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Acute kidney injury after gynaecological surgery – a systematic review and meta-analysis

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ABSTRACT

INTRODUCTION. Acute kidney injury (AKI) is an abruptly occurring loss of renal function, which includes both kidney injury and kidney impairment. It is associated with mortality and morbidity due to the increased risk of developing chronic kidney disease. The aim of this systematic review and meta-analysis was to determine the incidence of post-operative AKI in gynaecological patients without pre-existing kidney injury.

METHODS. Systematic searches were made for studies examining the association between AKI and gynaecological surgery published between 2004 and March 2021. The primary outcome was to compare two subgroups of studies; a screening group where AKI was diagnosed by systematic clinical screening and a non-screening group where AKI was diagnosed randomly.

RESULTS. Among the 1,410 records screened, 23 studies met the inclusion criteria, reporting AKI in 224,713 patients. The pooled incidence for post-operative AKI after gynaecological surgery in the screening subgroup was 7% (95% confidence interval (CI): 0.04-0.12). The overall pooled result for post-operative AKI after gynaecological surgery in the non-screening subgroup was 0% (95% CI: 0.00-0.01).

CONCLUSION. We found a 7% overall risk of post-operative AKI after gynaecological surgery. We found a higher incidence of AKI in the studies screening for kidney injury, illustrating that the condition is underdiagnosed when not screened for. An important risk exists of healthy women developing severe renal damage as AKI is a common post-operative complication with a potentially severe outcome that may be prevented in early diagnosis.

KEY POINTS

- Risk of post-operative acute kidney injury (AKI) after gynaecological surgery is 7% in studies screening for kidney injury.
- AKI is followed by a potentially severe outcome that may be prevented through early diagnosis.

The amount of surgical procedures performed in 2012 was estimated to be 312.9 million worldwide. Thus, global surgical volume is large and continuously growing [1]. With this global increase follows an increase in post-operative complications, which impact morbidity, length of hospitalisation and level of care at discharge. Major abdominal surgery, including a variety of gynaecological surgical procedures, is associated with increased post-operative complications and therefore increased morbidity. Gynaecological surgical procedures constitute almost 12% of all surgical procedures [2-4].

Kidney dysfunction is a well-known post-operative complication and is associated with increased morbidity and mortality [5]. This complication arises from a variety of acute conditions including acute kidney injury (AKI), acute renal failure and acute kidney syndrome [6]. Depending on the type of surgery and definition of kidney injury, the incidence of AKI varies from 1% to 37% [7-11]. The incidence of AKI is 12% in patients undergoing major abdominal surgery [12].

AKI is an abruptly occurring loss of renal function, which includes both kidney injury (structural damage) and kidney impairment (loss of function). This is followed by accumulation of waste products such as urea and other nitrogenous wastes [13]. Kidney hypoxia is recognised as a key pathogenic event in multiple forms of AKI [14]. AKI is associated with short- and long-term mortality and morbidity [5]. This is partly due to the increased risk of developing chronic kidney disease (CKD) and end-stage renal disease (ESRD) [15-17]. Studies have reported that 10-20% of patients surviving post-operative AKI develop CKD [18-20]. Both CKD and ESRD are associated with an elevated risk of death and reduced quality of life [21-26].

Approximately 30-40% of all AKI cases occur post-operatively [6]. Various comorbidities as age, intraoperative hypotension and increased BMI present as major risk factors in the development of post-operative AKI [27]. The association between intraoperative hypotension and post-operative AKI depends on various factors including severity and duration of intraoperative hypotension. During anaesthesia and various surgical procedures, intraoperative hypotension occurs, yet it is considered a modifiable risk factor [28].

During the past 20 years, three diagnostic tools for AKI have been developed: The Risk, Injury, Failure, Loss of kidney function and End-stage kidney disease (RIFLE) in 2004, the Acute Kidney Injury Networks (AKIN) in 2007 and the Kidney Disease Improving Global Outcomes (KDIGO) in 2012. These consensus AKI definitions are described in accordance with creatinine criteria and urine output (**Table 1**). The RIFLE criteria contain severity grades (Risk, Injury, Failure) and outcome classes (Loss, End-stage kidney disease), whereas the AKIN criteria differentiate between three stages and are a modification of the RIFLE criteria. As presented in Table 1, the KDIGO guidelines contain elements from both the RIFLE and the AKIN criteria.

TABLE 1 Acute kidney injury definitions for RIFLE, AKIN and KDIGO.

	Diagnostic tool					
	RIFLE		AKIN		KDIGO	
	stage	criteria	stage	criteria	stage	criteria
Creatinine	Risk	Increase of S creatinine ≥ 150% *Or* GFR decrease ≥ 25%	1	Increase of S creatinine ≥ 0.3 mg/dl *Or* Increase of 150-200% from baseline S creatinine	1	Increase of S creatinine ≥ 0.3 mg/dl *Or* Increase of 150-190% from baseline S creatinine
	Injury	Increase of S-creatinine of 200% *Or* GFR decrease ≥ 50%	2	Increase of 200-300% from baseline S creatinine	2	Increase of 200-290% from baseline S creatinine
	Failure	Increase S creatinine of 300% *Or* GFR decrease > 75% *Or* S creatinine rise ≥ 4 mg/dl	3	Increase of S creatinine ≥ 300% from baseline *Or* Increase of S creatinine ≥ 4.0 mg/dl with acute increase ≥ 0.5 mg/dl	3	Increase of S creatinine ≥ 300% from baseline *Or* Increase of S creatinine ≥ 4.0 mg/dl *Or* Renal replacement therapy
	Loss	Complete loss of kidney function for ≥ 4 wks	-	-	-	-
	ESKD	ESKD for ≥ 3 mos.	-	-	-	-
UO	Risk	UO < 0.5 ml/kg/h for 6 h	1	UO < 0.5 ml/kg/h > 6 h	1	UO < 0.5 ml/kg/h for 6-12 h
	Injury	UO < 0.5 ml/kg/h for 12 h	2	UO < 0.5 ml/kg/h > 12 h	2	UO < 0.5 ml/kg/h for ≥ 12 h
	Failure	UO < 0.5 ml/kg/h for 24 h *Or* Anuria for 12 h	3	UO < 0.3 ml/kg/h *Or* Anuria for 12 h	3	UO < 0.3 ml/kg/h for ≥ 24 h *Or* Anuria for ≥ 12 h

AKIN = Acute Kidney Injury Networks; ESKD = end-stage kidney disease; GFR = glomerular filtration rate; KDIGO = Kidney Disease Improving Global Outcomes; RIFLE = Risk, Injury, Failure, Loss of Kidney Function and End-stage Kidney Disease; UO = urine output.

The aim of this systematic review and meta-analysis was to determine the incidence of post-operative AKI in gynaecological patients without pre-existing kidney injury. This was done by comparing two subgroups of studies, a screening group where AKI was diagnosed by systematic clinical screening using consensus criteria and a non-screening group where AKI was diagnosed randomly. We hypothesised systematic clinical screening to be of significant value when diagnosing AKI after gynaecological surgery.

METHODS

Design

This systematic review and meta-analysis was conducted in accordance with the methods recommended by the meta-analysis of observational studies in epidemiology guidelines (MOOSE). The MOOSE checklist is presented in **Supplementary appendix TS1** (https://content.ugeskriftet.dk/sites/default/files/2023-05/a11220733-supplementary.pdf) [29]. The review was registered in the International Prospective Register of Systematic Reviews (PROSPERO, CRD42021247137).

Search strategy

The primary outcome was the incidence of post-operative AKI in patients who had undergone gynaecological surgery without pre-existing kidney injury.

Computer searches were conducted in the following electronic bibliographic databases: PubMed (Medline), Embase and the Cochrane Library. We searched for studies examining the association between AKI and gynaecological surgical procedures published between 2004 and March 2021. This time frame was in accordance with the establishment of the three AKI classifications. We searched for original articles in peer-reviewed journals excluding conference proceedings, publications in abstract form only, letters, case studies and reviews. The following keyword search terms and medical subject headings [MeSH] and [Emtree] were used in various combinations: ”acute kidney injury,” "acute renal injury," "acute renal insufficiency," "acute renal failure," "acute kidney failure," "gynecological surgery,” "gynecologic surgical procedure," "non-cardiac surgery," and "elective surgical procedure." The search was limited to human studies with no language restrictions. The search string is represented in **Supplementary appendix TS2**. In addition, reference lists of the primary research articles and review articles were examined to identify any potentially eligible studies. Publications were scanned and articles were selected for eligibility for further review based on the following inclusion criteria: provision of sufficient data calculating the association between AKI and gynaecological surgery.

The exclusion criteria were patients with preoperative AKI or CKD, patients who had per-operative mechanical injury of the urinary system, obstetric patients or patients who underwent any obstetrical procedure. Additionally, studies that failed to meet the minimum standards for methodological quality were excluded from the analysis.

Study quality

Two investigators (CR and IA) independently screened the literature and extracted data according to the predefined inclusion and exclusion criteria. Any discrepancy was resolved by consulting a third researcher (NK) and resolved through consensus among the investigators. Data extraction of the screening subgroup included: author, year of publication, study design, definition for AKI, type of gynaecological surgery, primary diagnosis (benign or malignant), cohort size, age and incidence of AKI. Data extraction of the non-screening subgroup included: author, year of publication, study design, type of gynaecological surgery, primary diagnosis, cohort size and incidence of AKI.

We used Rayyan for detecting possible duplicates. Risk of bias was assessed using the Newcastle-Ottawa Scale (NOS) for evaluating the quality of non-randomised studies in this meta-analysis. This quality assessment tool awards stars based on three categories: selection of the cohort, comparability of the study based on analysis or design and outcome of the study. Studies were included if they achieved at least three out of nine possible stars.

Statistical analysis

Statistical analysis was completed using The R Project for Statistical Computing (R), using R packages: meta, rmeta and metaphor. The test was two-tailed and statistical significance was set to $p < 0.05$.

The quantitative categorical variables were compared using the Cochrane Q test, a non-parametric analysis of the matched set of proportions, in the assessment of heterogeneity of this meta-analysis. The I^2 index was used to quantify the heterogeneity.

The occurrence of AKI was compared between groups by Fisher's exact test. $p < 0.05$ was considered significant. Fisher's exact test was used to calculate the level of significance using Social Science Statistics Version 2022. All of the included 23 studies provided data for Fisher's exact test hereby evaluating on the effectiveness of screening.

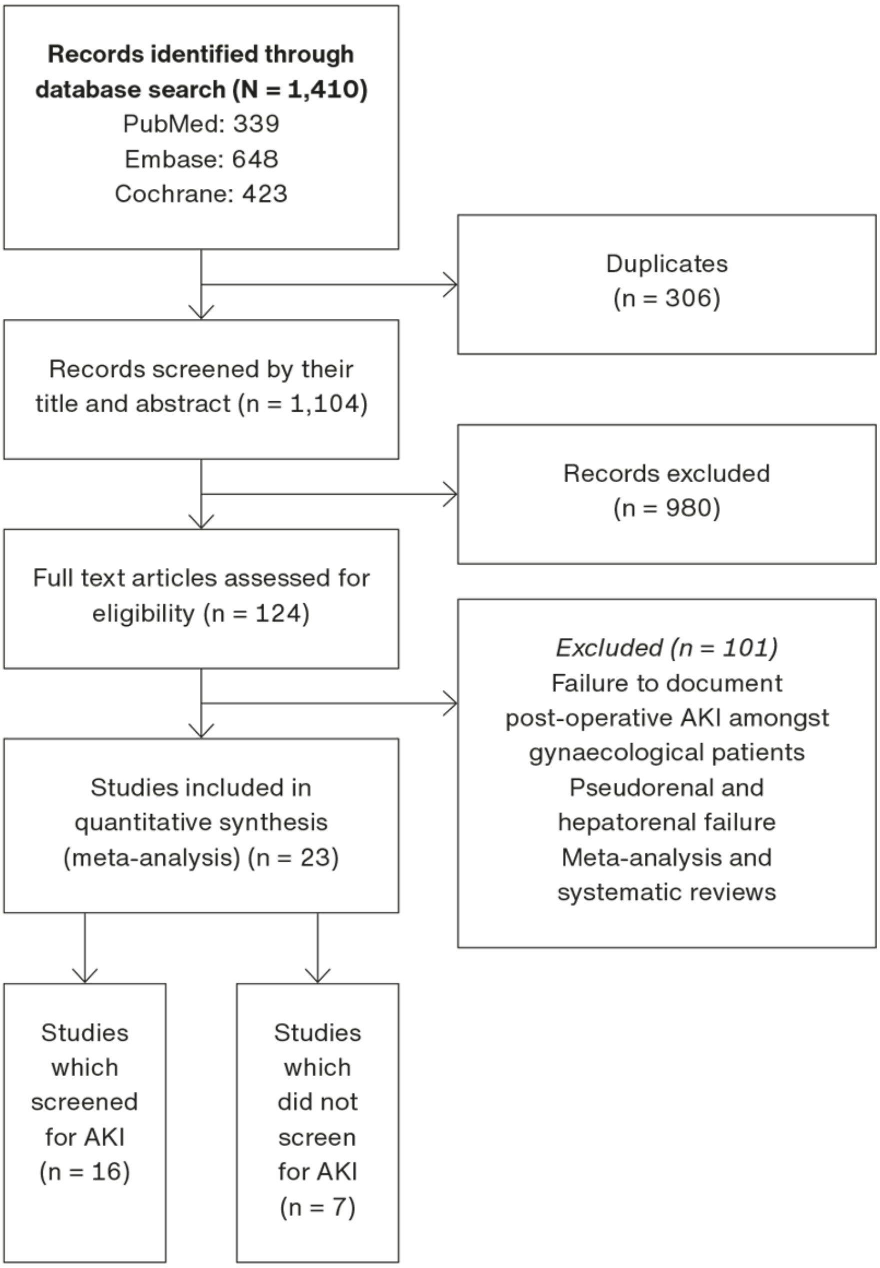
RESULTS

Literature search

A total of 1,410 records were identified. After removal of duplicates, 1,104 studies remained. Ultimately, a total of 23 studies were included and divided into two subgroups depending on diagnosis of AKI after gynaecological surgery. The studies meeting the inclusion criteria were all in English. The screening subgroup consisted of 16 studies in which 11,530 patients undergoing gynaecological surgery were systematically screened for AKI using the RIFLE, AKIN or KDIGO criteria. The non-screening subgroup consisted of seven studies in which 213,183 patients undergoing gynaecological surgery reported AKI, diagnosed with no clinical screening.

The literature screening procedure is presented in **Figure 1**. Among the 16 studies in the screening subgroup, nine were retrospective cohort and observational studies, four were prospective observational studies, one was a quasi-experimental time series, one was pilot matched-controlled study and one was post-hoc analysis of a randomised controlled pilot trial. The surgical procedures were undisclosed in seven of the remaining studies, concerning 623 patients. AKI was classified according to the RIFLE, AKIN and KDIGO classifications. Among the seven studies in the non-screening subgroup, six were retrospective cohort studies, and one was a case-control study. The surgical procedure was undisclosed in only one study concerning 621 patients.

FIGURE 1 Study inclusion flow chart.



AKI = acute kidney injury.

The NOS was used in quality assessment of the 23 included studies and is presented in Supplementary table 3 TS3.

Characteristics of included studies

Table 2 presents a detailed description of the screening subgroup containing 16 studies reporting post-operative AKI in gynaecological patients. All participants underwent gynaecological surgery due to either benign conditions (n = 801 based on one study) or gynaecological cancer (n = 2,529 based on six studies). However, the primary diagnoses were undisclosed in the remaining ten studies. The sample sizes ranged from three to 3,547 patients. The overall incidence of post-operative AKI ranged from 0% to 32%. The incidence of post-operative

AKI for benign surgery was 5%; and for gynaecological cancer, the range was from 3.12% to 29.16%.

TABLE 2 Details of the 16 studies in the screening subgroup and of the seven studies in the non-screening subgroup.

Reference	Study design	AKI definition	Type of gynaecological surgery (n)	Primary diagnosis (n)	Age, yrs	Gynaecological patients, n	Gynaecological patients with AKI, n	AKI incidence, %
Performed screening for AKI								
Chen et al., 2020 [32]	Single-centre retrospective observational study	KDIGO	-	Gynaecological cancer	Mean age *Propofol* No: 74, yes: 71 *Midazolam* No: 73, yes: 69 *Fentanyl* No 72, yes: 72	541: gynaecological patients in total 187: not screened for AKI 354: end	30	8.47: overall
Iyigun et al., 2019 [33]	Multicentre prospective observational study	KDIGO	-	-	-	52	8	15.38: overall
Li et al., 2019 [34]	Retrospective cohort study	KDIGO	-	-	-	25	8	32.00: overall
Hallqvist et al., 2018 [35]	Retrospective observational study	KDIGO	-	-	-	54	10	18.52: overall
Maheshwari et al., 2018 [36]	Retrospective cohort analysis	KDIGO	Hysterectomy, abdominal and vaginal (2,752) Other surgical procedures (795)	-	-	3,547	88: hysterectomy 17: other surgical procedures 105: total	2.96: overall
Russo et al., 2018 [31]	Pilot matched-controlled study	RIFLE	Radical hysterectomy, bilateral adnexectomy, bowel resection, peritonectomy and extended pelvic/periaortic lymphadenectomy	Ovarian cancer	Median age p = 0.55 GDHT: 49 Controls: 55	22: GDHT protocol 22: controls 44: total	3	6.82: overall
Salmasi et al., 2017 [37]	Retrospective cohort analysis	AKIN	Hysterectomyl, abdominal and vaginal	-	-	3,410	86	2.52 overall
Srisawat et al., 2018 [38]	Single-centre prospective cohort study	KDIGO	Laparoscopic abdominal surgery	-	-	3	0	0.00: overall
Hunsicker et al., 2017 [30]	Post-hoc analysis of a randomized controlled pilot trial	KDIGO	Laparotomy for cytoreductive surgery	Ovarian cancer	p = 0.14 Non-AKI: 53 AKI: 60	48	10: stage 1 1: stage 2 3: stage 3 14: total	29.16: overall
O'Connor et al., 2017 [12]	Retrospective cohort study	KDIGO	-	-	-	23	0	0.00: overall
Pourafkari et al., 2018 [39]	Prospective observational study	AKIN	-	-	-	97	1	1.03 overall
Sun et al., 2015 [28]	Retrospective cohort study	AKIN	Major abdominal surgery	Gynaecological cancer	p = 0.49	865	27	3.12: overall
Wu et al., 2015 [40]	Retrospective observational cohort study	KDIGO	-	-	-	18	0: 1st tertile 2: (2nd tertile) 2: (3rd tertile) 4: total	22.22: overall
Bell et al., 2014 [41]	Interrupted time series study	KDIGO	Abdominal excision of uterus, vaginal excision of uterus, other excisions of uterus, laparoscopic total hysterectomy, laparoscopic subtotal hysterectomy	-	-	403	17	4.22: overall
Biteker et al., 2014 [10]	Single-centre, prospective study	RIFLE	Major gynaecologic cancer surgery: abdominal hysterectomy and oophorectomy	Gynaecological cancer	-	59	6	10.17: overall
Vaught et al., 2015 [2]	Retrospective single-centre cohort study	RIFLE	Hysterectomy (1,349) Ovarian surgery (345) Vulvectomy (41) Colorecto-vaginal fistulas and rectocele surgery (39)	Benign (801) Gynaecological cancer (1,159)	Mean age Non-AKI: 53 All AKI: 60 RIFLE: 60 Injury: 59 Failure: 61	2,341	185: risk 65: injury 45: failure 295: total	5.00: benign 18.00: malignant 12.60: overall

Continues >

TABLE 2 CONTINUED Details of the 16 studies in the screening subgroup and of the seven studies in the non-screening subgroup.

Reference	Study design	AKI definition	Type of gynaecological surgery (n)	Primary diagnosis (n)	Age, yrs	Gynaecological patients, n	Gynaecological patients with AKI, n	AKI incidence, %
Did not perfom screening for AKI								
Kim et al., 2020 [42]	Retrospective cohort study	-	Hysteroscopic surgery (12.2%) Laparoscopic surgery (37.9%) Open/abdominal surgery (49.9%)	Myomectomies for symptomatic uterine fibroids: benign	Median age No transfusion: 38 Transfusion: 37	3,065: no transfusion 342: transfusion 3,407: total	0: no transfusion 2: transfusion 2: total	0.00: no transfusion 0.60: transfusion 0.06: overall AKI
Matsuo et al., 2020 [43]	Retrospective study	-	Open surgery, MIS, hysterectomy, adnexectomy, oophorectomy (73,707)	Early-stage ovarian cancer	Open surgery: 55.5 MIS: 52.4	68,885: open surgery 4,822: MIS 73,707: total	584	0.79: overall
Sears et al., 2020 [44]	Retrospective cohort study	-	Hysterectomy: abdominal, vaginal and laparoscopic surgery	Benign conditions	Abnormal laboratory values: 46.4 Normal laboratory values: 46 No laboratory values: 47.8	7,680: abnormal laboratory values 15,225: normal laboratory values 1,847: no laboratory values 24,752: total	7: abnormal laboratory values 6: normal laboratory values 1: no laboratory values 14: total	0.09: abnormal laboratory values 0.04: normal laboratory values 0.05: no laboratory values 0.06: overall
Ramzan et al., 2015 [45]	Retrospective cohort study	-	Panniculectomy, laparotomy, MIS	Endometrial cancer	Panniculectomy: 48 Laparotomy: 55.6 MIS: 55.5 Overall: 55.5	11: panniculectomy 208: laparotomy 332: MIS 551: total	1: panniculectomy 2: laparotomy 1: MIS 4: total	9.10: panniculectomy 1.00: laparotomy 0.60: MIS 0.73: overall
Ross et al., 2018 [46]	Case-control study	-	Cytoreductive surgery	Ovarian cancer	Median age ICU admissions: 66 Controls: 61	108: ICU admissions 216: controls 324: total	21	6.50: overall
Margulies et al., 2020 [47]	Retrospective cohort study	-	Laparoscopic and abdominal hysterectomy	Benign conditions	Laparoscopic: 47.2 Abdominal: 47.9	66,560: laparoscopic 43,261: abdominal 109,821: total	35: laparoscopic 64: abdominal 99: total	0.05: laparoscopic surgery 0.20: abdominal surgery 0.09: overall and/or dialysis
Vernooij et al., 2018 [48]	Retrospective cohort study	-	-	-	-	621: gynaecological patients in total 59: gynaecological patients examined for AKI	1	0.59: overall

AKI = acute kidney injury, AKIN = Acute Kidney Injury Networks; GDHT = goal-directed haemodynamic therapy; ICU = intensive care unit; KDIGO = Kidney Disease Improving Global Outcomes; MIS = minimally invasive surgery; RIFLE = Risk, Injury, Failure, Loss of Kidney Function and End-stage Kidney Disease.

Table 2 additionally presents a detailed description of the non-screening subgroup containing seven studies, reporting post-operative AKI in gynaecological patients. All participants underwent gynaecological surgery due to either benign conditions (n = 137,980 based on three studies) or gynaecological cancer (n = 184,403, based on four studies). The primary diagnosis was not reported in the remaining study. The sample sizes ranged from 324 to 109,821 patients. The incidence of post-operative AKI ranged from 0% to 6.5%. The incidence of post-operative AKI for benign surgery was between 0.06% and 0.09% and ranged from 0.73% to 6.5% for gynaecological cancer.

The inclusion and exclusion criteria of the included studies are presented in Supplementary table 4 TS4.

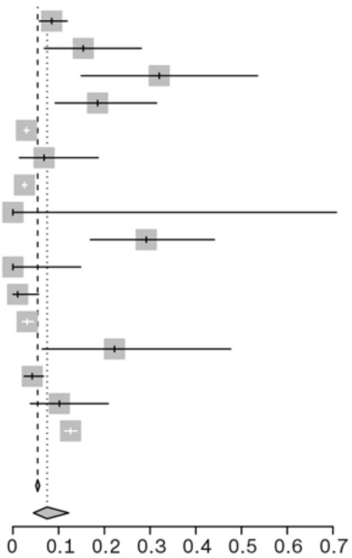
Meta analysis and Fisher's exact test

Separate meta-analyses were performed regarding both the screening and the non-screening subgroups. All of the 16 included trials in the screening subgroup provided data for the meta-analysis, see **Figure** 2A. The overall pooled result for post-operative AKI after gynaecological surgery was 0.07 (95% confidence interval (CI): 0.04-0.12). However, heterogeneity was observed between the studies (Cochran's Q test $p < 0.01$, $I^2 = 96\%$). All of the included seven studies in the non-screening subgroup provided data for the meta-analysis, see Figure 2B. The overall pooled result for post-operative AKI after gynaecological surgery was 0.004 (95% CI: 0.001-0.013). Heterogeneity was observed between the studies (Cochran's Q test $p < 0.01$, $I^2 = 99\%$). Significantly more heterogeneity was observed in the screening subgroup diagnosed with AKI than in the subgroup without screening ($p < 0.0001$).

FIGURE 2 Forest plot of risk of developing post-operative acute kidney injury. **A**. Based on the 16 included studies in the screening subgroup. **B**. Based on the seven included studies in the non-screening subgroup.

A

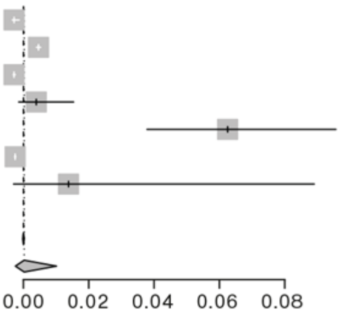
Reference	Events	Total	Proportion (95% CI)
Chen et al. [32]	30	354	0.08 (0.06-0.12)
Iyigun et al. [33]	8	52	0.15 (0.07-0.28)
Li et al. [34]	8	25	0.32 (0.15-0.54)
Hallqvist et al. [35]	10	54	0.19 (0.09-0.31)
Maheshwari et al. [36]	105	3,547	0.03 (0.02-0.04)
Russo et al. [31]	3	44	0.07 (0.01-0.19)
Salmasi et al. [37]	86	3,410	0.03 (0.02-0.03)
Srisawat [38]	0	3	0.00 (0.00-0.71)
Hunsicker et al. [30]	14	48	0.29 (0.17-0.44)
O'Connor et al. [12]	0	23	0.00 (0.00-0.15)
Pourafkari et al. [39]	1	97	0.01 (0.00-0.06)
Sun et a.l [28]	27	865	0.03 (0.02-0.05)
Wu et al. [40]	4	18	0.22 (0.06-0.48)
Bell et al. [41]	17	403	0.04 (0.02-0.07)
Biteker et al. [10]	6	59	0.10 (0.04-0.21)
Vaught et al. [2]	295	2,341	0.13 (0.11-0.14)
Fixed effect model		11,343	0.05 (0.05-0.06)
Random effects model			0.07 (0.04-0.12)



Heterogeneity: $I^2 = 96\%$, $\tau^2 = 0.9781$, $p < 0.01$

B

Reference	Events	Total	Proportion (95% CI)
Kim et al. [42]	2	3,407	0.00 (0.00-0.00)
Matsuo et al. [43]	584	73,707	0.01 (0.01-0.01)
Sears et al. [44]	14	24,752	0.00 (0.00-0.00)
Ramzan et al. [45]	4	551	0.01 (0.00-0.02)
Ross et al. [46]	21	324	0.06 (0.04-0.10)
Margulies et al. [47]	99	109,821	0.00 (0.00-0.00)
Vernooij et al. [48]	1	59	0.02 (0.00-0.09)
Fixed effect model		212,621	0.00 (0.00-0.00)
Random effects model			0.00 (0.00-0.01)



Heterogeneity: $I^2 = 99\%$, $\tau^2 = 2.8559$, $p < 0.01$

AKI = acute kidney injury; CI = confidence interval.

DISCUSSION

In our study, we found the overall incidence of post-operative AKI to be 7% in the screening group. The incidence of AKI had a wide range in these studies, with a low incidence in benign surgery and a higher incidence in patients undergoing surgery for gynaecological cancer. The pooled meta-analysis in the non-screening group found the that the incidence of AKI was very low. Again, the lowest incidence was reported in benign surgery compared with a higher risk in gynaecological cancer. Not only did the seven studies in the non-screening group report a very low incidence of kidney injury; the cohorts of gynaecological patients were large compared with the 16 studies in the screening group. This illustrates that renal injury after gynaecological surgery is significantly underdiagnosed in the non-screening group as the diagnosis of AKI requires systematic screening. Furthermore, a high degree of uncertainty exists in the comparison of the two subgroups due to lack of definition of AKI in the non-screening subgroup. The potential impact of this should be considered in future research. Patients undergoing gynaecological surgery are often hospitalised, operated and discharged on the same day. The post-operative rehabilitation and recovery occur at home, and the general practitioner undertakes clinical follow up, which additionally complicates setting the diagnosis of AKI post-operatively as serum creatinine is not monitored routinely.

The meta-analysis for both subgroups had a considerable level of heterogeneity (as the I^2 index was 96% and within the 90-100% interval in each group). The reported heterogeneity was high even though the analysis was focused on studies in the setting of gynaecological surgery. The most important reason for the high heterogeneity was assessed to be variation in the gynaecological surgical procedures. The surgical procedures in gynaecology range from minimal invasive surgical procedures of less than 30 minutes' duration to extensive laparotomy due to cancer lasting hours. This determines the extent of surgical stress response due to tissue damage and systemic inflammation, which is correlated with the risk of developing post-operative AKI [6]. The surgical stress response is due to direct or indirect tissue trauma followed by the release of cytokines, inflammatory mediators and acute-phase reactants. The release of these acute-phase reactants corresponds with both the level of stress response and the systematic inflammatory response [49]. Furthermore, perioperative hypotension due to hypovolemia and systemic inflammation are important determinants of post-operative AKI [6]. One eligible study reported the severity and duration of intraoperative hypotension [28]. The authors stratified the proportion of patients experiencing AKI in accordance with the duration of intraoperative hypotension for mean arterial pressure (MAP) thresholds of 55, 60 and 65 mmHg. A duration of > 20 minutes with a MAP below 65 mmHg doubled the risk of AKI. In this study, female gender presented as a protective factor in regards of post-operative AKI.

With more extensive surgical procedures follows a higher risk for post-operative AKI. This is in accordance with incidence reported by the included studies of both meta-analyses. In the screening group, the highest incidence of post-operative AKI with known surgical procedure in the screening group, was reported by Hunsicker et al. (29.16%) based on laparotomy for cytoreductive surgery due to ovarian cancer. The lowest incidences were reported by Srisawat et al. (0%) based on gynaecological laparoscopic abdominal surgery [30, 38]. Likewise, in the non-screening group, the highest incidence of post-operative AK with known surgical procedure was reported by Ross et al. (6.5%) based on cytoreductive surgery due to ovarian cancer [46]. The lowest incidence was reported by both Kim et al. (0.06%) and Sears et al. (0.06%), both based on hysterectomy due to benign conditions [42, 44]. However, a definite conclusion is not possible to draw as six of the 16 studies in the screening group lacked information on both type of gynecological surgery and primary diagnosis. Furthermore, one of the studies included procedures such as colorecto-vaginal fistulas and rectocele surgery [2]. However, these procedures constituted only 1.7% of the included gynaecological surgery cases, whereas the rest were abdominal procedures. Another important reason for the marked difference in the incidence of AKI may be differences in the study designs of the included trials as they cover five different types of trial.

Most patients who undergo gynaecological surgery are healthy females without previous kidney disease. It is important to diagnose AKI in these patients as the diagnosis increases their risk of developing CKD and ESRD later in life, followed by increased short- and long-term mortality and morbidity [15-17]. The development of progressive renal damage may be prevented with post-operative screening of AKI. Early diagnosis enables early treatment and prevents permanent injury, as AKI is often reversible. Fluid therapy and avoiding nephrotoxic medication are easy and relevant measures in the treatment for AKI. The use of nephrotoxic agents such as renin angiotensin system inhibitors and angiotensin-II receptor blockers reduces renal autoregulation. This autoregulation is important during surgery; as intraoperative hypotension is induced as part of the anaesthesia, this will impair renal perfusion and increase the risk of post-operative AKI. The severity of kidney injury is correlated with the duration of hypotensive episodes [6]. Preoperative optimisation, post-operative control and follow-up measures are particularly important in preventing AKI and the ensuing complications [50]. The lack of systematic clinical screening poses a major challenge in detecting AKI. As a result, AKI remains underdiagnosed and underreported in gynaecology.

Two groups seem to be in higher risk of post-operative AKI; patients who undergo abdominal surgery for gynaecological cancer and patients who undergo open abdominal surgery. It is relevant to monitor renal function prior to surgery by measuring creatinine and a urine strip. If protein is detected in the urine, a urine albumin/creatinine ratio may rule out underlying kidney disease that appears in 10% of the population. Creatinine should be repeated within 48 hours after surgery to detect early onset of AKI, and seven days after surgery to detect late-onset AKI. Patients diagnosed with stage 1 AKI may be discharged to their primary care physician for follow-up. Patients diagnosed with stage 2 or stage 3 AKI require assessment of a nephrologist.

To our knowledge this is the first systematic review and meta-analysis that assesses the incidence of post-operative AKI following gynaecological surgery, using the validated AKI definitions. This systematic review and meta-analysis included 16 eligible studies presenting data on 11,530 patients, which was a strength in the study. The inadequate reporting of the type of gynaecological surgery and the primary diagnosis within the included studies were limitations in our study. Furthermore, the significant heterogeneity limits the generalisability and validity of the overall results and it may be questioned whether a meta-analysis is the best method when heterogeneity is so high. Selection bias was addressed as the three investigators agreed on inclusion of eligible studies according to the predefined inclusion and exclusion criteria. Due to the number of included studies (n = 16), no methods were used to formally assess potential publication bias as the power of detecting bias increases with an increasing number of the included studies. For future research, we recommend systematic clinical screening for AKI using consensus definitions, report of type of gynaecological surgery and primary diagnosis.

CONCLUSION

In this meta-analysis, we found a 7% overall risk of post-operative AKI after gynaecological surgery, with the highest incidence being recorded in abdominal cytoreductive surgery (29.16%) and the lowest incidence registering in benign laparoscopic surgery (5%). We found a higher incidence of AKI in the studies screening for kidney injury, illustrating that the condition is underdiagnosed when not screened for. An important risk exists of healthy women developing severe renal damage as AKI is a relevant post-operative complication with a potentially severe outcome that may be prevented in early diagnosis.

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