates has been reported to be of significant advantage in terms of minor trauma, less blood loss, and shorter operative time, and is more likely to preserve the femoral head.^[12,13] However, its disadvantages are apparent as well, such as the high incidence of nonunion and femoral head necrosis.^[7] Therefore, despite an increasing number of studies on femoral neck fracture, it is still controversial regarding the optimal way of treating elderly patients.^[14]

In order to provide more recent and convincing evidence for the treatment of displaced femoral neck fractures, we performed the meta-analysis including more recent randomized controlled trials (RCTs) to evaluate mortality, reoperation rate, complications, and pain between patients treated either by AR or by IF.^[15–19] In addition, a trial sequential analysis (TSA) was used to determine whether there had been enough proof to convince us of the best option between AR and IF.

2. Materials and methods

2.1. Protocol and registration

This meta-analysis of RCTs was performed according to the preferred reporting items for systematic reviews and meta-analyses recommendations.^[20] A protocol for this meta-analysis has been registered on PROSPERO, and the registration number is CRD42017074991.

2.2. Literature searches

We conducted the literature search to find the papers involved in comparing AR to IF in the treatment of femoral neck fractures. Two independent reviewers systematically searched the electronic database—PubMed (1966 to July 1, 2018), Embase (1974 to July 1, 2018), and the Cochrane Library (1996 to July 1, 2018) with no restriction of language and geography. Our searching strategy involves the different combinations of search terms, including femoral neck fractures, AR, IF, and their respective alternatives. Also, we performed a manual search to identify relevant studies.

2.3. Inclusion criteria and exclusion criteria

Studies were included if they met the following eligibility criteria: RCTs, subjects older than 60 with femoral neck fractures (Garden Stage III or IV), studies comparing AR with IF, clinical outcomes including at least one of the following: mortality, reoperation rate, and complications.

Exclusion criteria: non-RCTs; studies did not focus on the displaced hip fracture; review articles, letters, conference abstracts, and case reports.

2.4. Data extraction

Two authors independently screened all available and relevant data from the included studies. The following characteristics were extracted: name of the first author, publication year, interventions and the number of patients both in AR and IF groups, the follow-up years, as well as the clinical results including mortality rate, reoperation rate, and complications (such as fixation failure, dislocation, nonunion, peri-prosthetic fractures, femoral head necrosis, infection, etc.).

2.5. Data synthesis

The primary outcome was the short-term (within 5 years) and long-term (over 5 years) mortality, reoperation risk, complication rate, and pain after the treatment, IF or AR. The secondary outcomes included the TSA results as well as the sensitivity analysis results.

2.6. Risk of bias and methodological quality assessment

We assess the methodological quality of each study based on The Cochrane Collaboration's tool.^[21] We primarily evaluated the following parts: randomization, allocation concealment, blinding, incomplete outcome data, and selective reporting. If there were any disagreement, we would discuss them again, and differences were resolved by a third reviewer. We also used GRADEpro to evaluate the quality of the eligible studies.^[22]

2.7. Trial sequential analysis

It is widely accepted that a qualified meta-analysis should be at least as good as a high-quality RCT, so rigorous standards for a meta-analysis should not be neglected. We, therefore, used TSA, which is capable of controlling the risks of type I and type II errors and then calculated required information size (RIS) needed by systematic review and meta-analysis, to evaluate the reliability and conclusiveness of the acquired studies on the major results.^[23,24] As previously described,^[25] TSA would create a trial sequential monitoring boundary by adjusting the random errors before the implementation of TSA. Also, the horizontal line of $Z=1.96$ acted as the traditional boundary of statistical significance in the process of TSA. See more details in supplementary file.

2.8. Statistical analysis

We conducted the meta-analysis by RevMan 5.3 software (The Nordic Cochrane Centre, Copenhagen, Denmark). We chose to compare the dichotomized results using RR and corresponding 95% CIs, and compare the continuous data using standard mean difference. Additionally, since both THA and HA were often seen being performed in the AR group, we made comparisons between the THA and IF, and between HA and IF, respectively. Chi-square and I^2 tests were used to check the heterogeneity among studies. If the heterogeneity was lower than 50%, a fixed-effects model was used; otherwise, a random-effects model would be used. Publication bias was evaluated by a funnel plot based on the outcomes.

3. Results

3.1. Included studies and characteristics

A total of 1,352 records were identified through database searching, but 31 studies were included at last for full review and meta-analysis (Fig. 1). Characteristics of the included studies were shown in Table 1.^[8–10,12,13,15–19,26–46] Figure 2 showed the risk of bias in the included trials. The quality assessment analysis indicated that the quality of the primary outcomes was moderate.

3.2. Clinical outcomes

3.2.1. Mortality. Twenty studies, on a total of 2,354 patients in AR group and 1,914 patients in IF group, provided the short-term mortality rate, whereas 14 studies, on a total of 1,391

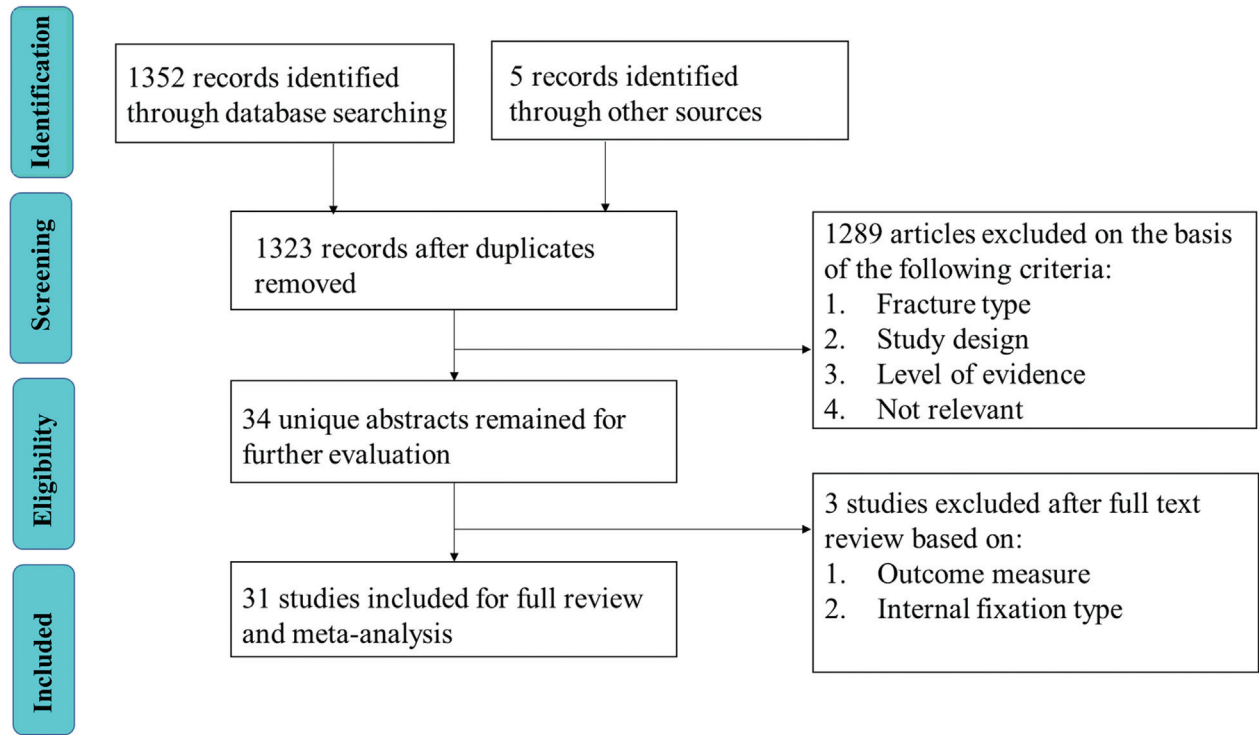


Figure 1. A flow chart of the process of screening literature we applied for this study is shown.

Table 1
Characteristics of included randomized controlled trials.

Study	Year	Interventions		Number of patients		Follow-up months
		Arthroplasty	Internal fixation	Arthroplasty	IF	
Soreide ^[31]	1979	HA	Olmed screws	53	51	14.5
Sikorski ^[10]	1981	HA	Garden screws	114	76	24
Svenningsen ^[33]	1985	HA	Compression screw /McLaughlin nail/ plate	59	110	36
Skinner ^[32]	1989	HA/THA	Sliding compression screws	180	91	12
van Vugt ^[8]	1993	HA	Dynamic hip screw	22	21	36
Jónsson ^[37]	1996	THA	Hansson hook pins	23	24	24
Neander ^[38]	1997	THA	Two parallel Olmed screws	43	57	18
Johansson ^[27]	2000	THA	Two parallel Olmed screws	50	50	24
Ravikumar ^[9]	2000	HA	Two von Bahr screws	47	53	60
vanDortmont ^[39]	2000	HA	Dynamic hip screw	29	28	24
Davison ^[29]	2001	HA	Compression hip screw / two-hole plate	187	93	60
Puolakka ^[40]	2001	HA	Three Ullevaal screws	15	16	24
Parker ^[13]	2002	HA	Three AO screws	229	226	12
Rogmark ^[41]	2002	HA/THA	Hansson hook pins or Olmed screws	192	217	24
Roden ^[42]	2003	HA	Two von Bahr screws	47	53	60
Tidermark ^[35]	2003	THA	Two cannulated screws	49	53	24
Blomfeldt ^[36]	2005	THA	Two cannulated screws	49	53	48
Björgul ^[43]	2006	HA	Olmed screws	455	228	72
Keating ^[28]	2006	HA/THA	Cancellous screws or sliding hip screw	180	118	24
Frihagen ^[12]	2007	HA	Two parallel cannulated screws	110	112	24
Heetveld ^[30]	2007	HA	Screws	109	115	24
Mouzopoulos ^[34]	2008	HA/THA	Richards plate-screw	71	38	48
Leonardsson ^[26]	2010	HA/THA	Hansson hook pins or Olmed screws	192	217	>60
Parker ^[44]	2010	HA	screws	229	226	180
Chammout ^[45]	2012	THA	Two cannulated screws	43	57	>60
Hedbeck ^[46]	2013	HA	Two cannulated screws	29	30	24
Cao ^[17]	2014	THA	Three hollow compression screws	157	128	60
Johansson ^[19]	2014	THA	Screw	68	78	>120
Stoen ^[18]	2014	HA	Screws	110	112	>60
Parker ^[15]	2015	HA	Screw/plate	26	30	12
Lu ^[16]	2017	HA	Cannulated screws	37	41	36.8

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bjergul 2006	+	+			+		
Blomfeldt 2005	+	+	+	+	+		
Cao 2014	+	+			+		
Chammout 2012	+	+			+		
Davison 2001	+	+	+		+		
Frihagen 2007	+	+	+		+		
Hedbeck 2012							
Heetveld 2007	-	+	+	+			
Johansson 2000	+	+			+		
Johansson 2014	+	+			+		
Jónsson 1996	+	+			+		
Keating 2006	+	+	+	+	+		
Leonardsson 2010	+	+			+		
Lu 2017							
Mouzopoulos 2008	+	-	+		+		
Neander 1997	+	+			+		
Parker 2002	+	+			+		
Parker 2010	+	+			+		
Parker 2015							
Puolakka 2001	+	+			+		
Ravikumar 2000	+	+			+		
Roden 2003	+	+			+		
Rogmark 2002	+	+			+		
Sikorski 1981	+	+					
Skinner 1989	-						
Soreide 1979	-						
Stoen 2014	+	+			+		
Svenningsen 1985	-	+			+		
Tidermark 2003	+	+	+	+	+		
van Dortmont 2000	+	+					
van Vugt 1993	+	+			+		

Figure 2. Risk of bias summary: judgements about each risk of bias item for each included study.

patients in AR group and of 1,380 patients in IF group, provided the long-term mortality rate. We found no differences either in short-term mortality (RR=1.07; 95% CI, 0.94–1.20; P=.24) (Fig. 3), or in long-term mortality (RR=1.02; 95% CI, 0.92–1.12; P=.86) (Fig. 4). We chose to use a fixed-effect model as

there was no significant heterogeneity between studies in all groups (P=.24, I²=17%, and P=.86, I²=0%, respectively).

The TSA was conducted in light of short-term and long-term mortality in control group of 19% and 37%, a relative risk increase in the experimental group of 15% and 1%, and diversity of 23% and 0%, respectively. The RIS was 8,204 and 5,449 participants. The cumulative Z curve (blue line) crossed neither the trial sequential monitoring boundaries (red inward slash) nor the conventional boundaries (black dotted line), but it entered the futility area (Fig. S1, <http://links.lww.com/OTAI/A11>). The TSA-adjusted 95% CI of RR was 0.90 to 1.27 and 0.85 to 1.19.

In an effort to provide more details on the effect of different types of AR on mortality, we also compared the short-term and long-term mortality between HA and IF group [14 studies of short-term mortality (labeled as A) and 5 studies of long-term mortality (labeled as B)], and between THA and IF group [(7 studies of short-term mortality (labeled as C) and 3 studies of long-term mortality (labeled as D)]. Similarly, the pooled analysis showed that there was no difference in comparison of the mortality of either THA or hip AR with IF at short-term and long-term follow-ups. Their statistical results were shown in sequence (Figs. 3 and 4): A (RR=1.08; 95% CI, 0.95–1.23; P=.25); B (RR=1.03; 95% CI, 0.90–1.16; P=0.69); C (RR=1.01; 95% CI, 0.71–1.43; P=0.97); D (RR=0.91; 95% CI, 0.75–1.11; P=.37). We used a fixed-effect model, as there was no significant heterogeneity (A: P=.06, I²=41%; B: P=.68, I²=0%; C: P=.07, I²=38%; D: P=0.71, I²=0%).

The TSA was conducted based on the incidence of short-term mortality in HA group in control group of 20%, a relative risk increase in the experimental group of 10%, and diversity of 49%. The RIS was 25,260 participants, 12.5% of which were accrued in our meta-analysis. The cumulative Z curve (blue line) crossed neither the trial sequential monitoring boundaries (red inward slash) nor the conventional boundaries (black dotted line), and the RIS was far from being reached (Fig. S2, <http://links.lww.com/OTAI/A11>). The TSA-adjusted 95% CI of RR was from 0.63 to 1.82.

3.2.2. Reoperation rate. Twenty-three studies, on a total of 2,383 patients in the AR group and of 1,914 patients in the IF group, provided the short-term reoperation rate, whereas 7 studies, on a total of 933 patients in the AR group and of 849 patients in the IF group, provided the long-term reoperation rate. There were statistical heterogeneities between studies in 2 groups (P<.00001, I²=74%; P=.03, I²=62%), so we used a random-effect model instead. The pooled results showed that AR group was associated with a lower short-term reoperation rate (RR=0.19; 95% CI, 0.13–0.28; P<.00001), and a lower long-term reoperation rate (RR=0.23; 95% CI, 0.17–0.33; P<.00001) (Figs. 5 and 6).

The TSA was conducted based on the rate of short-term reoperation in the control group of 30%, a relative risk reduction in the experimental group of 20%, and diversity of 56%. The cumulative Z curve (blue line) crossed the trial sequential monitoring boundaries, and conventional boundaries and the RIS was reached (Fig. S3, <http://links.lww.com/OTAI/A11>). The TSA-adjusted 95% CI of RR was adjusted from 0.14 to 0.19.

Again, we conducted the subgroup analysis of reoperation rate between THA and IF and HA and IF. The heterogeneity tests between THA and IF showed that it was present in both short-term and long-term reoperation rate (P=.96, I²=0%; P=.30, I²=16%), whereas the heterogeneity tests between HA and IF showed that there was no significant heterogeneity in long-term

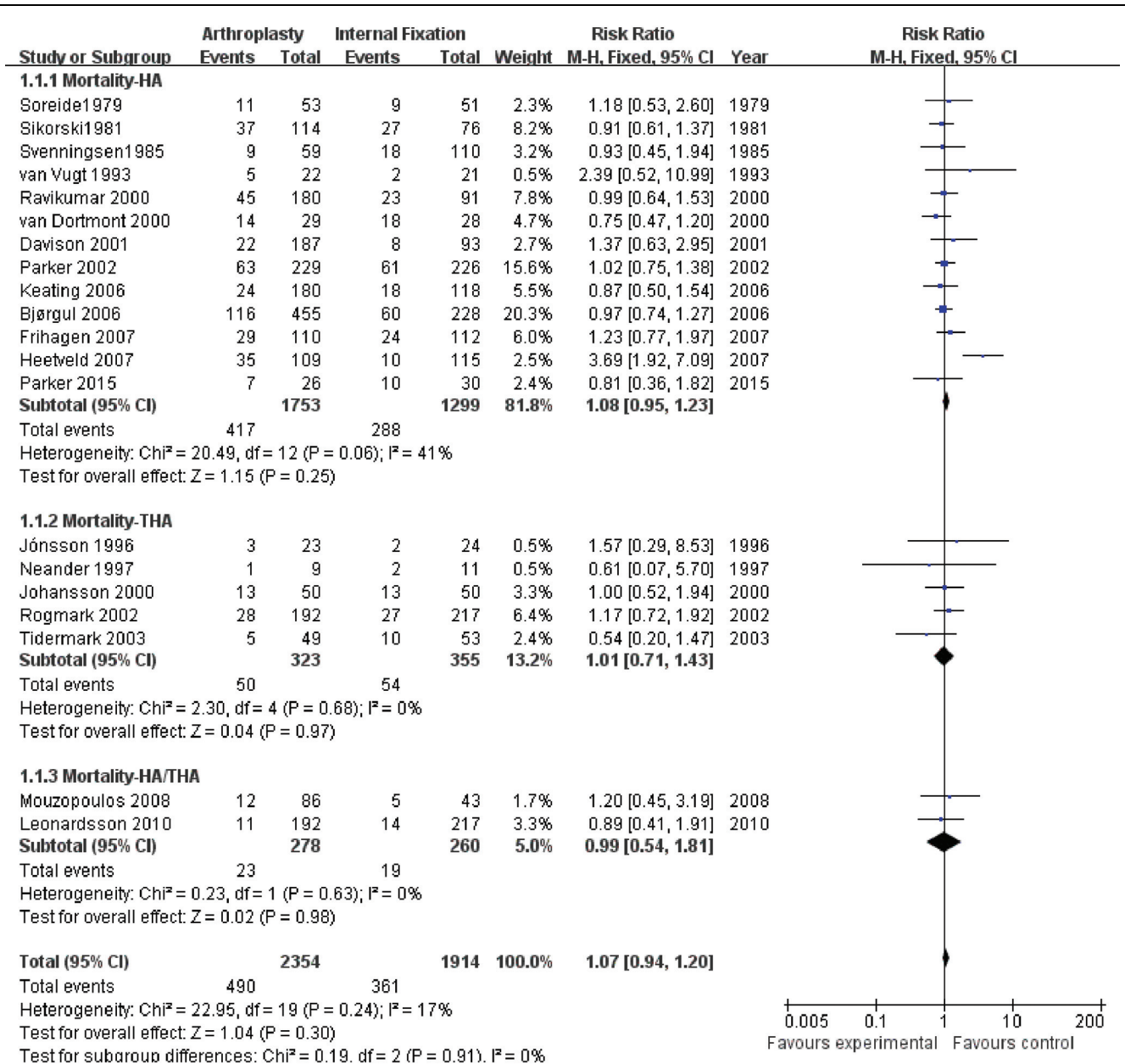


Figure 3. Forest plot of comparison of mortality at short term including the subgroups of Mortality-HA, Mortality-THA, and Mortality-HA/THA. Experimental = Arthroplasty, Control = Internal Fixation, M-H = Mantzel-Haenzel method.

reoperation rate ($P=.44$, $I^2=0\%$), but it was obviously heterogeneous in short-term reoperation rate ($P<.0001$, $I^2=74\%$). Therefore, the random-effect model was used for comparing short-term reoperation rate between HA and IF, whereas the fixed-effect model was used for all other comparisons. The pooled RRs for short-term and long-term reoperation rate after HA was compared to IF were 0.21 (95% CI, 0.13–0.35; $P<.00001$) and 0.17 (95% CI, 0.12–0.24; $P<.00001$), respectively, (Figs. 5 and 6). And the pooled RRs for short-term and long-term reoperation rate after THA was compared to IF were 0.11 (95% CI, 0.06–0.21; $P<.00001$) and 0.35 (95% CI, 0.23–0.53; $P<.00001$), respectively, (Figs. 5 and 6). It was clear that patients treated by AR (either THA or HA) were more likely to have fewer reoperations at short-term and long-term than patients treated by IF ($P<.00001$).

The TSA was conducted based on the rate of short-term reoperation in HA group in the control group of 30%, a relative risk reduction in the experimental group of 50%, and diversity of 74%. The cumulative Z curve (blue line) crossed the trial sequential monitoring boundaries and the conventional boundaries, and the RIS was reached (Fig. S4, <http://links.lww.com/OTAI/A11>). The TSA-adjusted 95% CI of RR was from 0.16 to 0.25.

3.2.3. Complications. Twenty studies, on a total of 1,740 patients in the AR group and of 1,693 patients in the IF group, provided the data of surgical complications as a whole, including the short-term and long-term complications. Due to the high heterogeneity ($P<.00001$, $I^2=83\%$; $P<.00001$, $I^2=89\%$), we used the random-effect model to perform the analysis. The pooled

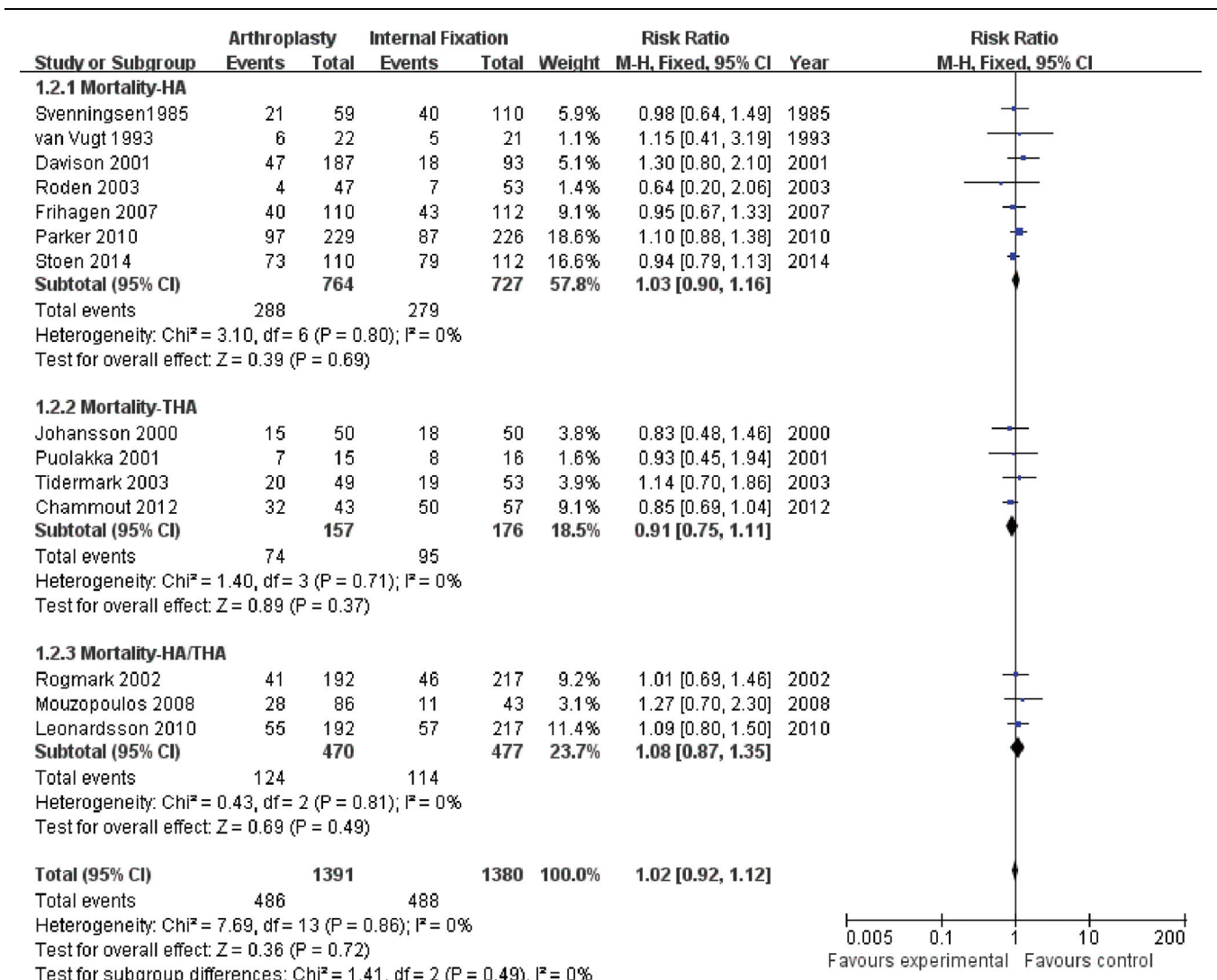


Figure 4. Forest plot of comparison of mortality at long term including the subgroups of Mortality-HA, Mortality-THA, and Mortality-HA/THA. Experimental = Arthroplasty, Control = Internal Fixation, M-H = Mantzel-Haenzel method.

analysis revealed a lower risk both at short-term (RR=0.37, 95% CI, 0.24–0.57; $P < .00001$) (Fig. 7) and long-term (RR=0.30, 95% CI, 0.16–0.57; $P < .0002$) (Fig. 8) of postoperative complications in the AR group when compared to that in the IF group, so we speculated that AR might be superior to IF regarding the postoperative complications.

Subgroup analysis showed that HA was also associated with a lower risk of complications both at short-term (RR=0.48, 95% CI, 0.27–0.85; $P = 0.01$) and at long-term (RR=0.17, 95% CI, 0.12–0.25; $P < 0.00001$) (Figs. 7 and 8) when compared to IF. As for THA, although it demonstrated a lower risk of complications at short-term (RR=0.20, 95% CI, 0.12–0.34; $P < .00001$) (Fig. 7), it did not show a statistically significant difference at long-term (RR=0.68, 95% CI, 0.23–1.97; $P = .48$) (Fig. 8). We used the random-effect model as well by virtue of their high heterogeneity ($P < .00001$, $I^2 = 83%$ at short-term; $P < .00001$, $I^2 = 89%$ at long-term).

We particularly removed the feeling of pain from various complications for the comparison between AR and IF because the degree of pain is one of the most critical factors that determine a patient’s quality of life. Similarly, we used the random-effect model on account of its high heterogeneity ($P < .00001$, $I^2 =$

85%). Moreover, the pooled RRs for postoperative pain after AR compared to IF were 0.50 (95% CI, 0.33–0.78; $P = .002$) (Fig. 9), so it seemed that patients treated by AR felt less pain than those treated by IF.

The TSA was conducted in light of short-term complications, total complications, and pain in the control group of 30%, a relative risk reduction in the experimental group of 30%, and diversity of 85%, 81%, and 89%, respectively. The RIS was 4,808, 5,848, and 7,003 participants, respectively. The cumulative Z curve (blue line) crossed the trial sequential monitoring boundaries (red inward slash) before the RIS has been reached (Fig. S5, <http://links.lww.com/OTAI/A11>). The TSA-adjusted 95% CI of RR was adjusted from 0.25 to 0.37, 0.21 to 0.30, and 0.48 to 0.80.

3.3. Sensitivity analysis

For those tests with high heterogeneity, we also performed the sensitivity analysis. We removed 1 study at a time and analyzed the rest to evaluate whether the overall result could have been significantly affected by 1 single study. The results of sensitivity analysis found that no single study had a significant influence on pooled RRs (Figs. S6–10, <http://links.lww.com/OTAI/A11>).

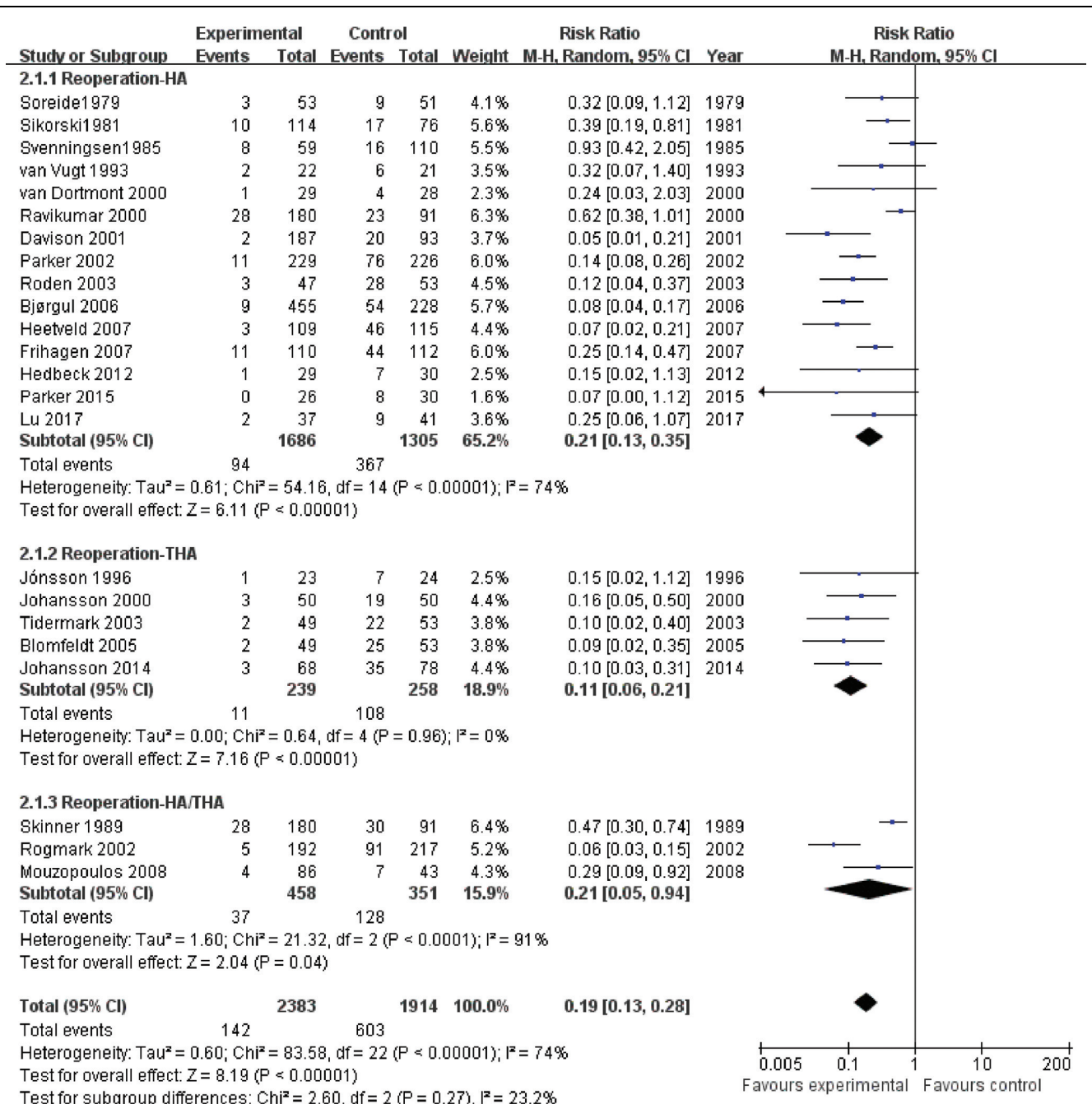


Figure 5. Forest plot of comparison of reoperation at short term including the subgroups of Reoperation-HA, Reoperation-THA, and Reoperation-HA/THA. Experimental = Arthroplasty, Control = Internal Fixation, M-H = Mantzel-Haenzel method.

3.4. Publication bias

In order to check for the underlying publication bias, we used the Begg funnel plot (standard error (SE) of the log RR). Also, the results showed no publication bias (Figs. S11–17, <http://links.lww.com/OTAI/A11>).

4. Discussion

Currently, the best treatment for patients with femoral neck fractures, particularly in elderly patients, is still undetermined. Previous evidence^[7] had shown that patients treated with AR were superior to those treated with IF on the whole. However, most of the studies they collected were observational studies and

lacked related quality control. Therefore, the reliability of their conclusions was limited. With the continuous advent of some new evidence of the comparison of AR and IF, we performed this meta-analysis of 31 RCTs in order to provide a latest and more reliable conclusion of the best treatment for patients with femoral neck fractures. The composite results revealed that compared to IF, AR was associated with fewer secondary operations and lower risk of postoperative complications, as well as no increased mortality. Additionally, AR was superior to IF with respect to the postoperative pain that patients suffered.

Mortality is one of the most essential clinical assessment criteria and possible crucial factors to determine whether patients should be treated with AR or IF. Patients treated by AR were

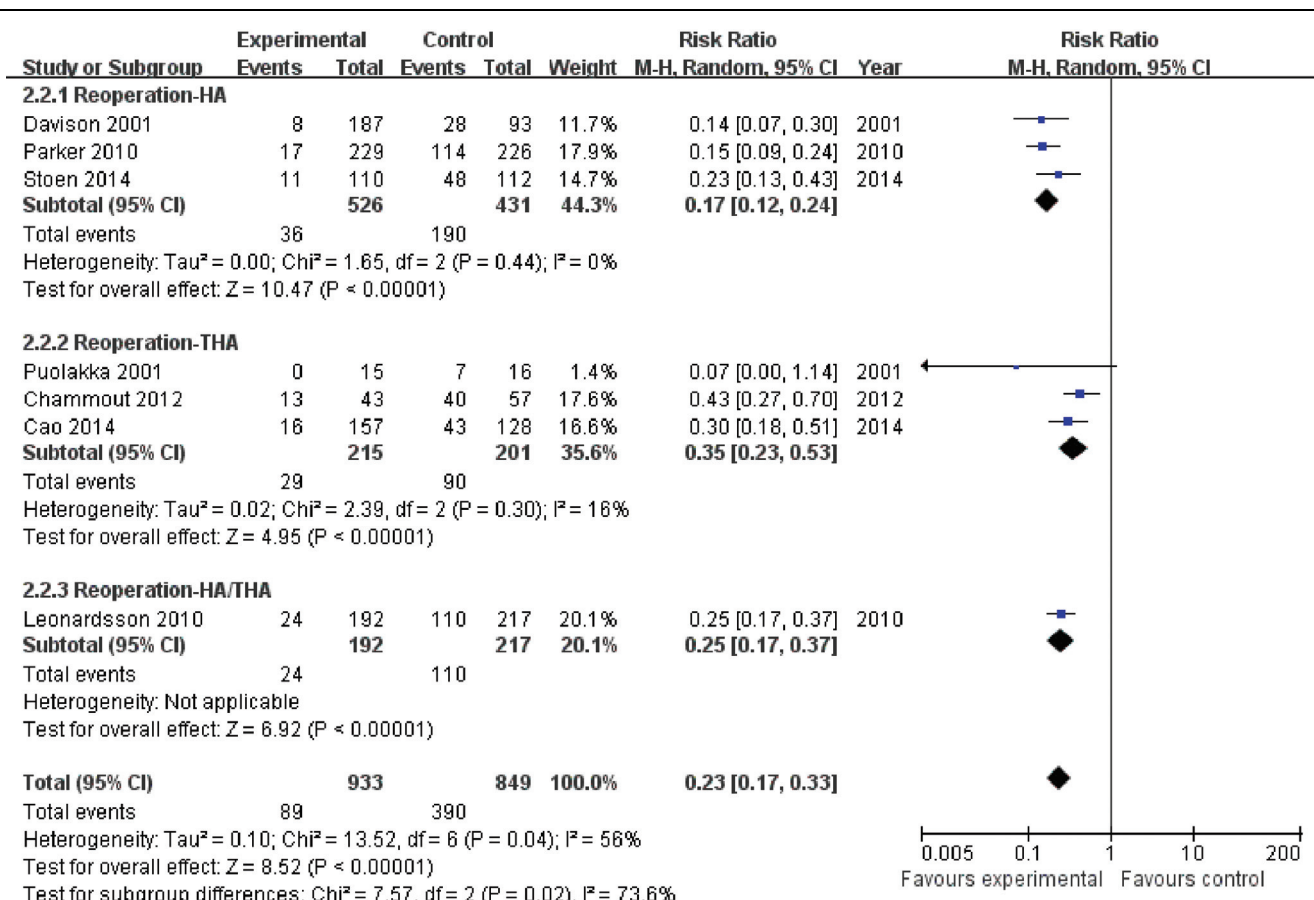


Figure 6. Forest plot of comparison of reoperation at long term including the subgroups of Reoperation-HA, Reoperation-THA, and Reoperation-HA/THA. Experimental = Arthroplasty, Control = Internal Fixation, M-H = Mantzel-Haenzel method.

allegedly characterized by higher mortality when compared to those treated by IF. Some studies^[6,26] showed that there was an increasing trend in the RR of mortality within the early 4 months after AR compared to the same period after IF. However, Hudson et al^[47] reported higher mortality in patients treated by IF when they took into consideration the age, gender, and comorbidities in their study. Nonetheless, in our meta-analysis, it suggests similar mortality for AR and IF in the treatment of patients with femoral neck fractures either within 5 years or more than five years. Also, similar to the comparison of AR and IF in the mortality, the results of the comparison between THA and IF or between HA and IF show no difference in mortality. In other words, the application of AR, regardless of THA or HA, for treating femoral neck fractures will not increase the possibility of death at short-term and long-term follow-ups.

The reoperation rate is also a key factor for assessing AR and IF. It has been reported that the reoperation rate after IF was changed from 30% to 50%^[48] and was far higher than that after AR.^[49] In our meta-analysis, similar results for IF were observed. We reported that AR could effectively reduce the risk of reoperation at short-term and long-term periods. Furthermore, THA or HA did not change the overall pooled effect of AR compared to IF in the reoperation rate. This can be partly attributed to the high risk of complications after IF, which will be discussed in detail later.

As for the occurrence of major postoperative complications, such as fixation failure, dislocation, nonunion, peri-prosthetic

fractures, femoral head necrosis, and infection, our meta-analysis revealed that compared to IF, AR was associated with a lower risk of complications either at short-term or at long-term follow-ups, or overall, which was likely to be attributed to lower risk of nonunion or femoral head necrosis.^[6,27]

Additionally, we compared AR and IF in the pain rate, which was significantly higher in the IF group. We believed that reasons behind this were that patients treated with IF, as reported by previous studies,^[7,9,13,28,29] were more likely to suffer from nonunion and femoral head necrosis, which would definitely increase the risk of pain.

Based on results from the sequential analysis, all the calculated RIS required to produce a reliable conclusion in mortality between AR (including THA and HA) and IF was far more than the number of patients we included. What's more, neither did the results of the current trial on mortality cross the traditional threshold (Z=1.96) nor the threshold of sequential analysis, meaning that, until now, we are still not sure which treatment, AR or IF, has higher mortality and further research is needed. However, unlike results from sequential analysis of mortality, results on reoperation rate, complications, and pain showed positive findings. Not only did they cross the traditional threshold (Z=1.96), but they also crossed the threshold of sequential analysis. In other words, the cumulative evidence from the comparison of the risk of reoperation and complications between AR (including THA and HA) and IF were reliable and conclusive. Therefore, there should be no need for further research on the

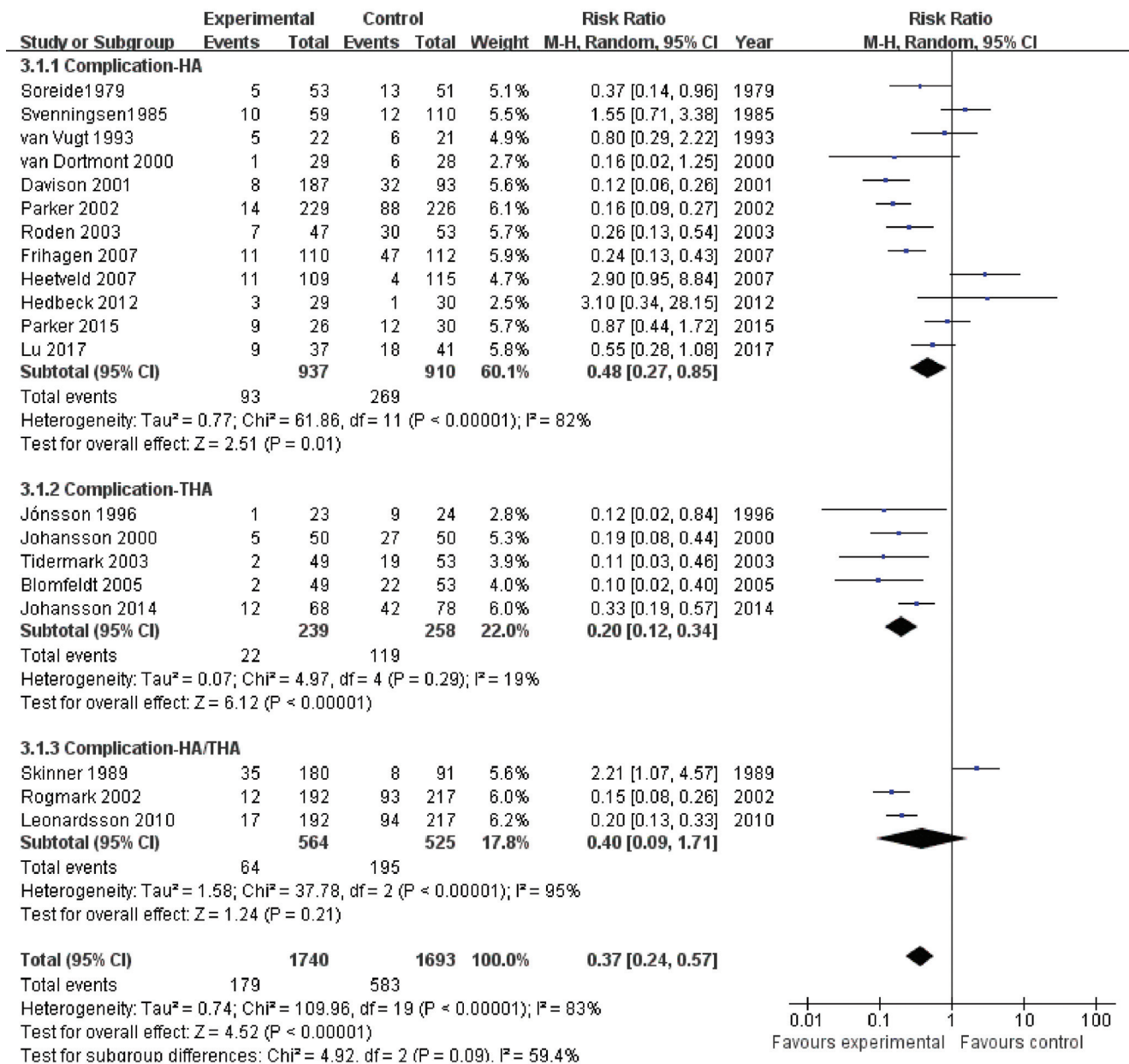


Figure 7. Forest plot of comparison of complication at short term including the subgroups of Complication-HA, Complication-THA, and Complication-HA/THA. Experimental = Arthroplasty, Control = Internal Fixation, M-H = Mantzel-Haenzel method.

comparison between AR and IF in terms of reoperation rate and postoperative complication.

However, there are 3 limitations to our study. First, some of the trials included in this meta-analysis may have deficiencies in the methodologic quality. For instance, there are 4 studies^[30-33] that adopted quasi-random or nonrandom methods to conduct their research. One study^[34] failed to conceal random allocation, and only several studies^[12,28-30,34-36] made it clear that they had used blinding for the type of treatment. For another, although we conducted the subgroup analysis on THA or HA, the effects of different types of AR (THA or HA, cemented or un-cemented) and IF (screws, plates, etc.) on the treatment outcomes were unavoidable. Besides, we included a relatively massive number of studies from 1979 to 2018, in which there may be some unknown biases and high heterogeneity. In addition, although there were some similar meta-analyses^[50-52] published before, our study here had its own advantages. First of all, far more recent

research and a considerable number of patients were included in our meta-analysis, which was more likely to offer reliable and convincing conclusions. Also, we applied many methods to evaluate the quality and heterogeneity of each RCT. Most importantly, when compared to other meta-analyses, this meta-analysis was highlighted by the application of TSA, that showed its outstanding advantages of evaluating the reliability and conclusiveness of the acquired studies on the major results. Under TSA, we could safely draw the conclusion that AR was indeed superior to IF concerning reoperation rate, complications, and post-operation pain in the treatment of the femoral neck fracture.

5. Conclusion

In summary, we recommend that the AR should be considered first in the treatment of elderly patients with displaced femoral neck fractures. And, as we have obtained sufficient evidence so far, more studies on the comparison of reoperation rate,

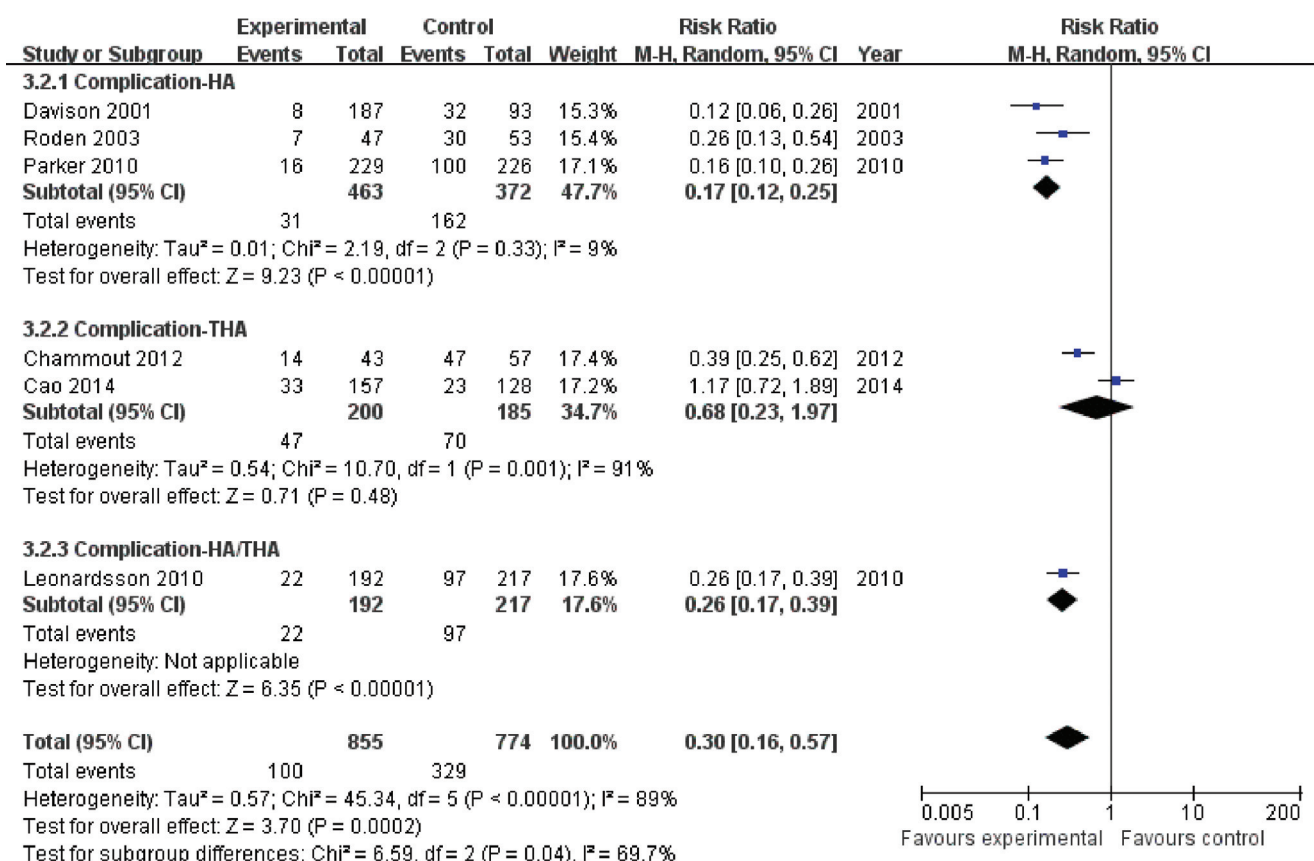


Figure 8. Forest plot of comparison of complication at long term including the subgroups of Complication-HA, Complication-THA, and Complication-HA/THA. Experimental = Arthroplasty, Control = Internal Fixation, M-H = Mantzel-Haenzel method.

complications, and postoperation pain between AR and IF might only outlive their usefulness in the future. Still, more well-designed and high-quality research with long-term follow-ups are needed to determine the optimal treatment with lower mortality.

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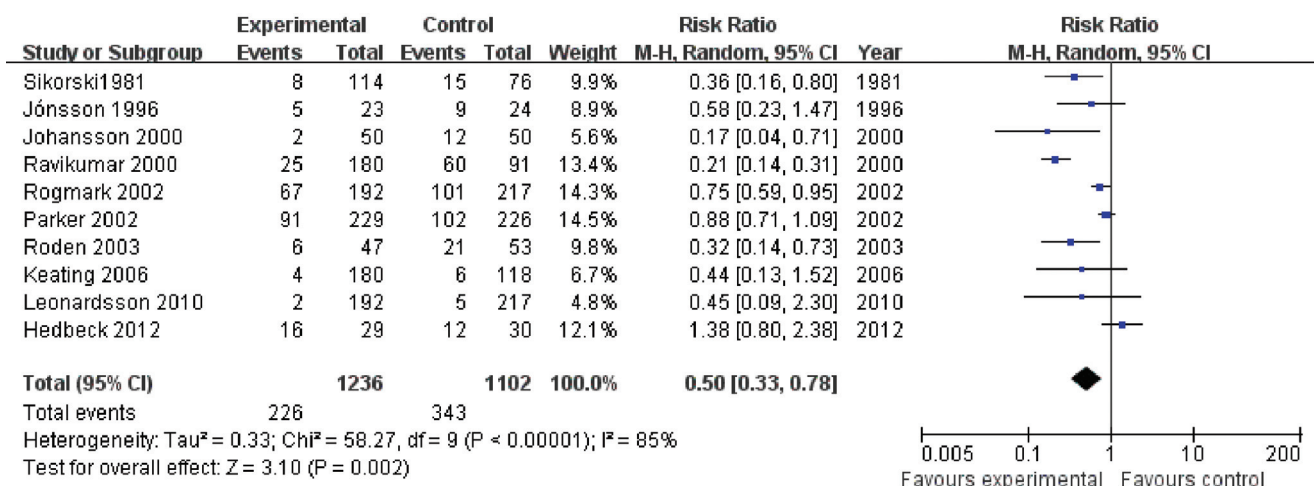


Figure 9. Forest plot of comparison of postoperative pain. Experimental = Arthroplasty, Control = Internal Fixation, M-H = Mantzel-Haenzel method.

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