

URINARY DIVERSION AFTER RADICAL CYSTECTOMY, ORTHOTOPIC NEOBLADDER VS ILEAL CONDUIT: A SYSTEMATIC REVIEW AND META-ANALYSIS OF POSTOPERATIVE COMPLICATION

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ABSTRACT

Objective: The purpose of this study is to compare orthotopic neobladder (ONB) and ileal conduit (IC) formation in terms of surgical outcome and complication. **Material & Methods:** Computerized bibliographic search on different databases related to this study. The PICO criteria method was applied to define research eligibility, per PRISMA recommendations and conducted a systematic review of the literature with meta-analysis. Weighted mean differences with 95 percent confidence intervals were used to compare continuous outcomes. **Results:** There were 479 publications were discovered and only 6 studies fulfilled the criteria included. The random-effect model's pooled result for urinary leakage complication revealed a significant difference of 1.62 between ONB and IC with higher incidence in neobladder group (95 percent CI, 1.85, 8.69, $P = 0.0004$) with non-significant heterogeneity ($Chi^2 = 0.65$, $df = 3$ ($P = 0.89$), $I^2 = 0\%$). Other complications (ileus complication, anastomosis site stenosis, sepsis, urinary infection) showed non-significant difference. **Conclusion:** Because of the heterogeneity in several aspects of the analyzed papers, further study comparing Orthotopic Neobladder and Ileal conduit in terms of complication following urinary diversion are needed to confirm superiority of ONB or IC as the urinary diversion of choice.

Keywords: Orthotopic neobladder, ileal conduit, urinary diversion, radical cystectomy.

ABSTRAK

Tujuan: Tujuan dari penelitian ini adalah untuk membandingkan pembentukan orthotopic neobladder (ONB) dan ileal conduit (IC) dalam hal hasil operasi dan komplikasinya. **Bahan & Cara:** Pencarian bibliografi terkomputerisasi pada database berbeda yang terkait dengan penelitian ini. Metode kriteria PICO diterapkan untuk menentukan kelayakan penelitian, sesuai rekomendasi PRISMA dan melakukan tinjauan literatur secara sistematis dengan meta-analisis. Perbedaan rata-rata tertimbang dengan interval kepercayaan 95 persen digunakan untuk membandingkan hasil yang berkelanjutan. **Hasil:** Terdapat 479 publikasi yang ditemukan dan hanya 6 penelitian yang memenuhi kriteria yang dimasukkan. Hasil gabungan model efek acak untuk komplikasi kebocoran urin mengungkapkan perbedaan signifikan 1.62 antara ONB dan IC dengan insiden lebih tinggi pada kelompok neobladder (95 persen CI, 1.85, 8.69, $P = 0.0004$) dengan heterogenitas tidak signifikan ($Chi^2 = 0.65$, $df = 3$ ($P = 0.89$), $I^2 = 0\%$). Komplikasi lain (komplikasi ileus, stenosis situs anastomosis, sepsis, infeksi saluran kemih) menunjukkan perbedaan yang tidak signifikan. **Simpulan:** Karena heterogenitas dalam beberapa aspek makalah yang dianalisis, penelitian lebih lanjut yang membandingkan Orthotopic Neobladder dan Ileal conduit dalam hal komplikasi setelah pengalihan urin diperlukan untuk memastikan keunggulan ONB atau IC sebagai pilihan pengalihan urin.

Kata kunci: Orthotopic neobladder, ileal conduit, diversifikasi urine, sistektomi radikal.

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INTRODUCTION

Every year about 357.000 new cases of bladder cancer are diagnosed yearly, and it is the cause of about 145.000 deaths. With numerous treatment modalities, radical cystectomy (RC) is still

the gold standard for managing muscle-invasive high-grade bladder cancer. Following RC, the patient will undergo a urinary diversion. The optimal type of urinary diversion (UD) after RC is still controversial because any form of diversion would have a different outcome on self-well-being, body

image, self-esteem, and, most importantly, urinary function.¹

Surgeons have used ileal conduit (IC) for decades as a "standard" urinary diversion for bladder cancer patients submitted to radical cystectomy. It has been understood as the most adequate, cost-effective, and reliable long-term solution and remains a commonly used diversion following radical cystectomy. However, during the last decades, this procedure has been questioned by the dissemination and better outcome of bladder substitutions.² a relevant section of the ileum is chosen, which should be around 15 cm proximal to the ileocecal valve. The conduit length is designed to provide for proper placement and tension-free anastomoses of the ureters to the proximal end of the conduit, with around 15 cm of ileum required for the diversion. Lifting the distal ileum and shining a light through to observe the avascular plane for the division to ensure adequate blood supply to the conduit can be used to visualize the mesenteric blood supply.³

Neobladder reconstruction is a surgical procedure to construct a new bladder and become another option for urinary diversion. Orthotopic diversions rely on the ileal segment's twofold folding to create a low-pressure reservoir.⁴ The distal division, 15 cm proximal to the ileocecal valve, is done in the same way as the ileal conduit, albeit the distal mesenteric division can be more profound to allow for more bowel segment movement into the pelvis. The neobladder is created by measuring approximately 55 cm of the bowel proximal to this distal divide. The intestine to be utilized for the neobladder is inserted into the pelvis in the same manner as the ileal conduit, while the anastomosed bowel is to be reconnected, and the mesenteric trap is closed in the same manner as the ileal conduit.³

OBJECTIVE

Few studies have reported comparing conduits and neobladders and found no specific superiority between the two procedures. Based on the previous study, we determined to systematically review and conduct a meta-analysis of the data of patients who underwent radical cystectomy that received orthotopic neobladder and ileal conduit formation in terms of surgical outcome and complication.

MATERIAL & METHODS

We performed a computerized bibliographic search on different databases: PubMed, ScienceDirect, Cochrane Library, and ClinicalTrials.Gov using the keywords: "Bladder cancer", "Cystectomy", "Orthotopic neobladder", "Ileal conduit", "Complication," and "Comparison." Two of the research team's investigators carried out the literature search independently. Data extraction was recorded on customized tables, and a third independent author handled any differences between the two independent authors. The following information was extracted: first author, country, journal, year of publication, study design (retrospective versus prospective), setting (single-center versus multi-center), number of patients, age (years), percentage of patients with bladder cancer, percentage of patients with ileal conduit group, percentage of the patient with orthotopic Neobladder group, the complication that arises in each group.

We applied the PICO method to define research eligibility, per PRISMA recommendations. The PICO criteria (population, intervention, control, and outcome) were used to develop the clinical question:

- Population: Patients undergoing radical cystectomy that received urinary diversion (either Neobladder or Ileal conduit)
- Intervention: Orthotopic Neobladder Urinary Diversion
- Comparison: Ileal Conduit Urinary Diversion
- Outcome: Postoperative/complications including urinary tract infection, leakage, sepsis, ileus, and anastomosis site stenosis

The inclusion criteria are all comparative study that examines postoperative complication of sepsis, ileus, and stenosis at anastomosis site in ileal conduit vs. orthotopic neobladder urinary diversion in a patient who underwent radical cystectomy. The exclusion criteria are all paper that is not in English or Bahasa Indonesia.

The papers were peer-reviewed by two writers (GA and MF). According to the guidelines of the "Cochrane Handbook for Systematic Reviews of Interventions" and "Preferred

Reporting Items for Systematic Reviews and Meta-Analysis" (PRISMA), we conducted a systematic review of the literature with meta-analysis. The Oxford Centre for EBM Standards assessed the article's quality.

The Cochrane Handbook for Systematic Reviews of Interventions was used to guide the

statistical approaches. Weighted mean differences with 95 percent confidence intervals were used to compare continuous outcomes.

The I2 tests and the Chi2 tests were used to assess the heterogeneity of the studies for each outcome: heterogeneity was considered significant if the I2 was greater than 50% with a P less than 0.10. A random-effect model was used when there was significant heterogeneity with an I2 value greater than 50%. Otherwise, a fixed-effect model was utilized in the case of non-significant heterogeneity. Funnel plots were used to see if there was any publication bias. Review Manager 5.4 was used to conduct the analyses.

Table 1. Characteristics of the studies.

Study	Population	Outcome
Gburek 1999 ⁵	ileal neobladder diversion in 62 men and 4 women (group 1) ileal conduit diversion in 66 men (group 2)	12 of 66 neobladder cases (18%), had a total of 16 perioperative complications and a 5% reoperation rate 12 of 66 conduit cases (18%) had a total of 17 perioperative complications and a 6% reoperation rate Mean hospital stay: 13-day each group
Parekh 2000 ⁶	117 with orthotopic reconstruction and 81 with ileal conduit during a 5-year time frame	The median operative time: ileal conduit - 201 minutes (range 140 to 373) orthotopic neobladder - 270 minutes (range 230 to 425) The median blood loss was 389 and 474 mL The median length of hospitalization -8 days (ileal conduit group) and 7 days (orthotopic neobladder group) Diversion-related complications recognized within 30 days that ultimately required a return to the operating room 3,4 % (neobladder) and 1,2% (ileal conduit)
Erber 2011 ⁷	146 with an ileal conduit and 115 with an ileal neobladder	69.1% and 69.6% of all patients who received an ileal conduit and ileal neobladder, respectively, developed early complications
Aboourmarzouk 2013 ⁸	39 with an ileal conduit and 24 with neobladder	No difference was found (P >0.05) regarding age, BMI, smoking history, TURBT pathology result, blood loss, blood transfusion requirement, conversion rates, length of hospital stay, morphine requirement, complications, or follow-up and quality of life
Mano 2018 ⁹	130 ileal conduit and 49 orthotopic neobladder patients	29% of neobladder patients and 8% of ileal conduit patients had a UTI episode (p=0.001). Diversion type was not associated with UTI. E.Coli was the most common pathogen in conduit patients (58%), and Klebsiella spp. in neobladder patients (29%).
Mohammed 2018 ¹⁰	64 ileal conduit and 49 W-neobladder patients	In ileal conduit group: wound complication was found in 33 cases (51.6%), leakage in 6 cases 9.4%), ileus in 12 (cases (18.8%), thromboembolic complication in 6 cases (9.4%) In w-neobladder group: wound complication was found in 21 cases (42.9%), leakage in 14 cases (28.6%), ileus in 14 cases (28.6%), and thromboembolic complication in 3 cases (6.1%).

RESULTS

Following a search of PubMed, ScienceDirect, Cochrane Library, and ClinicalTrials.Gov databases, 479 publications were discovered. After removing duplicates and papers that did not fulfill the inclusion criteria or had an exclusion criterion, six studies were chosen. The steps in the selection process are depicted in the PRISMA chart (Figure 1).

Table 1 lists the features of the studies that were chosen. In all six trials, IC patients were considerably older than ONB patients.

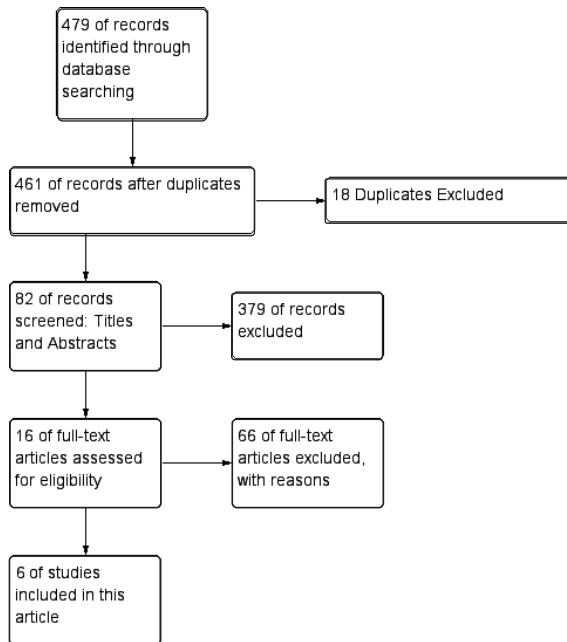


Figure 1. Prisma Flow Diagram.

Five studies including 371 participants reported the ileus complication after urinary diversion (Fig.2). The random-effect model's pooled results revealed a non-significant difference of 1.62 between ONB and IC (95 percent CI, 0.82, 3.21, P = 0.17) with moderate heterogeneity (Chi2 = 0.06, df = 4 (P = 0.81), I2 = 43%).

The Anastomosis site stenosis complication following urine diversion was documented in four investigations with 256 individuals (Fig.3). The pooled results of the random-effect model revealed a non-significant difference of 0.73 between ONB and IC (95 percent CI, 0.31, 1.72, P = 0.75) with non-significant heterogeneity (Chi2 = 1.23, df = 3 (P = 0.48), I2 = 0%).

In four studies involving 254 people, urinary leakage as a consequence of urinary diversion was reported (Fig.4). The random-effect model's pooled results showed a significant difference of 4.01 with higher incidence in neobladder group (95 percent CI, 1.85, 8.69, P = 0.0004) with non-significant heterogeneity (Chi2 = 0.65, df = 3 (P = 0.89), I2 = 0%).

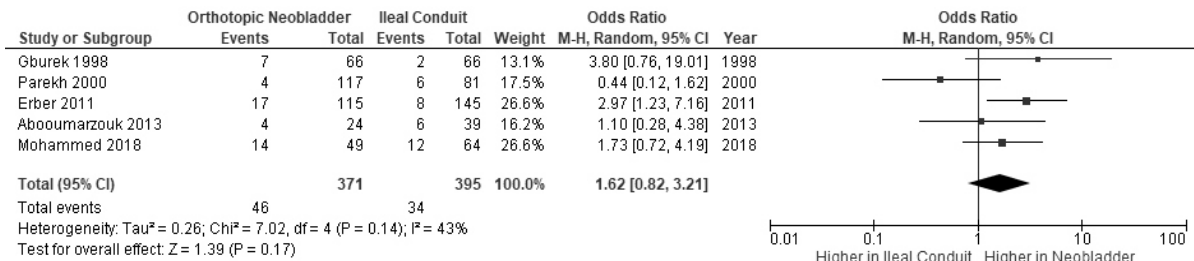


Figure 2. Forest Plot analysis for Ileus Outcome.

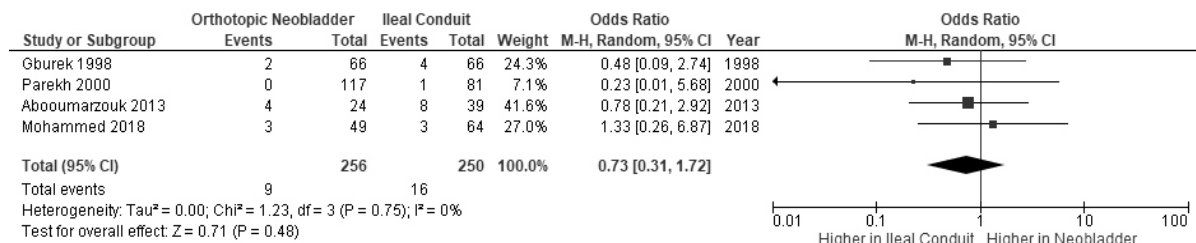


Figure 3. Forest plot analysis for Anastomosis Site Stenosis.

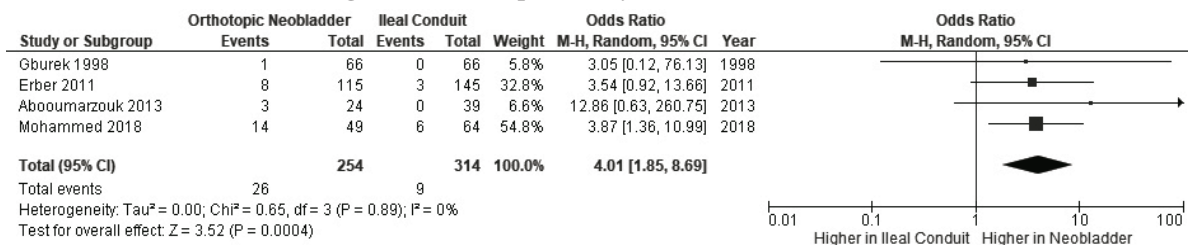


Figure 4. Forest plot analysis for urinary leakage.

In two studies involving 139 participants, sepsis incident following urine diversion was observed (Fig.5). The pooled findings of the random-effect model revealed a non-significant difference of 0.86 between ONB and IC (95 percent CI, 0.37, 1.97, $P = 0.76$) with non-significant heterogeneity ($\text{Chi}^2=0.00$, $\text{df}=1$ ($P=0.96$), $I^2=0\%$).

A urinary infection complication after urine

diversion was identified in four studies involving 280 people (Fig.6). The random-effect model's pooled findings indicated a non-significant difference of 1.17 between ONB and IC (95 percent CI, 0.26, 5.26, $P = 0.84$) with significant heterogeneity ($\text{Chi}^2=11.07$, $\text{df}=3$ ($P=0.01$), $I^2=73\%$).

For each of the six outcomes, funnel plots were analyzed. (Figure 7)

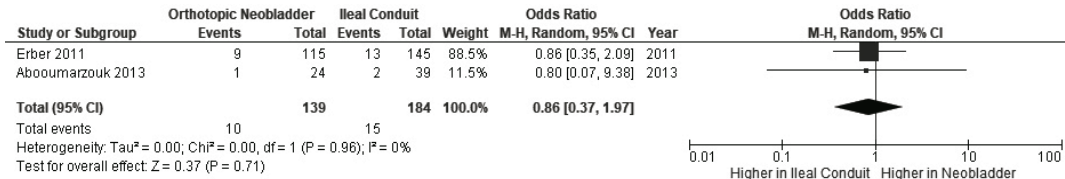


Figure 5. Forest plot analysis for Sepsis.

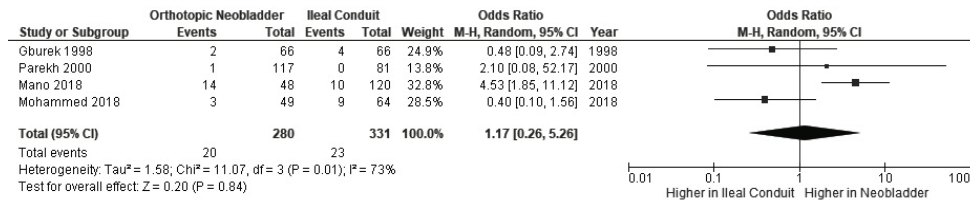


Figure 6. Forest plot analysis for Urinary Infection.

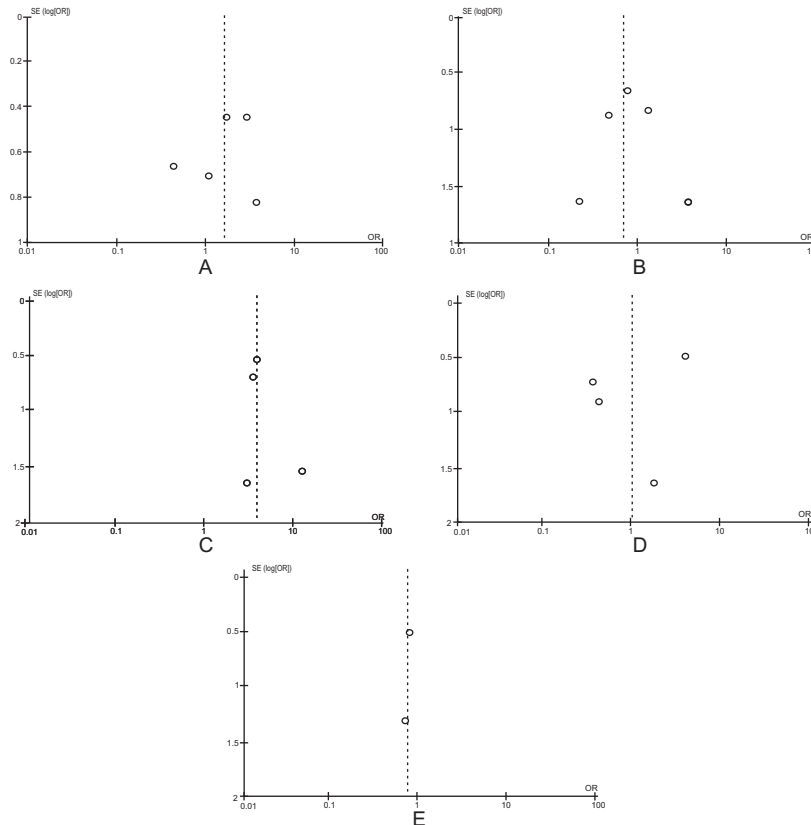


Figure 7. Funnel Plot. A) Ileus. B) Anastomosis Site Stenosis. C) Urinary Leakage. D) Sepsis. E) Urinary Tract Infection.

DISCUSSION

Radical cystectomy remains the treatment of choice for individuals with muscle-invasive bladder cancer. Cystectomy combined with any diversion is linked to a high rate of co-morbidity. This study looked at the differences in postoperative patient-perceived quality of life.¹¹

The ileal conduit is a technically simple and direct diversion to create. It is frequently chosen in older or comorbid patients because of the shorter operating time, limited bowel required for reconstruction, and decreased risk of morbidity. Despite these benefits, early and late problems are common, the most common being gastrointestinal, infectious, and wound issues in the early postoperative period.¹²

If the criteria of patient selection are met (patients having a good renal function and liver function and no evidence of direct invasion of disease in their urethra and prostate), an orthotopic neobladder is a chosen option for urinary diversion. The surgical time for a neobladder is typically thought to be longer than for a ureteroileocutaneous diversion. On the other hand, patients with a neobladder reported a substantially shorter duration of physical recovery than those with an ileal conduit. Patients with an NB, for example, needed only 1.4 weeks to be able to conduct the gentle physical exercise, compared to 3.12 weeks in the IC group. Only 29% of NB patients changed their everyday lives in the long run, whereas 72.7% of IC patients did.

This suggests that, despite enduring a more extensive surgical treatment, patients who had an NB required less time to recover and had a more significant change in their daily lives as compared to those who had a cystectomy and urine diversion.¹³ Although studies using objective definitions of incontinence based on pad weight report lower continence rates, most series report daytime continence approaching 90% and nighttime continence around 70%.¹⁴

We conducted this systematic review and meta-analysis to determine complications related to the urinary diversion the subject receives, whether Neobladder or Ileal Conduit. To the best of our knowledge, this is the first systematic review and meta-analysis that review the complication outcome of Neobladder and Ileal Conduit.

Our meta-analysis revealed a significant difference in urinary leakage complications related

to urinary diversion with Neobladder vs. Ileal conduit, with a higher incidence rate in Neobladder urinary diversion. While other complications of Ileus, Sepsis, UTI, and Anastomosis Site Stenosis, there is no significant difference. The time follow-up complication of each article was one month (earliest) to 50 months (longest).

The previous study showed that urinary leakage following ileal conduit diversion is a well-known complication, but the full scope of the problem has yet to be established. As stated in many other reports previously reported, underlying malignancy is a common denominator not only for loop leaks but for all types of postoperative problems. The occurrence of chronic postoperative azotemia without a concurrent rise in serum creatinine levels is a specific indicator of urine extravasation and should be investigated further.¹⁵ In this meta-analysis. However, we found that urinary leakage was higher in the neobladder than in the ileal conduit.

There have been reports of ileal neobladder leaks or ruptures in the literature. These are typically referred to as early neobladder problems and usually develop during the first three months of surgery. Chronic overdistension, presumably due to blockage from mucus plugs or traction from intraperitoneal adhesions to the bladder wall, has been suggested as a possible triggering factor for spontaneous perforation.¹⁶ Further analysis using more extensive and systematic clinical trials is needed to justify and better understand this different finding. Other complications could be compared between the two groups, including electrolyte imbalance after urinary diversion, vitamin B12 deficiency, metabolic acid-base disturbance, bone density-related disorder, etc.¹⁷ Further analysis and study about related complication is needed.

Our study has several limitations, including the choice article that is included as a cohort-secondly, the difference in the follow-up of each article. And the limited number of participants that are included in each study. To determine which urine diversion procedure is preferable, we suggested that a randomized trial with a more prominent subject is required. In addition, to follow-up, this trial should include comparisons of patient demographics, and post-operative data.

CONCLUSION

In conclusion, in terms of postoperative complications, this is the first meta-analysis and

systematic review of comparative studies on the impact of different types of urinary diversions. Because of the heterogeneity in several aspects of the analyzed papers, randomized controlled trials comparing Orthotopic Neobladder and Ileal conduit in terms of complication following urinary diversion are needed to confirm superiority of ONB or IC as the urinary diversion of choice.

REFERENCES

- Sanford T, Porten S, Meng MV. Molecular Analysis of Upper Tract and Bladder Urothelial Carcinoma: Results from a Microarray Comparison. *PLoS One.*; 10(8):e0137141.
- Siddiqui KM, Izawa JI. Ileal conduit: standard urinary diversion for elderly patients undergoing radical cystectomy. *World J Urol.* 2016; 34(1): 19-24.
- Chesnut GT, Rentea RM, Leslie SW. Urinary Diversions And Neobladders. *StatPearls*; 2021.
- Philip J, Manikandan R, Venugopal S, Desouza J, Javlé PM. Orthotopic neobladder versus ileal conduit urinary diversion after cystectomy a quality of life comparison. *Ann R Coll Surg Engl.* 2009; 91(7): 565-9.
- Gburek BM, Lieber MM, Blute ML. Comparison of studer ileal neobladder and ileal conduit urinary diversion with respect to perioperative outcome and late complications. *J Urol.* 1998 Sep; 160(3 Pt 1): 721-3.
- Parekh DJ, Gilbert WB, Koch MO, Smith JA Jr. Continent urinary reconstruction versus ileal conduit: a contemporary single-institution comparison of perioperative morbidity and mortality. *Urology.* 2000 Jun; 55(6): 852-5.
- Erber B, Schrader M, Miller K, Schostak M, Baumunk D, Lingnau A, Schrader AJ, Jentzmik F. Morbidity and Quality of Life in Bladder Cancer Patients Cystectomy and Urinary Diversion: A Single-Institution Comparison of Ileal Conduit versus Orthotopic Neobladder. *ISRN Urol.* 2012; 2012: 342796.
- Aboumarzouk OM, Drewa T, Olejniczak P, Chlosta PL. Laparoscopic radical cystectomy: neobladder or ileal conduit, debate still goes on. *Cent European J Urol.* 2014; 67(1): 9-15.
- Mano R, Goldberg H, Stabholz Y, Hazan D, Margel D, Kedar D, Baniel J, Yossepowitch O. Urinary Tract Infections After Urinary Diversion-Different Occurrence Patterns in Patients With Ileal Conduit and Orthotopic Neobladder. *Urology.* 2018 Jun; 116: 87-92.
- Mohammed, Ali H., Hassan, A., Abd ElAal, Abdallah A., Elbadry, Mohamed S., and Barsoum, Nady M. Evaluation of surgical outcomes and complications of patients who underwent ileal conduit (IC) urinary diversion in comparison with those who underwent orthotopic neobladder. *MJMR* 2018 Feb; 29: 97-99.
- Ritch CR, Balise R, Prakash NS, Alonzo D, Almengo K, Alameddine M, Venkatramani V, Punnen S, Parekh DJ, Gonzalo ML. Propensity matched comparative survival analysis following chemoradiation or radical cystectomy for muscle-invasive bladder cancer. *BJU Int.* 2018 May; 121(5): 745-751.
- Shabsigh A, Korets R, Vora KC, et al. Defining Early Morbidity of Radical Cystectomy for Patients with Bladder Cancer Using a Standardized Reporting Methodology. *Eur Urol* 2009; 55: 164–176.
- Hobisch A, Tosun K, Kinzl J, Kemmler G, Bartsch G, Hörtl L, Stenzl A. Quality of life after cystectomy and orthotopic neobladder versus ileal conduit urinary diversion. *World J Urol.* 2000 Oct; 18(5): 338-44.
- Nieuwenhuijzen JA, de Vries RR, Bex A, et al. Urinary Diversions after Cystectomy: The Association of Clinical Factors, Complications and Functional Results of Four Different Diversions. *Eur Urol* 2008; 53: 834–844.
- Hensle TW, Bredin HC, Dretler SP. Diagnosis and treatment of a urinary leak after ureteroileal conduit for diversion. *J Urol.* 1976 Jul; 116(1): 29-31.
- Liangos O, Aljohani KM, Faiz A, Jaber BL. An Ileal Neobladder Urinary Leak Mimicking Rapidly Progressive Glomerulonephritis. *Nephrology Research & Reviews.* 2012; 4(2): 66-68.
- Stein R, Rubenwolf P. Metabolic consequences after urinary diversion. *Front Pediatr.* 2014 Mar 10; 2: 15.