A systematic review and meta-analysis of the long-term outcomes of ileal conduit and orthotopic neobladder urinary diversion

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Abstract

Introduction: We aimed to perform a systematic review and meta-analysis on the long-term durability, incidence of complications, and patient satisfaction outcomes in ileal conduit (IC) and orthotopic neobladder (ONB).

Methods: A systematic electronic literature search was performed in Medline, Embase, Cochrane Library, and Scopus using MeSH and free-text search terms "Urinary diversion" AND "Ileal conduit" AND "Neobladder." The search concluded June 19, 2018. Inclusion criteria were those patients who had a cystectomy and required urinary diversion by either IC or neobladder. **Results:** In total, 32 publications met the inclusion criteria. Data were available on 46 787 patients (n=36 719 for IC and n=10 068 for ONB). Meta-analyses showed that IC urinary diversions performed less favorably than ONB in terms of re-operation rates, Clavien-Dindo complications, and mortality rates; odds ratios (ORs) and 95% confidence intervals (CIs) were 1.76 (1.24, 2.50) p<0.01, 1.16 (1.09, 1.22) p<0.01, and 6.29 (5.30, 7.48) p<0.01, respectively. ICurinary diversion performed better than ONB in relation to urinary tract infection rates andureteric stricture rates, OR and 95% CI 0.67 (0.58, 0.77) p<0.01 and 0.70 (0.55, 0.89) p<0.01,respectively.

Conclusions: Our results show that there is no significantly increased morbidity with ONB compared to IC. Selection of either urinary diversion technique should be based on factors such as tumor stage, comorbidities, surgical experience, and patient acceptance of postoperative sequalae.

Introduction

There are many conditions which necessitate removal of the urinary bladder using cystectomy.¹ The most common indication is cancer of the urinary bladder but in some cases cystectomy is indicated to treat benign disease such as interstitial cystitis.¹ Cystectomy therefore requires replacement of the urinary bladder with a procedure known as urinary diversion.¹ Urinary diversion is a form of urinary reconstruction and most commonly involves the use of a gastrointestinal (GI) segment to replace part or all of the function of the urinary bladder.¹ An optimal bladder replacement should be able to hold large intravesical volumes whilst maintaining low pressure values in order to restore normal function and preserve the upper urinary tracts.¹

Lifelong postoperative complications are common with any type of urinary diversion.¹ These can be divided into three broad groups, (i) Metabolic complications which are due to the intestinal segment's resorptive capacity, (ii) Neuromechanical aspects which affect storage volume and diversion compliance and (iii) Technical-surgical complications which result in postoperative morbidity.¹

Ileal conduit has long been considered the gold standard for replacement of the urinary bladder. However, orthotopic neobladder has a superior cosmetic appearance and better preservation of body image.² The aim of this systematic review and meta-analysis is to perform a robust comparison of ileal conduit and orthotopic neobladder urinary diversion and to provide practitioners with a summary of the global trends for reconstructive preferences in urinary diversion.

Methods

Search strategy

This review was planned and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).³

A systematic electronic literature search was carried out in Medline, Embase, Cochrane Library and Scopus. Using MeSH and free text terms, the search strategy was: "Urinary diversion" AND "Ileal conduit" AND "Neobladder". Titles and abstracts retrieved by the June 2018 search were screened independently by two authors (EB and ND), following the removal of duplicates. Where there was any uncertainty regarding inclusion, full texts were retrieved and assessed for inclusion. Excluded studies were listed with reasons given for their exclusion. Disagreements regarding the inclusion or exclusion of an article were resolved by discussion.

Eligibility criteria

Inclusion criteria were those patients who have had a cystectomy for any reason and required urinary diversion by either ileal conduit or orthotopic neobladder. Exclusion criteria were review articles, case reports, commentaries, letters, conference abstracts without sufficient outcome data and failure to meet the inclusion criteria.

Data extraction and outcomes

The following data were extracted from each study: author's name, journal of publication, year of publication, country of origin, study type, total number of patients and patient demographics (age, sex, body mass index [BMI]). Information regarding the following outcomes were recorded from each eligible study. The primary outcome measures were quality of life, measures of long-term durability (including re-operation, urinary tract infections (UTI) and ureteric stricture), post-operative morbidity, post-operative mortality and length of stay. Secondary outcome measures were physiological changes including active reflux, mucous, upper tract dilatation/hydronephrosis, renal scarring, metabolic changes, urinary stones, and health economics.

Statistical analysis

Data were presented as a mean \pm SD for continuous variables. Differences between outcomes measured were considered significant at p<0.05 (Stata). Meta-analysis was performed with Review Manager Version 5.3 software.⁴ The Mantel-Haenszel model was used for meta-analysis of dichotomous data and the inverse variance model for meta-analysis of continuous data.⁵

Results

Eligible studies

In total, 2907 articles were identified. Following the removal of duplicates (n=1458), 1449 articles were screened, of which 1417 were excluded as they did not meet the inclusion criteria. In total, 32 articles were included in the qualitative and quantitative analysis; see the PRISMA diagram in Figure 1 for the flow of studies through the review and the reasons for which studies were excluded.

Data were available for 46,787 patients in the studies included in this review (n=36,719 for ileal conduit and n=10,068 for orthotopic neobladders). Study characteristics are summarised in Table 1. In total there were 16 prospective case-control studies,⁶⁻²¹ one of which was a prospective case-control study with matched-pair analysis²⁰ and 16 retrospective case-control studies.^{2 22-36}

Patient demographics (including patient age, male to female ratio and patient BMI) were reported, if available; these are outlined in Table 2 and Table 3. The mean patient age between the ileal conduit and orthotopic neobladder groups was significantly different, 69.65 ± 5.84 in the ileal conduit group versus 61.07 ± 4.47 in the orthotopic neobladder group, 95% Confidence Interval (CI) 8.44, 8.71, p <0.01, with patients undergoing ileal conduit urinary diversion being older overall. The mean BMI of the ileal conduit group versus 23.7 ± 3.3 in the orthotopic neobladder group 95% CI 175, 2.25, p<0.01. The sex ratio in both groups was significantly different (11:2 male:female in the ileal conduit group versus 11:1 male:female in the orthotopic neobladder group, p <0.01).

Primary outcomes

Quality of life

Patient satisfaction, general measures of health status and disease specific measures of quality of life were not reported in a standardised manner across the studies. This precludes meaningful statistical analysis. Of the 32 included publications, 5 compared quality of life in patients with either diversion type.^{13 18 24 34 35} Using The European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire,³⁷ Navarro et al found a better acceptance in orthotopic neobladders versus ileal conduits.¹³ The scale used by the authors rates overall quality of life on a 7 point scale, where 1=Very Poor and 7=Excellent.³⁷ Sogni et al. also used the OLO-C30 questionnaire as well as the bladder cancer-specific module EORTC QLQ-muscle-invasive bladder cancer module 30 (BLM 30)³⁸ and found that the quality of life reported in both groups was comparable but with a non-significant higher quality of life rating seen in the orthotopic neobladder group.³⁴ Erber *et al* also used the OLO-C30 questionnaire and reported overall quality of life as 58 ± 25.3 in the ileal conduit group and 72.3 ± 19.5 in the neobladder group.²⁴ Sherwani et al used a simple satisfaction scale of "Very Good", "Good", "Poor" to compare quality of life between the two groups and reported higher ratings in the orthotopic neobladder group.¹⁸ Finally, Thulin et al had patients rate quality of life as "high", "moderate" or "low".³⁵ Of these, 68% of patients with an orthotopic neobladder reported their quality of life as "high" compared to 53% of ileal conduit recipients.³⁵

Measures of long-term durability

The measures of long-term durability included in this review were re-operation rates, UTI rates and ureteric stricture rates. The meta-analysis of these outcomes are detailed in Figure 2.

Of the 32 studies included in this review, 9 examined re-operation rates. The rate of reoperation was significantly greater in patients with an ileal conduit compared to patients undergoing orthotopic neobladder formation [Odds Ratio (OR) 1.76: 95% Confidence Interval (CI) 1.24, 2.50, p < 0.01]; see Figure 2A.

The incidence of UTI rates was reported in 11 studies. The incidence of UTI was significantly less in patients with an ileal conduit versus patients with an orthotopic neobladder [n = 1048/4013, 26.1% versus n = 433/1425, 30.4% respectively, OR 0.67: 95% CI 0.58, 0.77, p < 0.01]. This is reported in Figure 2B.

Ureteric stricture rates in both groups were reported in 9 publications. The incidence of the ureteric stricture was statistically less significant in patients undergoing ileal conduit urinary diversion versus patients with orthotopic neobladder, shown in Figure 2C [n = 249/3533, 7.0% versus n = 109/1241, 8.8% respectively, OR 0.70: 95% CI 0.55, 0.89, p < 0.01].

Complications

Post-operative morbidity, reported in 21 publications, was described using the Clavien-Dindo classification in 12 publications. ^{6 7 10 14 15 19-22 26 28 33 39}.

The incidence of post-operative morbidity was significantly higher in patients undergoing ileal conduit urinary diversion versus those undergoing orthotopic neobladder urinary diversion as shown in Figure 3A [n = 15659/25264, 61.9% versus n = 5102/8478, 60.1% respectively; OR 1.16~95% CI 1.09, 1.22, p < 0.01]. Subgroup analysis of patients who suffered Clavien-Dindo 1-2 (minor) complications showed that patients undergoing ileal conduits were less likely to suffer a minor complication than those undergoing orthotopic neobladder urinary diversion, as shown in Figure 3B, this was not statistically significant [n = 1016/1802~56.4% versus n = 573/1029, 55.7%; OR 0.89 95% CI 0.75, 1.06, p = 0.21]. Subgroup analysis of those who suffered Clavien-Dindo 3-5 (major) complications showed that patients with ileal conduits were significantly more likely to suffer a major complication than those with orthotopic neobladders, as shown in Figure 3C [n = 375/1802, 20.8% versus n = 184/1029, 17.9%; OR 1.25~95% CI 1.02, 1.53, p = 0.03].

Mortality

Post-operative mortality was reported in 21 publications The mortality rate in patients with ileal conduit urinary diversion is significantly higher than that of patients undergoing orthotopic neobladder [n = 3227/33656, 9.6% versus n = 142/8810, 1.6%; OR 6.29 95% CI 5.30, 7.48, p < 0.01] as demonstrated in Figure 4.

Length of stay

Seven publications reported length of stay for ileal conduit and orthotopic neobladder groups as a mean \pm SD as outlined in Figure 5. Length of stay was shorter in the ileal conduit group compared to the orthotopic neobladder group 17.56 \pm 8.61 days versus 19.93 \pm 7.85 days with a mean difference of -0.74 [95% CI -1.30, -0.18, p < 0.01].

Eleven other publications reported length of stay as median and range and these are outlined in Table 4.

Secondary outcomes

Physiological changes

For the purpose of this review, physiological changes following urinary diversion were defined as: active reflux, upper tract dilation or hydronephrosis, mucous, metabolic changes urinary stones and renal scarring.

The incidence of active reflux was reported in 2 of the 32 included publications. The forest plot in Figure 6A shows that patients undergoing ileal conduit urinary diversion are at lower risk of active reflux than those undergoing orthotopic neobladder, this was not statistically significant [n = 0/147 versus n = 1/81 respectively; OR 0.17 95% CI 0.01, 4.31 p = 0.28]. The incidence of upper tract dilatation/hydronephrosis was reported in 3 of the 32 included publications. Analysis shows that patients with ileal conduit urinary diversion are more likely to have hydronephrosis than those with orthotopic neobladders, shown in Figure 6B [n = 23/568,

4.0% versus n = 9/297, 3.0% respectively, OR 1.56~95% CI 0.67, 3.62, p = 0.30]; again, not statistically significant.

The incidence of mucous production was less in patients with ileal conduit than those with orthotopic neobladder [n = 1/135, 0.7% versus n = 3/99, 3% respectively; OR 0.58 95% CI 0.08, 3.98, p = 0.58]. This was not statistically significant. This is demonstrated in Figure 6C. The incidence of metabolic change is less in patients with an ileal conduit versus orthotopic neobladder, shown in Figure 6D. [n = 26/280 4.5% versus n = 37/330, 11.2% respectively: OR 0.57 95% CI 0.32, 1.03, p = 0.06]. This finding was not statistically significant

The incidence of urinary stones was lower in patients with ileal conduit urinary diversion compared to orthotopic neobladder [n=167/4719, 3.5% versus n=85/1319, 6.4% respectively; OR 0.49 95% CI 0.37, 0.64, p < 0.01]. This is shown in Figure 6E. This was statistically significant.

There were no data reported in any of the included studies regarding the incidence of renal scarring in patients with either urinary diversion.

Health economics

None of the studies included in this review examined or made any comment on the economic impact of either ileal conduit or orthotopic neobladder urinary diversion precluding a comparison of cost of intervention or assessment of cost-benefit relationship.

Discussion

This study is a comprehensive review comparing ileal conduit and orthotopic neobladder urinary diversions. The choice of urinary diversion has significant implications for both the patient in terms of their future health and quality of life and for the surgeon and their methods. The choice of which urinary diversion to use also depends on many factors such as surgical skill, urethral disease or patient acceptance.¹ It is therefore imperative that a thorough comparison is made of the outcomes of IC and ONB to provide practitioners with a comprehensive summary of the data to aid surgical and patient decision making.

It demonstrates that there is an overall preference towards ileal conduit urinary diversion and a tendency for this type of diversion to be performed in older patients. It also showed a higher re-operation rate and rate of post-operative morbidity and mortality in those patients who underwent an ileal conduit urinary diversion. Orthotopic neobladder urinary diversions, however, performed worse in terms of UTI, ureteric stricture, urinary stone rates.

In this study, comparison of patient age in the two groups showed that patients IC urinary diversion were significantly older than those patients undergoing ONB diversion. It can be reliably assumed that older patients have greater comorbidities so interpretation of results may be affected by this finding. Younger patients, likely with fewer comorbidities, tend to have a ONB diversion, possibly due to the widely accepted belief that ONB has a greater risk of perioperative complications due to its technical complexity. ² This is therefore likely to confound data relating to post-operative complication rates in each group. The larger numbers of ileal conduits performed in these studies compared to orthotopic neobladders demonstrates the preference for

ileal conduit as the choice of urinary diversion. This is likely to be multifactorial as addressed previously, including patient preference, surgical skill and other patient factors such as age or comorbidity.

From the included publications there was a better acceptance and quality of life in patients with orthotopic neobladder diversions than those with ileal conduit⁴⁰. However it is worth bearing in mind that each type of urinary diversion has inherently different challenges associated with it.⁶ According to meta-analysis there is a higher rate of UTI in the orthotopic neobladder group, potentially as orthotopic neobladders often require self-catheterisation which comes with the associated risk of bacterial inoculation.³⁵ Meta-analysis also demonstrated a significantly higher risk of ureteroileal stricture in patients with an orthotopic neobladder than those with an ileal conduit urinary diversion, possibly due to the use of an anti-reflux mechanism in ureterointestinal anastomosis, however an antireflux mechanism was only used for ONB in two of the publications included in this review. This highlights the importance of forming a low pressure reservoir.¹

The studies included for analysis in this review focused predominantly on reporting perioperative data regarding ileal conduit urinary diversion and orthotopic neobladders, revealing a dearth of information on long-term outcomes of these two types of urinary diversion. This may explain the paucity of evidence relating to the long-term complications of urinary diversion.¹ Meta-analysis of those publications which reported post-operative morbidity using Clavien-Dindo shows a significantly higher morbidity in ileal conduit compared to orthotopic neobladder.^{67 10 14 15 19-22 26 28 33} This is potentially explained by noting that within this systematic review, patients undergoing ileal conduit tended to be older and have higher grade tumours, which may increase the risk of death independent of diversion type. It must also be considered that minor (CD 1-2) complications may be under reported given that many of the publications included in this review were retrospective case controls.²⁷

Meta-analysis of mortality rates between ileal conduit and orthotopic neobladder urinary diversion showed a significantly increased risk of death in those patients undergoing ileal conduit diversion compared to patients with orthotopic neobladders. However, patients undergoing ileal conduit tend to be older and have higher grade tumours, which may increase the risk of death independent of diversion type.²

Meta-analysis of mean \pm SD of length of stay demonstrated a significantly longer length of stay in patients undergoing orthotopic neobladder. Length of stay is sometimes dependent on the practice of individual institutions and thus it cannot be assumed that orthotopic neobladder urinary diversion always results in an increased length of stay but it is still an important consideration when deciding which type of urinary diversion to use.

With the exception of stones (which were significantly more likely in orthotopic neobladder), meta-analysis of the physiological changes considered in this review showed no statistically significant results. Nonetheless, consideration of physiological changes such as hydronephrosis, vesicoureteric reflux, mucous production, metabolic changes and urinary stones

is important when deciding between ileal conduit and orthotopic neobladder, particularly in patients with pre-existing conditions.

A cost-benefit comparison is a crucial aspect of assessing any intervention and there seems to be a complete lack of any such analysis in contemporary literature. This is certainly an aspect of urinary diversion which requires further study. In countries where universal or socialised healthcare does not exist, the type of urinary diversion a patient receives may depend on their ability to pay for this type. ⁴¹

The main limitation of this meta-analysis is that the studies included for analysis consist of retrospective or prospective case-control studies. Other limitations include the small sample sizes contained within most publications, limiting the generalisability of the findings of this review and the non-standard reporting of outcomes. Thirdly, some data points were presented as median and range which precluded any analysis regarding these figures. Lastly, there is the potential for significant selection bias in all publications in that those undergoing orthotopic neobladder have lower stage tumours and would therefore have better postoperative outcomes in terms of recovery and mortality rates. ²⁰

However, this is a very robust analysis involving large numbers of patients with extensive follow up, using standardised questionnaires, and involves data from multiple institutions. This analysis also includes international publications and so is representative of global trends for reconstructive preferences in urinary diversion.

Conclusions

This systematic review and meta-analysis does not support the widely held perception that orthotopic neobladder is associated with increased risk of post-operative morbidity, however the reason for this may be multifactorial. Our findings demonstrated that orthotopic neobladder was associated with a lower rate of major (Clavien-Dindo 3-5) complications than the ileal conduit. However, larger cohort studies are required to reach a definitive conclusion as to which type of diversion is superior. Our results also reinforce that the selection of which type of urinary diversion to perform should be based on careful pre-operative counselling taking into account patient factors such as tumour stage and comorbidities, surgical skill and patient acceptance of the sequalae of either type of urinary diversion.

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Figures and Tables

Fig 1.

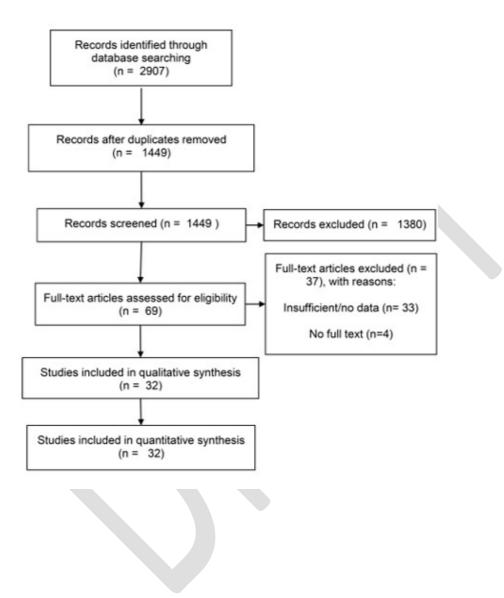


Fig 2.

Α

	llealCon	duit	Orthotopic Neo	obladder		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Abe T et al. 2014.	71	493	16	175	39.6%	1.67 [0.94, 2.96]	
Erber et al 2012	25	146	12	115	21.8%	1.77 [0.85, 3.70]	+
Gburek BM et al. 1998.	9	66	10	66	16.9%	0.88 [0.33, 2.34]	
Gore JL et al. 2010.	21	1252	2	109	7.1%	0.91 [0.21, 3.94]	
Hofer M et al. 2012.	21	245	2	63	5.7%	2.86 [0.65, 12.53]	
Monn MF et al. 2014.	3	13	2	55	1.2%	7.95 [1.17, 53.82]	
Parekh DJ et al. 2000.	7	81	4	117	5.9%	2.67 [0.76, 9.45]	
Popov Z et al. 2007.	2	32	0	52	0.7%	8.61 [0.40, 185.21]	
Sherwani A et al. 2009.	2	13	0	4	1.2%	1.96 [0.08, 49.26]	
Total (95% CI)		2341		756	100.0%	1.76 [1.24, 2.50]	•
Total events	161		48				· · · · · · · · · · · · · · · · · · ·
Heterogeneity: Chi ² = 6.9	8, df = 8 (P	= 0.54)	: I ² = 0%				
Test for overall effect: Z	= 3.14 (P =	0.002)					0.01 0.1 1 10 100 Favours IC Favours ONB

в

	llealCon	duit	Orthotopic Neo	bladder		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixed, 95% CI
Collins et al 2013	0	43	4	70	0.7%	0.17 [0.01, 3.23]	+	
Gburek BM et al. 1998.	1	66	2	66	0.4%	0.49 [0.04, 5.56]		
Hofer M et al. 2012.	29	245	10	63	3.1%	0.71 [0.33, 1.55]		
Jung J et al. 2006.	3	29	4	19	0.9%	0.43 [0.09, 2.20]		
Kim SH et al. 2014.	15	161	12	147	2.5%	1.16 [0.52, 2.56]		
Mano R et al. 2018.	10	130	14	49	4.1%	0.21 [0.09, 0.51]		
Nieuwenhuijzen JA et al. 2008.	26	118	24	62	5.3%	0.45 [0.23, 0.88]		
Sherwani A et al. 2009.	0	13	4	4	1.4%	0.00 [0.00, 0.24]	+	
Tan WS et al. 2017.	13	100	9	34	2.5%	0.42 [0.16, 1.08]		
Thulin H et al. 2010.	73	190	59	180	8.1%	1.28 [0.83, 1.96]		
van Hemelrijck et al 2013	878	2918	291	731	70.9%	0.65 [0.55, 0.77]		
Total (95% CI)		4013		1425	100.0%	0.67 [0.58, 0.77]		•
Total events	1048		433					
Heterogeneity: Chi2 = 26.88, df =	10 (P = 0.0	003); l ²	= 63%				0.01	0.1 1 10 10
Test for overall effect: Z = 5.65 (F	P < 0.00001	1)					0.01	Favours IC Favours ONB

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	llealCon	duit	Orthotopic Neo	bladder		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
Collins et al 2013	1	43	3	70	1.5%	0.53 [0.05, 5.28]	
Gburek BM et al. 1998.	3	66	1	66	0.6%	3.10 [0.31, 30.55]	
Jung J et al. 2006.	1	29	4	19	3.1%	0.13 [0.01, 1.31]	
Kim SH et al. 2014.	7	161	4	147	2.6%	1.63 [0.47, 5.67]	
Nieuwenhuijzen JA et al. 2008.	13	118	5	62	3.8%	1.41 [0.48, 4.16]	
Popov Z et al. 2007.	2	32	0	52	0.2%	8.61 [0.40, 185.21]	,
Proic A et al. 2017.	10	66	4	60	2.3%	2.50 [0.74, 8.44]	
Thulin H et al. 2010.	3	100	1	34	1.0%	1.02 [0.10, 10.15]	
van Hemelrijck et al 2013	209	2918	87	731	84.9%	0.57 [0.44, 0.74]	
Total (95% CI)		3533		1241	100.0%	0.70 [0.55, 0.89]	•
Total events	249		109				
Heterogeneity: Chi2 = 16.22, df =	8 (P = 0.04	 I² = 5 	1%				
Test for overall effect: Z = 2.93 (I	P = 0.003)	3533 - 2					0.01 0.1 1 10 100 Favours IC Favours ONB

Fig 3.

A

	liea/Cor	tiubr	Orthotopic Neol	bladder		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events.	Total	Weight	M-H. Fixed, 95% CI	M-H, Fixed, 95% CI
Abe T et al. 2014.	350	493	129	175	2.3%	0.87 [0.59, 1.29]	
Abournarzouk OM et al. 2014.	14	39	12	24	0.4%	0.56 [0.20, 1.57]	
Angulo et al 2014	2	8	- 4	12	0.1%	0.67 [0.09, 4.93]	
antonelli A et al. 2016.	59	85	52	85	0.7%	1.44 [0.76, 2.72]	
ollins et al 2013	46	43	55	70		Not estimable	
e Nunzio C et al. 2013.	201	217	102	112	0.4%	1.23 [0.54, 2.81]	
ecaestecker K et al. 2016.	38	40	35	32		Not estimable	
rber et al 2012	101	140	80	115	1.1%	0.98 [0.58, 1.67]	
iore JL et al. 2010.	827	1252	197	109		Not estimable	£
lofer M et al. 2012.	107	245	37	63	0.8%	1.50 (0.85, 2.00)	+
im SH et al. 2014.	78	161	7	147	0.2%	18.80 (8.28, 42.66)	
Ionn MF et al. 2014.	68	130	19	55	0.6%	1.81 [0.95, 3.47]	
avaro M et al. 2013.	15	17	33	37	0.1%	0.91 [0.15, 5.52]	
azmy M et al. 2013.	48	67	69	91	0.7%	0.81 [0.39, 1.65]	
euwenhuigen JA et al. 2008.	87	118	100	62		Not estimable	
opov Z et al. 2007.	20	32	26	62	0.3%	1.67 (0.68, 4.09)	
oghmann et al 2014	328	349	171	186	0.6%	1.37 [0.69, 2.73]	
oghmann F et al. 2013.	10142	18782	3203	6282	91.8%	1.13 [1.07, 1.19]	
herwani A et al. 2009.	6	13	2	4	0.1%	0.86 (0.09, 8.07)	
an WS et al. 2017.	120	100	40	34		Not estimable	
an Hemelrijck et al 2013	2942	2918	720	731		Not estimable	
otal (95% CI)		26264		8478	100.0%	1.16 [1.09, 1.22]	
lotal events	15659		5102				
leterogeneity: Chi ² = 54.85. cf =	14 (P < 0.	(10000					
est for overall effect: Z = 5.21 (0.1 0.2 0.5 1 2 5 1 Favours IC Favours ONB

в

	ItealCor	dult	Orthotopic Neo	bladder		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
Abe T et al. 2014.	249	493	106	175	28.5%	0.66 [0.47, 0.94]	
Aboumarzouk OM et al. 2014.	14	39	12	24	3.5%	0.56 [0.20, 1.57]	
Angulo et al 2014	1	8	3	12	0.8%	0.43 [0.04, 5.06]	
Antonelli A et al. 2016.	66	85	66	85	5.4%	1.00 [0.49, 2.06]	
De Nunzio C et el. 2013.	100	217	63	112	9.5%	1.14 [0.67, 1.93]	+-
Decaestecker K et al. 2016.	31	.40	30	32	2.8%	0.23 [0.05, 1.15]	
Kim SH et al. 2014.	26	147	38	161	11.0%	0.70 [0.40, 1.22]	
Monn MF et al. 2014.	115	139	25	55	2.2%	5.75 [2.89, 11.46]	
Nazmy M et al. 2013.	32	67	33	91	5.4%	1.61 [0.85, 3.06]	
Neuwenhuijzen JA et al. 2008.	25	118	10	62	3.8%	1.40 [0.62, 3.14]	
Roghmann et al 2014	244	349	146	186	21.1%	0.64 [0.42, 0.97]	-
Tan WS et al. 2017.	47	100	21	34	6,1%	0.55 [0.25, 1.22]	
Total (95% CI)		1902		1029	100.0%	0.89 [0.75, 1.06]	
Total events Heterogeneity: Chi ^a = 44.64, df =	1. 40	00001);	573 P = 75%				0.01 0.1 1 10 10
Test for overall effect: Z = 1.26 (P = 0.21)						Favours IC Favours ONB

С

	RealCor	duit	Orthotopic Neol	bladder		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95%-CI
Abe T et al. 2014	101	493	23	175	15.9%	1.70 [1.04, 2.78]	
Aboumarzouk OM et al. 2014	2	.39	1	24	0.7%	1.24 [2.11, 14.50]	
Angulo et al 2014	1	8	1	12	0.4%	1.57 [0.08, 29.41]	
Antonelli A et al. 2016.	11	85	9	85	4.6%	1.26 [0.49, 3.20]	
De Nunzio C et al. 2013.	35	217	19	112	12.4%	0.94 [0.51, 1.74]	-
Decaestecker K et al. 2016.	7	40	6	32	2.7%	1.15 (0.33, 4.02)	
Kim SH et al. 2014.	34	147	28	161	12.1%	1.43 [0.82, 2.60]	+
Monn MF et al. 2014.	31	139	15	55	0.8%	0.77 [0.37, 1.67]	
Nazmy M et al. 2013.	16	67	36	91	13.7%	0.48 (0.24, 0.97)	
Neuwenhuijzen JA et al. 2008.	32	118	15	62	8.4%	1.17 (0.57, 2.37)	
Roghmann et al 2014	84	349	25	186	14.6%	2.04 [1.25, 3.32]	
Tan WS et al. 2017.	21	100	25 7	34	4.9%	1.03 [0.39, 2.68]	-
Total (95% CI)		1802		1029	100.0%	1.26 [1.02, 1.63]	
Total events	375		184				
leterogeneity Ch2 = 15.68. df =	11 (P=0.	15); P =	30%				the star is the star
Test for overall effect Z = 2.14 (P = 0.031						0.01 0.1 1 10 10 Favours IC Favours ONB

Fig 4.

	llealCor	nduit	Orthotopic Neol	bladder		Odds Ratio		Odd	Is Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fb	ed, 95% Cl
Abe T et al. 2014.	4	493	1	175	0.9%	1.42 [0.16, 12.82]	6	-	
Aboumarzouk OM et al. 2014.	2	39	1	24	0.7%	1.24 [0.11, 14.50]			
Antonelli A et al. 2016.	1	85	1	85	0.6%	1.00 [0.06, 16.25]			-
Collins et al 2013	1	43	1	70	0.5%	1.64 [0.10, 26.97]			
Gburek BM et al. 1998.	0	66	0	66		Not estimable			
Kim SH et al. 2014.	3	161	3	147	1.9%	0.91 [0.18, 4.59]			+
Monn MF et al. 2014.	3	139	2	55	1.8%	0.58 [0.09, 3.60]			-
Nahar B et al. 2018.	993	10197	20	692	21.4%	3.63 [2.31, 5.68]			
Nieuwenhuijzen JA et al. 2008.	3	118	2	62	1.6%	0.78 [0.13, 4.81]		-	-
Parekh DJ et al. 2000.	0	81	0	117		Not estimable			
Popov Z et al. 2007.	1	32	0	52	0.2%	5.00 [0.20, 126.52]		_	
Roghmann et al 2014	17	349	4	186	3.1%	2 33 [0 77, 7.03]			
Roghmann F et al. 2013.	224	18782	50	6282	46.9%	1.50 [1.11, 2.05]			
Sogni F et al. 2008.	3	53	2	32	1.5%	0.90 [0.14, 5.70]			
Tan WS et al. 2017.	3	100	1	34	0.9%	1.02 [0.10, 10.15]		_	-
van Hemelrijck et al 2013	1969	2918	54	731	17.8%	26.01 [19.51, 34.69]			
Total (95% CI)		33656		8810	100.0%	6.29 [5.30, 7.48]			•
Total events	3227		142						~
Heterogeneity: Chi2 = 215.11, df	= 13 (P < 0	0.00001)	$1^2 = 94\%$				0.01	0.1	1 10
Test for overall effect: Z = 20.93	(P < 0.000	01)						Favours IC	- 51
								. around its	

Fig 5.

	liea	Cond	uit	Orthotog	ic Neobl	adder		Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI		
Abournarzouk OM et al. 2014.	9.3	2.3	39	9.4	1.3	24	39.3%	-0.10 [-0.99, 0.79]	•		
Sburek BM et al. 1998.	13	7	66	13	8.75	66	4.3%	0.00 [-2.70, 2.70]	+		
Gm SH et al. 2014.	19.3	18.8	147	21.6	12.5	161	2.4%	-2.30 [-5.90, 1.30]	-		
kahar B et al. 2018.	10.3	10.4	10197	10.8	10.9	692	44.5%	-0.50 [-1.34, 0.34]	•		
hopov Z et al. 2007.	41	13.5	32	46	12.25	52	0.9%	-5.00 [-10.74, 0.74]	-		
Sherwani A et al. 2009.	15	2.25	13	19.7	2.25	4	4.9%	-4.70 [-7.22, -2.18]	-		
iogni F et al. 2008.	15	6	53	19	7	32	3.7%	-4.00 [-6.91, -1.09]	-		
Total (95% CI)			10547			1031	100.0%	-0.74 [-1.30, -0.18]			
teterogeneity: Chill = 19.71, df	= 6 (P =)	0.003)	I* = 709	6				2 N N	100 50 0 5		
fest for overall effect: Z = 2.60	(P = 0.00)	(9)							Favours IC Favours		

Fig. 6

А

llealCor		Orthotopic Neob	ladder		Odds Ratio	Odds Ratio
Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
0	29	0	19		Not estimable	
0	118	1	62	100.0%	0.17 [0.01, 4.31]	· •
	147		81	100.0%	0.17 [0.01, 4.31]	
0		1				
						0.01 0.1 1 10 100
= 0.28)						Favours IC Favours ONB
	Events 0 0	Events Total 0 29 0 118 147 0	Events Total Events 0 29 0 0 118 1 147 1 1 0 1 1	Events Total Events Total 0 29 0 19 0 118 1 62 147 81 0 1	Events Total Events Total Weight 0 29 0 19 0 19 0 118 1 62 100.0% 147 81 100.0% 0 1	Events Total Events Total Weight M-H, Fixed, 95% CI 0 29 0 19 Not estimable 0 118 1 62 100.0% 0.17 [0.01, 4.31] 147 81 100.0% 0.17 [0.01, 4.31] 0

	llealCon	duit	Orthotopic Neo	bladder		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Abe T et al. 2014.	19	493	4	175	61.1%	1.71 [0.57, 5.11]	
Collins et al 2013	1	43	3	70	24.0%	0.53 [0.05, 5.28]	
Popov Z et al. 2007.	3	32	2	52	14.9%	2.59 [0.41, 16.39]	
Total (95% CI)		568		297	100.0%	1.56 [0.67, 3.62]	+
Total events	23		9				
Heterogeneity: Chi ² =	1.16, df = 2	(P=0.	56); l ² = 0%				101 01 10 100 100
Test for overall effect:	Z = 1.04 (F	P = 0.30)				0.01 0.1 1 10 100 Favours IC Favours ONB

С

	llealCon	duit	Orthotopic Neo	bladder		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
Navaro M et al. 2013.	0	17	3	37	77.2%	0.28 [0.01, 5.76]	
Nieuwenhuijzen JA et al. 2008.	1	118	0	62	22.8%	1.60 [0.06, 39.75]	
Total (95% CI)		135		99	100.0%	0.58 [0.08, 3.98]	-
Total events	1		3				
Heterogeneity: Chi ² = 0.60, df = 1	1 (P = 0.44)); I ² = 09	6				0.01 0.1 1 10 100
Test for overall effect: Z = 0.55 ()	P = 0.58)						Favours IC Favours ONB

D

	llealCon	duit	Orthotopic Neo	bladder		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
Cho A et al. 2017.	2	32	11	62	23.5%	0.31 [0.06, 1.49]	
Navaro M et al. 2013.	4	17	9	37	14.5%	0.96 [0.25, 3.69]	
Neuwenhuijzen JA et al. 2008.	20	118	16	62	58.2%	0.59 [0.28, 1.24]	
Parekh DJ et al. 2000.	0	81	0	117		Not estimable	
Popov Z et al. 2007.	0	32	1	52	3.8%	0.53 [0.02, 13.36]	
Total (95% CI)		280		330	100.0%	0.57 [0.32, 1.03]	•
Total events	26		37				
Heterogeneity: Chi2 = 1.15, df = 1	3 (P = 0.76)); 1º = 09	6				0.01 0.1 1 10 100
Test for overall effect: Z = 1.86 (P=0.06)						0.01 0.1 1 10 100 Favours IC Favours ONB

Е

	llealCon	duit	Orthotopic Neol	bladder		Odds Ratio	Odds	Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixe	d, 95% CI
Gburek BM et al. 1998.	2	66	1	66	0.8%	2.03 [0.18, 22.96]		
Gore JL et al. 2010.	21	1252	7	109	10.0%	0.25 [0.10, 0.60]		
Kim SH et al. 2014.	2	161	2	147	1.6%	0.91 [0.13, 6.56]		_
Popov Z et al. 2007.	0	32	1	52	0.9%	0.53 [0.02, 13.36]		
Tan WS et al. 2017.	1	100	0	34	0.6%	1.04 [0.04, 26.14]		
Thulin H et al. 2010.	4	190	6	180	4.7%	0.62 [0.17, 2.25]		-
van Hemelrijck et al 2013	137	2918	68	731	81.5%	0.48 [0.35, 0.65]		
Total (95% CI)		4719		1319	100.0%	0.49 [0.37, 0.64]	•	-
Total events	167		85					
Heterogeneity: Chi ² = 4.33,	df = 6 (P =	0.63); 1	² = 0%					1 10 100
Test for overall effect: Z = 5	5.13 (P < 0	00001)					0.01 0.1 Favours IC	1 10 100 Favours ONB

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Table 1. Summary of studies included in the meta-analysis for ileal conduit and orthotopic neobladder								
Author (year) Origi		Journal	Type of study	Level of evidence	IC (N)	ONB (N)		
Abe et al, 2014	Japan	Int J Urol	RCC	3b	493	175		
Aboumarzouk et al, 2014	Poland	Cent European J Urol	PCC	3b	39	24		
Angulo et al, 2014	Spain	Urology	PCC	3b	8	12		
Antonelli et al 2016	Italy	Clin Genitourin Cancer	PCC	3b	85	85		
Belotti et al, 2012	Italy	Anticancer Research	PCC	3b	223	111		
Cho et al, 2017	Korea	Renal Failure	RCC	3b	33	62		
Collins et al, 2013	Sweden	Eur Urol	PCC	3b	43	70		
De Nunzio et al, 2013	Italy	Eur J Surg Oncol	PCC	3b	217	112		
Decaestecker et al, 2016	Belgium	European Urology, Supplements	PCC	3b	40	32		
Erber et al, 2012	Germany	IRSN Urol	RCC	3b	23	34		
Gburek et al, 1998	USA	Journal of Urology	RCC	3b	66	66		
Gore et al, 2010	USA	Journal of Urology	RCC	3b	1252	109		
Hofer et al, 2012	USA	Journal of Urology	PCC	3b	245	63		
Jung et al, 2006	Korea	Korean Journal of Urology	PCC	3b	29	19		
Kim et al, 2014	Korea	Jpn J Clin Oncol	RCC	3b	161	147		
Mano et al, 2018	Israel	Urology	RCC	3b	130	49		
Monn et al, 2014	USA	Urologic Oncology: Seminars and Original Investigations	RCC	3b	139	55		
Nahar et al, 2018	USA	Journal of Urology	RCC	3b	10197	692		
Navarro et al, 2008	Chile	Urology	PCC	3b	17	37		
Nazmy et al, 2013	USA	Journal of Urology	PCC	3b	67	91		
Nieuwenhuijzen et al, 2008	The Netherlands	Eur Urol	PCC	3b	118	62		

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Parekh et al, 2000	USA	Urology	RCC	3b	81	117
Popov et al, 2007	Republic of	Acta chirurgica lugoslavica		3b	32	52
	Macedonia	Acta chirurgica tugostavica	RCC	30	32	52
Prcic et al, 2017	Bosnia and	Med Arch	PCC	3b	66	60
	Herzegovina	mea Arch		30	00	00
Roghmann et al, 2013	USA	Can Urol Assoc J	RCC	3b	18782	6282
Roghmann et al, 2014	Germany	Int J Urol	RCC	3b	349	186
Roghmann et al, 2017	Germany	Journal of Urology	PCC	3b	510	294
Sherwani et al, 2009	India	Int J Health Sci (Qassim)	PCC	3b	13	4
Sogni et al, 2008	Italy	Urology	RCC	3b	53	32
Tan et al, 2017	United Kingdom	Eur Urol Focus	PCC	3b	100	34
Thulin et al, 2010	Sweden	BJU Int	RCC	3b	190	180
van Hemelrijck et al, 2013	Sweden	BJU Int	RCC	3b	2918	720

IC: ileal conduit; ONB: orthotopic neobladder; PCC: prospective case-control; RCC: retrospective case-control.

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Table 2. Patient demographics from papers where age was reported as a mean ± standard deviation									
Author (year)	Age (conduit)	Age	Male/female	Male/female	BMI	BMI			
	ge (containe)	(neobladder)	(conduit)	(neobladder)	(conduit)	(neobladder)			
Aboumarzouk et al, 2014	60±7.11	57±8.68	34/5	24/0	27.2 ± 2.3	27.96±2			
Antonelli A et al 2016	63±8.8	63.5±6.7	69/16	72/13	NR	NR			
Belotti et al, 2012	70.4±8.1	60.6±0.9	183/34	90/21	26.3±4.3	26.3±3.6			
Cho et al, 2017	69.5±8.1	64.5±8.6	23/10	52/10	NR	NR			
Collins et al, 2013	69.9±6.7	59.8±9.0	31/11	62/8	24.8±3.1	26.1±3.4			
De Nunzio et al, 2013	71±9.75*	$63 \pm 0.25^{*}$	NR	NR	$26.4\pm6^{*}$	25±3.25*			
Decaestecker et al, 2016	$71{\pm}1.5^{*}$	63±1.25*	29/11	27/5	$26{\pm}4.25^{*}$	$26 \pm 3.75^*$			
Gburek B et al, 1998	69±11.75*	62±12.75*	66/0	62/4	NR	NR			
Hofer et al, 2012	$69.7 \pm 3.75^*$	59.7±15	NR	NR	NR	NR			
Jung et al, 2006	65.6±9.9	60.8±8.3	NR	NR	NR	NR			
Kim et al, 2014	67.1±8.9	59.4±9.4	115/32	156/5	23.6±3.3	24±3.1			
Monn et al, 2014	72.6±10	59.6±9	107/32	49/6	NR	NR			
Nahar et al, 2018	68.8±10.1	62.8±10	8835/1362	663/29	NR	NR			
Parekh et al, 2000	68±12.75*	60±13.5*	48/33	97/20	NR	NR			
Roghmann et al, 2013	69.6	60.8	81/19	91/9	NR	NR			
Sherwani et al, 2009	59	53.3	NR	NR	NR	NR			
Thulin et al, 2010	70.1	64.3	134/56	165/15	NR	NR			

*Estimated standard deviation based on the Range Rule of Thumb. BMI: body mass index; NR: not reported.

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Table 3. Patient demographics from papers where age was reported as a median and range								
Author (year)	Age (conduit)	Age (neobladder)	Male/female (conduit)	Male/female (neobladder)	BMI (conduit)	BMI (neobladder)		
Abe et al, 2014	70 (37–89)	63 (25–86)	364/129	164/11	23 (14.6–35.1)	23.3 (16–31.5)		
Angulo et al, 2014	74.5 (70-82.2)	66 (61.5–75)	5/3	12/0	27.7 (23.2–31.8)	27.3 (25.5–28.5)		
Erber et al, 2012	70 (64–75)	62 (56–66)	98/48	110/5	NR	NR		
Mano et al, 2018	72 (65–78)	60 (53–65)	112/18	43/6	NR	NR		
Nieuwenhuijzen et al, 2008	70 (46–85)	62 (32–73)	88/30	59/3	NR	NR		
Roghmann et al, 2014	72 (67–76)	61 (55–67)	256/93	158/28	27.3 (24.6–29.8)	26.1 (23.8–29.2)		
Sogni et al, 2008	78.9 (75–88)	77.5 (75–82)	NR	NR	NR	NR		
Tan et al, 2017.	67.4 (60.4–74.3)	54.5 (48.6–61.6)	75/25	28/6	27.2 (23.4–31)	27.3 (23–28.5)		
6	67.4 (60.4–74.3)	. ,						

BMI: body mass index; NR: not reported.

Table 4. Studies where length of stay is reported as median and range								
	Ile	eal conduit	Orthotopic neobladder					
Author (year)	n	Median	n	Median				
		(range)	11	(range)				
Abe et al, 2014	493	39 (3–257)	175	42 (18–364)				
Angulo et al, 2014	8	9.5 (8–11)	12	8.5 (7.2–10.7)				
Antonelli et al, 2016	85	17	85	21				
Belotti et al, 2012	223	20 (16–24)	111	24 (20–29)				
Collins et al, 2013	43	9 (6–142)	70	9 (4–78)				
Decaestecker et al, 2016	40	10 (5–36)	32	11 (6–39)				
Monn et al, 2014	139	8 (6–10)	55	7 (6–8)				
Nieuwenhuijzen et al, 2008	118	17 (6–53)	62	15 (8–44)				
Parekh et al, 2000	81	8 (5-60)	117	7 (5–28)				
Roghmann et al, 2014	349	19 (16–24)	70	9 (17–23)				
Tan et al, 2017	100	10 (8–15.5)	34	11 (8.5–14)				