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Original Article

Efficacies of surgical treatments based on Harris hip score in elderly patients with femoral neck fracture

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Abstract: Aim: To compare the efficacies of four surgical treatments, i.e., total hip arthroplasty (THA), internal fixation (IF), hemiarthroplasty (HA), and artificial femoral head replacement (artificial FHR), by performing a network meta-analysis based on Harris hip score (HHS) in elderly patients with femoral neck fracture. Methods: In strict accordance with specific inclusion and exclusion criteria, randomized controlled trails (RCTs) were screened and selected from a larger group of studies that were retrieved through a comprehensive search of scientific literature databases, further complimented by manual search. The resultant high-quality data from final selected studies were analyzed using Stata 12.0 software. Results: A total of 3680 studies were initially retrieved from database search, and 15 RCTs were eventually incorporated into this meta-analysis, containing 1781 elderly patients who had undergone various surgical treatments for femoral neck fracture (THA group = 604; HA group = 604; IF group = 495; artificial FHR group = 78). Our major result revealed a statistically significant difference in HHS of femoral neck fracture when HA and IF groups were compared with THA. No differences were detected in the HHS of femoral neck fracture undergoing artificial FHR and THA. The surface under the cumulative ranking curves (SUCRA) value of HHS, in elderly patients with femoral neck fracture after surgery, revealed that IF has the highest value. Conclusions: The current network meta-analysis results suggest that IF is the superlative surgical procedure for femoral neck fracture patients, and IF significantly improves the HHS in femoral neck fracture patients.

Keywords: Femoral neck fracture, total hip arthroplasty, hemiarthroplasty, internal fixation, artificial femoral head replacement, randomized controlled trials

Introduction

Femoral neck fracture, also known as hip fracture, is an common consequences of injuries in the elderly population, which frequently occurs in the proximal end of the femur close to the hip, mainly due to osteoporosis [1]. The incidence of femoral neck fractures is 2-4 cases per 10,000 in under-65 age group [2], however, the incidence climbs steeply to 28/10,000 among men and 64/10,000 among women, respectively, in population aged over-70 [3]. Femoral neck fracture is characterized by a fragility fracture resulting from minor trauma or a fall in a person who has weakened osteoporotic bone, while in people with normal bone, the most femoral neck fractures are due to high-energy trauma such as sports injuries, car accidents and falling from heights [4]. An elderly patient with femoral neck fracture has often sustained a low-energy fall, and is accompanied by severe pain with inability to bear weight, and the affected extremity is frequently shortened and externally rotated compared to the normal leg [5]. Treatment for femoral neck fractures varies with patient's age and the fracture pattern, and mainly includes total hip arthroplasty (THA), hemiarthroplasty (HA), internal fixation (IF) and artificial femoral head replacement [6, 7].

THA is the main method for hip replacement, and patients treated with THA benefit from the advantages of shorter operation times, reduced dislocation rates, less blood loss, less complex surgery, and lower initial costs [8]. HA is an excellent choice for femoral neck fractures in elderly patients, but this method has the disadvantages of higher rates of reoperation and inferior long term functional results than THA for treatment of acute, displaced femoral neck fractures [9]. IF is one of the main options for curing femoral neck fractures, containing open reduction internal fixation (ORIF) and closed reduction internal fixation (CRIF) [10]. IF is associated with shorter operating time, less blood loss, and less initial surgical trauma, but it has a high reoperation rate, typically varying between 10-57% [11]. Artificial femoral head replacement (artificial FHR) is regarded as an ideal and reliable method for treating elderly patients with femoral neck fracture and contributes to fast reconstruction of hip joint function, and for its distinct advantages of less trauma, simple operation procedure and early rehabilitation after surgery [12]. Accumulating evidence has demonstrated that these four treatments have significant efficacy in elderly patients with femoral neck fractures [3, 13, 14]. However, conflicting opinions exist on ranking the effectiveness of these four treatments in elderly patients with femoral neck fracture [15, 16].

Traditional meta-analyses combine the outcomes of homogeneous studies within the same topic, and it is not feasible to simultaneously compare more than two interventions [17]. However, a network meta-analysis can indirectly compare three or more procedures, using a common comparator, and can also combine direct and indirect comparisons simultaneously for comparing several intervention methods [18, 19]. Therefore, to identify the optimal surgical treatment for elderly patients with femoral neck fracture, we performed a network meta-analysis based on published studies, and ranked the efficacies of the four surgical treatments (THA, HA, IF and artificial FHR).

Materials and methods

Search strategy

A literature search of public databases (PubMed, EBSCO, Ovid, Springerlink, Wiley, Web of Science, Cochrane Library, Wanfang database and VIP database) was conducted to retrieve relevant studies published prior to October, 2014. The studies were identified using the following combination of keywords and free words: ("femoral neck fractures" or "femoral neck fracture" or "femur neck fractures" or "femur neck fracture") and ("general surgery" or "surgical procedures, operative" or "surgery, general" or "surgery" or "operative procedures" or "surgery, ghost" or "operative surgical procedure" or "procedure, operative" or "procedure, operative surgical"). Manual search of cross-reference was performed to identify additional relevant studies.

Study selection criteria

Studies were screened using the following inclusion criteria for eligibility: (1) study design: randomized controlled trail (RCT), (2) interventions: THA, HA, IF and artificial FHR applied for the treatment of femoral neck fractures, (3) subjects investigated: clinically diagnosed as elderly femoral neck fracture patients, (4) end indicators: Harris hip scores (HHS) of femoral neck fracture in elderly patients after surgery. The exclusion criteria were: (1) insufficient data, (2) non-RCT, (3) duplicate publications, (4) study without significant comparison between surgeries.

Data extraction and quality assessment

All data from eligible trials were extracted by two investigators independently using a predefined form, and the following information was collected: surname of the first author, publication year, country, ethnicity, language, disease, study design, intervention, gender, age and one year HHS. Disagreement on study eligibility was resolved by a third reviewer after reexamination, until consensus was achieved on every item. Two or more investigators evaluated the quality of enrolled studies on the basis of Collaboration's tool for assessing risk of bias [20]. The risk of bias covers six domains, including random sequence generation, allocation concealment, blinding of participants or blinding outcome assessment, incomplete outcome data, selective reporting and other bias. The detailed assessment criteria were standard as follows: (1) whether allocation sequence is generated properly, (2) whether the method used to conceal the allocation sequence is appropriate, (3) whether the intended blinding is effective, (4) whether the incomplete outcome data are dealt with appropriately, (5) state how selective outcome reporting was examined and what was found, (6) whether any other important concerns about bias is covered in the other domains in the tool.

Statistical analysis

Statistical analysis was conducted with the STATA statistical software (Version 12.0, Stata

Table 1. Baseline characteristics of included studies

First author	Year	Country	Ethnicity	Disease	Intervention		Age (years)		Gender (M/F)	
					T1	T2	T1	T2	T1	T2
Wani IH [29]	2014	India	Asians	neck of femur	C	A	65.16	65.04	26/24	34/16
Stoen RO [14]	2014	Norway	Caucasians	neck of femur	C	B	83.4 (80.1-85.1)		57/165	
Guo Y [30]	2013	China	Asians	neck of femur	C	D	65.3 ± 3.1	64.2 ± 2.9	18/12	16/14
Guo Y [30]	2013	China	Asians	neck of femur	C	A	65.3 ± 3.1	63.8 ± 2.4	18/12	15/15
Guo Y [30]	2013	China	Asians	neck of femur	D	A	64.2 ± 2.9	63.8 ± 2.4	16/14	15/15
Cadossi M [31]	2013	Italy	Caucasians	neck of femur	B	A	84.2 (73-98)	82.3 (71-96)	13/28	8/34
Tang J [33]	2011	China	Asians	neck of femur	C	D	58.9 ± 5.3	65.3 ± 6.7	24/30	16/32
Tang J [33]	2011	China	Asians	neck of femur	C	A	58.9 ± 5.3	77.3 ± 6.5	24/30	18/32
Tang J [33]	2011	China	Asians	neck of femur	D	A	65.3 ± 6.7	77.3 ± 6.5	16/32	18/32
vanden Bekerom MP [32]	2011	Netherlands	Caucasians	neck of femur	B	A	80.3 (70.2-93.9)	82.1 (70.1-95.6)	22/115	25/90
Nicolaides V [16]	2011	Greece	Caucasians	neck of femur	C	B	64	72	32/38	18/17
Nicolaides V [16]	2011	Greece	Caucasians	neck of femur	C	A	64	72	32/38	18/17
Nicolaides V [16]	2011	Greece	Caucasians	neck of femur	B	A	72	72	18/17	18/17
Hedbeck CJ [7]	2011	Sweden	Caucasians	neck of femur	B	A	80.7 ± 5.1	80.5 ± 5.1	54/6	47/13
Giannini S [34]	2011	Italy	Caucasians	neck of femur	B	A	82.6 (68-92)	80.7 (65-89)	NR	NR
Mouzopoulos G [35]	2008	Greece	Caucasians	neck of femur	C	B	75.38 ± 4.62	74.24 ± 3.77	12/26	10/24
Mouzopoulos G [35]	2008	Greece	Caucasians	neck of femur	C	A	75.38 ± 4.62	73.07 ± 4.93	12/26	9/28
Mouzopoulos G [35]	2008	Greece	Caucasians	neck of femur	B	A	74.24 ± 3.77	73.07 ± 4.93	10/24	9/28
Macaulay W [36]	2008	USA	Caucasians	neck of femur	B	A	77 ± 9	82±7	9/14	10/7
Frihagen F [37]	2007	Norway	Caucasians	neck of femur	C	B	83.2 ± 7.65	82.5 ± 7.32	25/87	32/78
Blomfeldt R [38]	2007	Sweden	Caucasians	neck of femur	B	A	80.7 (70-89)	80.5 (70.2-89.7)	6/54	13/47
Johansson T [39]	2006	Sweden	Caucasians	neck of femur	C	A	84 (75-101)		34/109	
Squires B [40]	1999	UK	Caucasians	neck of femur	B	A	71	69	NR	NR

T, treatment; M, male; F, female; A, total hip arthroplasty; B, hemiarthroplasty; C, internal fixation; D, artificial femoral head replacement; NR, not reported.

Corporation, College Station, TX, USA). Standard mean difference (SMD) with 95% confidence intervals (95% CI) was calculated by applying fixed-effects model or random-effects model for evaluating the effects of different surgeries on HHS of femoral neck fracture in elderly patients. Z test was employed to detect the significance of overall effect size [21]. Heterogeneity was assessed with Cochran's Q-statistic test and qualified by I^2 test [22, 23]. If P value less than 0.05, heterogeneity was considered statistically significant. The I^2 test provides a measure of the degree of heterogeneity in the results. Values of 0~25% are considered to represent no heterogeneity, 25~50% to modest heterogeneity, 50~75% to large heterogeneity and 75~100% to extreme heterogeneity. A random-effects model was applied if there was significant heterogeneity ($P < 0.05$ or $I^2 > 50\%$), otherwise, a fixed-effects model was employed ($P_h > 0.05$ or $I^2 < 50\%$) [24]. Network meta-analysis synthesizes data by collecting a network of studies regarding more than two interventions. The colligation of direct evidence and indirect evidence enhances the accuracy in evaluation and generates a relative ranking of all interventions for the studied estimates [25]. In each closed loop, we utilize the inconsistency factor (IF) to evaluate the heterogeneity among studies. If the 95% confidence intervals (95% CI) of IF values are truncated at zero, it suggests that the direction of the IF is unimportant [26]. Funnel plots were utilized to identify whether there is small-study effects, so as to provide further confirmation for the reliability of the results [27]. The assumption of consistency models allows the presence of heterogeneity of the intervention effects among studies while no significant differences was found in study design. After the generation of heterogeneity matrix, frequentist method was used for the fitted model to calculate the ranking probabilities [28].

Results

Included studies

A total of 3680 articles were retrieved after the initial computer search and manual search of cross-reference lists. And, 530 articles were

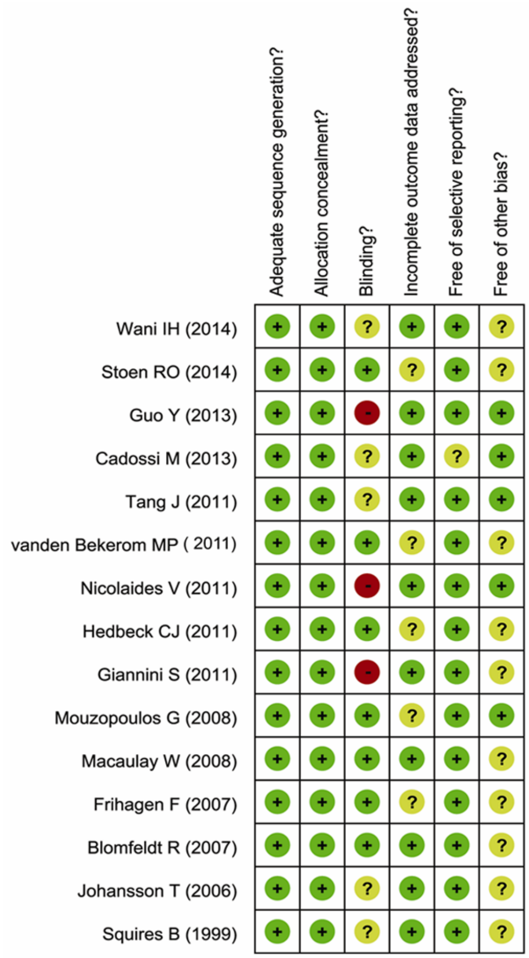

Figure 1. The methodological quality of assessment for the enrolled studies on the basis of Collaboration's tool for assessing risk of bias.

excluded for duplicates, 450 for letters, reviews and meta-analyses, 353 for non-human studies and 1807 for irrelevant to research topic, and 540 full-text articles remained for further assessment. Further elimination of the studies was as follows: 120 studies for non-RTC, 105 for irrelevant to IF, and 124 for irrelevant to THA, 129 for irrelevant to HA, 46 for irrelevant to artificial FHR and 1 study for incomplete data or weakly correlated data. Finally, a total of 15 studies, published between 1999 and 2014, were selected according to our inclusion criteria, and contained 1781 cases of elderly patients with femoral neck fracture [7, 14, 16, 29-40]. Based on the surgical procedure, 604 cases were in THA group, 604 cases in HA group, 495 cases in IF group and 78 cases in artificial FHR group. Of these 15 eligible studies, 3 studies were performed in Asians and 12

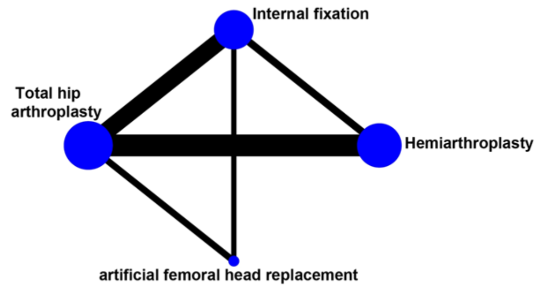

Figure 2. The evidence network of all enrolled studies involving the four inventions in this network meta-analysis (total hip arthroplasty, hemiarthroplasty, internal fixation and artificial femoral head replacement).

studies in Caucasians. Four of the studies were three-arm trials and 11 studies were two-arm trials, containing a total 23 comparisons. The baseline characteristics and Cochrane assessment of risk of bias are showed in **Table 1** and **Figure 1**, respectively.

Evidence network

As shown in **Figure 2**, the connecting lines represent direct comparisons between two interventions, and interventions without connections can be indirectly compared through network meta-analysis. The width of lines represents the number of included studies and the nodes size represents overall sample size of the intervention. The color of lines represents the risk of bias of enrolled articles. This study included four treatments for elderly patients with femoral neck fracture, namely, THA, HA, IF and artificial FHR.

Contribution plot of network meta-analysis

Each direct comparison in our current network meta-analysis contributed differently to the evaluation of the network summary effects and the details are shown in **Figure 3**: (1) nine of the studies had direct comparison between THA and HA, whose percentage contribution to HA & IF, HA & artificial FHR were 50% and 50%, respectively, and 33.3% for the whole network meta-analysis, (2) six of the studies had the direct comparison between THA and IF, whose percentage contribution to HA & IF, IF & artificial FHR were 50% and 50%, respectively, and 33.3% for the whole network meta-analysis, (3) two of the studies had the direct comparison between THA and artificial FHR, whose percent-

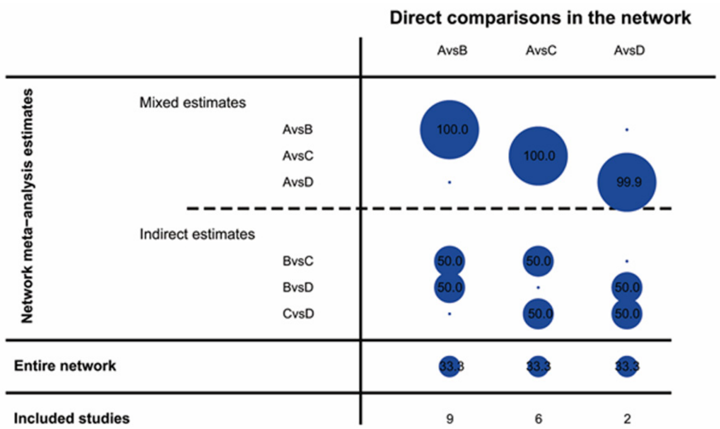

Figure 3. Contribution plot of enrolled studies about each direct comparison among four inventions in this network meta-analysis (A: total hip arthroplasty, B: Hemiarthroplasty, C: Internal fixation, D: Artificial femoral head replacement).

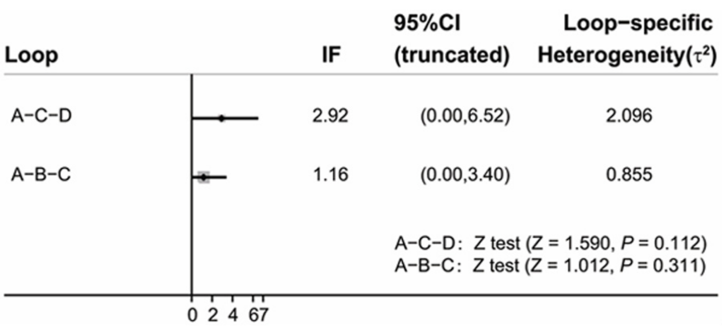

Figure 4. Inconsistency test for direct and indirect comparison in this network meta-analysis (A: Total hip arthroplasty, B: Hemiarthroplasty, C: Internal fixation, D: Artificial femoral head replacement).

age contribution to HA & artificial FHR, IF & artificial FHR were 50% and 50%, respectively, and 33.3% contribution to the whole network meta-analysis.

Evaluating and presenting assumptions of network meta-analysis

Inconsistency plot was utilized to test the heterogeneity among studies in closed loop of the present network meta-analysis. As shown in **Figure 4**, this network meta-analysis consists of two triangular loops, including THA-IF-artificial FHR and THA-HA-IF. The 95% CI of IF values are truncated at zero, suggesting there is no evidence of significant inconsistency. The *P* values of the two triangular loops (both $P > 0.05$) further confirmed the existence of consistency the direct comparisons and indirect comparisons of these two triangular loops.

Comparisons of efficacy

The results of this network meta-analysis showed that there was statistical significance for the HHS of femoral neck fracture in elderly patients with the treatment of HA and IF when compared with THA (HA: SMD = 0.0004, 95% CI = 0.0001~0.036, *P* = 0. 001, IF: SMD = 0.0001, 95% CI = 0.0001~0.012, *P* < 0. 001). While there was no statistical significance for the HHS of femoral neck fracture in elderly patients between the treatment of artificial FHR and THA (SMD = 0.0019, 95% CI = 0.0001~4.437, *P* = 0. 113). After ignoring covariance, further analysis still demonstrated that there was statistical significance for the HHS of femoral neck fracture in elderly patients among the comparisons of THA with HA and IF (HA: SMD = 0.0005, 95% CI = 0.0001~0.043, *P* = 0. 001, IF: SMD = 0.0001, 95% CI = 0.0001~0.009, *P* < 0. 001). However, there was no statistical significance for the HHS of femoral neck fracture in elderly patients between artificial FHR and THA ($P > 0.05$) (**Table 2**). Relative efficacy of the four surgical treatments shows in **Figure 5** (black corresponds to 95% CI and red corresponds to 95% predictive intervals).

Ranking of interventions

The treatment relative ranking of estimated probabilities of HHS of femoral neck fracture in elderly patients after four surgeries indicated the surface under the cumulative ranking curves (SUCRA) values of the four interventions were 1.9% for THA, 65.2% for HA, 82.1% for IF, 50.8% for artificial FHR, and IF had the highest rank. Besides, the treatment relative ranking of predictive probabilities of HHS of femoral neck fracture in elderly patients after four surgeries revealed the SUCRA values of four interventions was 12.8% for THA, 62.2% for HA, 71.9% for IF, 53.1% for artificial FHR, and IF still had the highest rank, further confirmed that IF is

Table 2. Comparisons of the difference of Harris hip score in neck of femur patients treated with 4 surgeries

Comparisons	Harris hip score (correlation not ignored)					Harris hip score (correlation ignored)				
	SMD	95% CI LL	95% CI UL	Z	P	SMD	95% CI LL	95% CI UL	Z	P
B vs. A	0.00038	0.00001	0.0359	-3.4	0.001	0.00047	0.00001	0.0434	-3.32	0.001
C vs. A	0.00008	0.00001	0.0119	-3.72	< 0.001	0.00007	0.00001	0.0092	-3.83	< 0.001
D vs. A	0.00186	0.00001	4.4373	-1.58	0.113	0.00165	0.00001	3.8105	-1.62	0.105

SMD, standard mean difference; LL, lower limit; UL, upper limit; A, total hip arthroplasty; B, hemiarthroplasty; C, internal fixation; D, artificial femoral head replacement.

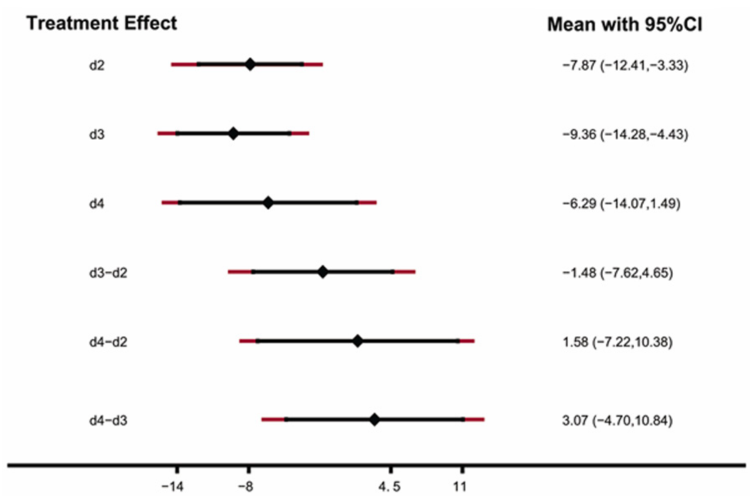

Figure 5. The confidence intervals of estimates of four inventions (Black corresponds to 95% confidence intervals and red corresponds to 95% predictive intervals).

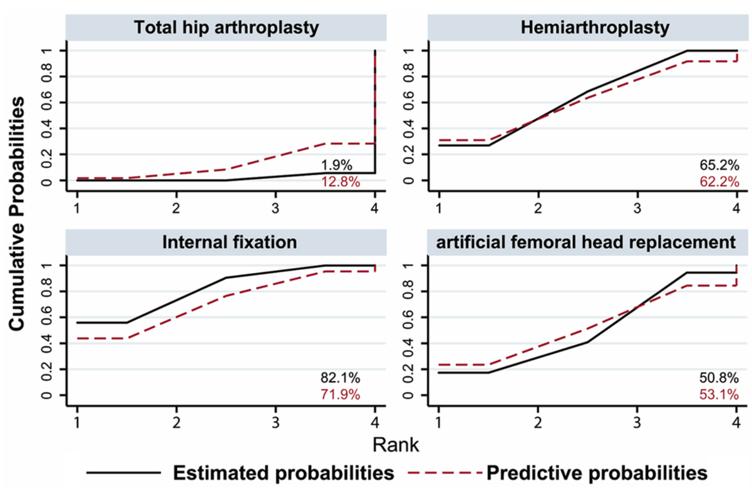

Figure 6. Plots show the surface under the cumulative ranking curves (SUCRC) values of shoulder scores of clavicular fracture patients treated with four inventions (d2, hemiarthroplasty, d3, internal fixation, d4, artificial femoral head replacement).

the optimal and effective treatment for femoral neck fractures in elderly patients (**Figure 6**).

Assessment of publication bias

The funnel plots in **Figure 7** showed that all the included studies symmetrically distribute around the vertical line (x = 0), suggesting that no existence of small-study effect in the network.

Discussion

Femoral neck fractures frequently occur in elderly patients of over-60 age group, although they can occur in both sexes and at all ages. The incidence of femoral neck fracture has increased significantly owing to longer life expectancy, improvements in medical technology and increased vehicular traffic, in case of accident-related fractures [41]. Treatment options for femoral neck fracture in elderly patients include TAH, IF, HA and artificial THR. However, the optimal and the most effective treatment of femoral neck fracture in elderly patient is vigorously debated based on opinions, in the absence of scientific studies that systematically compared the procedures [29]. Consequently, to explore the optimal surgical treatment for femoral neck fracture patients, we performed a network-analysis and, based on our results, we propose IF as the optimal surgical treatment after comparing SUCRA values of 4 most popular surgical intervention procedures (TAH, IF, HA and artifi-

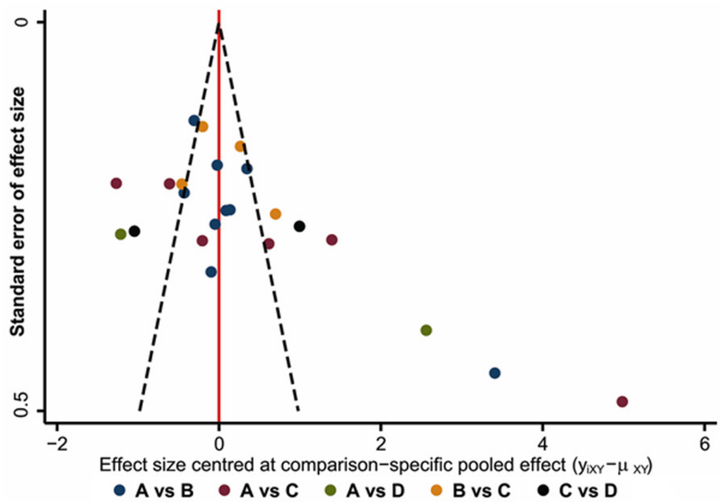

Figure 7. Funnel plot to confirm the risk of publications bias for the fifteen included literature (A: Total hip arthroplasty, B: Hemiarthroplasty, C: Internal fixation, D: Artificial femoral head replacement).

cial THR) in femoral neck fracture, under both the treatment relative ranking of estimated probabilities and the treatment relative ranking of predictive probabilities. In clinics, IF is already the treatment of choice, and the feasibility of IF varies depending on the bone quality, surgical technique, type of fracture, and surgeon's experience [42]. IF maintains the femoral head and the natural hip joint, in case the head and fracture unites do not undergo avascular necrosis. A study showed that femoral neck fractures in the young, healthy, and active patients with good bone quality are almost always treated using reduction with IF due to the advantages of minimal blood loss, short operating time, and low infection rate [43]. Patients with femoral neck fracture undergoing THA have a higher rate of dislocation, possibly due to relative laxity of the hip capsule, violation of the hip capsule during the acute injury and poor compliance in this often physically and cognitively debilitated older patient population [44]. The treatment with HA for femoral neck fracture contribute to long-term problems such as loss of function, acetabular wear and loosening with corresponding pain. Furthermore, HA may be associated with destruction of the articulating acetabular cartilage (prosthetic arthritis), especially in patients leading active, independent lifestyles, which can result in the development of debilitating activity related hip pain and the need for conversion surgery [14]. Recent studies claimed that there was a higher intra-operative blood loss and an increased incidence of dislocation in patients receiving artificial THR. Accordingly, THR was recommended only for patients aged below 70, or in the presence of advanced radiological osteoarthritis (OA) or rheumatoid arthritis (RA) [31]. Therefore, IF is considered as the optimal treatment in elderly patients with femoral neck fracture.

Since a single trial usually compares only few selected treatments, it is difficult to integrate information on the relative efficacy of all regimens for the same indication. Similarly, conventional direct meta-analysis also fails to measure the relative effect between diverse treatments as it only synthesizes trials with a same pair of comparators. Network meta-analysis compares a set of treatments for a specific disease simultaneously through a common comparator treatment. The merits of our network meta-analysis mainly focused on following points. First, we compared interventions indirectly for the absence of head-to-head trial and try to get more precise efficacy estimates by evaluating direct and indirect comparisons. Second, this is the first network meta-analysis to compare the efficacies of four surgical treatments (THA, HA, IF and artificial FHR) based on HHS in elderly patients with femoral neck fracture. Third, the 95% CI of IF values are truncated at zero, suggesting there is no significant inconsistency in our network meta-analysis. There are also some limitations in this network meta-analysis. First, only 15 RCTs were enrolled in our study, the number of included studies was comparatively small. Second, due to limitations of available data and information in the enrolled studies, only four surgical treatments for elderly patients with femoral neck fracture were considered and other surgical treatments were not considered, which may affect the overall outcomes of this network meta-analysis.

Conclusion

This network meta-analysis strongly supports that IF is the optimal surgical treatment for femoral neck fracture patients, and IF significantly improves the HHS in femoral neck fracture patients. However, our outcomes needs to be further confirmed based on high-quality RCT studies with more detailed and complete information.

Acknowledgements

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Disclosure of conflict of interest

None.

Abbreviations

THA, total hip arthroplasty; IF, internal fixation; HA, hemiarthroplasty; artificial FHR, artificial femoral head replacement; HHS, Harris hip score; RCTs, randomized controlled trails; SUCRA, surface under the cumulative ranking curves; ORIF, open reduction internal fixation; CRIF, closed reduction internal fixation; SMD, Standard mean difference; OA, osteoarthritis; RA, rheumatoid arthritis.

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