A Meta-Analysis of Acute Kidney Injury in Patients Undergoing Hip Fracture Surgery: Prevalence and Risk Factors

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Abstract

Objective: Acute kidney injury(AKI) was a frequent complication following hip fracture surgery, but recent studies reported inconsistent findings. The purpose of our study was to systematically clarify the prevalence and risk factors of AKI after hip fracture surgery.

Methods: Pubmed, Embase, and Web of Science were searched from the inception to March 2020 to identify observational studies investigating the prevalence and risk factors of AKI in patients undergoing hip fracture surgery. Pooled prevalence and odds ratios(ORs) with 95% confidence intervals(CIs) were estimated using random-effect model. Publication bias was evaluated with a funnel plot and statistical test. All the statistical analyses were performed using STATA version 12.0.

Results: A total of 11 studies with 16,421 patients were included in the current meta-analysis. The pooled prevalence of AKI in patients undergoing hip fracture surgery was 17%(95%CI, 14%-21%). Postoperative serum albumin(OR 1.80; 95%CI, 1.38–2.36) was a significant predictor for AKI. Age(OR 1.01; 95%CI, 0.95–1.07) and ACE inhibitors(OR 1.38; 95%CI, 0.92–2.07) were also associated with increased risk of AKI, but the results were not statistically significant. No significant publication bias was identified through statistical tests(Egger's test, p = 0.258 and Begg's test, p = 0.087).

Conclusions: The pooled AKI following hip fracture surgery was approximately 17%. Postoperative serum albumin was a potential significant risk factor for AKI.

Introduction

The worldwide population is continuously aging, thereby leading to an increase in the prevalence of osteoporotic hip fractures.[1,2] A recent statistical estimation predicts that the patients receiving surgical interventions for hip fracture will double by 2050 owing to the aging of population.[3] Furthermore, hip fracture is a major public health challenge, for it causes serious morbidity, death, and socioeconomic burden.[3]

Acute kidney injury (AKI) is a clinical syndrome featured with a sudden impairment in glomerular filtration and correlates with complex etiologies and pathophysiological processes. Every year, about 13.3 million cases are diagnosed with this intractable syndrome all over the world.[4,5] Worse still, it has been estimated that AKI results in a considerably mortality (1.7 million deaths per year) globally.[4,5] Notably, AKI is a common postoperative complication in patients undergoing surgical interventions for hip fracture, which closely correlated with prolonged hospital stay, various morbidity and increased mortality[6,7] Therefore, to adequately understand the landscape of prevalence and risk factors of AKI may largely help to improve outcomes of patients undergoing hip fracture surgery. Nevertheless, the reported prevalence of AKI associated with hip fracture surgery ranged widely from 5–60% currently. This remarkable range change may be caused by different AKI definition, inconsistent follow-up durations and small sample size, and so on. It is common sense that an inaccurate estimation of AKI prevalence will prevent clinicians to grasp an overview of the disease burden and its natural history, and this makes it hard for them to evaluate whether specific treatment strategies are effective for preventing AKI. Additionally, positively monitoring and coping with the risk factors for AKI may also do good to AKI prevention.[8,9]

Therefore, in this study we performed a meta-analysis and systematic review to summarize the prevalence and associated risk factors for AKI in patients undergoing surgical treatment for hip fracture.

Methods

This meta-analysis was undertaken according to the guideline of the Meta-analysis of Observational Studies in Epidemiology(MOOSE) checklist and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis(PRISMA) statement.[10,11]

Search Strategy And Study Selection

A systematic literature search of Pubmed, Embase, and Web of Science was conducted from inception to March 2020 to retrieve studies that reported the prevalence and risk factors of AKI in patients undergoing surgical interventions for hip fracture. The systematic search strategy was established using the terms of "acute kidney injury", "hip fracture surgery" and their variants. A manual search for potentially eligible studies was performed as well by screening the references of the included literature.

Selection Criteria

Eligible studies should be cohort studies, case-control studies, or cross-sectional studies, which must provide the data to estimate prevalence and risk factors of AKI in patients undergoing surgery for hip fracture. Only studies published in English were considered. The Retrieved studies were individually evaluated for eligibility by the two investigators independently. Discrepancies in eligible study selection were resolved via discussion and mutual consensus.

Data Abstraction And Quality Assessment

We applied the pre-designed table to extract the following information: first author, publication year, study period, country, operation type, case number, the number of patients with AKI, AKI definition and risk factors of AKI. The primary outcome was the prevalence of AKI after surgery for hip fracture. The secondary outcome was the odds ratio (OR) with corresponding 95% confidence interval (CI), which evaluated the relevant risk factors of AKI after surgery for hip fracture. Furthermore, only ORs with CIs generated from the multivariate analysis in the included studies were extracted. Two authors independently assessed the risk of bias of each eligible study according to the Newcastle-Ottawa Scale (NOS) score.[12]

Statistical analysis

The prevalences of AKI after surgery for hip fracture were extracted from eligible studies. Pooled estimated prevalences and 95% CIs were calculated with a random effect model. Odds ratios (ORs) with 95% CIs for risk factors were combined with a random effect model when substantial statistical heterogeneity existed across the included studies. Only candidate risk factors reported in two or more eligible studies on multivariable model were subjected for meta-analysis. I^2 statistic was applied to evaluate the statistical heterogeneity across eligible studies was assessed using with P value for $Q < 0.05$ or statistic $I^2 > 50\%$ regarded as substantial heterogeneity.[13,14] Meta-regression analysis on publication time, sample size and NOS score were used to explore the potential source of heterogeneity. Sensitivity analysis was undertaken by deleting one study each step to investigate the influence of single study on the overall pooled estimated prevalence of AKI after surgery for hip fracture. Subgroup analyses based on region, sample size, study design, AKI Definition, and NOS score for the primary outcome were conducted to explore the prevalence of AKI in sub-populations. Publication bias was evaluated by Begg's and Egger's tests, in which $P < 0.05$ and asymmetric funnel plot indicated significant publication bias.[15,16] A two-sided $P < 0.05$ was identified as statistical significance. All the statistical analyses were performed using STATA 12.0 (Stata Corporation, College Station, TX, USA).

Results

Study selection and characteristics

A total of 810 items were identified through systematically searching three databases. Furthermore, the full texts of 57 articles were screened for possible eligibility following removing duplicated and irrelative items. Eventually, a total of 11 studies with 16,421 patients were included in the current meta-analysis.[3,6,17–25] The flow chart of study selection was summarized in Fig. 1. The publication time of included studies ranged from 2010 to 2020. Seven studies were performed in Asia[6,18,19,21,22,24,25], while the other four in Europe[3,17,20,23]. The operation types, study design, and AKI definition of included studies were also different from each other. The whole NOS score of included studies ranged from 6 to 8 points, which suggested that the quality of included studies were moderate to high level. The detailed baselines characteristics and quality assessment of included studies were showed in Table 1 and Table 2.

Table 1
Baseline characteristics of included studies in the meta-analysis

Study/year	**Study period**	**Country**	**Operation**	**Age(years)**	**N with AKI**	**N total**	**AKI Definition**	**Study design**
Craig 2012[17]	September and November 2010	United Kingdom	Surgery for fractured neck of femur	Study group (80.3 years); control group (83.6 years)	13	100	An increase in serum creatinine by over 50% of baseline	Historical cohort study
Ulucay 2012 [18]	2007–2010	Turkey	Surgery for femoral neck fracture	> 65 years	25	163	AKIN classification	Prospective cohort study
Marty 2016 [3]	May-October 2012	France	Hip fracture surgery	83(75–92) years	29	48	AKIN classification	Prospective cohort study
Pedersen 2016 [20]	2005–2011	Denmark	Hip fracture surgery	> 65 years	1717	13529	KDIGO classification	Regional cohort study
Hong 2017 [19]	2010–2012	Korea	Hip fracture surgery	> 65 years	95	450	AKIN classification	Retrospective cohort study
Shin 2018 [6]	2011–2016	Korea	Surgery for intertrochanteric fracture of the proximal femur	> 60 years	57	481	KDIGO classification	Retrospective cohort study
Frenkelrutenberg 2019 [21]	2012–2016	Israel	Surgery for fragility hip fractureS	> 65 years	55	217	AKIN classification	Retrospective cohort study
Jang 2019 [22]	2011–2015	Korea	Femoral neck fracture surgery	77.6(65–97) years	44	248	KDIGO classification	Retrospective cohort study
Rantalaiho 2019 [23]	2017–2018	Finland	Hip fracture surgery	> 65 years	40	475	KDIGO classification	Retrospective cohort study
Kang 2020 [24]	2011–2016	Korea	Hip fracture surgery	70.1 years	25	550	AKIN classification	Case–control study
Küpeli 2020 [25]	January (1–7), 2018	Turkey	Hip fracture surgery	> 65 years	28	160	KDIGO classification	Retrospective descriptive study

AKI, Acute Kidney Injury; KDIGO, Kidney Disease Improving Global Outcome; AKIN, Acute Kidney Injury Network

Table 2
NOS score of included studies in the meta-analysis

Study	Selection	Comparability	Exposure	Total Score
Craig 2012[17]	2	2	3	7
Ulucay 2012 [18]	3	2	3	8
Marty 2016 [3]	3	2	3	8
Pedersen 2016 [20]	3	2	3	8
Hong 2017 [19]	3	2	2	7
Shin 2018 [6]	3	2	3	8
Frenkelrutenberg 2019 [21]	2	2	3	7
Jang 2019 [22]	3	2	3	8
Rantalaiho 2019 [23]	2	2	3	7
Kang 2020 [24]	2	2	3	7
Küpeli 2020 [25]	2	2	2	6
NOS, Newcastle-Ottawa Scale				

Postoperative Aki In Patients Undergoing Hip Fracture Surgery

All the included studies reported the prevalence of postoperative AKI in patients undergoing hip fracture surgery. The pooled prevalence of AKI following hip fracture surgery was 17% (95%CI, 0.14–0.21) with substantial heterogeneity(I^2 = 95%)(Fig. 2). Meta-regressions were conducted to explore the potential sources of statistical heterogeneity. The results indicated that publication time(p = 0.368), sample size(p = 0.593), and NOS score(p = 0.558) may not be the potential sources of statistical heterogeneity. Also, we performed stratified analyses to explore the prevalence of AKI in subgroup patients. In subgroup analyses stratified by region, the prevalence of AKI in Asia(22%) was higher than that in Europe(12%). When stratified by sample size, the prevalence of AKI in sample size > 500(40%) was higher than that in sample size ≤ 500(15%). In subgroup analysis by study design, the prevalence of AKI in the subgroup of cohort study(14%) was lower than that in other subgroup(43%). Interestingly, the prevalences of AKI in subgroup stratified by AKI definition and NOS score were basically the overall pooled prevalence of AKI. The detailed results of subgroup analyses were showed in Table 3. We also undertook the sensitivity analysis to explore the influence of individual included studies on the overall pooled estimate. We found that the pooled prevalence of POD basically remained stable, which indicated that pooled result was robust and credible(Fig. 3). We further evaluated the potential publication bias using the funnel plot and statistical tests. The funnel plot seemed to be asymmetric, but the statistical results indicated that the publication bias was not statistically significant (Egger's test, p = 0.258 and Begg's test, p = 0.087; Fig. 4).

Table 3
Subgroup analysis for the prevalence of AKI in Patients Undergoing hip fracture surgery

Outcomes	Number of trials	Pooled prevalence with 95%CI	I^2 (%)
Primary analysis	11	0.17(0.14–0.21)	95
Region			
Asia	7	0.22(0.15–0.29)	93.9
Europe	4	0.12(0.07–0.18)	97
Sample size			
> 500	2	0.40(0.02–0.79)	96.5
≤ 500	9	0.15(0.11–0.18)	94
Study design			
Cohort study	9	0.14(0.11–0.18)	94.1
Others	2	0.43(0.11–0.76)	94.3
AKI Definition			
Self-definition	1	0.12(0.06–0.18)	
KDIGO	5	0.17(0.09–0.25)	96.7
AKIN	5	0.20(0.15–0.25)	92.4
NOS score			
> 7	5	0.17(0.12–0.21)	92.2
≤7	6	0.20(0.12–0.29)	95.9

AKI, Acute Kidney Injury; CI, Confidence interval; KDIGO, Kidney Disease Improving Global Outcome; AKIN, Acute Kidney Injury Network

Risk factors for AKI in patients undergoing hip fracture surgery

We also explore the potential risk factors associated with AKI in patients undergoing hip fracture surgery. A total of seven studies reported AKI-associated risk factors on multivariate or adjusted model(Table 4).[3,6,18,20,22–24] Of these identified risk factors, pooled estimate indicated that postoperative serum albumin(2 studies; OR 1.80; 95%CI, 1.38–2.36; Table 5) was a significant predictor for AKI in patients undergoing hip fracture surgery. Age(3 studies; OR 1.01; 95%CI, 0.95–1.07; Table 5) and ACE inhibitors(2 studies; OR 1.38; 95%CI, 0.92–2.07; Table 5) were also associated with increased risk of AKI in patients undergoing hip fracture surgery, but the results were not statistically significant.

Table 4
Risk factors associated with AKI on multivariate model in patients undergoing hip fracture surgery

Study	Risk factors on multivariate model
Ulucay 2012 [18]	Age, years: (OR 1.049, 95%CI 0.984–1.118); Gender (female):(OR 2.643, 95%CI 0.909–7.686); Potassium: (OR 1.688, 95%CI 0.693–4.110); eGFR:(OR 0.945, 95%CI 0.921–0.963)
Marty 2016 [3]	Preop RI:(OR 0.03, 95%CI 0.01–75228);Postop RI:(OR 1.6*10^{12}, 95%CI 3779 – 679*10^{18}); GFR Preop:(OR 9.7, 95%CI 0.88–107); Age, years: (OR 0.92, 95%CI 0.84–1.01)
Pedersen 2016 [20]	Obese patients for AKI 1 stage(HR 1.4, 95%CI 1.1–1.8), AKI 2 stage(HR 1.9, 95%CI 1.3-3.0), AKI 3 stage(HR 2.8, 95%CI 1.5–4.9)
Shin 2018 [6]	Age (years):(OR 1.022, 95%CI 0.983–1.064); Chronic kidney disease:(OR 3.879, 95%CI 1.885–7.981);ACE inhibitors(OR 1.751, 95%CI 0.928–3.302);NSAIDs(OR 0.718, 95%CI 0.339–1.291); Koval score(OR 1.067, 95%CI 0.916–1.244);Postoperative serum albumin(OR 1.972, 95%CI 1.029–3.779); Postoperative drained blood volume(OR 1.003, 95%CI 0.999–1.007)
Jang 2019 [22]	Type of operation(OR 0.33, 95%CI 0.09–0.94); Diabetes mellitus:(OR 2.36, 95%CI 0.80–7.01);Previous renal disease(OR 2.57, 95%CI 0.60–3.24);ACE inhibitor(OR 1.43, 95%CI 0.50–1.17); Hemoglobin(OR 1.43, 95%CI 0.50–1.17);BUN(OR 1.03, 95%CI 0.99–1.08);eGFR(OR 1.02, 95%CI 0.99–1.04); Intraoperative hypotension(OR 5.14, 95%CI 1.54–20.35)
Rantalaiho 2019 [23]	Dementia(RR 2.37, 95%CI 1.00–4.98); Preoperative sCr:(RR 1.01, 95%CI 1.01–1.02)
Kang 2020 [24]	Hospitalization(OR 1.24, 95%CI 0.96–1.57);EBL(OR 1.54, 95%CI 1.32–2.44);Postoperative serum albumin(OR 1.77, 95%CI 1.52–2.74)
AKI, Acute Kidney Injury; OR, odds ratio; CI, Confidence interval; eGFR, estimated glomerular filtration rate; GFR: glomerular filtration rate;preop RI: preoperative doppler renal resistive index; postop RI:postoperative doppler renal resistive index; HR, hazard ratio; ACE inhibitors = angiotensin-converting enzyme inhibitors; NSAIDS = Non-steroidal antiinflammatory drugs; BUN, blood urea nitrogen; EBL: estimated blood loss	

Table 5
Meta-analysis of risk factors for AKI in Patients undergoing hip fracture surgery

Outcomes	Number of trials	OR (95% CI)	I^2(%)
Age	3	1.01(0.95–1.07)	63.7
ACE inhibitors	2	1.38(0.92–2.07)	0
Postoperative serum albumin	2	1.80(1.38–2.36)	0
eGFR	2	0.98(0.91–1.06)	95.1
AKI, Acute Kidney Injury; OR, odds ratio; CI, Confidence interval; ACE inhibitors, angiotensin-converting enzyme inhibitors; eGFR, estimated glomerular filtration rate			

Discussion

The current meta-analysis revealed that AKI was a relatively frequent complication in patients undergoing hip fracture surgery with pooled prevalence ranging from 14 to 21%. Additionally, postoperative serum albumin was identified to be a significant risk factor for AKI following hip fracture surgery.

The current meta-analysis based on 11 observational studies indicated that the overall pooled prevalence of AKI following hip fracture surgery was 17% with substantial heterogeneity. Considering that the significant heterogeneity may impair the credibility of the pooled estimate, meta-regression was performed to explore the potential sources of statistical heterogeneity. Furthermore, we identified that publication time, sample size, and NOS score may not be associated with significant heterogeneity. Furthermore, we conducted subgroup analysis and sensitivity analysis to explore the prevalence of AKI in sub-population. Interestingly, the results of subgroup analysis and sensitivity analysis were basically consistent with the overall pooled effect, which suggested that the pooled estimate was robust and reliable. A previous meta-analysis showed that the overall estimated prevalence rates of AKI in patients undergoing total hip arthroplasties are 6.3%.[26] Obviously, the prevalence of AKI following total hip arthroplasties was lower than that in patients undergoing hip fracture surgery. Regardless of the fact that the exact causes for these differences were largely unclear, but surgical workers should attach more importance to the potential AKI in patients undergoing hip fracture surgery. In the study, we also investigated the risk factors for AKI following hip fracture surgery. Pooled analysis showed that postoperative serum albumin was a significant indicator for AKI in patients undergoing hip fracture surgery. Consistent with our results, some previous studies also found that serum albumin level was a potential risk factor for AKI. Thongprayoon et al. revealed that there existed a U-shape correlation between serum albumin levels and AKI in hospitalized patients.[27] Dos Santos and coworker found that low serum albumin concentration was associated with increased risk of AKI in critically ill patients.[28] Mechanically, a recent study found that 5-Lypoxygenase products induced by albumin overload may be responsible for renal tubulointerstitial injury.[29] Other risk factors including age, ACE inhibitors, and eGFR were possible predictors for AKI, although the pooled results were not statistically significant. Collectively, perioperative management methods aimed at these risk factors may decrease the risk of AKI after hip fracture surgery.

There also existed several limitations in the current study. Firstly, our meta-analysis showed substantial statistical heterogeneity, which may potentially impair the reliability of the pooled estimate. Subsequently, we performed meta-regression to explore the sources of statistical heterogeneity and none of significant factors were identified to be responsible for heterogeneity. A possible interpretation is that multiple clinical and methodological difference across included studies, but not individual factor contribute to the significant statistical heterogeneity. Irrespective of the statistical heterogeneity, the results of subgroup analysis and sensitivity analysis were basically consistent with the overall pooled effect, which showed the robustness and reliability of the pooled estimate. Secondly, we evaluated the potential publication bias using the funnel plot and statistical tests. The statistical results showed that the publication bias was not statistically significant, but the funnel plot seemed to be asymmetric. Considering the inconsistence, the potential publication bias still cannot be excluded, although we performed a systematic literature search in the meta-analysis. Thirdly, some risk factors reported in included studies were not pooled for meta-analyses owing to limited studies, which may bias the authentic effects for AKI. The pooled analysis based on two studies found that ACE inhibitors may not be a significant risk factor for AKI following hip fracture surgery. Actually, many studies found that ACE inhibitors was a significant predictor for AKI.[30–32] Also, many risk factors including chronic kidney disease, intraoperative hypotension, and dementia were reported to be significant predictors for AKI, but we did not included for further pooled analyses owing to that they were reported in the limited studies. Therefore, the limited studies may bias the authentic estimates in the current meta-analysis. Accordingly, the results in our meta-analysis may be relatively conservative and should be interpreted in caution.

Take together, the current meta-analysis revealed that the pooled AKI in patients undergoing hip fracture surgery was approximately 17%. Postoperative serum albumin was identified to be a potential significant risk factor for AKI. Further high-quality studies should be warranted to systematically clarify the prevalence and risk factors of AKI following hip fracture surgery.

Abbreviations

AKI: Acute kidney injury; CI: Confidence interval; OR: odds ratio

Declarations

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Author contributions

Yan-Li Zhang and Yan-Chuang Pu designed this meta-analysis. Yan-Li Zhang, Yan-Chuang, Pu, Jin Wang, and Zi-Cai Li extracted data. Jin Wang, Zi-Cai Li, and Hu-Lin Wang performed statistical analysis. Yan-Li Zhang and Yan-Chuang Pu wrote this manuscript.

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Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors

Consent for publication

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Competing interests

The authors declare that they have no competing interests.

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Figures

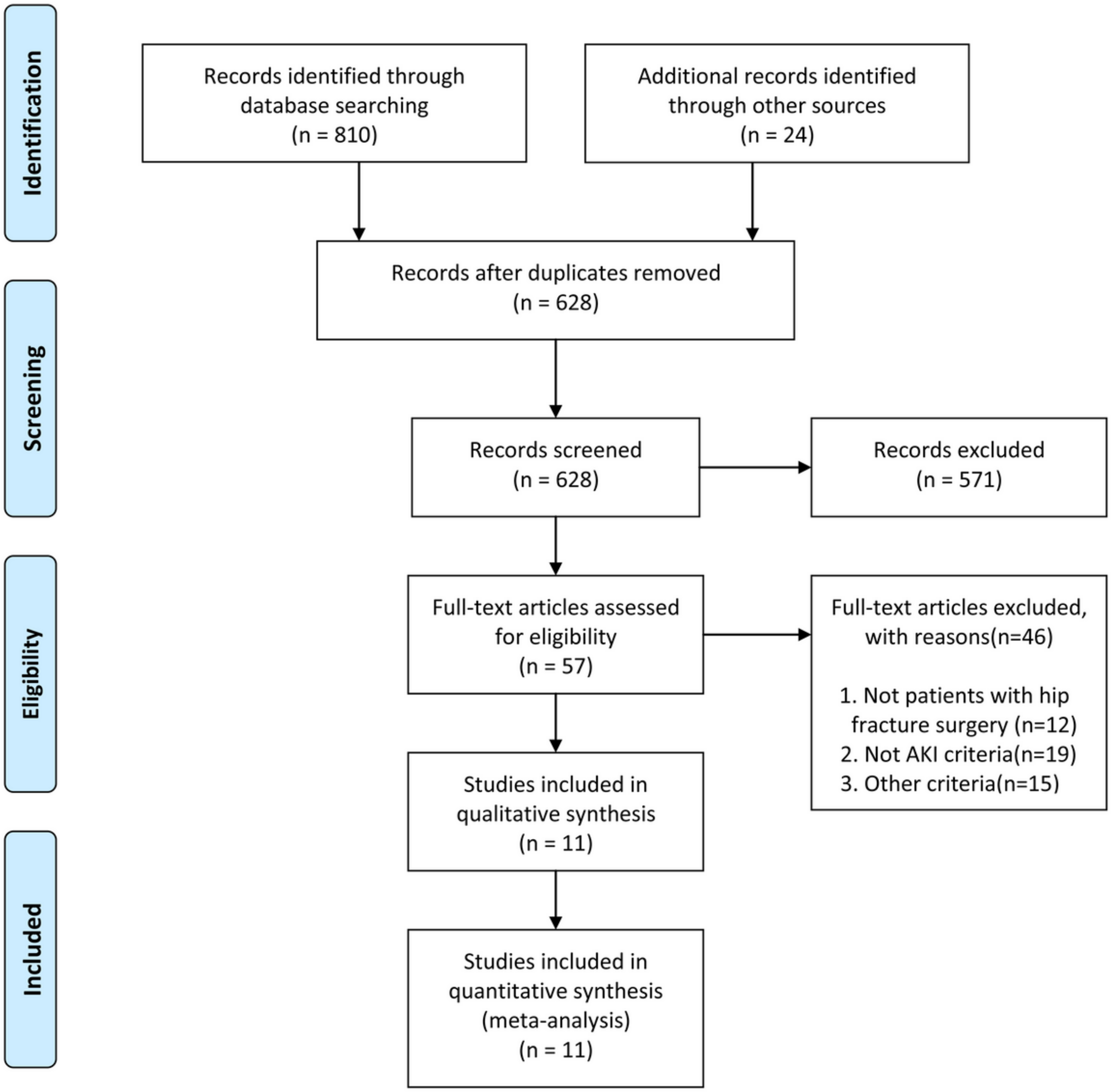

Figure 1

Flow diagram of the selection of studies for this meta-analysis

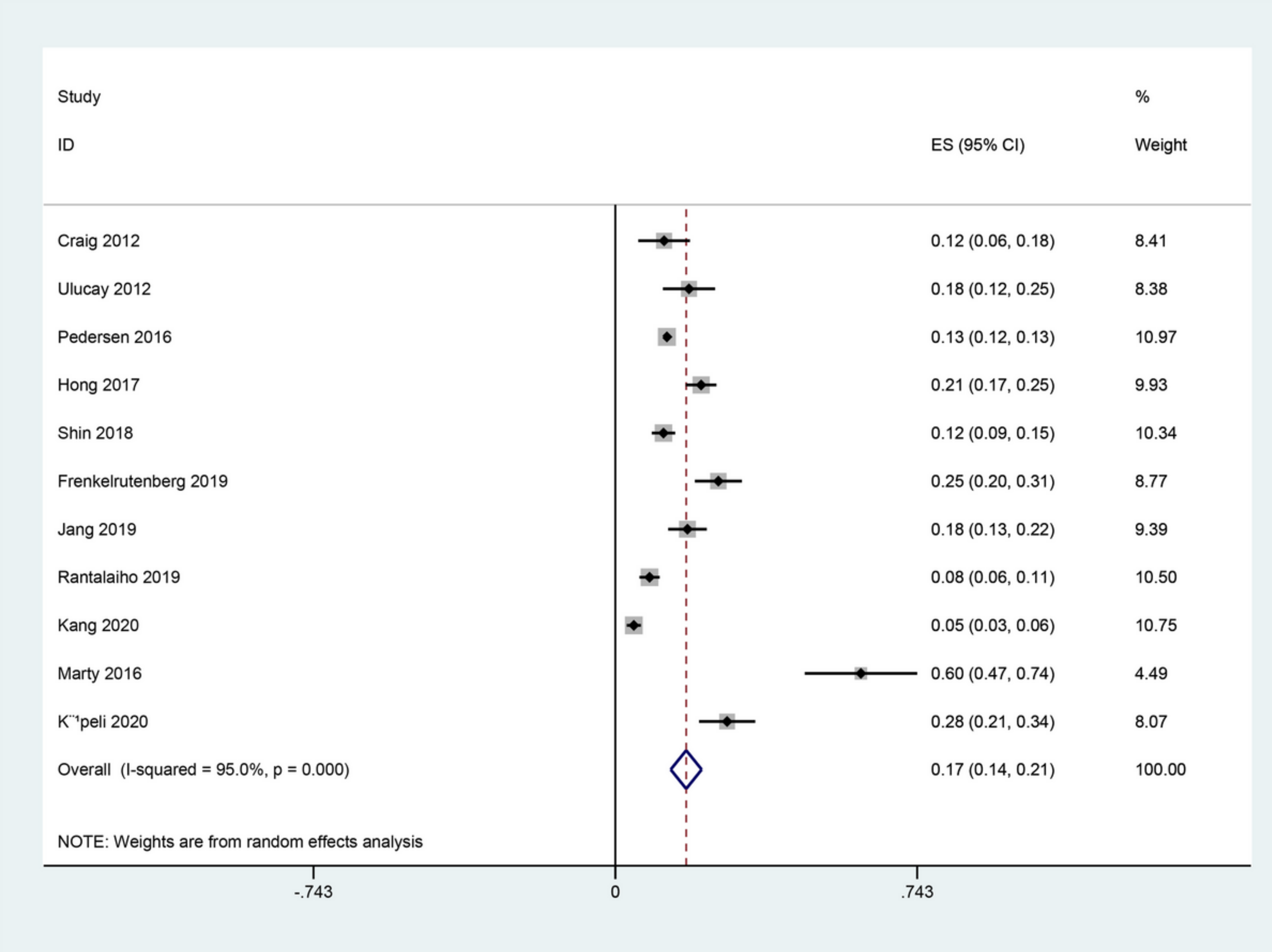

Figure 2

Forest plot for prevalence of AKI in patients undergoing hip fracture surgery using random-effects mode.

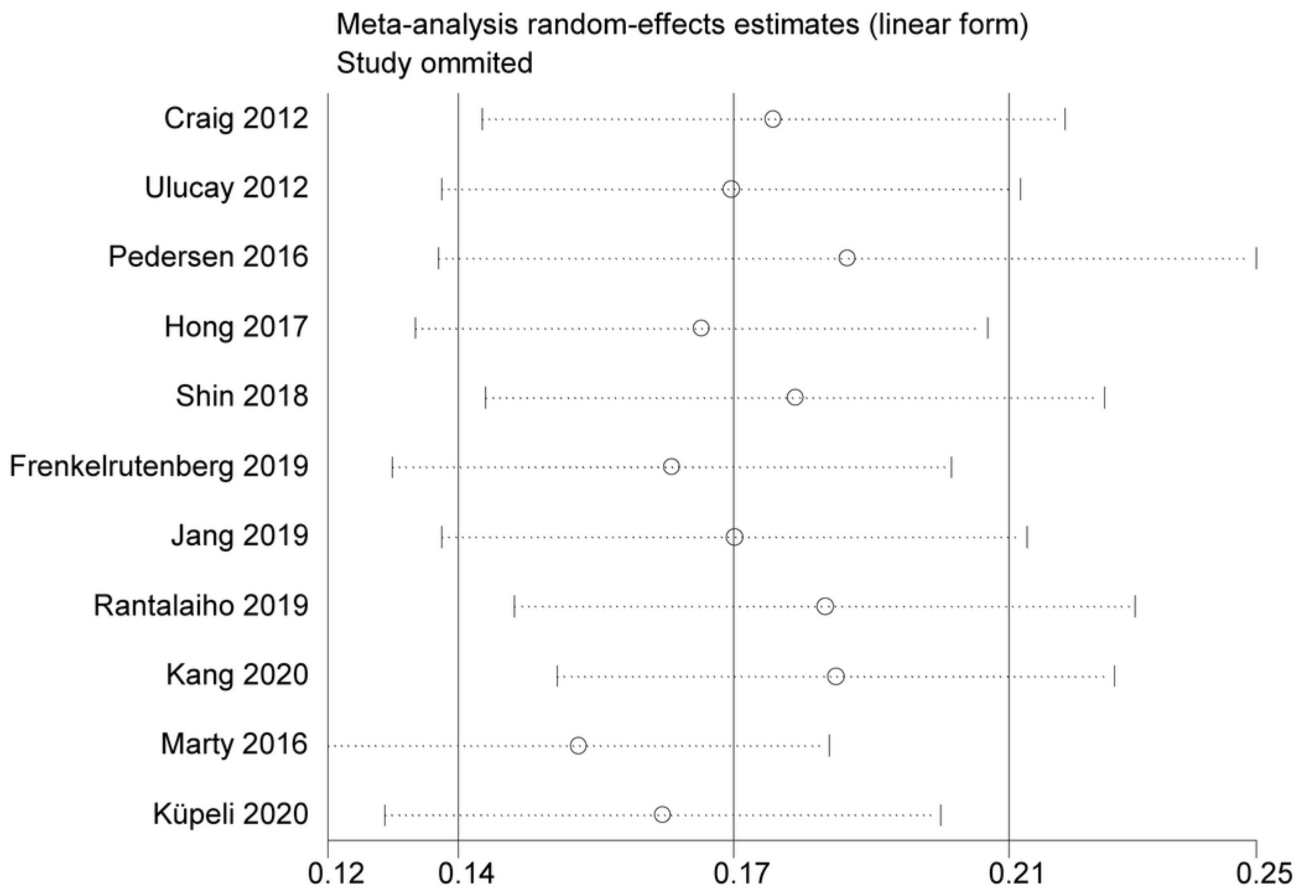

Figure 3

Sensitivity analysis for prevalence of AKI in patients undergoing hip fracture surgery in the meta-analysis.

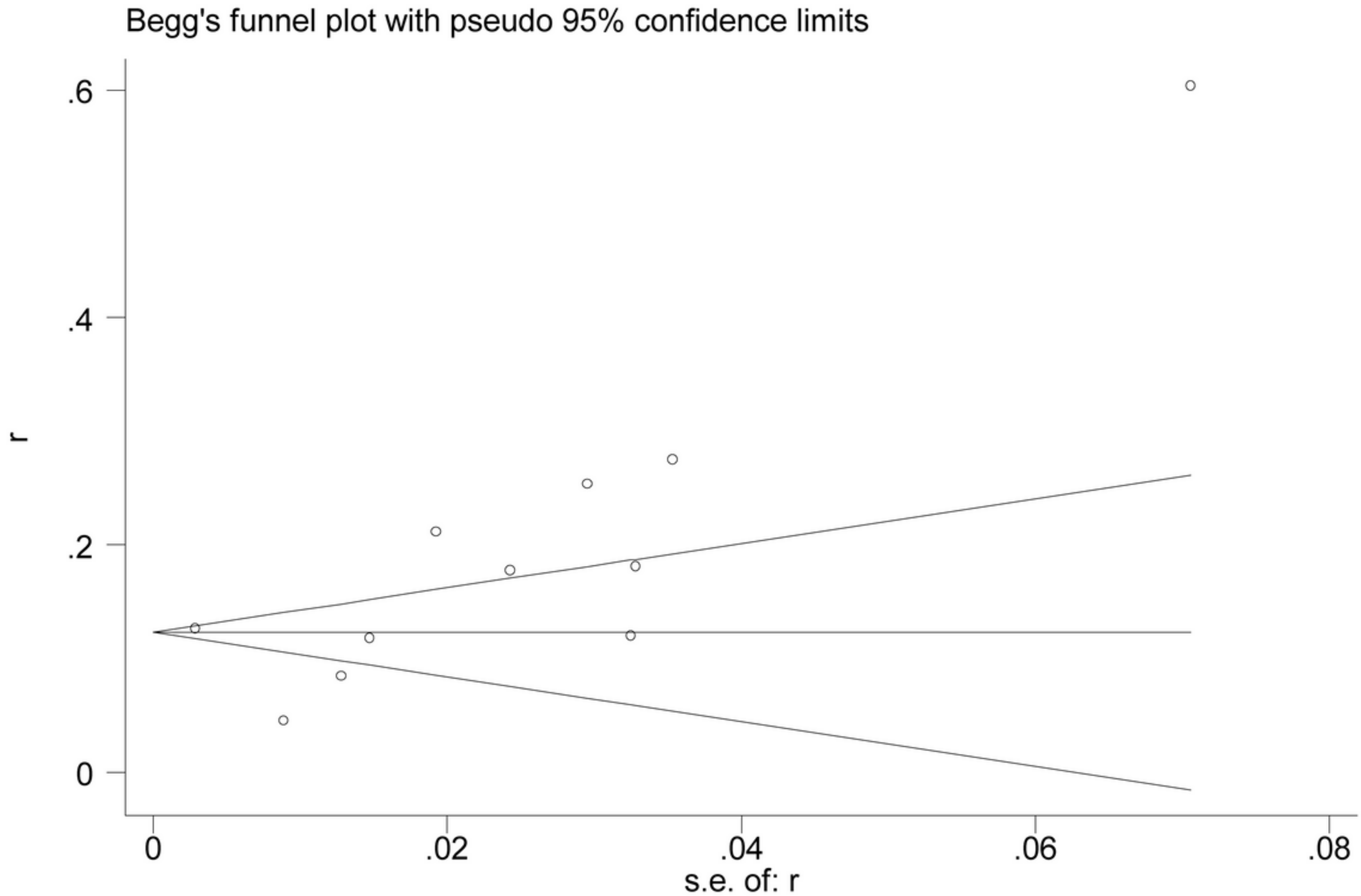

Figure 4

Funnel plot for prevalence of AKI in patients undergoing hip fracture surgery. (Egger's test, p = 0.258 and Begg's test, p = 0.087).