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Comparison of long-term outcomes between ileal conduit and transuretero-cutaneostomy urinary diversion after radical cystectomy: a systematic review and meta-analysis

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ABSTRACT

Background: Urinary diversion in bladder cancer treatment has been a distinguished topic of interest due to varying approaches available. Amongst them, ileal conduit (IC) and transuretero-ureterostomy (TUU) have been popular options in clinical practice. This study would like to compare the long-term outcomes of IC and TUU in patients undergoing RC procedures.

Materials and methods: Literature searches were conducted in MEDLINE, CENTRAL, and EMBASE. Duration of hospitalization, complication rate, quality of life, and survival rate were selected as outcomes. Risk of bias was assessed using the ROBINS-I tool. Outcome measure was pooled using forest plot in Review Manager V.5 for Macintosh. Heterogeneity was measured using the DerSimonian and Laird random-effects model.

Results: Eighteen matching interventional studies were included, 3 were prospective studies. The total number of included samples was 3,689; 1,172 patients of the TUU and 2,517 of IC group. The IC procedure associates with longer hospitalization [mean difference 3.80 [95% confidence interval (CI): 2.27–5.32), $p < 0.001$, $I_2 = 92\%$]. Duration of intensive care did not differ significantly. There were no differences in major complication rates [odds ratio (OR) = 1.45, 95% CI: 0.74–2.84, $p = 0.27$, $I_2 = 54\%$]: stone formation (OR = 1.07, 95% CI: 0.51–2.23, $p = 0.48$, $I_2 = 0\%$), and renal function deterioration (OR = 0.81, 95% CI: 0.39–1.68, $p = 0.57$, $I_2 = 0\%$) between the TUU and IC groups. Quality of life decreased in both groups, and only occurred in the early days after the stoma placement phase. Survival rates were not different among the groups.

Conclusion: TUU is a better UD option as it offers shorter time of hospitalization, with the similar major complications, quality of life, and survival rate compared to IC.

Key words: ileal conduit; long-term outcome; radical cystectomy; transuretero-ureterostomy; bladder cancer

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Introduction

Bladder cancer is the second most common urinary tract malignancy, affecting mostly patients aged 65 years or older [1]. The incidence of bladder cancer doubles in seniors over 85 years of age compared to those aged 65 to 69 years, and the incidence in people aged 85 years and above will double by 2030 [2]. In the US, it was estimated that 32% of bladder cancer patients were aged between

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75 and 84 years [3]. At the same time, many elderly patients are expected to have diabetes mellitus, congestive heart failure, and coronary artery disease as comorbidity. Therefore, invasive therapy becomes challenging to adjust for these patients' comorbidities and age-related physiological changes. The treatment of choice could not only concern short-term postoperative outcomes but also the quality of life, probability of remission, and other long-term outcomes that affect the patient's function in terms of carrying out their daily activities.

According to the NCCN Clinical Practice Guidelines in Oncology, radical cystectomy (RC) is indicated for muscle invasive bladder cancer (MIBC) and high-risk non-muscle invasive bladder cancer (NMIBC) [4]. This invasive procedure is associated with excellent perioperative outcomes, with long-term morbidity ranging from 19% to 64% [5]. Lymph node dissection and urinary diversion (UD) also remain standard care along with the RC.

The UD could be divided into two types according to their urine reservoir manipulation: continent reservoirs and non-continent reservoirs. Continent UD is a long and technically more complex procedure than the non-continent UD but offers a good quality of life improvement. However, the reoperation and complication rates were also higher [6–8]. Therefore, non-continent UD is more recommended, especially for the elderly. In addition, improved quality of life in patients receiving non-continent UD has also been recently documented [9].

Ileal conduit (IC) is the more commonly used procedure for UD, as it was supported by a lot of evidence [10]. On the other hand, the transuretero-ureterostomy (TUU) has a lower risk of complication and is more appropriate when bowel segments cannot be used for internal reservoirs or in elderly patients [11]. Although various reports have documented the incidence of stoma stenosis, the latest modified TUU techniques allow patients to achieve better catheter-free rates [9]. Thus, the basic reasoning behind what type of UD should be chosen for the patient remains unclear. Additionally, literature reviews comparing both types of UD are lacking. This review aims to compare the long-term outcomes of IC and TUU in patients undergoing RC procedures.

Materials and methods

This meta-analysis was constructed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines by Cochrane, with the aim of comparing the long-term outcomes of IC and TUU urinary diversion following the RC procedure. The PICO of this review was explained later in the eligibility criteria section.

Eligibility criteria

All clinical studies evaluating the long-term outcome of patients who underwent TUU or IC urinary diversion after radical cystectomy were included in this review. Literature reviews, systematic reviews or meta-analyses, editorial letters, animal studies, non-English written articles, and/or studies in peer review (unpublished) were excluded from this study. The assessment of the eligibility of the studies was carried out independently by each author.

Literature searching strategy

A literature search was conducted on three electronic databases (EMBASE, MEDLINE, and CENTRAL) using five search engines (Pubmed, EBSCO Host, Proquest, EMBASE, and Cochrane). The keywords were adjusted to each search engine specification: ((((ureterostomy) OR (transuretero-ureterostomy)) OR (cutaneostomy)) AND (radical cystectomy)) AND ((((ileal conduit) OR (bricker conduits)) OR (ileal loop urinary diversion) OR (ileal loop urinary diversion).

We collected all the articles on the initial search with the EndNote X9 for Macintosh. Duplicated articles were deleted and continued to each author's title and abstract screening process independently. The full-text assessment was carried out on all articles that passed the screening stage, which each author carried out. Study quality was assessed using the Risk of Bias In Non-randomized Studies - of Intervention (ROBINS-I) tool by each author.

Data extraction and outcomes of interest

We extracted the data needed, including the form of the author's name, year of publication, study design, sample size, and all outcomes of interest, as attached in Table 1. As we aimed to assess long-term patient outcomes, all outcomes were collected from events that occurred ≥ 30 days postoperatively, except for the duration of hospitalization.

Table 1. The eligibility criteria for study inclusion

Aspect	Criteria
Participant	Patients with urinary diversion (ureterostomy or conduit) following RC for the first time. No restrictions on age, sex, race, or patient co-morbidities.
intervention	Illeal conductive urinary diversion. Sigmoidal conduit and colon conduit were excluded. IC was not restricted to a specific technique.
Comparator	TUU. Other stomal approaches (e.g., nephrostomy) were excluded.
Outcome*	Duration of hospitalization All major complications (Clavien-Dindo classification system grade ≥ III) Deterioration of renal function Quality of life Survival rate (overall and disease-specific survival rate)

*outcome of interest was explained further in the Data Extraction and Outcomes of Interest section. RC — radical cystectomy; IC — ileal conduit; TUU — transuretero-ureterostomy

The outcome intended as a major complication is any postoperative complication with the Clavien-Dindo classification system grade ≥ III. Late surgical complications were defined as all complications associated with the surgery which occurred at least 30 days after surgery. Any important complication (such as wound healing, stone formation, and urinary leakage) was also extracted. Deterioration of renal function is defined as a decline of estimated glomerular filtration rate (eGFR) ≥ 20% over baseline, while the quality of life was assessed using any validated instruments [such as EORTC Core Quality of Life questionnaire (EORTC-QLQ-C30) and Functional Assessment of Cancer Therapy for patients undergoing radical cystectomy (FACT-Bl-Cys)].

Statistical analysis

The rate of complications, renal function deterioration, and survival were recorded and transformed into dichotomous outcomes; while the duration of hospitalization and quality of life were directly used as a continuous outcome. These outcomes were then pooled using a forest plot. Effect size measurement was calculated using a fixed-effect model when heterogeneity ($I^2 < 50\%$), using Review Manager 5 for Macintosh by Cochrane.

Results

We found 584 studies in the initial literature search, with a total of 430 duplication-free articles. Twenty-five studies matched the clinical questions proposed in this study and were included in the full-text analysis. Two studies were not available in English, two studies were single-armed, one study combined several types of conduct in the analysis, one study combined IC and TUU in one arm, and one other study had an inadequate sample making statistical inferential analysis impossible.

Characteristics and quality of studies

We found 18 eligible studies, consisting of 3 prospective and 15 retrospective studies. The total number of patients included was 3,689 samples, with 1,172 patients receiving TUU procedures and 2,517 patients receiving IC procedures. The risk assessment of bias using ROBINS-I tools by all authors independently shows that there are two studies with a critical risk of bias and three studies with a high risk of bias. Most of the studies had a moderate risk of bias, and five studies had a low risk of bias. More complete data regarding the risk of bias for each study included is presented in Table 2.

Length of stay

Most of the studies reported a higher duration of hospitalization in the IC group [11–17]. Four other studies reported no significant difference in duration of hospitalization in the IC and TUU groups. In the perioperative period, Deliveliotis et al. [11] reported that the TUU group required shorter intensive care than the IC group. While Fuschi et al. [14] and Long et al. [15] reported that the duration of intensive care did not differ significantly between the two groups, although the non-intensive stay was longer in the IC group.

Only three studies reported the duration of hospitalization with an outcome measure that could

Table 2. Characteristic and bias risk of included studies

No.	Author	Follow-up	Design	Sample sizes	Quality assessment							
					D1	D2	D3	D4	D5	D6	D7	Overalls
1	Adamczyk et al., 2021	30 days	Retrospective	210 (TUU)/183 (IC)	Mods	Mods	Low	Low	Low	Low	Low	Low
2	Arman et al. 2020	12 months	Prospective	23 (TUU)/22 (IC)	Cri	Cri	Low	Low	Mods	Mods	Low	Hi
3	Delieriotis et al. 2005	Not mentioned	Retrospective	29 (TUU) /25 (IC)	Mods	Low	Low	Low	Mods	Mods	Low	Mods
4	De Nunzio et al. 2013	90 days	Prospective	138 (TUU)/217 (IC)	Hi	Mods	Low	Low	Low	Mods	Low	Mods
5	Fuschi et al., 2022	6 months	Retrospective	41 (TUU)/37 (IC)	Hi	Mods	Low	Low	Mods	Mods	Low	Mods
6	Gacci et al., 2013	36 months	Retrospective	16 (TUU)/16 (IC)	Hi	Mods	Low	Low	Mods	Mods	Low	Mods
7	Huang et al. 2021	Not mentioned	Retrospective	301 (TUU)/1093 (IC)	Mods	Mods	Low	Low	Low	Low	Mods	Mods
8	Kadoriku et al., 2022	90 days	Retrospective	25 (TUU)/25 (IC)	Mods	Mods	Low	Low	Low	Low	Low	Low
9	Khalilullah et al 2021	24.8 months	Retrospective	22 (TUU)/30 (IC)	Low	Low	Low	Low	Mods	Low	Low	Low
10	Kilciler et al. 2006	37 ± 9.35 months	Retrospective	34 (TUU)/67 (IC)	Cri	Cri	Low	Low	Cri	Hi	Low	Hi
11	Knaps et al. 2004	5.4 years	Retrospective	4 (TUU)/195 (IC)	Cri	Cri	Low	Low	Cri	Hi	Mods	Cri
12	Longo et al. 2016	42.7 (12–72) months	Retrospective	35 (TUU)/35 (IC)	Mods	Low	Low	Low	Mods	Mods	Low	Mods
13	Nishikawa et al. 2014	60 months	Retrospective	42 (TUU)/40 (IC)	Mods	Mods	Low	Low	Low	Low	Mods	Mods
14	Pycha et al. 2008	16 (5–14) months	Prospective	41 (TUU)/55 (IC)	Low	Mods	Low	Low	Mods	Low	Low	Low
15	Saika et al. 2007	4 (0.3–11.2) years	Retrospective	31 (TUU)/56 (IC)	Cri	Hi	Low	Low	Mods	Mods	Hi	Hi
16	Suzuki et al., 2019	24 months	Retrospective	109 (TUU)/123 (IC)	Mods	Low	Low	Low	Cri	Mods	Low	Mods
17	Wuethrich et al. 2016	22 (0.04–147) months	Retrospective	11 (TUU)/178 (IC)	Cri	Cri	Low	Low	Cri	Hi	Mods	Cri
18	Xie et al. 2021	60 months	Retrospective	60 (TUU)/ 120 (IC)	Mods	Mods	Low	Low	Low	Low	Low	Low

Domain	Judgment
D1: bias due to confounding D2: Bias due to selection of participants D3: Bias in classification of intervention D4: Bias due to deviation from the intended intervention D5: bias due to missing data D6: Bias in the measurement of the outcomes D7: bias in reporting results	Cri: critical risk of bias Hi: high risk of bias Mod: moderate risk of bias Low: low risk of bias

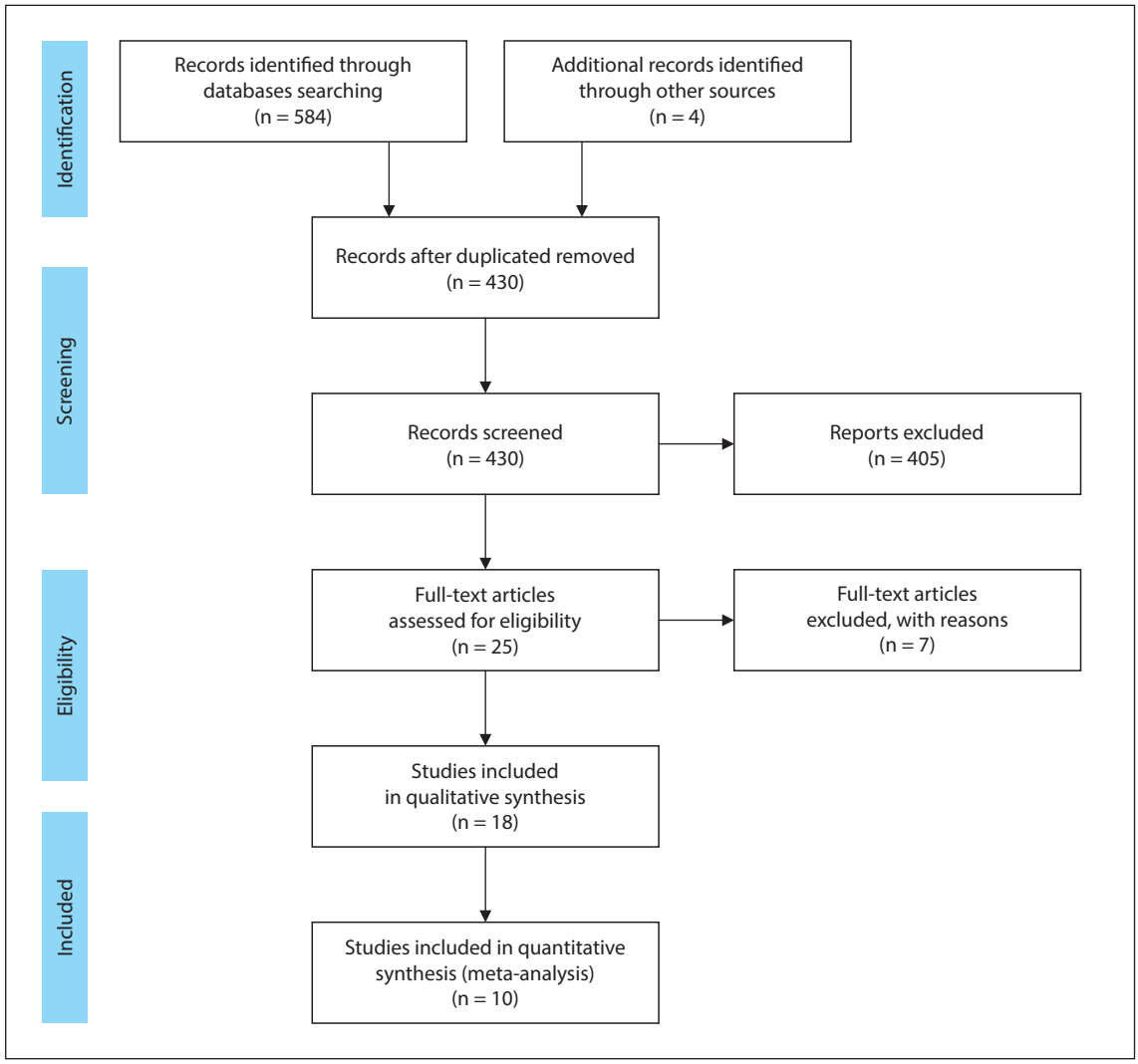

Figure 1. Literature search flow

be further analyzed using a forest plot. We found a pooled mean difference in hospital stay of 3.80 [95% confidence interval (CI): 2.27–5.32] days in the IC group, with a $p < 0.001$ ($I_2 = 92\%$). The duration of intensive care did not differ significantly between the TUU and IC groups ($p = 0.96$, $I_2 = 85\%$).

Late complications

DeNunzio et al. [12] and Fuschi et al. [14] reported a higher complication rate (CDCS grade ≥ 3) in the IC group. In contrast, six other studies reported no difference in the proportion of major complications (CDCS grade ≥ 3) between the two groups [9, 13, 18–21]. Moreover, Kadoriku et al. [18] reported no significant difference in the proportion of major complications in 2 different periods, 30 days and 90 days postoperatively. Arman et al. [9] added that the difference in the proportion of major complications was not found to be significant, either in TUU or cutaneous-ureterostomy (double stoma).

A forest plot pooling the OR estimate for major complication rate shows no difference in the proportion of major complication rates between the TUU and IC groups [OR = 1.45 (95% CI: 0.74–2.84), $p = 0.27$]. Heterogeneity was recorded at 54% (I_2); thus, the random-effect model calculation was implemented.

Several studies also reported late surgical complications that were not classified using the CDCS grading system. Khalilullah et al. [16] reported five stoma stenoses, one anastomotic stricture in the TUU group, one anastomotic stricture, and one entero-cutaneous fistula in the IC group. Urinary leakage was reported in 5 patients (14.3%) in the IC

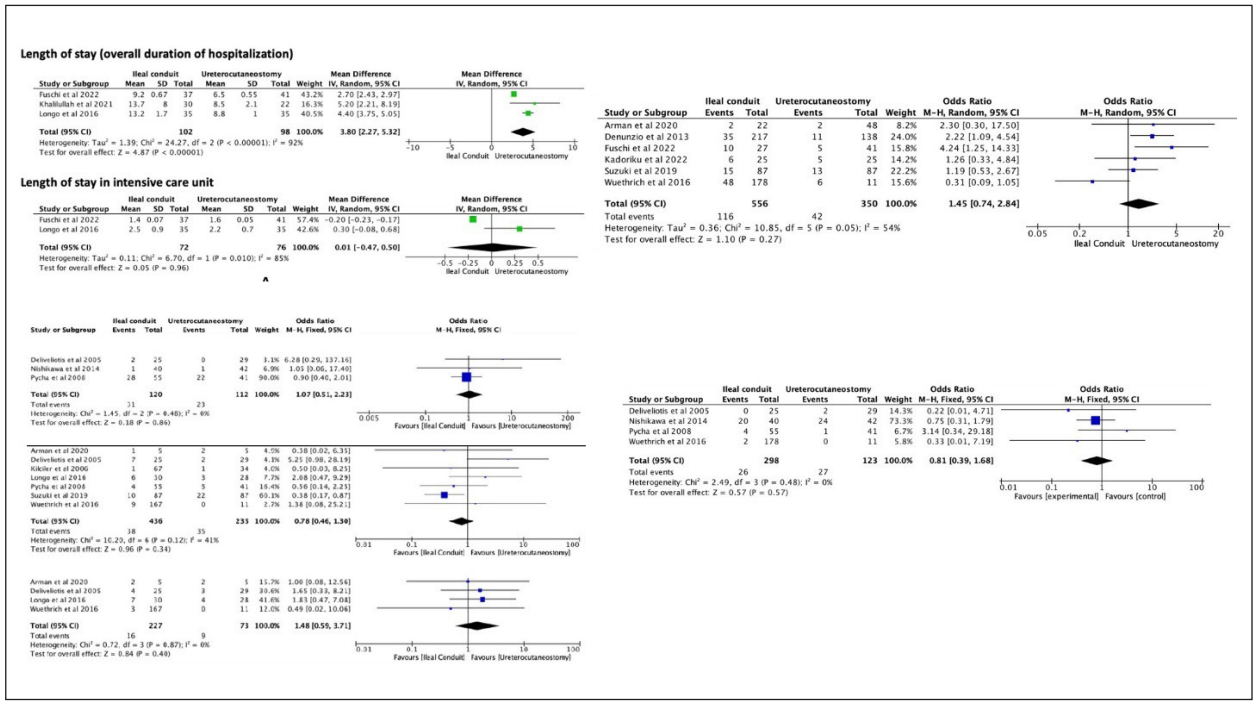

Figure 2. Forest plot for: Length of stay after surgery (**A**), major complication rate (**B**), stone formation, urinary tract infection, surgical-site infection rate (**C**), and renal function deterioration rate (**D**)

group, while none of the TUU group's patients experienced this complication [15]. Pycha et al. [22] reported a significantly higher rate of late surgical complications in the IC group; most of those complications caused a deterioration of renal function.

There are three studies reported the event of stone formation. Deliveliotis et al. [11] found stone formation in the IC group only (8%), while Nishikawa et al. [23] and Pycha et al. [22] reported the occurrence of renal calculi in both groups; however, the rate difference was not statistically significant [11, 22, 23]. The forest plot was presented in Figure 2.

Suzuki et al.[19]n = 123; cutaneous ureterostomy, n = 109 reported the incidence of postoperative recurrent pyelonephritis following the TUU was significantly higher than IC (p = 0.030). However, others reported no significant difference of urinary tract infection rate among the groups [9, 11, 15, 17, 20, 22]. The surgical-site infection rate was also not significantly different between the TUU and IC groups. The forest plot of these results was presented in Figure 2.

Renal function

A median reduction of eGFR was reported in all groups. However, the incidence of eGFR reduction > 20% was higher in the TUU group. [19] Wuethrich et al. [20] reported an incidence of renal failure of < 2% in the IC group, while Deliveliotis et al. [11] found no incidence of renal failure in the IC group. Nishikawa et al. [23] reported a relatively higher incidence of renal failure in the TUU group than IC. Knaps et al. [24] reported a less than 10% renal failure rate in the TUU group.

In general, there was no difference in the incidence of decreased kidney function between the two types of urinary diversion. The odds risk for the IC group to experience a decrease in kidney function was 0.81 (95% CI: 0.39–1.68, p = 0.57, I_2 = 0%).

Quality of life

Various parameters can be used to assess the quality of life of post-RC patients. Arman et al. [9] reported that the quality of life of the IC group was higher than that of the ureterostomy (TUU and DSCU), based on the EORTC-QLQ-C30 and FACT-Bl-Cys parameters. Gacci et al. [25] used three types of parameters to assess the patient's QoL and reported no significant difference in the QoL of the TUU and IC groups. Moreover, Saika et al. [26] also compared the quality of life outcomes of TUU and IC patients with those of orthotopic neobladder and reported no difference in patient quality of life between the three types of UD.

Survival rate

Almost all studies agree that the two groups have no significant difference in survival rate and survival time. Huang et al.[27] reported that the median survival time for the TUU group was 19 (95% CI: 15–26) months, and for the IC group it was 19 (95% CI: 16–24) months (p = 0.652). Only Wuethrich et al.[20] reported that the TUU group had a worse survival rate and survival time than the IC group (Tab. 8).

Discussion

This study successfully compared the long-term outcomes of TUU and IC procedures in post-RC patients. There were 18 studies with 3,689 post-RC patients, consisting of 1,172 TUU patients and 2,517 IC patients. Despite the high postoperative morbidity rates, RC procedures are the standard of care for localized treatment of MIBC and high-risk NMIBC [4, 21]. Following the RC, a urinary diversion is a mandatory intervention. TUU and IC have become the most favored urinary diversion options, considering their cost and less invasive approach than the continent's urinary diversion [19, 28]. The choice among these two options are based on the patient's preference and disease characteristics [29].

IC urinary diversion includes manipulating the ileum as a medium to pass urine from the ureter to the extracorporeal stoma. This action has consequences of a longer surgery time and a higher risk of postoperative infection compared to the TUU procedure [12]. A significantly higher blood volume loss has also been reported in various studies [11, 29]. This would increase the hospitalization duration, which is higher in IC patients. Adamczyk et al. [13] reported that IC becomes a significant predictor of prolonged hospital stay (> 7 days) compared to TUU, with an odds ratio of 6.13 (95% CI: 3.40–11.39, p < 0.001). Our meta-analysis found that the IC group had a significantly higher mean duration of hospitalization than the TUU group, with a mean difference of 3.80 (95% CI: 2.27–5.32; p < 0.001; I_2 = 92%). However, the time required for intensive care was not significantly different between the two groups.

Various studies report different things related to postoperative complications. Some reported higher rates of major complications in the IC group [11, 12, 14], and some did not report any significant difference in the incidence of complications between the two groups [9, 19]. Deliveriotis et al. [11] consistently reported a higher incidence of complications in the IC group, in the perioperative period up to 90 days postoperatively, with baseline characteristics of the two groups being not significantly different. Although several studies disagreed that the incidence of major complications was higher in the IC group, none of these studies reported a higher incidence of major complications in the TUU group.

Longo et al. [15] reported urinary leakage in 5 patients in the IC group, while none in the TUU group. In this case, the two groups have the same sample size. Kilciler et al. [17] reported two events of stomal stenosis, three events of anastomotic stricture, and one pyelonephritis in the TUU group. Five stomal stenoses, four anastomotic strictures, one pyelonephritis, and four ileuses were found in the IC group. The high incidence of long-term complications reported in the IC group may result in a higher number of patient readmissions to the operating room [19], increasing the cost of treatment.

The long-term complication of concern is reduced renal function, as urinary diversion has been associated with a long-term decline in renal function [30]. Decreased renal function has been documented in both groups. Suzuki et al. [19] reported median renal function in the TUU group of TUU of 55.9 (14.4–111.3) and IC of 56.8 (19.3–112.7) at 24 months postoperatively (p = 0.458), with a baseline eGFR that was not significantly different between the two groups. In general, there was no significant difference in the proportion of renal function decline >20% rate between the two groups (OR = 0.81, 95% CI: 0.39–1.68, p = 0.57, I_2 = 0% for IC versus TUU).

All UD actions decrease the patient's quality of life, as the patient will experience a decrease in the aesthetic function of the body due to the installation of a stoma and the need for money and time to conduct stoma care. Zewude et al. [31] reported that 66% of patients lost sexual function, and only 11% could adapt well and were satisfied with their present condition. This condition occurs primarily in the early days after stoma placement. Fuschi et al. [14] reported lower patient quality of life scores at the third month of stoma insertion in

the TUU group [52.4, 95% CI: 50.3–54.5; effect sie (ES): 1.62] and IC [52.2, 95% CI: 49.4–55.0; ES: 1.61) However, the quality of life scores increased at the sixth month in both groups.

Only Arman et al. [9] reported a higher health-related quality of life (HR-QoL) in the IC group than in the TUU. This was related to the lower catheter-free rate in the TUU group. Another study with a more extended observation period agreed that the quality of life for the TUU and IC groups was not significantly different. Khalilullah et al. [16] observed patients' QoL for more than 12 months post-UC, reporting no significant difference in QoL between the two groups.

The 5-year survival rate of patients undergoing RC, which is generally indicated for high-risk NMIBC or MIBC, is reported to vary between 54–68% [32, 33]. Urinary diversion has reportedly associates with the patient survival. However, various other factors were found to have a much more significant effect, including tumor staging, lymph node involvement, and ASA score [34]. Almost all studies agree that there is no difference in the survival rate of the TUU and IC groups. Only Wuethrich et al. [20] reported that TUU has a lower cancer-specific survival rate [hazard ratio (HR) = 3.416 (95% CI: 1.169–9.978); p = 0.025]. TUU was also reported to have a lower overall survival rate [HR = 2.696, 95% CI: 1.306–5.569; p = 0.007]. However, this study had a skewed sample proportion between the IC and TUU groups. A total of 178 IC patients were included, while there were only 11 patients in the TUU group. In addition, the patient's baseline characteristics were also found to be significantly different in terms of age, ASA score, and preoperative kidney function.

The difference in long-term outcomes of the TUU and IC groups was significantly found in the duration of hospitalization. Increased duration of hospitalization is associated with an increased risk of nosocomial infection [35]. The elderly, for whom the local prevalence of MIBC peaks, have decreased immune function. Exposure to nosocomial infections due to a higher duration of hospitalization will worsen the patient's prognosis. On the other hand, these two groups (TUU and IC) do not show a significant difference in long-term complications rate and survival. The decrease in quality of life only occurred in the early days after stoma placement phase and experienced an increase in quality of life scores over time. During the catheter-free period, the two groups had no significant difference in quality of life.

This meta-analysis successfully compared the long-term outcomes of UD, specifically TUU and IC. We reviewed studies from various types of populations making the results of this meta-analysis able to be extrapolated in various clinical settings. However, there are some limitations we should underline. First, most studies were based on medical records. This retrospective approach might lead to a failure to control the measurement bias. Second, most of the outcomes of interest are reported in different outcome measures, making it unable to carry out a meta-analysis of these outcomes, and the synthesis of the outcomes result was only carried out narratively. Third, a small number of included studies have a risk of critical bias, mainly due to the unequal distribution of samples between groups and significant differences in baseline characteristics.

Conclusion

To conclude, TUU is a better UD option for patients undergone RC, as it offers a shorter hospitalization duration, with the no difference major complication, quality of life changes, and survival rates compared to IC.

Conflict of interest

Authors declare no conflict of interest.

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None declared.

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