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ORIGINAL ARTICLE

Outcome comparison between ileal conduit and orthotopic neobladder:

An extended literature review

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Introduction

Bladder cancer is the 10th most common malignancy worldwide and represents a burden on both patients and healthcare providers. The management strategy for muscle-invasive bladder cancer is radical cystectomy with urinary diversion. Ileal conduit has been regarded as the main method of urinary diversion for several years. Orthotopic neobladder has been its main competitor since the development of newer techniques.

Aim

The aim of this extended literature review to evaluate the evidence and outline arguments in favour or against ileal conduit and orthotopic neobladder with a special focus on morbidity, mortality, sexual dysfunction, tumour recurrence, renal function and quality of life.

Methodology

A total of 17 relevant studies were identified – 15 cohort studies and 2 systematic reviews. These were appraised to establish rigour, reliability and validity.

Results

Evidence from contemporary literature demonstrates that ileal conduit and orthotopic neobladder offer comparable outcomes when it comes to morbidity, mortality, relapse rates and acute or chronic kidney disease. However, neobladder could be the better option in consideration for the patient's sexual function and quality of life.

Conclusions

These findings were used to develop graded recommendations which could be applied to local clinical practice.

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Bladder cancer is the 10th most common malignancy worldwide.[1] Radical cystectomy is the recommended elective treatment for muscle-invasive bladder cancer. In males, radical cystectomy involves removal of the bladder, prostate, and seminal vesicles; in females, the bladder, ovaries, uterus, cervix and anterior vagina are resected.[2] Radical cystectomy then requires reconstruction of the lower urinary tract through urinary diversion.[3]

Oncological, physiological, social and technical issues, along with patient preference are factors that need to be taken into consideration when decided on the type of urinary diversion. For more than 30 years, the ileal conduit has been considered the gold standard urinary diversion method. However, since 1980, a number of orthotopic neobladders have been developed and improved. The most popular neobladder described is the Studer's method.[4]

In 2015, according to the British Association of Urological Surgeons (BAUS) Section of Oncology's radical cystectomy dataset, 80.6% of patients received an ileal conduit and only 6.9% had a neobladder.[5] Current practice relies heavily on the urologist's judgment in determining what type of urinary diversion is opted for. Controversies over this choice are partly due to the lack of effective ways of outcome assessment and unawareness of disease-specific problems related to ileal conduit and orthotopic neobladder.

An extended literature review to examine the evidence surrounding this topic was therefore performed to determine which method of urinary diversion offers the most favourable outcomes.

Aim

The aim of this literature review is to critically appraise the evidence for and against ileal conduit and orthotopic neobladder, taking into account patient health-related quality of life, symptoms, complication rates, mortality and long-term oncological outcomes. The findings of the literature review were used in the development of graded recommendations for clinical practice as the intended end-product.

Methodology

The PICO method (Table 1) was used to formulate the clinical question, which in turn assisted the development of a search strategy. The clinical question developed is: *In patients who undergo radical cystectomy for bladder cancer, how do ileal conduit and orthotopic neobladder as methods of urinary diversion compare in terms of postoperative outcomes?*

A systematic literature search was conducted using Ovid via Embase, Medline and Joanna Briggs Institute EBP Database. The keywords used were 'bladder cancer' AND 'radical cystectomy' AND 'urinary diversion' AND 'neobladder' AND 'ileal conduit' AND 'outcomes'. Another search using Pubmed was done using a combination of free text words and Medical Subject Heading (MeSH) terms to increase the sensitivity of the search. The database was searched using the following keywords: 'radical cystectomy' AND 'urinary diversion' AND 'neobladder' AND 'ileal conduit' AND 'outcomes'. The Cochrane Library database was also searched using the keywords 'radical cystectomy' AND 'ileal conduit' AND 'neobladder'.

Table 1 Acronym PICO to formulate a clinical question

PICO model for clinical questions	
Patient/Problem	Radical cystectomy for bladder cancer
Intervention	Ileal conduit as a method of urinary diversion following cystectomy
Comparison	Orthotopic neobladder as a method of urinary diversion following cystectomy
Outcomes	Morbidity and mortality Sexual dysfunction Tumour recurrence Renal function and metabolic abnormalities Quality of life

Inclusion criteria were articles on human subjects, both males and females, over 18 years of age, published between 2007 and 2017, that provided a direct comparison between ileal conduit and orthotopic neobladder and reported on at least one outcome measured after radical cystectomy. No restriction was made on origin of study. The search was limited to publications in the English language.

The search using Ovid via Embase, Medline and Joanna Briggs Institute EBP Database yielded 83 articles, of which 11 were relevant to the topic after screening abstracts and titles (**Table 2).** Reference listing was done with backward chaining employed to retrieve pertinent publications. Three further relevant articles were found.

The Pubmed database search yielded 127 articles, of which 10 were deemed to be relevant. Seven of these had already been identified in the previous search and were eliminated. No further relevant studies were identified from the Cochrane Library database search.

A total of 15 cohort studies and 2 systematic reviews were critically appraised using the

Table 2 Search results using Ovid via Embase, Medline and Joanna Briggs Institute EBP Database

	Keyword	Number of articles
1	bladder cancer	70976
2	radical cystectomy	13032
3	urinary diversion	16328
4	Ileal conduit	4295
5	neobladder	3520
6	outcomes	1489108
7	1 and 3 and 3 and 4 and 5 and 6	108
8	limit 7 to English language	100
9	limit 8 to human	89
10	limit 9 to year 2007-2017	83

Critical Appraisal Skills Programme (CASP) appraisal tool. The evidence grading tool applied for all studies is the Scottish Intercollegiate Guidelines Network (SIGN) grading system as described by Harbour & Miller (2001).[6] Grading of Recommendations was also done according to system by Harbour and Miller (2001).[6]

Results

Morbidity and mortality

Radical cystectomy with any type of urinary diversion is a complication-prone surgery, with the risk of developing a complication ranging from 16-66%.[7-8] A wide range of complications are quoted in different studies which can be attributed to the use of different reporting systems. The main finding in the study by Erber et al. (2012)[9] was the significantly higher incidence of ileus in patients undergoing ileal conduit. The authors also report better survival outcomes with orthotopic neobladder. In comparing the type, incidence and severity of 90-day morbidity, Abe et al. (2014)[10] revealed that overall complication rate did not vary between ileal conduit and orthotopic neobladder. More importantly, the type of urinary diversion was an independent risk factor for overall complications. Along with the study by Kim et al. (2014),[11] there was no significant difference in 90-day mortality. Aboumarzouk et al. (2014)[12] found no significant difference in comparison of individual and grouped complications, a finding reproduced in the study by Kim et al. (2014)[11] and Antonelli et al. (2015).[13]

Observations relating to morbidity must be interpreted with caution due to the confounding effect of heterogeneity in age, comorbidities and distribution of prognostic parameters between groups. The results are confounded by the propensity for surgeons to recommend neobladder to young healthy individuals. None of the studies identified any statistically significant difference in overall complications rate. The misconception that neobladder, being a more technically challenging type of surgery, is automatically associated with more complications is therefore unfounded.

1. Sexual dysfunction

Sexual dysfunction is one of the complications which is often overlooked, in the process of prioritising other outcomes such as cure with minimal risk of recurrence. The reported rate of sexual dysfunction after radical cystectomy is between 14%-80%.[14] The only study which directly addressed this issue was by Asgari et al. (2013)[15] which concluded that following an initial drop in erectile function, orthotopic neobladder patients demonstrated a significant improvement in sexual desire compared to their ileal conduit counterparts. In this study, no attempt at nerve-sparing was undertaken. The improved sexual desire in the neobladder group can be attributed to a less drastically altered body image.

The studies by Goldberg et al. (2016)[16] and Cerruto et al. (2016),[17] although not focused on sexual function as the primary outcome, also pointed out more favourable results in erectile function with orthotopic neobladder.

2. Tumour recurrence

Local recurrence of bladder cancer after radical cystectomy is often a result of surgical failure. Ileal conduit was favoured for a long time since it was thought to provide better cancer clearance than neobladder. However, the study by Pejcic et

al. (2007)[18] demonstrated no significant difference in recurrence rates between the two. The construction of a neobladder is therefore supported whenever there is the absence of tumour at the bladder neck or at the intramural or juxtavesical ureteral segment at cystectomy. With an improved understanding of pathology behind invasive bladder cancer, the majority of patients without prostatic or bladder neck involvement can now be offered neobladder without compromising cancer control.[19]

3. Renal function and metabolic abnormalities

Urinary diversion is associated with hyperchloremic metabolic acidosis and electrolyte metabolism abnormalities owing to absorption of ammonium through the intestinal mucosa. It is often believed that the metabolic challenge posed by ileal conduit is less than that of orthotopic neobladder due to a shorter bowel segment used and the absence of a reservoir.[20] However, Cho et al. (2017)[21] showed no significant differences in biochemical profiles between ileal conduit and neobladder. The authors also outlined a relationship between decreased renal function and acid-base status.

The incidence of acute kidney injury after radical cystectomy is 31-38% and is associated with higher incidence of chronic kidney disease and mortality.[22] According to Joung et al. (2016),[23] the incidence of acute kidney injury, its associated intensive care admission rate and length of hospital stay did not differ significantly between the two groups.

Jin et al. (2011)[24] showed that irrespective of the type of urinary diversion, a substantial proportion of radical cystectomy patients experience deterioration in renal function. However, the authors report better long term renal function with neobladder as compared to ileal conduit when patients were exposed to diabetes and hypertension.

Nishikawa et al. (2014)[25] observed renal deterioration in 46.2% of the study population after radical cystectomy, with hypertension and pyelonephritis being independent predictive risk factors. Yet, no significant differences were found between ileal conduit and neobladder.

4. Quality of life

Health-related quality of life, being a multifaceted and subjective concept, was the most challenging outcome to quantify in this literature review. Various questionnaires were encountered in the assessment of quality of life, thus it is difficult to achieve comparability of results. Not all questionnaires used in the appraised papers have been validated and they are very heterogenous in the assessed domains.

The urological community remains unconvinced regarding the quality of life benefits of neobladder over ileal conduit. However, most of the papers argue in favour of orthotopic neobladder, relying on perceived functional benefits and preservation of body image.[19-26] This, however, could be a reflection of selection bias since younger healthier patients with more favourable tumours are usually encouraged to receive a neobladder.

On the other hand, complications related to neobladder management are also highlighted, such as incontinence and reduced bladder control and sensation.[17] Counter arguments for ileal conduit can be put forward, especially since significantly higher urinary function scores were achieved

in comparison to neobladder, as shown in the papers by Huang et al. (2015),[27] Goldberg et al. (2016)[16] and Cerruto et al. (2016).[17]

Conclusion

After analysis of some conflicting evidence, the key results do not demonstrate any benefits of orthotopic neobladder over ileal conduit in terms of morbidity, mortality, renal function and recurrence, indicating that they are equally safe procedures. However, significant benefits can be appreciated with neobladder with regards to sexual function and quality of life, giving it a more appealing role particularly in younger patients. The recommendations shown in **Table 3** were developed as the end product of the critical appraisal of papers included in this literature review. They can provide a basis for future developments in such a dynamic and constantly evolving specialty as urological oncology. However, preceding the introduction of formal guidelines, more high level evidence derived from well-designed randomised controlled trials is required.

Table 3 Recommendations for practice

Recommendation 1 – Grade C
Based on current evidence, the choice of either ileal conduit or orthotopic neobladder as the method of urinary diversion following radical cystectomy does not significantly impact relapse rates for bladder malignancy, but ileal conduit is associated with lower survival rates. Erber et al. (2012) – Level 2+ Goldberg et al. (2016) – Level 2+ Kim et al. (2014) – Level 2++ Pejcic et al. (2007) – Level 2-.
Recommendation 2 – Grade C
Current best evidence suggests that the choice of urinary diversion after radical cystectomy translates into no significant difference in mortality rates between ileal conduit and orthotopic neobladder. Abe et al. (2014) – Level 2+ Aboumarzouk et al. (2014) – Level 2- Kim et al. (2014) – Level 2++ Jin et al. (2011) – Level 2+
Recommendation 3 – Grade C

It is suggested that ilela conduit and orthotopic neobladder following radical cystectomy may be associated with different rates of individual postoperative complications, but the overall complication rate is not significantly different.

Abe et al. (2014) – Level 2+

Crozier et al. (2016) – Level 2-

Aboumarzouk et al. (2014) – Level 2-

Kim et al. (2014) – Level 2++

Antonelli et al. (2015) – Level 2++

Recommendation 4 – Grade D

Current best evidence suggests that opting for orthotopic neobladder as the method of urinary diversion following radical cystectomy translates into longer operating time.

Abe et al. (2014) – Level 2+

Aboumarzouk et al. (2014) – Level 2-

Crozier et al. (2016) – Level 2-

Recommendation 5 – Grade C

Based on current evidence, orthtotopic neobladder offers the most benefits in sexual function outcomes and is the recommended option of urinary diversion after radical cystectomy whenever feasible, especially in younger men.

Asgari et al. (2013) – Level 2+

Goldberg et al. (2016) – Level 2+

Cerruto et al. (2016) – Level 2+

Recommendation 6 – Grade C

Current best evidence recommends the early identification and intervention for risk factors associated with renal impairment in attempt to minimize the decline in postoperative renal function in both ileal conduit and orthotopic neobladder patients. However, the proportion of patients developing chronic renal dysfunction does not significantly differ amongst the two methods of urinary diversion.

Nishikawa et al. (2014) – Level 2+

Jin et al. (2011) – Level 2+

Recommendation 7 – Grade C

According to current evidence, the formation of orthotopic neobladder after radical cystectomy leads to more favourable health-related quality of life outcomes in several domains in comparison to ileal conduit.

Philip et al. (2009) – Level 2-

Huang et al. (2015) – Level 2+ Singh et al. (2014) - Level 2+ Crozier et al. (2016)- Level 2- Cerruto et al. (2016) – Level 2+
Recommendation 8 – Grade C
It is suggested that ileal conduit after radical cystectomy offers more benefit in term of urinary function when compared to the orthotopic neobladder alternative. Huang et al. (2015) – Level 2+ Goldberg et al. (2016) – Level 2+ Cerruto et al. (2016) – Level 2+

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