Systematic Review And Meta-Analysis: Risk Factors Of Acute Kidney Injury In Major Abdominal Surgery

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ABSTRACT: Background and objective: Acute kidney injury (AKI) is a common complication in patients undergoing major abdominal surgery. Various recent studies reported an incidence of AKI after surgery ranging from 6.7 to 32%. Risk factors for AKI in this setting may be procedure-related factors, post-operative complications and several patient-related include age, gender, comorbid disease Diabetes Melitus (DM), Hypertension (HT), Cardiovascular disease (CVD), and physical status. This study aimed to explore the risk factors of AKI in major abdominal surgery

Methods: We conducted a systematic literature search from PubMed and Cochrane Library. We included articles describing AKI in the setting of major abdominal surgery, published from 2015 until now, and cohort study design. This review was registered with PROSPERO (CRD42020216405)

Results: From 478 articles, 4 articles met our inclusion criteria describing AKI outcomes in varied population 683-3751. Prevalence of AKI 8,8 %. Age patient risk AKI in major abdominal surgery with Mean difference was 3.04 (95% CI = 1.83-4.25; P <0.00001). Meta-analysis of the four studies showed that Male had a pooled Odds ratio (OR) of 1.79 (95% CI = 1.04-3.08; P = 0.04) , DM OR 1.64 (95% CI 1.36-2.03; P <0.00001), HT pooled OR 1.90 (95% CI = 1.30-2.78; P = 0.0009), CVD has an OR of 1.58 (95% CI = 0.91-2.75; P = 0.10), physical status ASA≥ 3 (The American Society of Anesthesiologists) score has pooled OR 1.70 (95% CI = 1.16-2.49; P = 0.007)

Conclusion: Risk factors of AKI in major abdominal surgery setting are higher significantly in male, and patient with comorbid disease DM and HT had a significantly high risk of AKI, as well as physical status score ASA ≥ 3.

KEYWORDS: AKI, risk factors, major abdominal, surgery, major surgery

1. INTRODUCTION

Acute kidney injury is a poor predictor of short- and long-term outcomes, as well as a significant risk factor for the development of chronic kidney disease (CKD) [1,2]. Incidence of AKI is 13.3 million cases every year, and 11.3 million in developing countries [3]. To diagnose AKI, there are several criteria used around the world, RIFLE (Risk-Injury-Failure-Loss-End Stage Renal Failure), AKIN (Acute Kidney Injury Network), and KDIGO (Kidney Disease Improving Global Outcome) [1,4,5]. One-third of AKI in a hospital are caused by surgical intervention, but AKI as a complication after surgery is often undiagnosed[6]. Risk factors for AKI can be associated with patient and surgical intervention. There are several risk factors for AKI in patients with major abdominal surgery of older age, DM, HT, CVD, type of surgery, duration of surgery, use of vasoactive drugs, and intraoperative erythrocyte transfusion[78,9].Recognizing the risk factors for complications of AKI after surgery is expected to be a reference for predictors of AKI. Therefore, a systematic review and meta-analysis of the risk factors for AKI in major abdominal surgery is needed.

2. MATERIAL AND METHODS

2.1 Study selection and eligibility criteria

We included all original research articles describing AKI in the setting of major abdominal surgery, patients >18 years old, cohort study design, articles published after 2015, and in English. We prospectively excluded studies that do not report AKI in major abdominal surgery, surgery on urological, gynecological, vascular, and transplant, preexisting CKD, and Renal Replacement Therapy. No ethical approval will be needed because data from previously published studies in which informed consent was obtained by primary investigators will be retrieved and analyzed.

2.2 Literature search

We conducted a systematic literature search from the PubMed and Cochrane library database in April - August 2020. Our search strategy combined the following search terms mapped to the appropriate MeSH subject headings, exploded in the following Boolean expression: (AKI OR acute kidney injury OR acute renal failure) AND (incidence OR risk factors) AND (major surgery: operation OR surgery OR major surgery OR postoperative). Identical results were removed. The remaining studies were screened for relevance by title and abstract. Further reading and investigation according to inclusion and exclusion were done to search for potentially relevant studies. Our systematic review was registered with PROSPERO (CRD42020216405) and we adhered to the PRISMA (the Preferred Reporting Items for Systematic Reviews and MetaAnalyses).

2.3 Data extraction

Data extraction was performed using standardized forms that include generic information (first author, year, place), sample size, study design, age, gender, design, type of surgery, the comorbid disease which consists of HT, DM, and CVD, and ASA-PS scores≥3. Data extraction was performed independently by two authors (EB and HK)

2.4 Statistical analysis

Statistical analysis was performed using Review Manager V.5.4 (RevMan). We anticipated heterogeneity in terms of sample size with fixed and random effects models. Statistical heterogeneity between studies was analyzed using the Higgins I^2 test to estimate odds ratios (ORs) for dichotomous data and mean differences for continuous data[10] and explored graphically at the forest plot. The non-overlapping 95% CI results showed heterogeneity. The $\chi 2$ test was performed to assess homogeneity with a cut-off value of 10% (0.10). Interpretation of heterogeneity according to the Cochrane guidelines was 0–40% low heterogeneity, 30–60% moderate heterogeneity, 50–90% substantial heterogeneity, and 75–100% substantial heterogeneity. The Z score was calculated to get the overall effect, with the results of the analysis being significant if the P-value <0.05.

3. RESULTS

3.1 Study selection

Our systematic search identified a total of 278 titles from which a total of 4 articles describing AKI outcomes in patients undergoing major abdominal surgery. As many as 247 records were excluded after screening the title or abstract. After evaluating and assessing 31 potential studies, 27 studies were removed because 16 articles: are not a cohort study, have various types of surgery, outcomes are not AKI, have special populations, are not in English, 11 articles' total NOS score was less than 7. The selection process is shown in Fig. 1.

3.2 Study characteristics

The total patient varied from 683-3751 from 4 studies. Pooled prevalence of AKI varied between 5.8 -25.9%. The proportion of males varied from 60.7-65%, and patients who had a history of comorbid DM varied from 15.9 to 31%, CVD 1.6-5.85%, and HT was between 30-87%. The total number of AKI patients setting major abdominal surgery with DM, HT, CVD, and ASA-PS scores≥ 3 was less than those without AKI. The basic characteristics of the study are shown in Table 1

Table 1

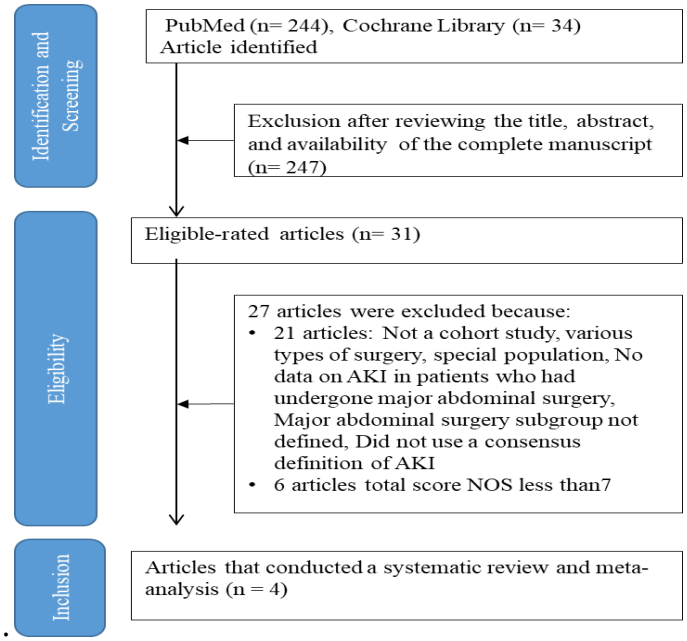
Study characteristic

No	Author, year	Study design	No.enroll	AKI vs No AKI						
				total	Male	Age years (Mean±SD)	CVD	DM	HT	ASA-PS ≥3
1.	Kee, 2019 [11]	Retrospective	683	177 vs 506	104 vs 311	60,9±13 vs 56,8±13,6	12 vs 28	40 vs 46	68 vs 146	NA

2.	Mizota, 2017[12]	Retrospective	3560	226 vs 3334	181 vs 2001	66,25± 9,6 vs 65,25± 12,59	7 vs 50	58 vs 508	117 vs 961	26 vs 208
3.	Mizota, 2018[14]	Retrospective	3751	216 vs 3493	176 vs 2112	67,25±9,6 vs 62,75±12,59	9 vs 53	54 vs 547	112 vs 1026	28 vs 222
4.	STAR Surg, 2018[13]	Prospective	949	175 vs 774	126 vs 491	NA	6 vs 34	61 vs 234	153 vs 672	81 vs 321
AKI: Acute kidney Injury, CVD: Cardiovascular Disease, DM: Diabetes mellitus, HT: Hypertension, ASA-PS: *The American Society of Anesthesiologist Physical Status* score, NA: *not available*										

3.3 Risk of AKI patient-related factors

One study was not included in the meta-analysis to determine the relationship between age and risk of AKI because the data were presented in the centered mean. The results of the meta-analysis showed that the mean difference between ages was 3.04 (95% CI = 1.83-4.25; P <0.00001) and was significantly higher in the AKI group than without AKI. The risk of AKI in major abdominal surgery was 1.79 times higher in males (OR of 1.79 (95% CI = 1.04-3.08; P = 0.04)) and statistical heterogeneity among the four studies was significant (P <0.00001). The pooled OR females had 0.56 (95% CI = 0.32-0.96; P = 0.04) and statistical heterogeneity between the four studies was also significant (P <0.00001). Meta-analysis of the four studies showed that DM had an OR of 1.64 (95% CI 1.36-2.03; P <0.00001), HT had an OR of 1.90 (95% CI = 1.30-2.78; P = 0.0009), CVD had a pooled OR of 1.58 (95% CI = 0.91-2.75; P = 0.10). Meta-analysis of the three studies showed that score ASA-PS $\geq$ 3 had an OR of 1.70 (95% CI = 1.16-2.49; P = 0.007). The risk of AKI patient-related factors of the study is shown



In fig 2-5

Fig. 1. Prisma Flowchart

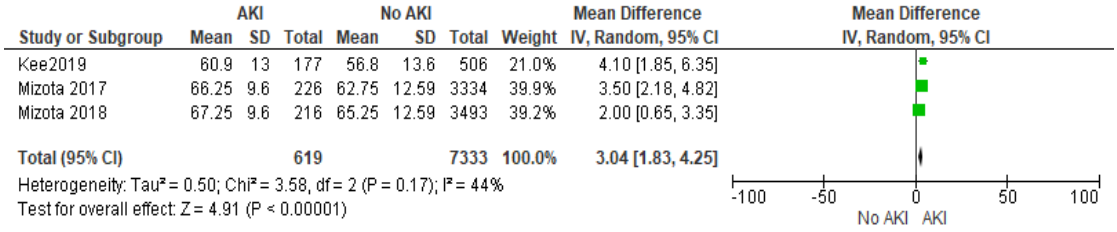
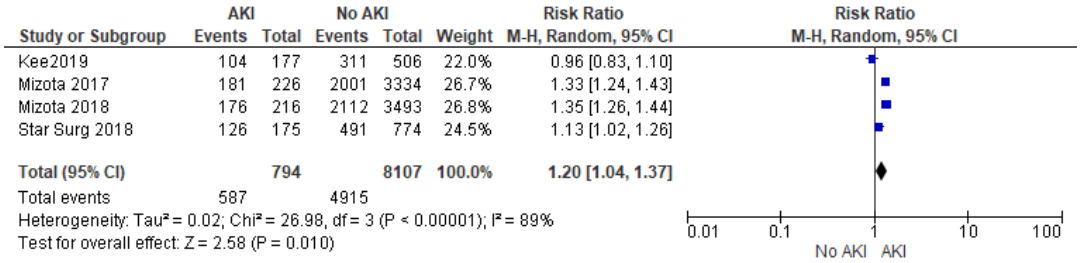


Fig.2. Analysis and forest plot of the mean difference in the age against the risk of AKI in major abdominal surgery

A.



B.

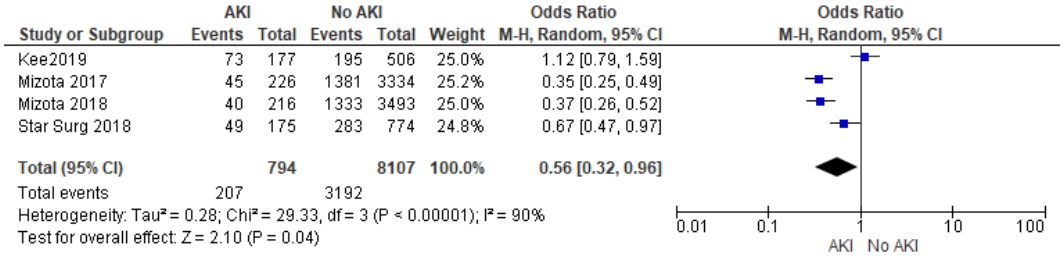
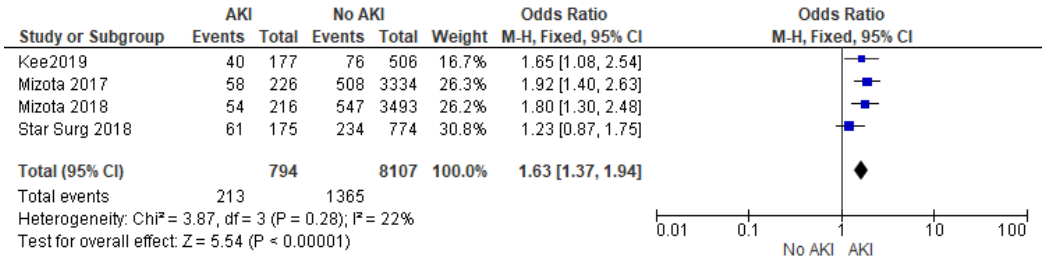
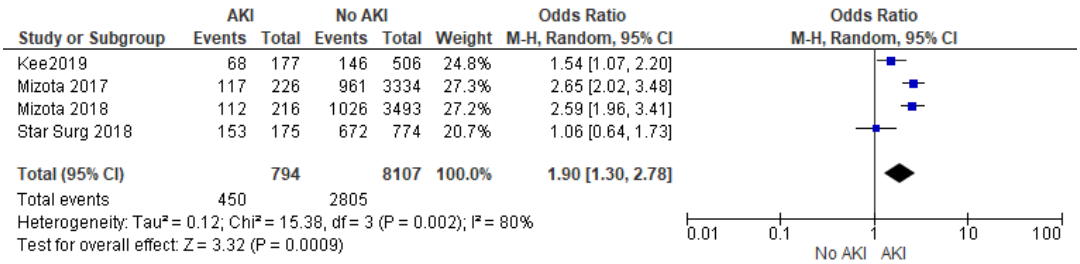


Fig.3. Analysis and forest plot of gender A) male and B) female against the risk of AKI in major abdominal surgery

A



B.



C

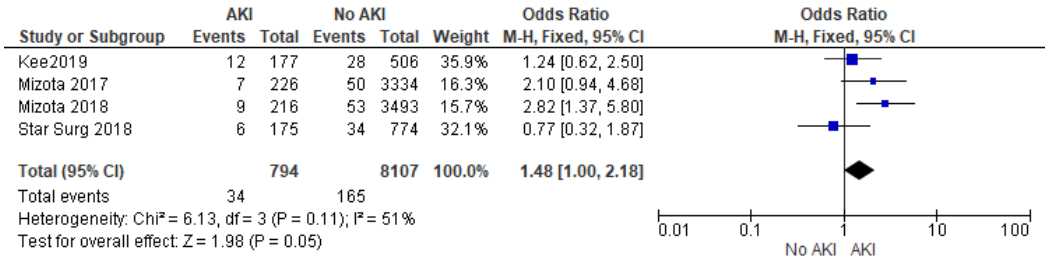


Fig.4: Analysis and forest plot of A) DM, B) HT, C) CVD against the risk of AKI in major abdominal surgery

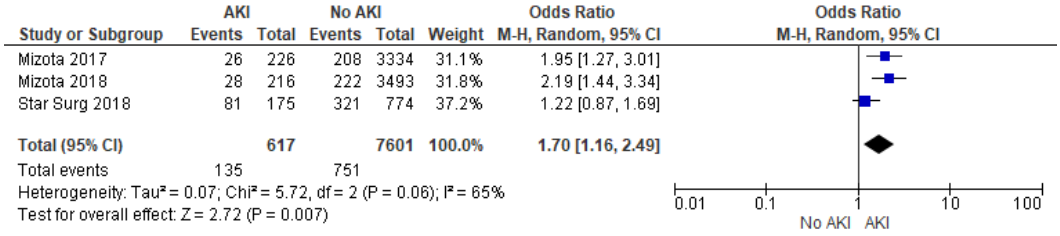


Fig.5: Analysis and forest plot of score ASA-PS $\geq$ 3 against the risk of AKI in major abdominal surgery

4. DISCUSSION

From a systematic review of the four studies, it was found that the number of subjects who underwent major abdominal surgery varied from 683 to 3.751 patients. The population of major abdominal surgery in the study of Kee et al was colorectal surgery. Two studies by Mizota et al in 2017 and 2018 covered surgery that included liver, colorectal, pancreatic, and esophageal resections. One study by Star Surg et al included patients undergoing major gastrointestinal and liver surgery. It appears that the four studies in this systematic review have a considerable variation in the type of major abdominal surgery. O'Connor et al in 2015 on 19 cohort studies found an incidence of GgGA 13.4% (95% CI = 10.9-16.4) and there was a significant heterogeneity (I^2 = 99%) among all studies. Major abdominal surgery including mixed, hepatobiliary, major gynecology, upper gastrointestinal, and colorectal. [8,11–14]

Risk of AKI-related age was found that the mean difference was 3.04 (95% CI = 1.83-4.25; P <0.00001), this mean age difference was significantly higher in the AKI group than without AKI. As we get older there is a decrease in the capacity of the kidneys to adapt to hemodynamic changes, the renal plasma flow is lower, and the renal response to vasodilation factors is also reduced. Elderly patients are also more frequently exposed to drugs that can affect kidney function, such as diuretics and contrast media agents. [15,16]

According to KDIGO, female is one of the risk factors for susceptibility to AKI. Long et al's study reported that female had a higher risk of AKI abdominal surgery setting with an OR of 0.68 (99% CI = 0.47-0.98). Significant risk of AKI major abdominal surgery setting for both male OR 1.79 (95% CI = 1.04-3.08; P = 0.04) and female OR 0.56 (95% CI = 0, 32-0.96; P = 0.04). From the results of this meta-analysis, male had 1.79 times the risk of AKI occurrence and female had a 44% renoprotective effect. [1,15]

Throughout our study, this study was the first meta-analysis to evaluate comorbid risk factors, particularly DM, HT, and CVD for the incidence of AKI in major abdominal surgery. Especially for DM and HT, no further evaluation of the history of treatment was carried out, whereas CVD in this meta-analysis was the majority of the history of congestive heart failure. Diabetes mellitus is known to be a risk factor for susceptibility to AKI occurrence. Hyperglycemia has been shown to predispose the kidneys to ischemia, microvasculopathy, and interstitial inflammation[1,17]. In this study, it was found that DM has an OR of 1.64 (95% CI = 1.36-2.03; P <0.00001). Biteker et al conducted a multivariate analysis of the risk factors of AKI, found that DM has a risk of 1.53 times (95% CI = 1.19-3.46; P = 0.001) and is an independent risk factor for AKI. [6]

Hypertension in this metanalysis was found to have an OR of 1.9 (95% CI = 1.30-2.78; P = 0.0009) but statistical heterogeneity among the four studies was significant. Star Surg et al specifically evaluating perioperatively of patients taking ARB or ACE-I reported that HT was more common in patients with ARB than without ARB. In another study by Kim et al, it was found that HT was a strong predictor of AKI (adjust RR 1.50 [1.40–1.61]) in intra-abdominal surgery. [18] The study of Tomozawa et al reported the risk of AKI in surgical liver resection in which patients with a history of HT had an adjusted OR of 2.10 (95% CI = 1.11-3.97). Uncontrolled hypertension can result in the arteries around the kidneys narrowing, weakening, or hardening, resulting in insufficient blood flow to the kidney tissue and the kidneys losing their ability to filter blood and regulating fluids, hormones, acids, and salts in the body. Surgery causes an increase in catabolic hormones and cytokines which increase the secretion of antidiuretic hormones, activate RAAS, increase aldosterone, also cause sodium and water retention and loss of potassium. [18,19]

Previous studies by Pan et al found that the risk of CVD was OR 1.85; P = 0.007, in this study the OR is 1.58 (95% CI = 0.91-2.75; P = 0.10). History of CVD in AKI patients undergoing major non-cardiovascular surgery has been shown to have a high risk of mortality in hospitalization. Long et al found a higher risk of AKI in patients with congestive heart failure OR 3.07 (99% CI = 1.74-5.41; P <0.001). [15,20]

The study by Kee et al that did not assess ASA-PS score as a risk factor for AKI, this study only analyzed three studies. The results showed that physical status score ASA-PS $\geq$ 3 had an OR of 1.7 (95% CI = 1.16-2.49; P = 0.007) and statistical heterogeneity among the three studies was not significant. This result is different from the study by Teixeira et al, which reported that the ASA-PS 4/5 score had a much higher OR of 9.1 (95% CI = 2.9-27.5; P <0.0001). The much greater variation in the total number of patients in this meta-analysis was the first to evaluate ASA-PS scores as a risk factor for AKI.[21]

4.1 Limitation

To our knowledge, this is the first meta-analysis to assess the risk factors of AKI in patients related to major abdominal surgery. Our limitations were the heterogeneous types of major abdominal surgery and various data reported in the median, interquartile range (IQR), and centre mean. This study only evaluated four studies, two studies using one data source, gray publications were excluded, and only used two search databases. Therefore, we realize that there is a publication bias.

5. CONCLUSION

In patients who underwent major abdominal surgery, the risk factor of AKI is higher in male, while patients with comorbid disease DM and HT have a higher risk of AKI, as well as score ASA-PS $\geq$ 3

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