



Intracorporeal versus extracorporeal urinary diversion after robot-assisted radical cystectomy: a pooled analysis

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Background: To compare intracorporeal urinary diversion (ICUD) with extracorporeal urinary diversion (ECUD) after robot-assisted radical cystectomy (RARC) for surgery safety, postoperative recovery, complication, and prognosis.

Methods: We performed a literature search on PubMed, Embase, Medline and the Cochrane Library based on all randomized controlled trials (RCTs) and observational comparative studies related to study topics published before July 14th, 2020. Then systematic review and meta-analysis was performed.

Results: 13 retrospective studies containing 4,755 patients were identified. In terms of surgery safety, with similar operative time, ICUD group showed less estimated blood loss (EBL) ($P < 0.0001$) and lower blood transfusion rate ($P = 0.006$). In terms of postoperative recovery, with similar hospital stay, ICUD group showed earlier recovery on flatus ($P < 0.001$) and oral intake ($P < 0.0001$). In aspect of complications, there were no significant differences between ICUD and ECUD groups, except for gastrointestinal system complications. ICUD group had lower gastrointestinal complications rate than ECUD group ($P = 0.002$). In aspect of prognosis outcomes, with similar mortality, ICUD group had lower recurrence rate than ECUD group ($P = 0.004$).

Conclusions: Based on the current evidence, ICUD procedure is excellence in surgery safety, postoperative recovery, complications, and prognosis. However, the observational studies reduced the level of evidence, larger randomized trials are needed to confirm these findings.

Keywords: intracorporeal urinary diversion (ICUD); extracorporeal urinary diversion (ECUD); robot-assisted radical cystectomy (RARC); bladder cancer

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Introduction

In year 2019, 80470 bladder cancer cases with 17,670 deaths have been reported in America alone (1). Radical cystectomy (RC) is the most important therapy for high-risk non-muscle invasive bladder cancer and muscle-invasive bladder cancer (2). With technological progress, the application of minimally invasive surgery such as robot-

assisted radical cystectomy (RARC) (3) has been increasing applied in advanced bladder cancer all over the world. For instance, in the U.S, the RARC ratio of radical cystectomy increased from 0.6 percent in 2004 to 18.5 percent in 2012 (4).

As the complexity nature of the procedure, extracorporeal urinary diversion (ECUD) is a preferred option in tradition. With development of robotic surgery, a new direction for

reconstructive surgery is emerging, enabling surgeons to choose intracorporeal urinary diversion (ICUD) to complete the procedure (5,6). The advantages of ICUD procedure include smaller incision, less pain, decreased bowel exposure and lower risk of electrolyte disorders (7), it is now increasingly applied in clinical practice as an alternative to ECUD procedure.

Despite several studies have reported the perioperative outcomes, complications, and oncological outcomes of ICUD and ECUD after RARC, but no consensus on the differential comparative effectiveness of ICUD versus ECUD has been reached. Therefore, we conducted this latest systematic review and meta-analysis to compare the perioperative results, complication results, and oncological results of patients between ICUD and ECUD.

Methods

We carried out this research on the basis of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (8) and present this article in accordance with the PRISMA reporting checklist (available at <http://dx.doi.org/10.21037/gs-20-740>). Prospero ID: CRD42020175036 (<http://www.crd.york.ac.uk/PROSPERO>).

Search strategy

We did a computer retrieval on literature published before July 14th, 2020 in English through PubMed, Embase, Medline and the Cochrane Library. The following string terms were used [Title/Abstract]: robot AND cystectomy AND intracorporeal AND extracorporeal. We reviewed all abstracts and reviews related to the theme. Further, we filtered references from original articles by manual search. When two or more studies involving the same population range, we select the most complete or up-to-date research results.

Inclusion and exclusion criteria

Studies were included if they done comparison between ICUD after RARC and ECUD after RARC, and reported perioperative outcomes, complications result and oncological results, both RCTs or NRCTs such as prospective and retrospective studies were qualified. We excluded reviews, editorials, comments, meeting abstracts

and articles not in English. Studies that provided adequate information for estimating relative risk (RR) or hazard ratio (HR) by a 95% confidence interval (95% CI) were included.

Data extraction

Two authors extracted and summarized the data independently. In case of disagreement, it is up to the senior author's decision. The results were distributed into five categories: baseline characteristics, surgery safety, postoperative recovery, complication results and prognosis outcomes. Estimated blood loss (EBL), blood transfusion rate, operative time were classified into surgery safety. Hospital stay, time needed to bowl recovery, time needed to resume oral intake were categorized into postoperative recovery. Clavien-Dindo complications grade and organ system are the standards for the complications results, which were subdivided into 30 d-complications, grade ≥ 3 of 30 d-complications, 90 d-complications, grade ≥ 3 of 90 d-complications, 90 d-mortality, gastrointestinal system, genitourinary system, metabolism system and wound/skin system. Recurrence rate and mortality rate were categorized in prognosis outcomes.

Statistical analysis and quality assessment

Because all included literatures were case-control studies, so we applied the Newcastle-Ottawa Scale to assess quality (9). When the score was 7 or more, it was classified as high-quality studies. Eventually, twelve studies gained high quality grade.

Review Manager 5.3 (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen) were used to complete the meta-analysis. Weighted mean difference (WMD) and odds ratio (OR) with 95% CI were used for continuous variables and dichotomous variables, respectively. When the results were expressed in quartiles, we choose statistical algorithms to calculate the standard deviation. Besides, statistical heterogeneity was evaluated using chi-square test with a significance set at $P < 0.10$. The degree of heterogeneity was measured by value of I-squared (I^2) ($I^2 < 25\%$: no heterogeneity; $I^2 = 25-50\%$: moderate heterogeneity; $I^2 > 50\%$: large heterogeneity). When the heterogeneity was large, we used the random-effects model and if not, we used the fixed-effects model. Funnel plot was used to assess publication bias. Subgroup analysis was

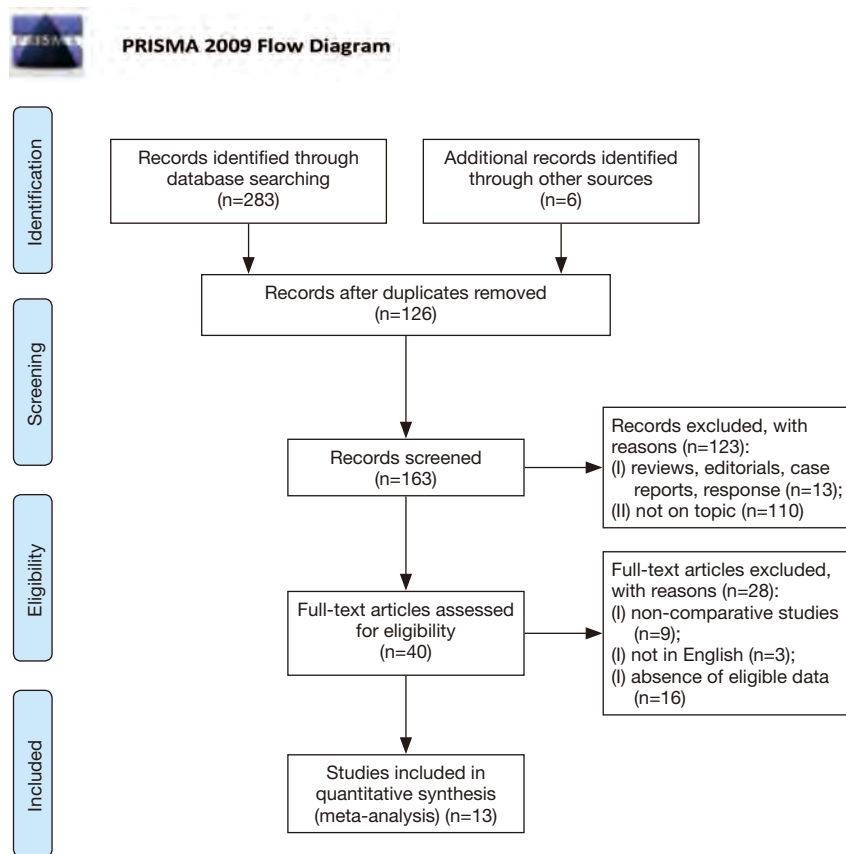


Figure 1 Flow chart of studies selection.

conducted to compare valuables between ICUD group and ECUD group. We conducted a sensitivity analysis by the leave-one-out cross validation to assess the stability of the pooling results by Stata/SE 15.1.

Results

Study selection and characteristics

The preliminary search results a total of 283 articles (*Figure 1*) (10). After removing duplicates, the remaining 163 articles were filtered by title and abstract. On the basis of our inclusion and/or exclusion criteria, we ruled out 123 articles and then evaluated the full text of the remaining 40 studies. After further filtering with inclusion criteria, thirteen retrospective studies (6,11-21) containing 4,755 cases were included in the final analysis. These studies were published between 2010 and 2020 with six been from America, four from Europe and three from South Korea. ICUD was regarded as the experimental arm, ECUD was

regarded as the control arm. The baseline features of the patients including age, body mass index (BMI), American Society of Anesthesiologists (ASA) score, pathological tumor stage and pathological node stage were summarized in *Table 1*.

Surgery safety and postoperative recovery

In regard of surgery safety, the pooled data of 3694 patients from the ten studies were evaluated operative time which showed no significant differences between the two groups (WMD: 20.25; 95% CI: -12.51 to 53.00; $P=0.23$) (*Figure 2A*). With large heterogeneity ($I^2=95\%$; $P<0.01$), a random-effect model was used. The pooled data from the eight studies, total 3206 patients were evaluated estimated blood loss (EBL) which showed less EBL in the ICUD group than that in ECUD group (WMD: -95.25; 95% CI: -129.99 to -60.52; $P<0.001$) (*Figure 2B*). With large heterogeneity ($I^2=57\%$; $P=0.02$), a random-effect model was used. 3461 patients from six studies were evaluated blood

Table 1 Baseline features of included patients

Author	Year	Region	Design	NOS score	No (ICUD/ ECUD)	Age (median and IQRs)	BMI (median and IQRs)	ASA score (≥3) (%)	pT ≥T3 (%)	pN >N0 (%)	Follow-up (months)
Aboumohamed	2014	USA	R	7	42/40	73/71	28.2/27.9	50/40	33/30	9.5/17.5	30/30
Ahmed	2014	UK	R	7	167/768	66/68	28/27	47/52	38/41	20/24	12/17
Bertolo	2019	USA	R	7	60/66	69/73	29.5/27.8	98/97	39/39	20/14	18/18
Guru	2010	USA	R	6	13/13	71 (60 to 81)/ 66 (51 to 85)	NR	NR	13/54	23/36	NR
Hussein	2017	USA	R	7	1,094/1,031	67/68	27.3/27.5	44/53	38/39	18/19	11/17
Shim	2020	South Korea	R	7	84/278	64.4/65.3	24.2/23.7	NR	33.3/31.3	26.2/18.3	35/35
Kang	2012	South Korea	R	7	4/38	69.5/62.2	26.4/24.8	25/53	0/24.4	NR	NR
Lenfant	2018	France	R	7	74/34	65 (62 to 73)/ 68 (59 to 76)	25.9 (23.7 to 28.0)/ 26.2 (24.1 to 28.9)	14.9/41.2	NR	19.2/0	15/28
Pruthi	2010	USA	R	7	12/20	60.9/66.9	27.6/27.4	NR	NR	NR	NR
Pyun	2016	South Korea	R	7	26/38	65.4/63.1	24.8/24.9	NR	26.9/21.1	NR	NR
Tan	2018	UK	R	7	59/68	69 (62 to 74)/ 71 (66 to 76)	26.5 (23.9 to 30.2)/ 27.0 (24.5 to 29.6)	NR	32.3/36.8	16.9/16.2	NR
Kingo	2017	Denmark	R	7	38/12	68.3/68.1	27.3/24.3	5.3/16.7	13.2/25.0	NR	NR
Zhang	2020	USA	R	7	301/375	69.0 (61.0 to 75.0)/ 70.0 (63 to 75)	27.5 (23.9 to 30.9)/ 28.0 (25.0 to 31.7)	NR	32.6/27.8	NR	26/26

NOS score, Newcastle-Ottawa Scale score; ICUD, intracorporeal urinary diversion; ECUD, extracorporeal urinary diversion; BMI, body mass index; ASA, American Society of Anesthesiologists score; pT, pathological tumor grade; pN, pathological N grade; IQRs, interquartile ranges; NR, not reported.

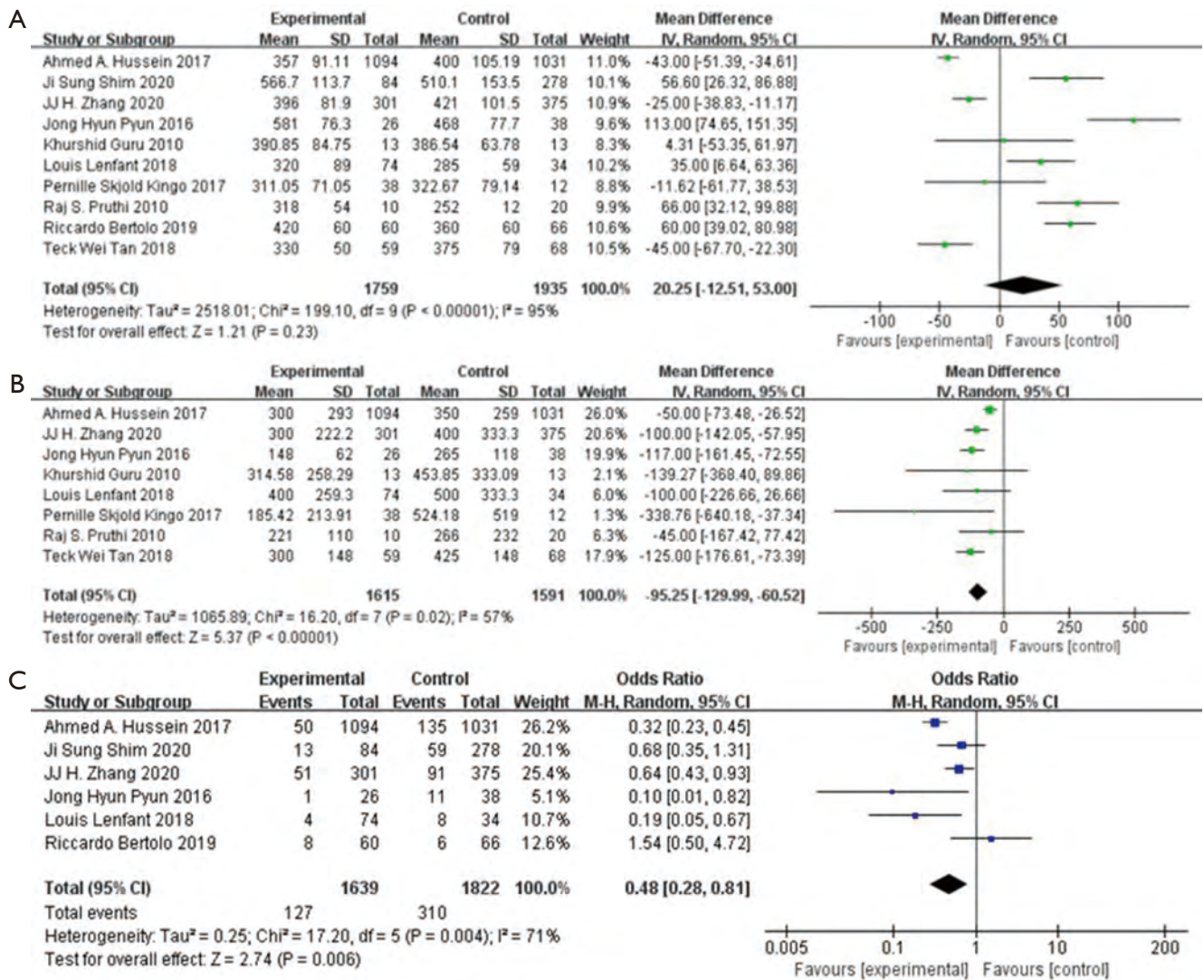


Figure 2 Forest plot for surgery safety. (A) Operative time; (B) EBL; (C) blood transfusion rate. EBL, estimated blood loss.

transfusion rate which showed lower blood transfusion rate in the ICUD group than that in ECUD group (OR 0.48; 95% CI: 0.28 to 0.81; P=0.006) (Figure 2C). With large heterogeneity (I²=71%; P=0.004), a random-effects model was applied.

In regard of postoperative recovery, 3638 patients from eight studies had record on hospital stay, no significant difference was shown between the two group (WMD: -0.46; 95% CI: -1.80 to 0.89; P=0.50) (Figure 3A). There was large heterogeneity (I²=90%; P<0.001), a random-effect model was used. Analysis of 426 patients from two studies indicated that patients in ICUD group need shorter time to begin oral intake (WMD: -0.92; 95% CI: -1.30 to -0.54; P<0.001)

(I²=0%; P=0.64) (Figure 3B) and shorter time to bowl recovery (WMD: -14.42; 95% CI: -20.77 to -8.07; P<0.001) (I²=0%; P=0.60) (Figure 3C). As no heterogeneity between ICUD and ECUD groups, fixed-effect models were applied.

Complication results according to Clavien-Dindo grade

The pooled data from the seven studies, total 4,127 patients were evaluated 30 d-complication which indicates no significant difference between the ICUD group and the ECUD group (OR 1.13; 95% CI: 0.73 to 1.75; P=0.58) (Figure 4A). With large heterogeneity (I²=83%; P<0.001), a random-effect model was applied. 3167 patients

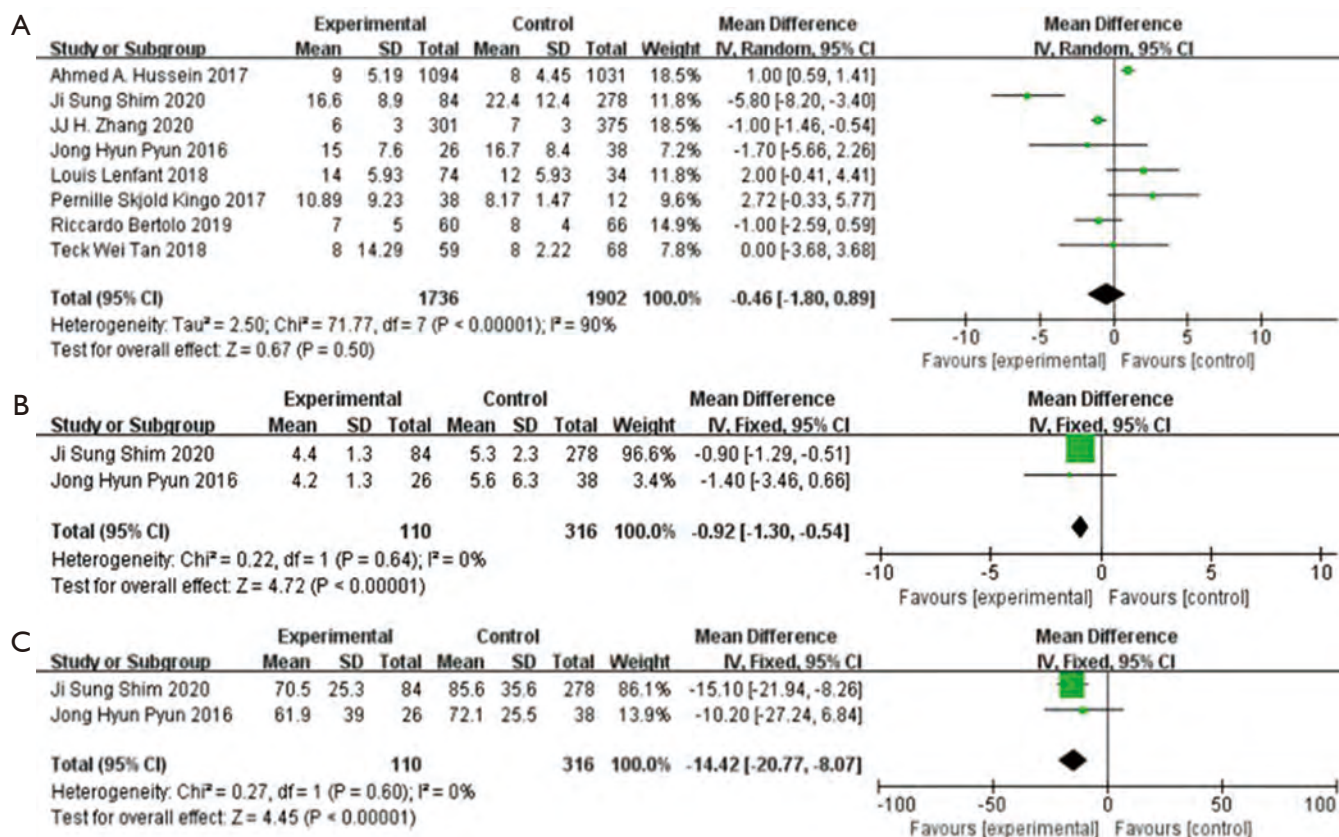


Figure 3 Forest plot for postoperative recovery. (A) Hospital stay; (B) time to oral intake; (C) time to flatus.

from six studies have assessment data on grade ≥ 3 of 30 d-complications, no significant difference between two groups was found (OR 1.20; 95% CI: 0.53 to 2.72; P=0.66) (Figure 4B). With large heterogeneity (I²=82%; P<0.001), a random-effect model was applied. From the seven studies which assessed 90 d-complications in 4415 patients, no significant difference was identified between two groups (OR 0.81; 95% CI: 0.57 to 1.15; P=0.24) (Figure 4C). With large heterogeneity (I²=65%; P=0.01), a random-effect model was applied. From the eight studies which assessed grade ≥ 3 of 90 d-complications in 4465 patients, consistently no significant difference between ICUD group and ECUD group was found (OR 0.95; 95% CI: 0.65 to 1.40; P=0.80) (Figure 4D). With large heterogeneity (I²=53%; P=0.04), a random-effect model was applied. Again, from the four studies which assessed 90 d-mortality in 3,863 patients, no significant difference between two groups (OR 0.83; 95% CI: 0.55 to 1.26; P=0.39) was identified (Figure 4E). With no heterogeneity (I²=0%; P=0.47), a fixed-effect model was applied.

Complication results according to organ system

Furthermore, complications were subdivided according to the organ system into gastrointestinal system, genitourinary system, wound/skin system, and metabolism system. Analysis on the pooled data of 2,001 patients from the six studies which have complications data from gastrointestinal system showed that patients in ICUD group had lower gastrointestinal complications rate than that in ECUD group (OR 0.67; 95% CI: 0.51 to 0.87; P=0.002) (Figure 5A). As no heterogeneity (I²=0%; P=0.82), a fixed-effect model was applied. From the six studies which assessed complications in genitourinary system in 2001 patients, no significant difference was found between two groups (OR 1.24; 95% CI: 0.92 to 1.67; P=0.16) (Figure 5B). With moderate heterogeneity (I²=41%; P=0.13), a fixed-effect model was applied. From the four studies which assessed complications in wound/skin system in 1199 patients, no significant difference was identified between two groups (OR 0.83; 95% CI: 0.42 to 1.66; P=0.60) (Figure 5C). With no heterogeneity (I²=0%; P=0.41), a

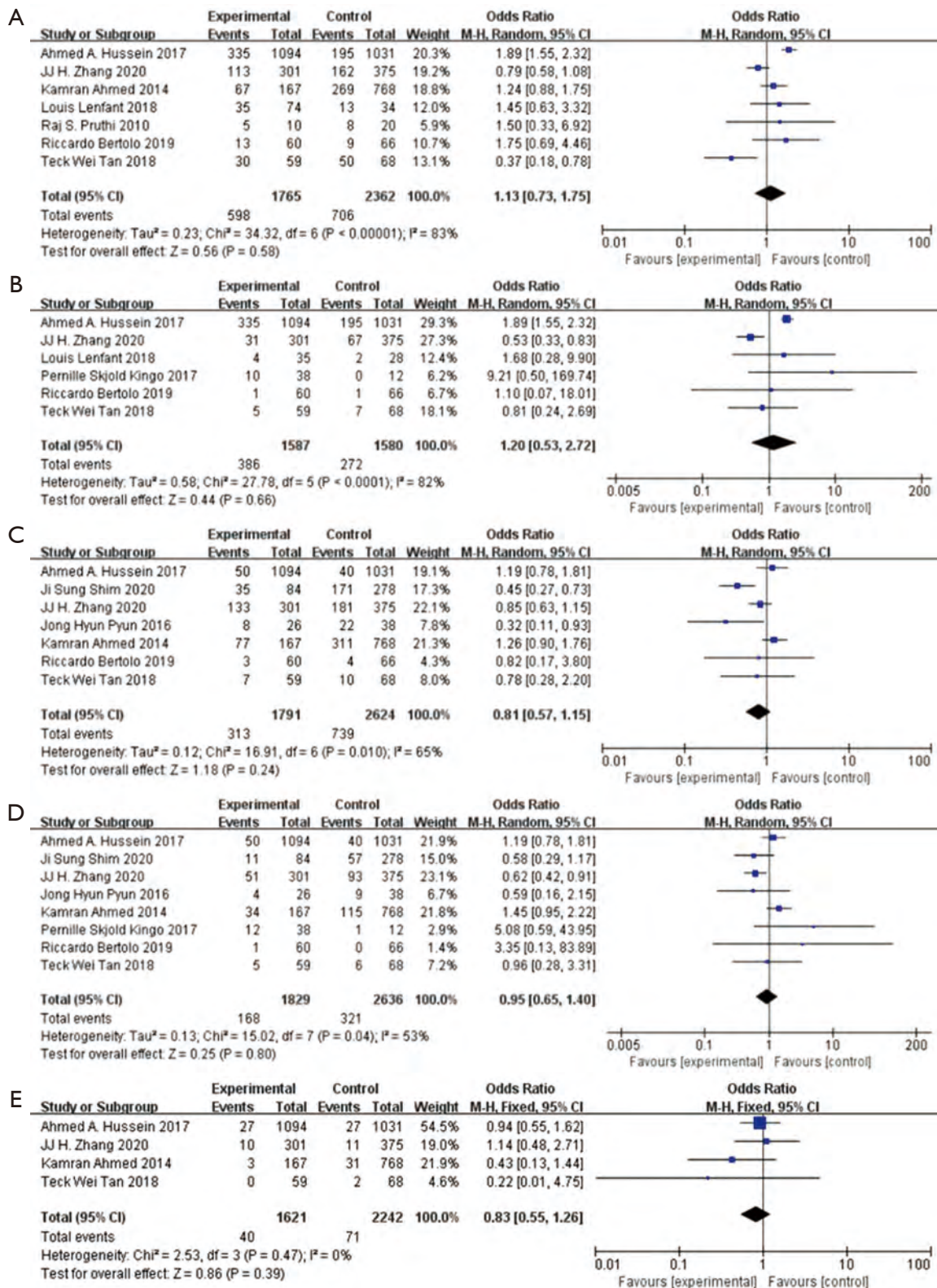


Figure 4 Forest plot for complications according to Clavien-Dindo grade. (A) 30 d-complications; (B) grade ≥3 of 30 d-complications; (C) 90 d-complications; (D) grade ≥3 of 90 d-complications; (E) 90 d-mortality.

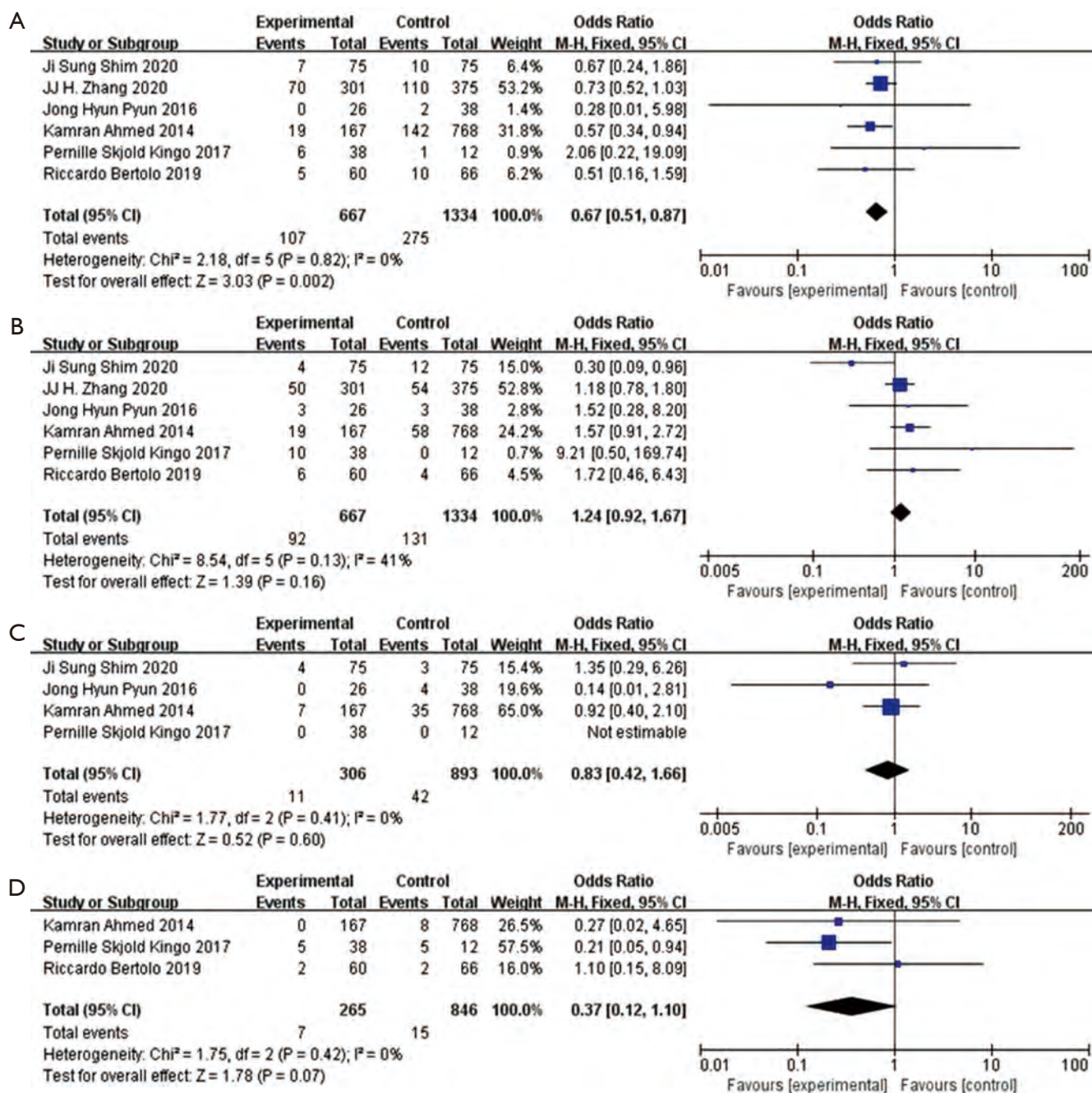


Figure 5 Forest plot for complications according to organ system. (A) Gastrointestinal complication; (B) genitourinary complication; (C) wound/skin complication; (D) metabolism complication.

fixed-effect model was applied. The pooled data from the three studies involving 1,111 patients with complications evaluated in metabolism system, no significant difference was shown between two groups (OR 0.37; 95% CI: 0.12 to 1.10; P=0.07) (Figure 5D). As no heterogeneity (I²=0%; P=0.42), a fixed-effect model was applied.

On the basis of data from included studies, we analyzed four common complications: urinary tract infection, ureteral anastomosis leakage, ileus and acute kidney injury (AKI). Urinary tract infection evaluated from the pooled data of three studies included 852 patients, no significant difference was identified between two groups (OR 1.07; 95% CI:

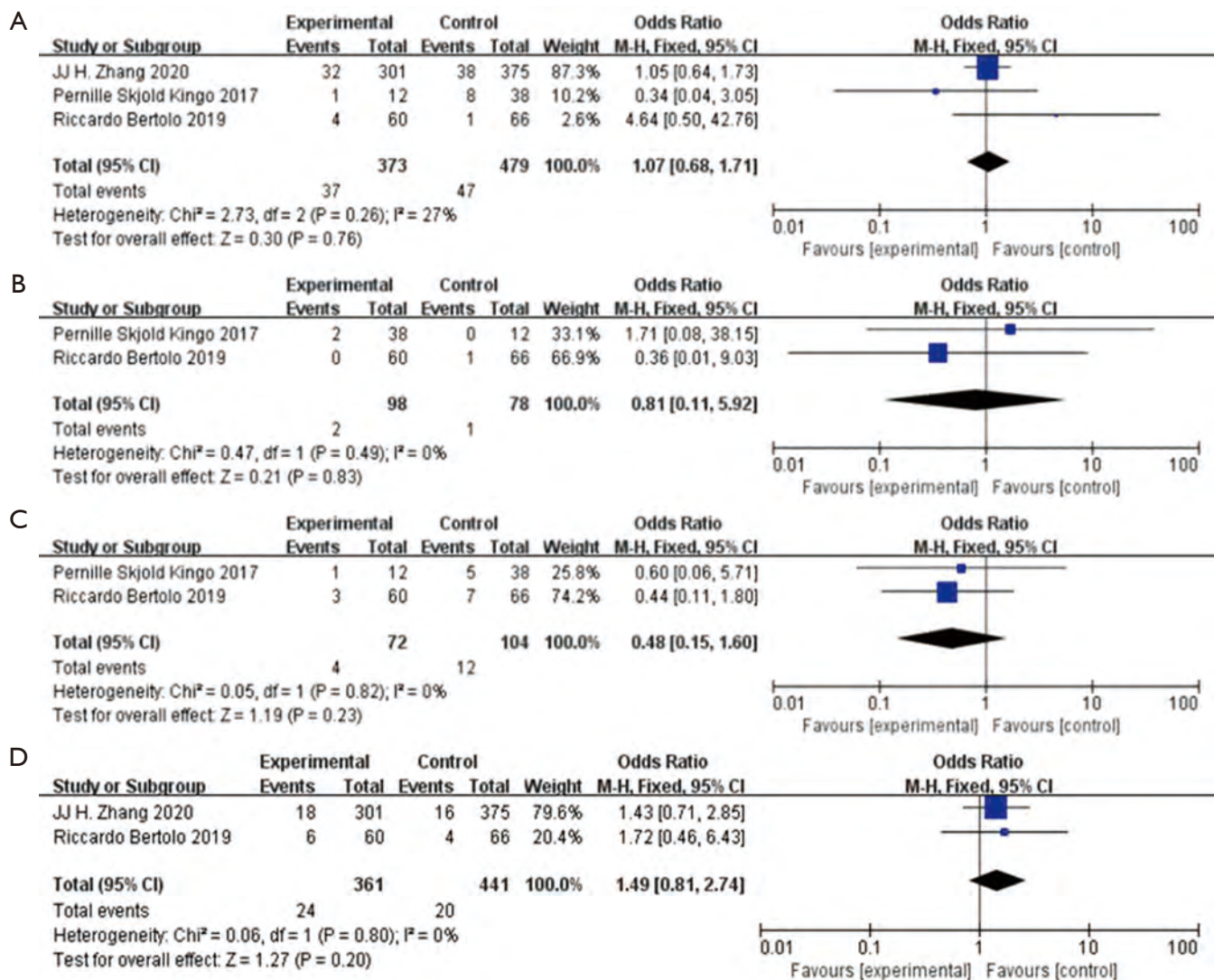


Figure 6 Forest plot for specific complications. (A) Urinary tract infection; (B) ureteral anastomosis leakage; (C) ileus; (D) AKI. AKI, acute kidney injury.

0.68 to 1.71; $P=0.76$) (Figure 6A). With no heterogeneity ($I^2=27\%$; $P=0.26$), a fixed-effect model was applied. Ureteral anastomosis leakage was assessed from the pooled data of two studies involving 176 patients, no significant difference was found between two groups (OR 0.81; 95% CI: 0.11 to 5.92; $P=0.83$) (Figure 6B). With no heterogeneity ($I^2=0\%$; $P=0.49$), a fixed-effect model was applied. Ileus was evaluated from the pooled data of three studies included 852 patients, no significant difference was identified between two groups (OR 0.48; 95% CI: 0.15 to 1.60; $P=0.23$) (Figure 6C). With no heterogeneity ($I^2=0\%$; $P=0.82$), a fixed-effect model was applied. AKI was assessed from pooled

data of two studies involving 802 patients, no significant difference was shown between two groups (OR 1.49; 95% CI: 0.81 to 2.74; $P=0.20$) (Figure 6D). With no heterogeneity ($I^2=0\%$; $P=0.80$), a fixed-effect model was applied.

Prognosis outcomes

The average follow-up time was 21.3 months in ICUD group and 23.3 months in ECUD group among the included studies. From the three studies which assessed recurrence rate in 2,613 patients, ICUD group showed lower recurrence rate than ECUD group (OR 0.74; 95% CI: 0.61 to 0.91; $P=0.004$)

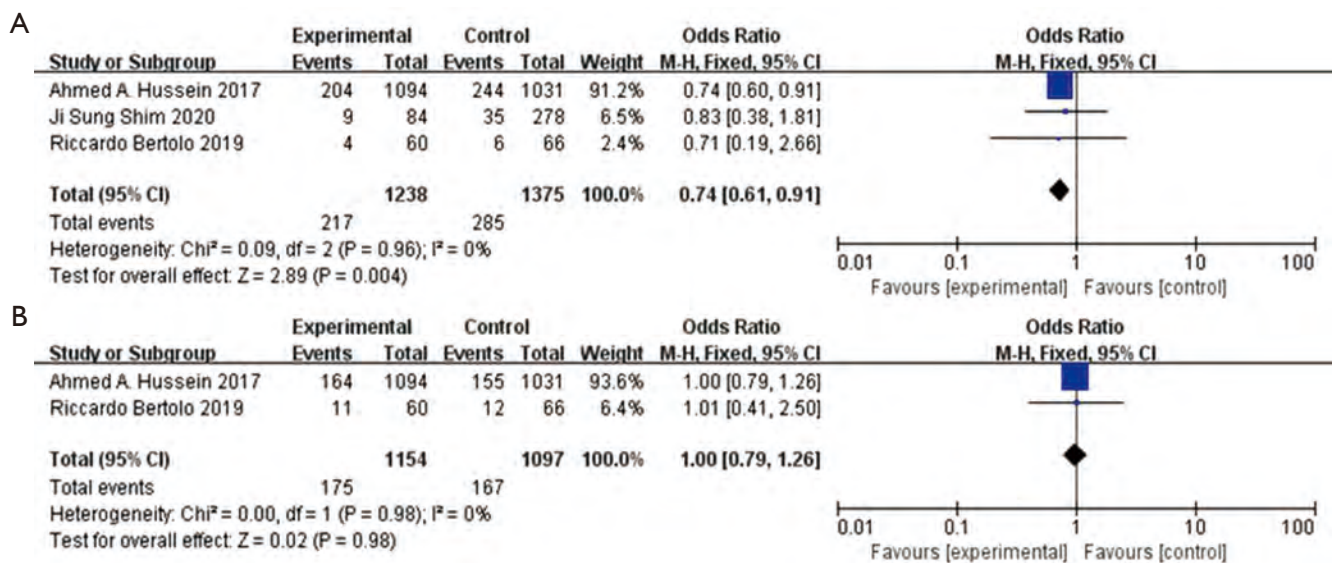


Figure 7 Forest plot for prognosis outcomes. (A) Recurrence; (B) mortality.

(Figure 7A). With no heterogeneity ($I^2=0\%$; $P=0.96$), a fixed-effect model was applied. From the two studies which assessed mortality rate in 2,251 patients, no significant difference was shown between two groups (OR 1.00; 95% CI: 0.79 to 1.26; $P=0.98$) (Figure 7B). With no heterogeneity ($I^2=0\%$; $P=0.98$), a fixed-effect model was applied.

Subgroup analysis

Based on the baseline features we collected, we divided patients into three categories. Age >65 or age ≤ 65 , BMI >27 or BMI ≤ 27 , publication of year >2016 or publication of year ≤ 2016 .

In aspect of operation time, transfusion rate and metabolism system, the results changed after subgroup stratification. other results were as same as total group (Figures S1-S7). A total of 564 patients from four studies evaluated operation time, in which when patients mean age ≤ 65 , ICUD group had longer operation time than ECUD group (WMD: 65.79; 95% CI: 35.51 to 96.06; $P<0.001$) (Figure 8A). With large heterogeneity ($I^2=71\%$; $P=0.02$), a random-effect model was applied. 120 patients from three studies with publication time before 2016 were evaluated on operation time, ICUD group showed longer operation time than ECUD group (WMD: 64.81; 95% CI: 10.96 to 118.66; $P=0.02$) (Figure 8B). With large heterogeneity ($I^2=80\%$; $P=0.007$), a random-effect model was applied. 2,927 patients from three studies were evaluated on transfusion rate, when patient's mean age >65 , no significant difference was

existed between two groups (OR 0.58; 95% CI: 0.29 to 1.17; $P=0.13$) (Figure 9A). With large heterogeneity ($I^2=83\%$; $P=0.003$), a random-effect model was applied. 2,927 patients from three studies were evaluated on transfusion rate, in patients whose BMI >27 , no significant difference was identified between two groups (OR 0.58; 95% CI: 0.29 to 1.17; $P=0.13$) (Figure 9B). With large heterogeneity ($I^2=83\%$; $P=0.003$), a random-effect model was applied. 985 patients from two studies were evaluated on complication rates in metabolism system, ICUD group showed lower rates than ECUD group when patient's BMI >27 (OR 0.23; 95% CI: 0.06 to 0.93; $P=0.04$) (Figure 10). With no heterogeneity ($I^2=0\%$; $P=0.88$), a fixed-effect model was applied.

Sensitivity analysis and publication bias

A sensitivity analysis was performed (Figures S8-S11) by leave-one-out cross validation to assess the stability of pooled results. After deleting the studies with heterogeneity, the overall OR did not change significantly. Consequently, the results of meta-analysis are fairly convincing.

Funnel plots were used to assess the risk of publication bias. A few asymmetries were found (Figures S12-S15) which indicated a publication bias.

Discussion

With more surgical performance and doctor experience,

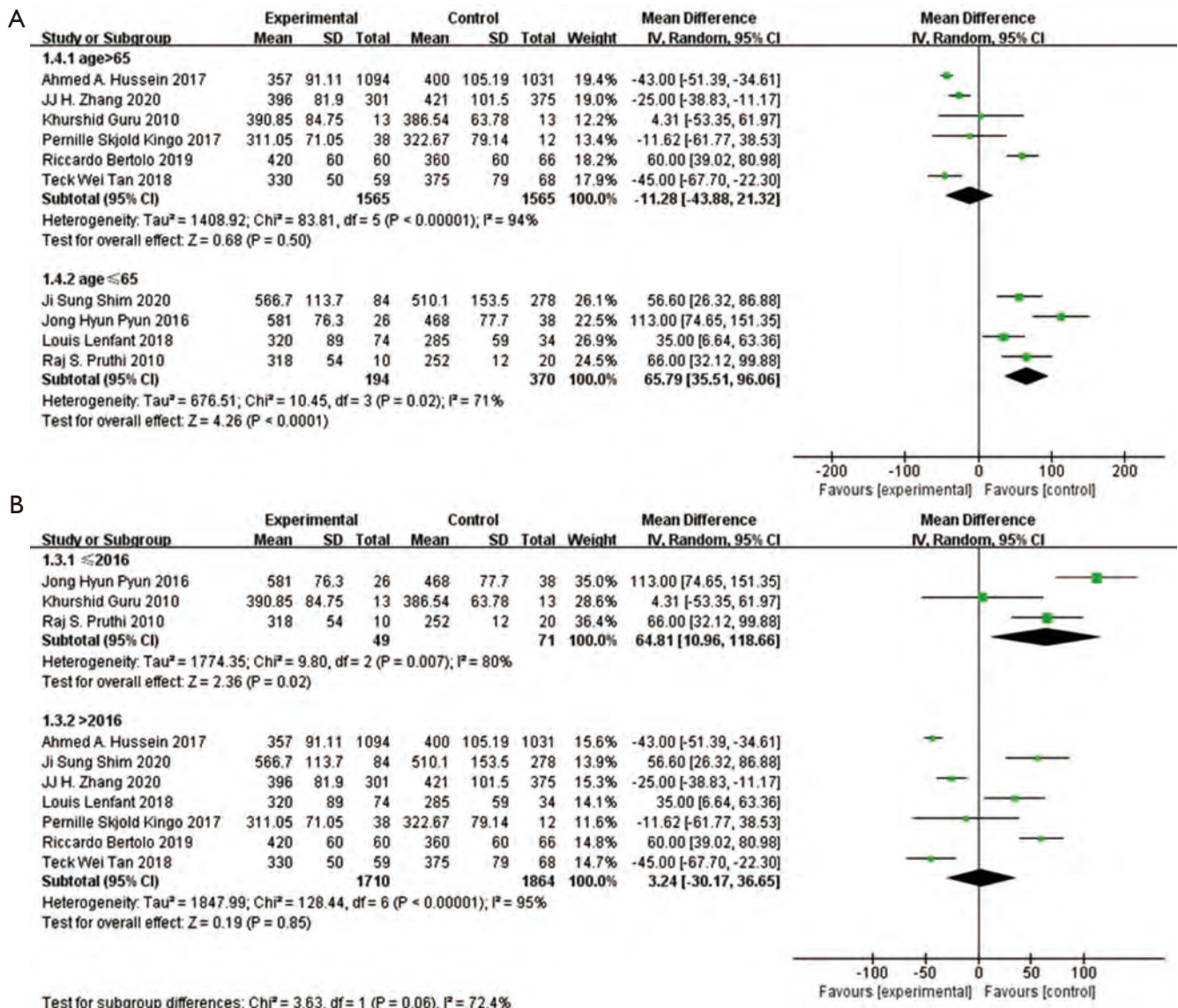


Figure 8 Subgroup analysis. (A) Operation time of patients in age >65 or age ≤65; (B) operation time of patients in BMI >27 or BMI ≤27.

potential benefits of ICUD are becoming recognized increasingly. Especially under the rapid development of robotic surgery, it is now feasible to perform RC with ICUD (22). However, the results of the studies comparing robot-assisted ICUD and robot-assisted ECUD are controversial, so we performed this meta-analysis to have a conclusion.

In regard of surgery safety, with similar operation time, ICUD group showed less EBL and lower blood transfusion rate than ECUD group. It indicates that ICUD procedure is trustworthy in terms of surgical safety. In one hand, surgeons who can conduct ICUD are experienced with

excellent surgical techniques, EBL and transfusion rate reduced in their surgery probably due to their expertise. In the other hand, due to the high-risk nature of the procedure in ICUD, surgeons may choose only “ideal” patients to do ICUD. Hence, we think there may be some kind of selection bias exist between procedures. In the subgroup analysis about operation time, we found that operation time in ECUD group was shorter in the studies published before 2016. First of all, we consider that the earlier the studies published, the lower the popularity of robotic surgery. Secondly, Hayn *et al.* reported that the number of cases needed to “complete” the learning curve for RARC

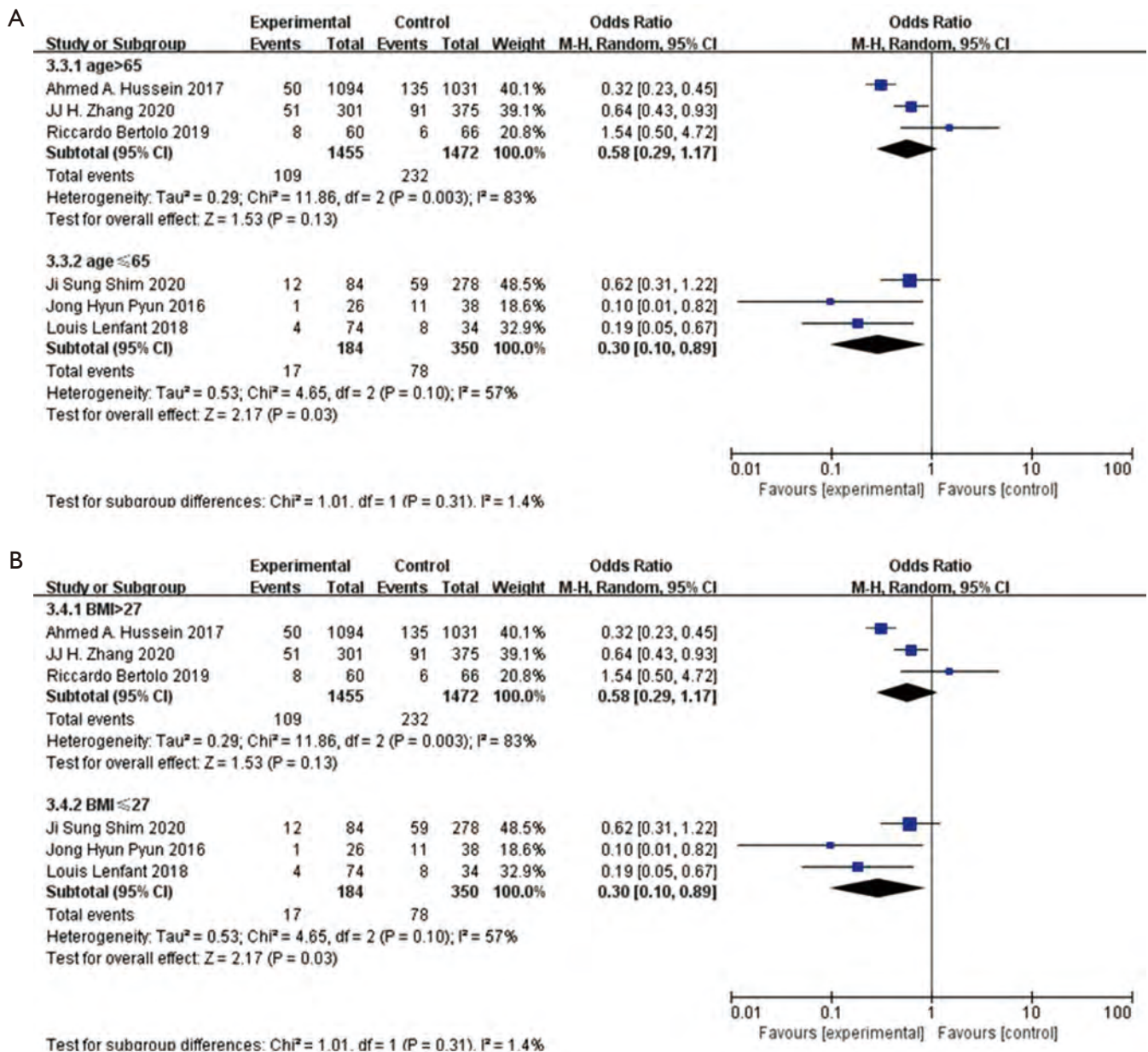


Figure 9 Subgroup analysis. (A) Transfusion rate of patients in age >65 or age ≤65; (B) transfusion rate of patients in BMI >27 or BMI ≤27.

is suggested to be thirty (23), nevertheless, the amount of ICUD in the included studies published before 2016 was below 30. With slow uptake of ICUD and long learning curve, experienced surgeons performing this approach are still limited. Larger multicenter studies are needed to verify the outcome.

In regard of postoperative recovery, with similar hospital stay, ICUD group need shorter time to bowl recovery and shorter time to resume oral intake. Firstly, minimized

skin incision lengths lead to less pain which might reduce analgesic use and may allow an earlier return to normal activities. That could be the cause of quicker bowel function recovery. Furthermore, more mobilization of ileum leading to later restoration of bowel function (24). A recent randomized trial (25) which observed changes in several markers within 5 days after surgery, including interleukin-6, C-reactive protein, procalcitonin, white blood cell count, and cortisol, found that intracorporeal anastomosis is

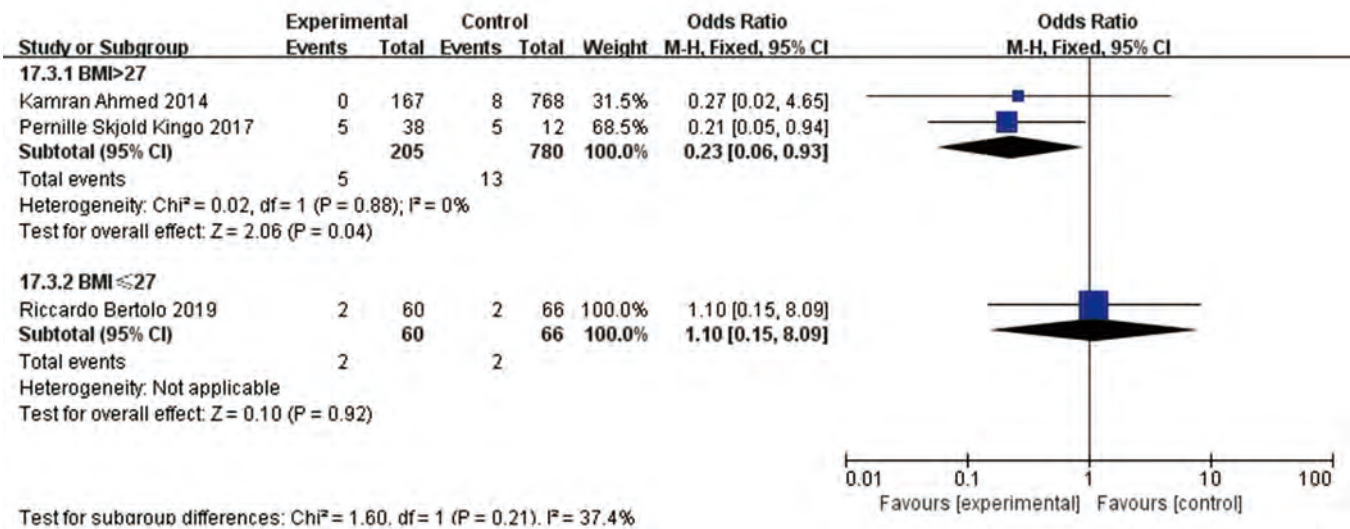


Figure 10 Subgroup analysis: complications in metabolism system of patients in BMI >27 or BMI ≤27.

associated with significantly less surgical stress response and earlier gastrointestinal recovery compared to extracorporeal anastomosis.

In terms of complications, there were no significant difference between ICUD and ECUD groups according to Clavien-Dindo grade. In addition, there were also no significant differences between ICUD and ECUD groups in genitourinary complication, metabolism complication and wound/skin complication. Moreover, there were no significant differences between two groups in four common complications: urinary tract infection, ureteral anastomosis leakage, ileus, and AKI. However, the rate of gastrointestinal complication was lower in ICUD group. Roscio *et al.* argued that extraction of the ileum through surgery incision has more chance to have tissue trauma and contamination (26), which probably causes ileus, diarrhea, gastrointestinal bleeding, and gastritis. On the other hand, minimized surgical incision in ICUD group means a lot of advantages. Ahmed *et al.* has been demonstrated that the longer time the peritoneum is exposed to the air, the greater the chance of intestinal inflammation, which may lead to intestinal paralysis or ileus (14). In addition, reducing the time of intraabdominal visceral contents exposing to ambient air can result in reduced surgical stress response, consequentially it has advantages to patient's recovery (27). Theoretically, the narrow space in the abdominal cavity will cause difficulty in uretero-intestinal anastomosis and increase the probability of anastomotic leakage, but this

is not the case in our study. In the subgroup analysis of metabolism complications in patients whose BMI >27, ICUD group had a lower rate of that than ECUD group. We speculate that less bleeding and earlier oral intake probably are the reasons. As we all know, large amount of blood loss can cause many complications, including metabolism complications. In addition, oral intake in the early period of post-operation can effectively replenish protein and electrolytes in the body.

The limitations of the meta-analysis are as follow. Firstly, all articles were retrospective. Without random sequence generation and blinding, it could increase the risk of selection bias. Secondly, most of the included studies did not separately discuss the specific data on two main urinary diversion surgery: ileal conduit and orthotopic neobladder, so we couldn't analyze the effect of different urinary diversion. Thirdly, the studies we included did not consider ERAS as a factor affecting postoperative recovery, so the results probably changed based on different postoperative care. Last but not the least, there were large heterogeneity in several results, which caused a limitation in terms of generalizability of the study.

Conclusions

Based on the current evidence, ICUD has better performance than ECUD on surgery safety, postoperative recovery, complications, and prognosis. However, the observational studies reduced the level of evidence, larger

randomized trials are needed to confirm these findings.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/gs-20-740>). XZ serves as an unpaid Associate Editor of *Gland Surgery* from Mar 2015 to Feb 2021. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work and ensuring questions related to the accuracy or integrity of any part of the work be appropriately investigated and resolved.

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Supplementary

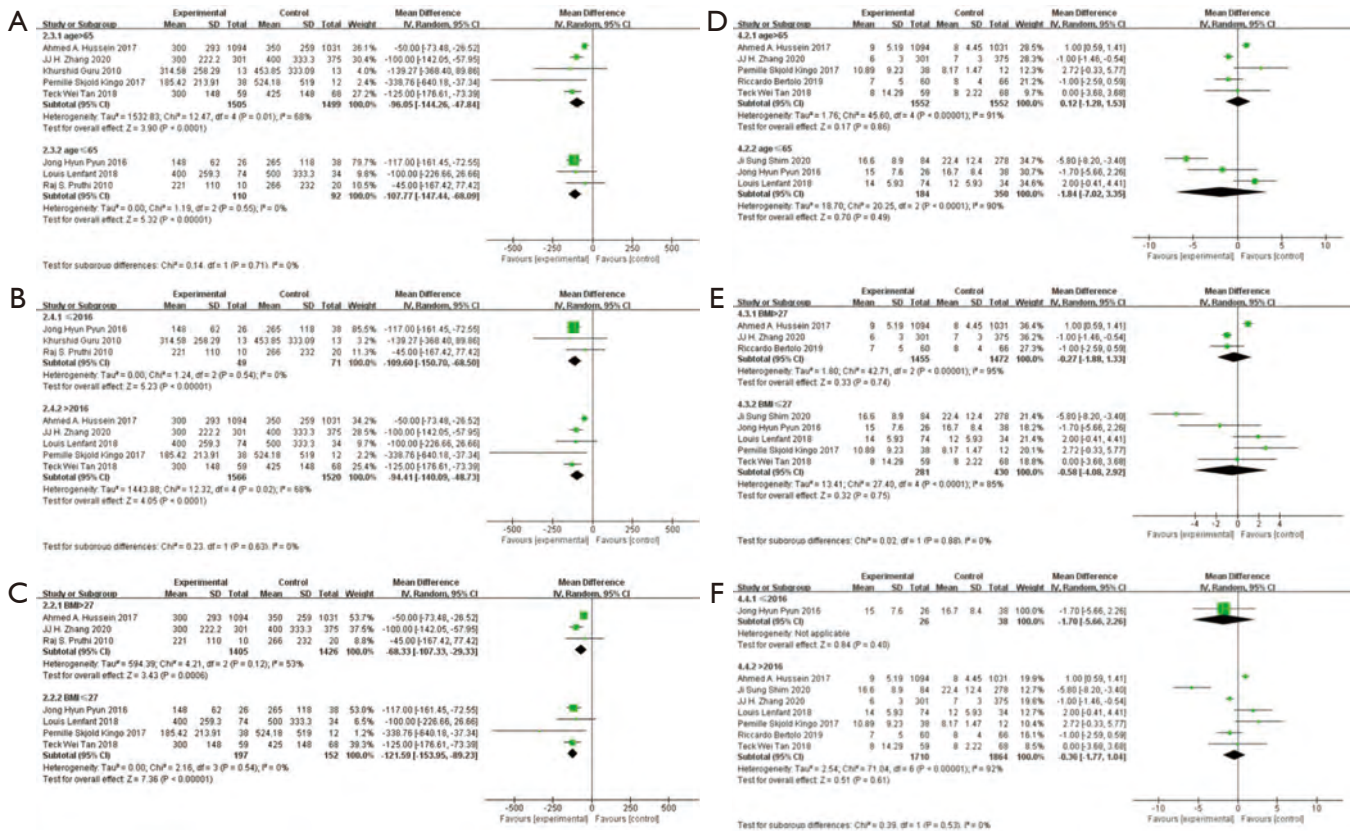


Figure S1 Subgroup analysis for surgery safety and postoperative recovery. (A) EBL of patients in age >65 or age ≤65; (B) EBL of patients in BMI >27 or BMI ≤27; (C) EBL of patients in publication of study >2016 or ≤2016; (D) hospital stay of patients in age >65 or age ≤65; (E) hospital stay of patients in BMI >27 or BMI ≤27; (F) hospital stay of patients in publication of study >2016 or ≤2016.

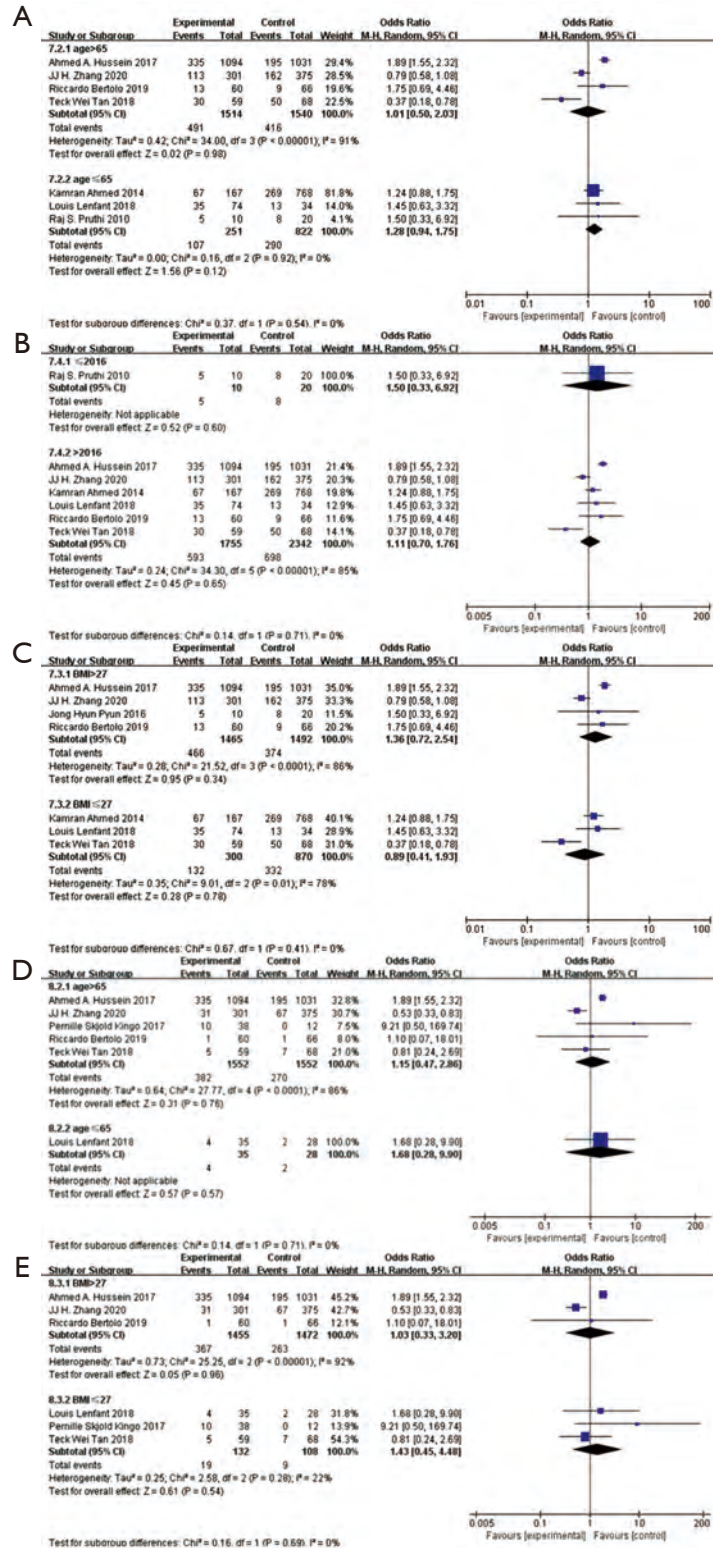


Figure S2 Subgroup analysis for complications according to Clavien-Dindo grade. (A) 30 d-complications of patients in age >65 or age ≤65; (B) 30 d-complications of patients in BMI >27 or BMI ≤27; (C) 30 d-complications of patients in publication of study >2016 or ≤2016; (D) grade ≥3 of 30 d-complications of patients in age >65 or age ≤65; (E) grade ≥3 of 30 d-complications of patients in BMI >27 or BMI ≤27; (F) grade ≥3 of 30 d-complications of patients in publication of study >2016 or ≤2016.

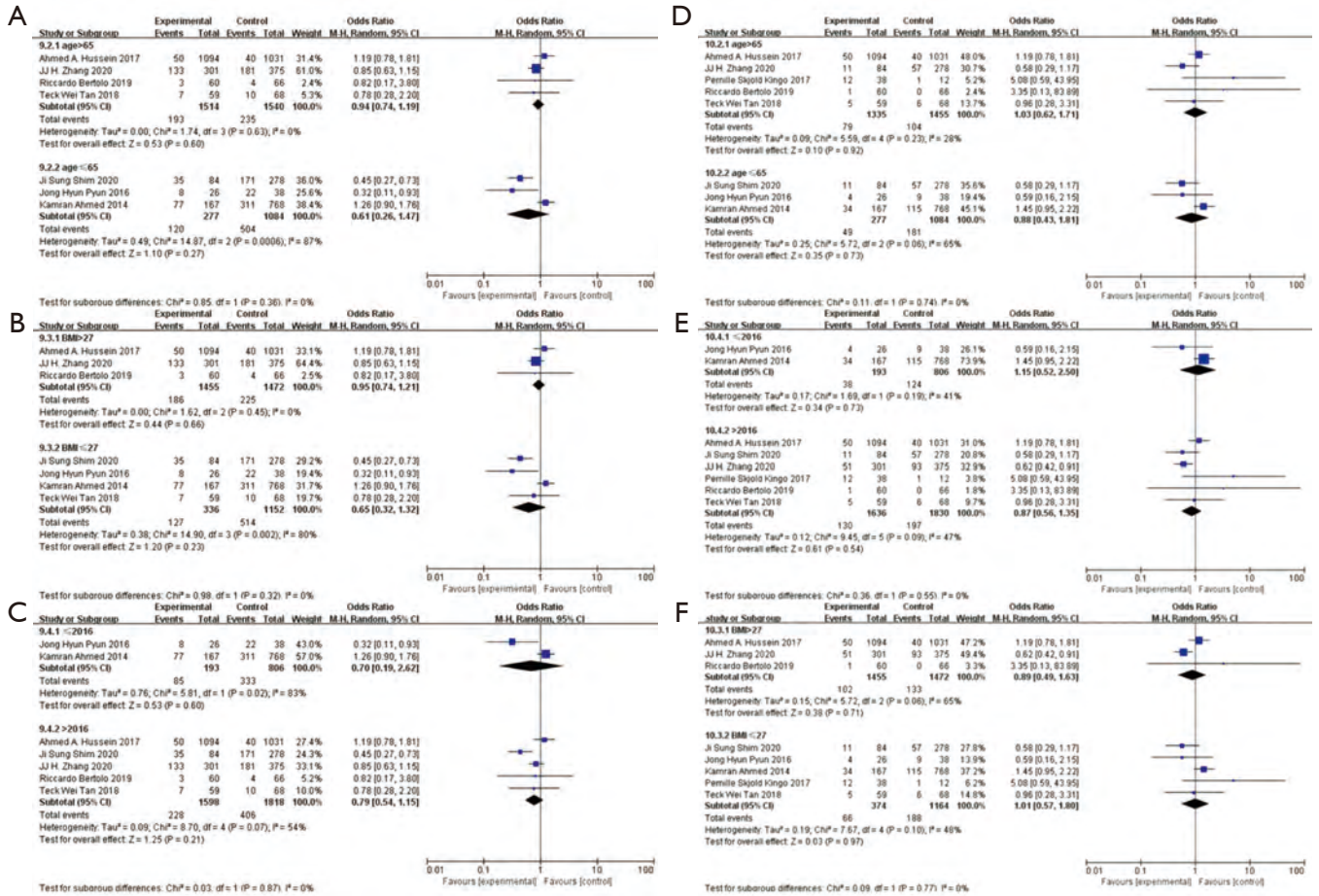


Figure S3 Subgroup analysis for complications according to Clavien-Dindo grade. (A) 90 d-complications of patients in age >65 or age ≤65; (B) 90 d-complications of patients in BMI >27 or BMI ≤27; (C) 90 d-complications of patients in publication of study >2016 or ≤2016; (D) grade ≥3 of 90 d-complications of patients in age >65 or age ≤65; (E) grade ≥3 of 90 d-complications of patients in BMI >27 or BMI ≤27.

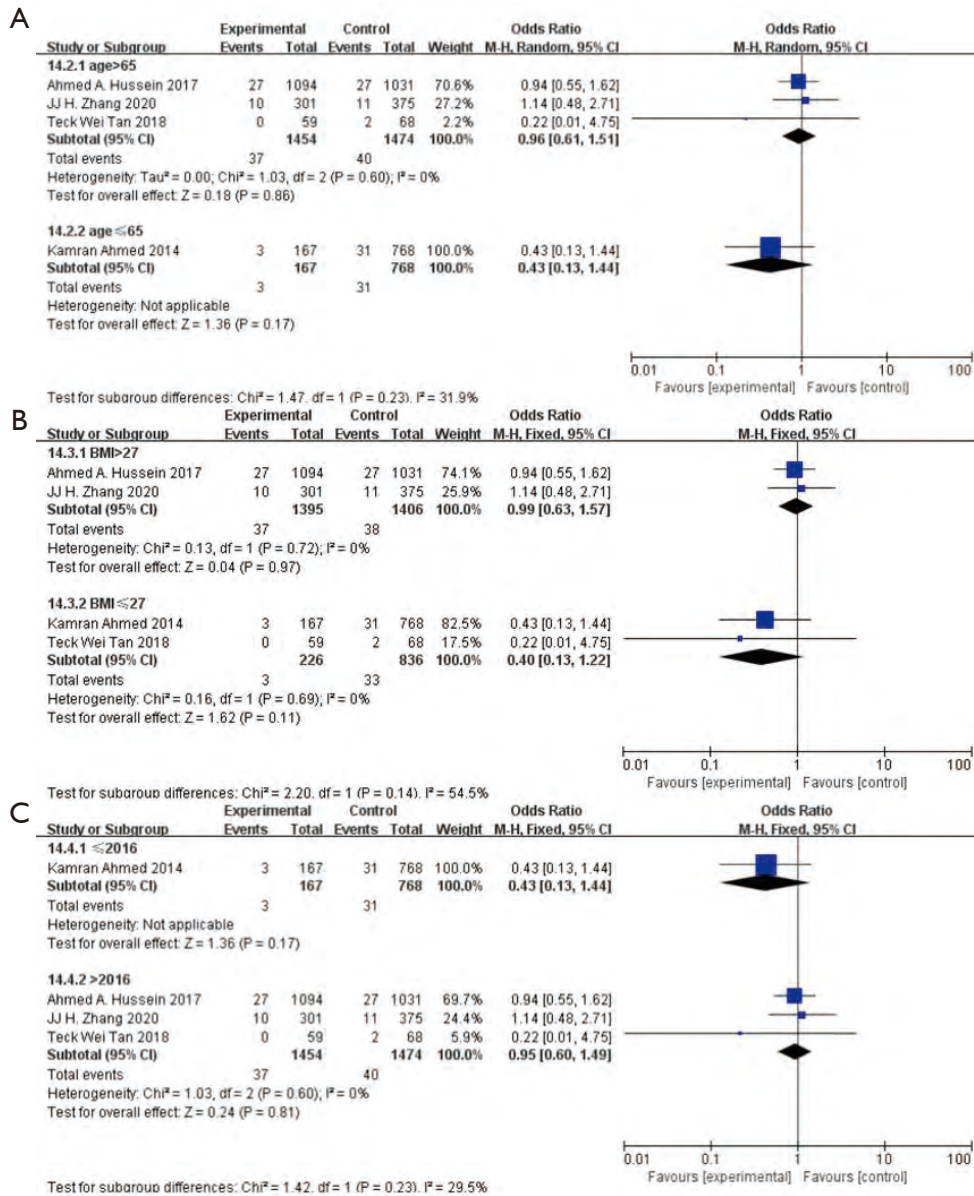


Figure S4 Subgroup analysis. (A) 90 d-mortality of patients in age >65 or age ≤65; (B) 90 d-mortality of patients in BMI >27 or BMI ≤27; (C) 90 d-mortality of patients in publication of study >2016 or ≤2016.

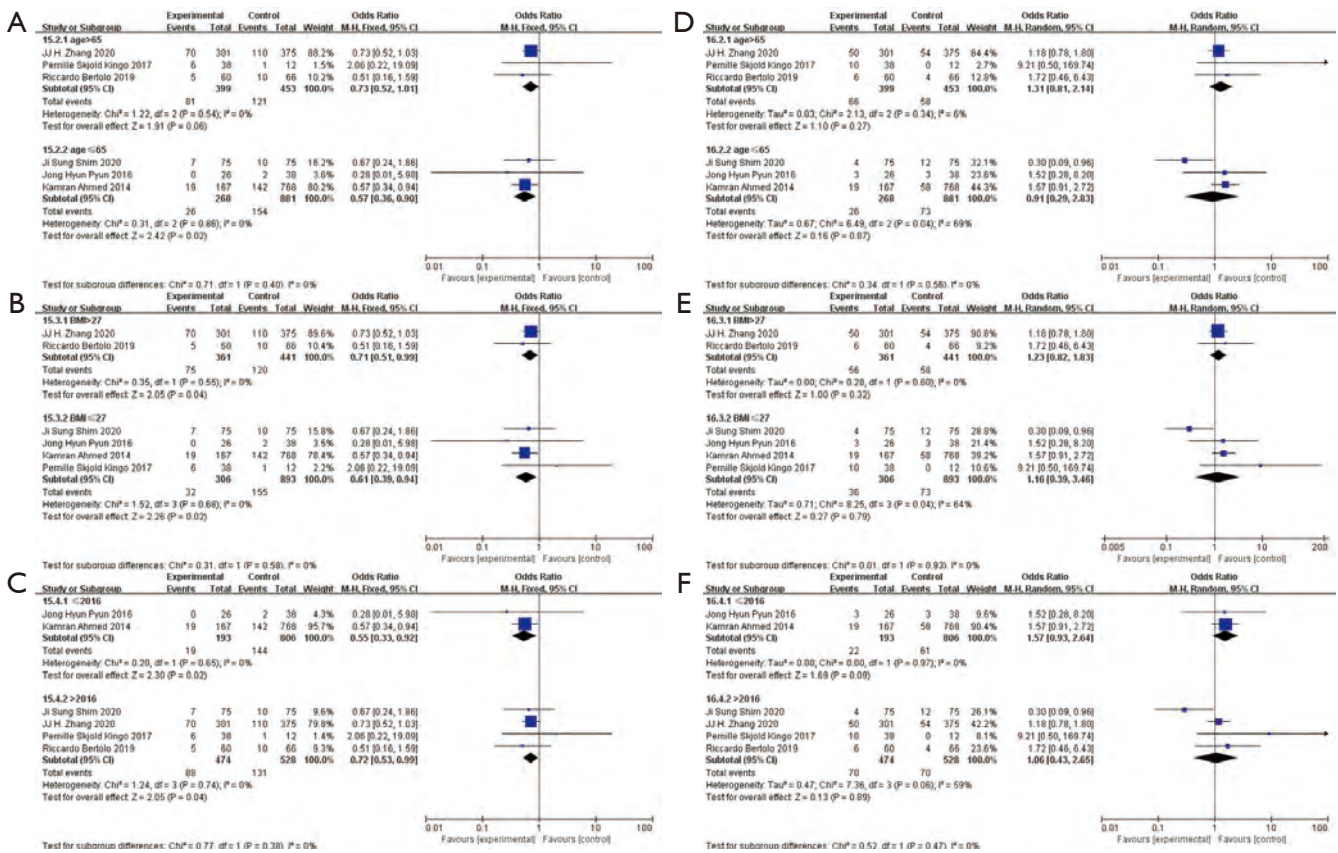


Figure S5 Subgroup analysis for complications according to organ system. (A) gastrointestinal complications of patients in age >65 or age ≤65; (B) gastrointestinal complications of patients in BMI >27 or BMI ≤27; (C) gastrointestinal complications of patients in publication of study >2016 or ≤2016; (D) genitourinary complications of patients in age >65 or age ≤65; (E) genitourinary complications of patients in BMI >27 or BMI ≤27; (F) genitourinary complications of patients in publication of study >2016 or ≤2016.

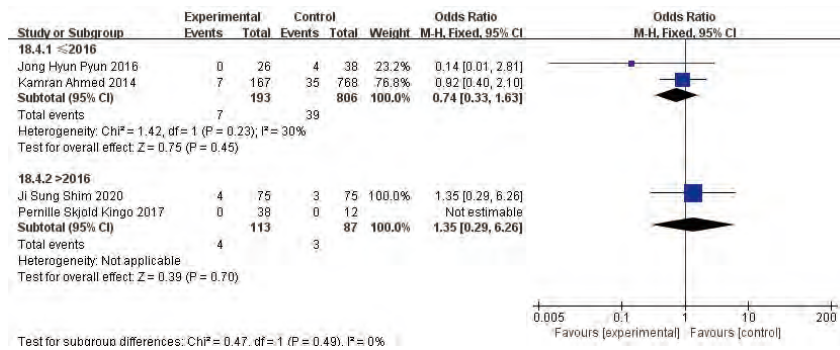
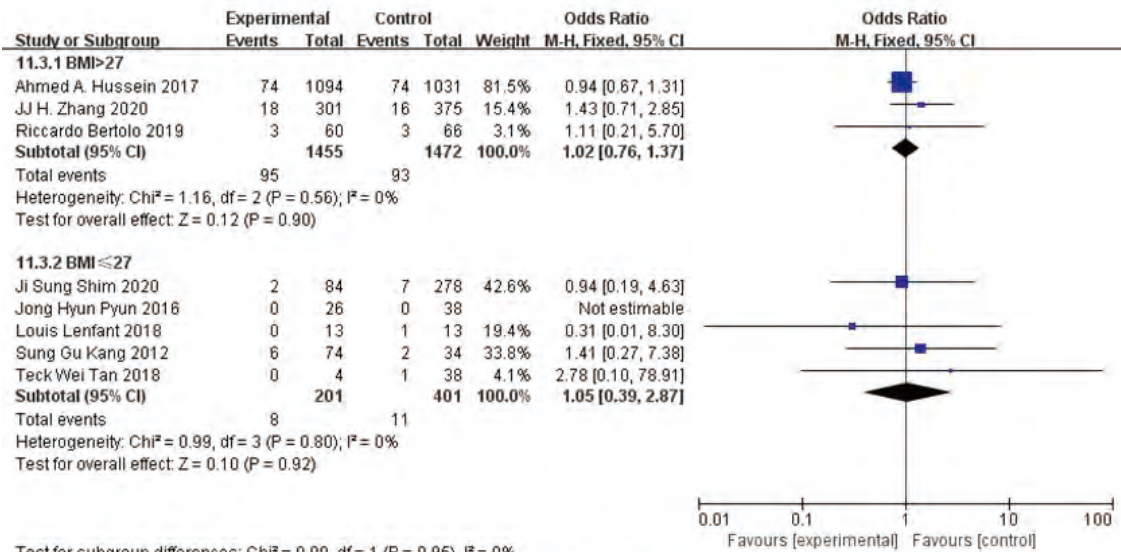


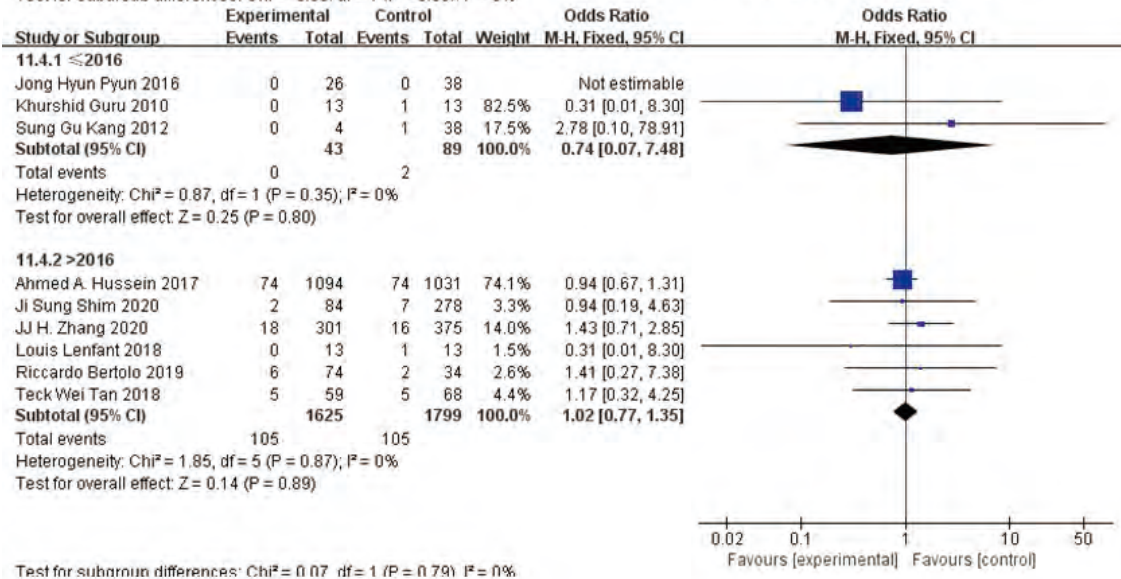
Figure S6 Subgroup analysis for complications according to organ system: wound/skin complications of patients in publication of study >2016 or ≤2016.

A



Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.95), I² = 0%

B



Test for subgroup differences: Chi² = 0.07, df = 1 (P = 0.79), I² = 0%

Figure S7 Subgroup analysis. (A) Positive surgical margin of patients in BMI >27 or BMI ≤27; (B) positive surgical margin of patients in publication of study >2016 or ≤2016.

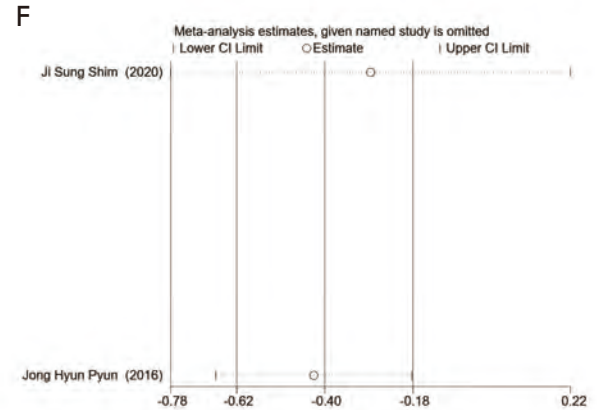
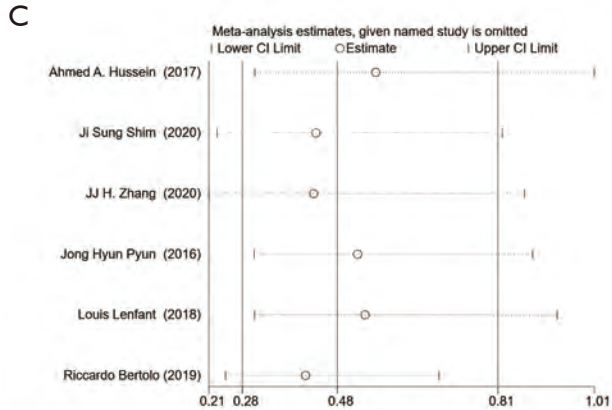
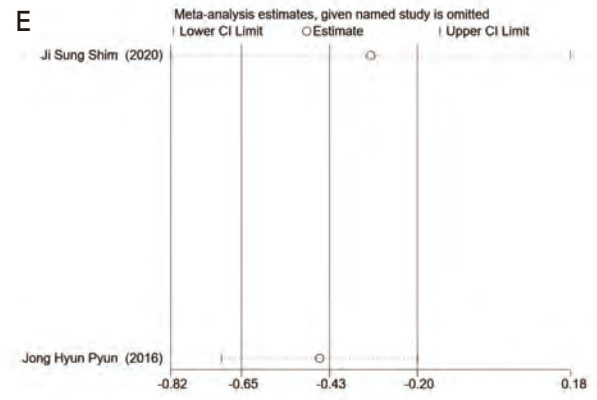
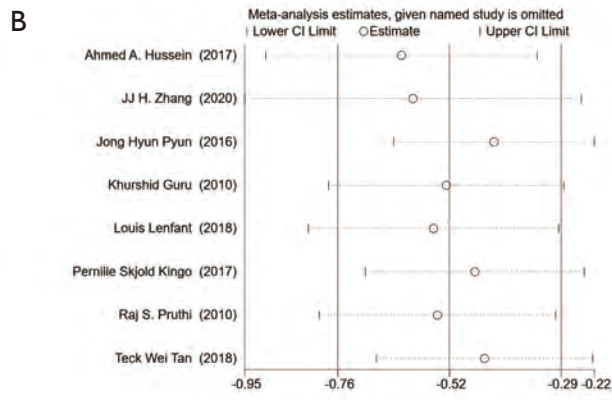
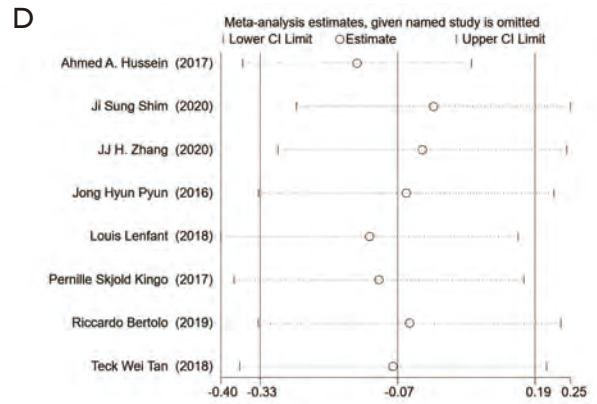
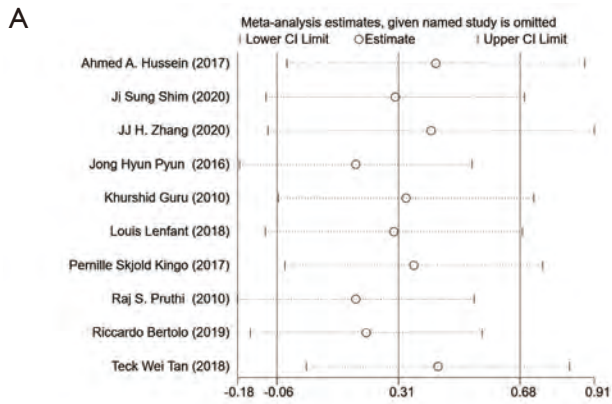


Figure S8 Sensitivity analysis for surgery safety and postoperative recovery. (A) Operation time; (B) EBL; (C) transfusion rate; (D) hospital stay; (E) time to flatus; (F) time to oral intake.

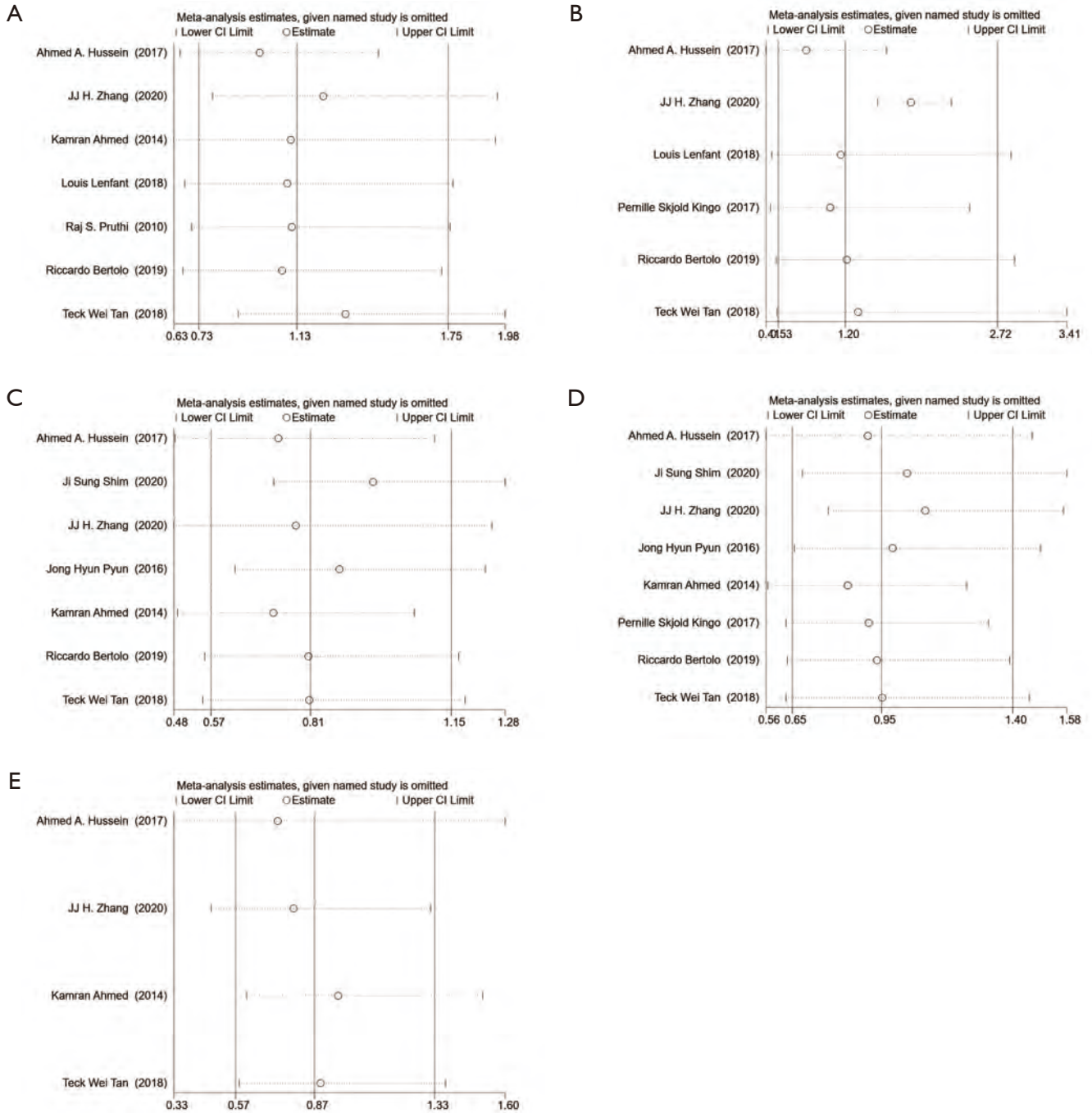


Figure S9 Sensitivity analysis for complications according to Clavien-Dindo grade. (A) 30 d-complications; (B) grade ≥ 3 of 30 d-complications; (C) 90 d-complications; (D) grade ≥ 3 of 90 d-complications; (E) 90 d-mortality.

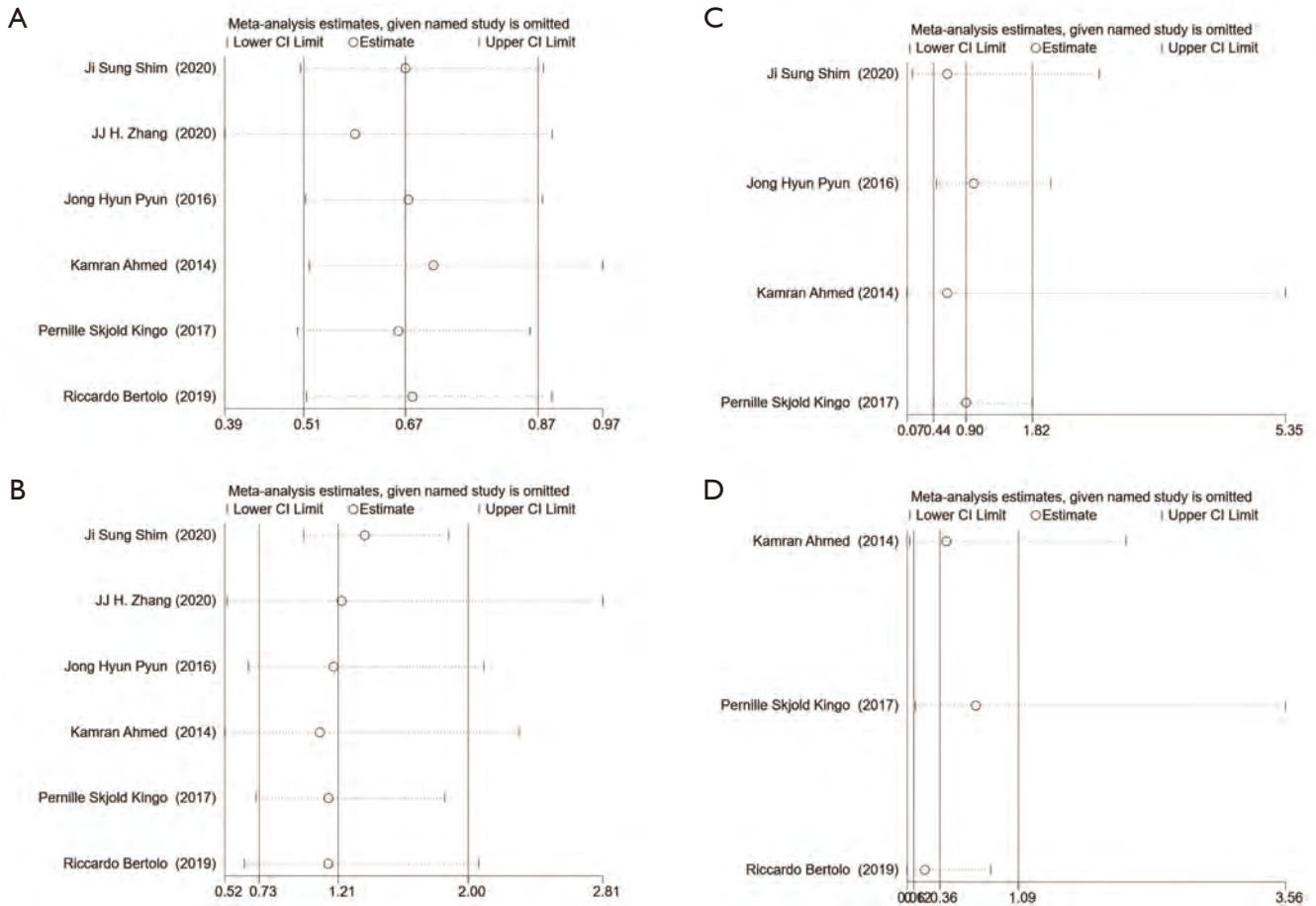


Figure S10 Sensitivity analysis for complications according to organ system. (A) Gastrointestinal; (B) genitourinary; (C) wound/skin; (D) metabolism.

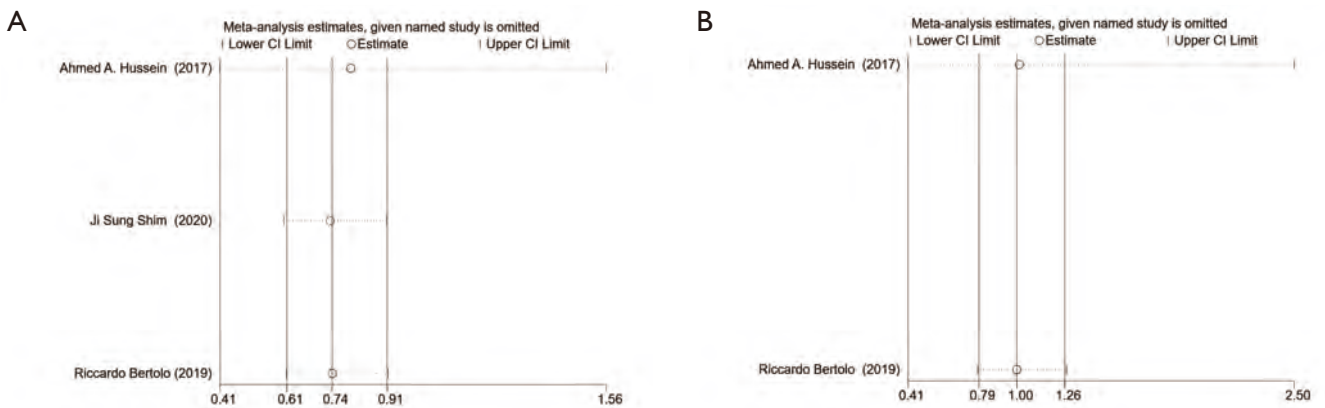


Figure S11 Sensitivity analysis for prognosis results. (A) Recurrence; (B) mortality.

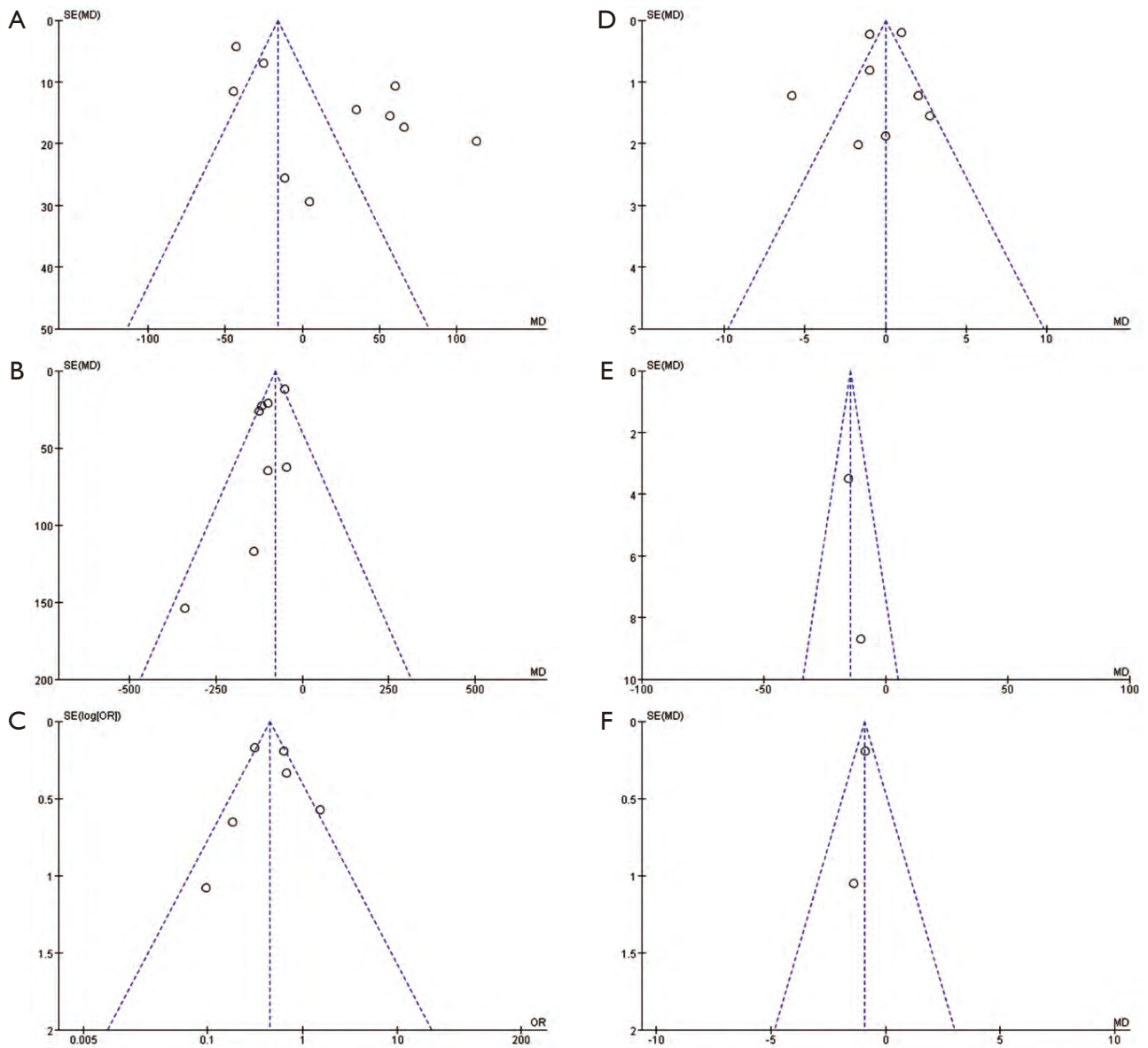


Figure S12 Funnel plot for surgery safety and postoperative recovery. (A) Operation time; (B) EBL; (C) transfusion rate; (D) hospital stay; (E) time to flatus; (F) time to oral intake.

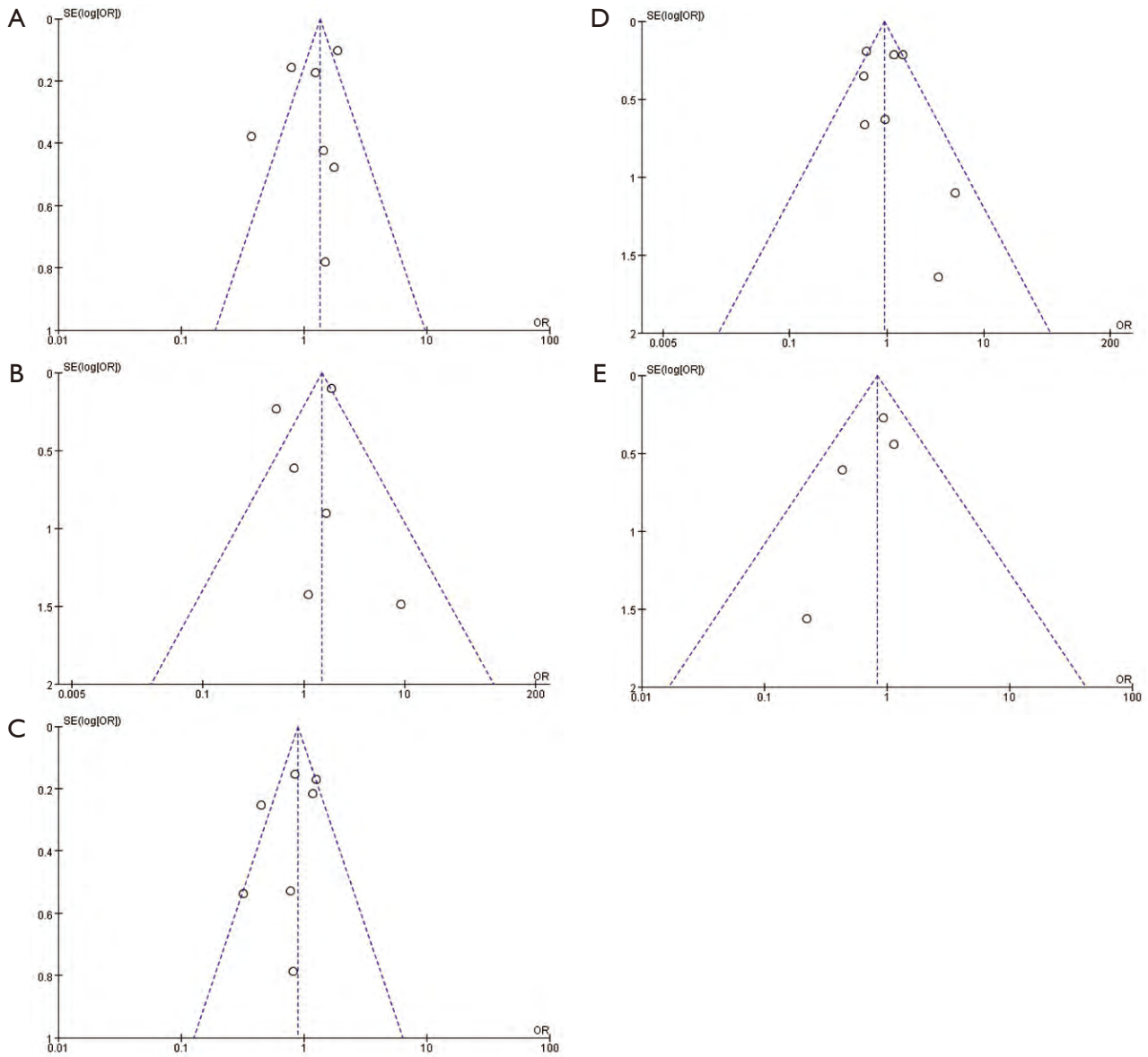


Figure S13 Funnel plot for complications according to Clavien-Dindo grade. (A) 30 d-complications; (B) grade ≥ 3 of 30 d-complications; (C) 90 d-complications; (D) grade ≥ 3 of 90 d-complications; (E) 90 d-mortality.

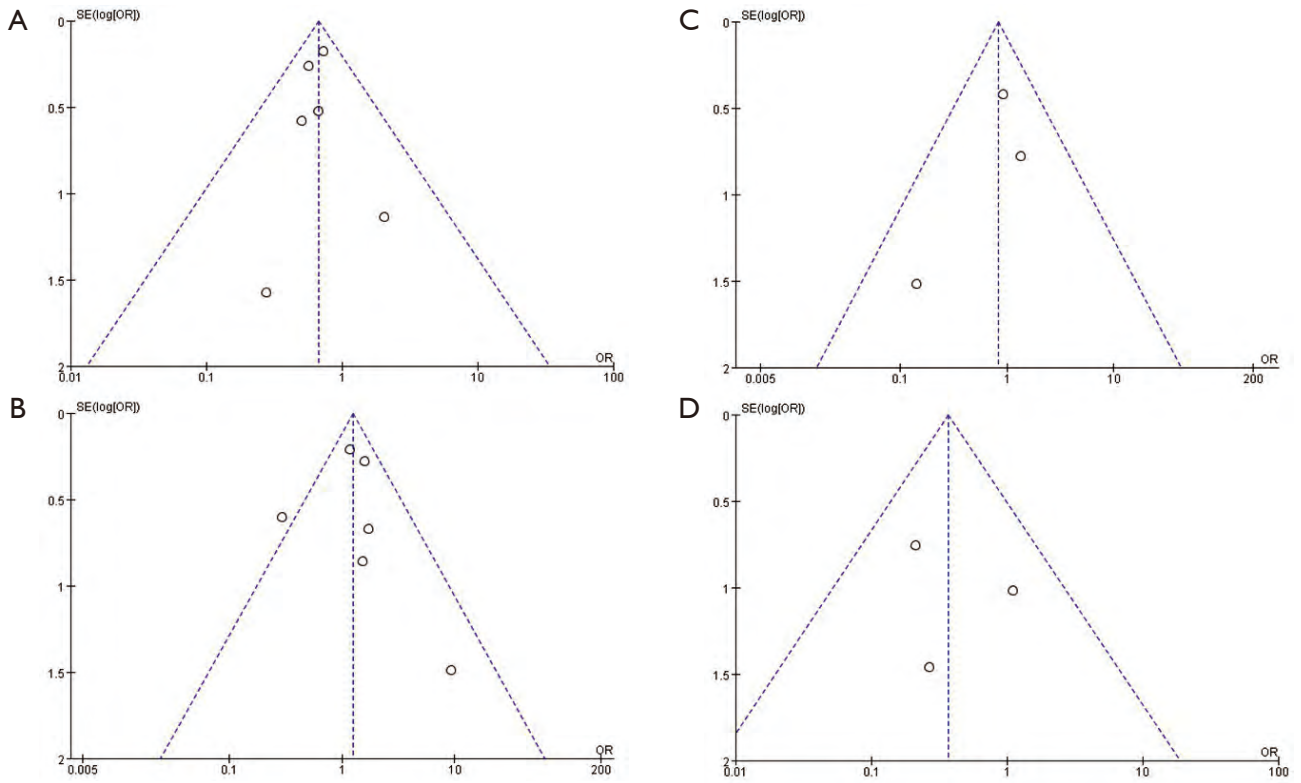


Figure S14 Funnel plot for complications according to organ system. (A) Gastrointestinal; (B) genitourinary; (C) wound/skin; (D) metabolism.

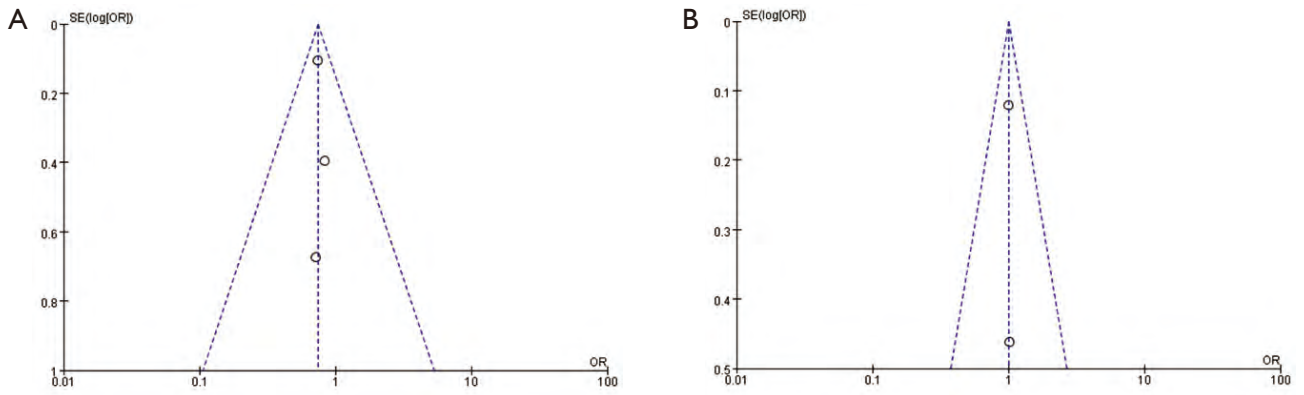


Figure S15 Funnel plot for positive surgery margin and prognosis results. (A) Recurrence; (B) mortality.