Original Article

Does prostatectomy with the bladder neck reconstruction technique result in shorter recovery times to urinary continence: a meta-analysis

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Abstract: Background: It has been reported that one of the major complications of prostatectomy is postoperative incontinence. Owing to mixed and inconclusive results, we conducted a meta-analysis to systematically summarize and clarify the association between the bladder neck reconstruction technique (BNR) and postoperative continence.

Methodology/main results: A systematic search of studies on the association of the bladder neck reconstruction technique and postoperative continence was conducted in PubMed, Scopus, and Web of Science databases. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were used to pool the effect size. At 1 month, the fixed-effect model pooled OR was 1.31 (95% CI: 0.85-2.20, P = 0.216) with a small heterogeneity (P = 0.377 and I² = 0%). At 3 month, the pooled OR with the random effect model was 1.59 (95% CI, 0.98-2.59; P = 0.062), and the greater heterogeneity was investigated by the method of sensitivity analysis, subgroup analysis and even meta-regression; At 6 and 12 month, the fixed model and the random model were used, respectively. The pooled OR was 0.89 (95% CI, 0.45-1.75; P = 0.729) at 6 month and 1.31 (95% CI, 0.52-3.28; P = 0.563) at 12 month. Conclusions: Our meta-analysis suggests that BNR could not improve the earlier recovery rate from urinary incontinence after prostatectomy at 1, 3, 6 and 12 month. However, the results should be interpreted with caution due to limited sample and heterogeneity. Large-scale and well-designed studies are needed to validate our findings.

Keywords: Bladder neck reconstruction, postoperative incontinence, prostatectomy, meta-analysis

Introduction

Prostate cancer is the second most common malignancy in men with more than 1 million new cases being diagnosed and 300,000 cases are dead every year worldwide [1, 2]. Prostatectomy is one of the major forms of therapy for localized prostate cancer. However, postoperative incontinence, which is reported to vary widely, from 2.5% to 87% [3], is a major complication of prostatectomy. Some published studies have introduced several modified surgical techniques that could improve the incontinence symptom, such as puboprosthetic ligament sparing [4], seminal vesicle sparing techniques [5], posterior rhabdosphincter reconstruction [6, 7], apical dissection modifications [8], anatomic bladder neck preservation [9], total reconstruction of the vesicourethral junction [10].

Bladder neck reconstruction (BNR) is also a method reported to improve urinary continence. It was derived from the intussusception stitch technique applied in open radical prostatectomy (ORP) procedures [11], and then it developed into the bladder neck plication stitch technique in robot-assisted radical prostatectomy (RARP) [12]. In the past more than 10 years, several studies have been conducted to resolve this issue, with the results of which were quite different, nay contradictory. It was still unclear whether BNR were effective for patients with prostatectomy. It is of importance to improve operative technique and patients’ life quality to reassess this issue in depth, so we performed this systematic review and meta-analysis to assess all the published evidence involving RCTs and non-RCTs, therefore an unambiguous evidence shall be given about whether prostatectomy with BNR could result in shorter recov-
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Evidence times to urinary continence at 1, 3, 6 and 12 months after surgery.

Evidence acquisition

Literature search and article selection

A systematic review was performed using PubMed, Scopus, and Web of Science in April 2015 to identify relevant studies. Searches were restricted to publications in English. Separate searches were done by the terms of following searches: radical prostatectomy, urinary incontinence, intussusception of the bladder neck, bladder neck plication stitch.

Two reviewers (DKG, WHC) separately screened retrieved database files and the full text of potentially eligible studies for relevance. Study selection was proceeded according to the search strategy based on the PRISMA Statement [13] (Figure 1). Only studies making a comparison between surgeries with and without the procedure of BNR were included for further screening. Detailed data could be acquired to calculate the odds ratios (ORs) and 95% confidence interval (CI). Cited references from the selected studies retrieved in the search were also assessed for significant papers. Comment, review, meeting abstract and editorial were not included as they were not considered methodologically appropriate. Disagreements were resolved by consensus or by discussion with the supervisor (YMW).

Assessment of study quality

The level of evidence (LE) was rated for each included study according to the criteria provided by the Oxford Centre for Evidence-based Medicine published in 2009. We used the modified Jadad scale [14] for quality assessment of RCTs, and the Newcastle-OttawaQuality Assessment Scale published in 2000 (NOS)
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Table 1. The modified Jadad scale

<table>
<thead>
<tr>
<th>Eight items</th>
<th>Answer</th>
<th>Score</th>
<th>Choi et al. [1]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Was the study described as randomized?</td>
<td>Yes</td>
<td>+1</td>
<td>*+1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Was the method of randomization appropriate?</td>
<td>Yes</td>
<td>+1</td>
<td>*+1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>-1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not described</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Was the study described as blinding?*</td>
<td>Yes</td>
<td>+1</td>
<td>*+0.5</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Was the method of blinding appropriate?</td>
<td>Yes</td>
<td>+1</td>
<td>*+1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>-1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not described</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Was there a description of withdrawals and dropouts?</td>
<td>Yes</td>
<td>+1</td>
<td>*+1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Was there a clear description of the inclusion/exclusion criteria?</td>
<td>Yes</td>
<td>+1</td>
<td>*+1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Was the method used to assess adverse effects described?</td>
<td>Yes</td>
<td>+1</td>
<td>*+0</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Was the method of statistical analysis described?</td>
<td>Yes</td>
<td>+1</td>
<td>*+1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

*Double-blind got 1 score, single-blind got 0.5 score; *means meeting the item requirement and can get the score behind.

Table 2. Newcastle-Ottawa quality assessment scale (for case-control studies)

<table>
<thead>
<tr>
<th>Study</th>
<th>Selection</th>
<th>Comparability</th>
<th>Exposure</th>
<th>Total score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walsh et al.</td>
<td>d)</td>
<td>b)</td>
<td>a)</td>
<td>a)</td>
</tr>
<tr>
<td>Sakai et al.</td>
<td>b)</td>
<td>a)</td>
<td>a)</td>
<td>a)</td>
</tr>
<tr>
<td>Wille et al.</td>
<td>d)</td>
<td>a)</td>
<td>a)</td>
<td>a)</td>
</tr>
<tr>
<td>Lee et al.</td>
<td>d)</td>
<td>a)</td>
<td>a)</td>
<td>a)</td>
</tr>
</tbody>
</table>

*means meeting the item requirement and can get the score behind.

Table 3. Characteristics of studies included in the meta-analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Published year</th>
<th>Study design</th>
<th>Operative technique</th>
<th>LE</th>
<th>Case, n</th>
<th>Study quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walsh et al.</td>
<td>2002</td>
<td>nRCT</td>
<td>ORP</td>
<td>3b</td>
<td>45</td>
<td>64</td>
</tr>
<tr>
<td>Wille et al.</td>
<td>2005</td>
<td>nRCT</td>
<td>ORP</td>
<td>3b</td>
<td>127</td>
<td>132</td>
</tr>
<tr>
<td>Sakai et al.</td>
<td>2005</td>
<td>nRCT</td>
<td>ORP</td>
<td>3b</td>
<td>24</td>
<td>48</td>
</tr>
<tr>
<td>Lee et al.</td>
<td>2011</td>
<td>nRCT</td>
<td>RARP</td>
<td>3b</td>
<td>159</td>
<td>175</td>
</tr>
<tr>
<td>Choi et al.</td>
<td>2014</td>
<td>RCT</td>
<td>RARP</td>
<td>2b</td>
<td>79</td>
<td>79</td>
</tr>
</tbody>
</table>

LE = level of evidence; RCT = randomised controlled trial; nRCT: non randomised controlled trial. Inte.: intervention group; Cont.: control group. *Using Jadad scale (score from 0 to 8), see Table 1. **Using Newcastle-Ottawa Scale (score from 0 to 9), see Table 2.
applied for a semi-quantitative assessment of studies, in which five or more stars indicate a high quality. The scoring processes of four non-RCTs were shown in Table 2.

Statistical analysis

A meta-analysis was performed to assess the overall outcomes of the radical prostatectomy with and without BNR at different postoperative times. The association was calculated using ORs and 95% CIs. The statistical significance of the summary OR was determined using the Z test, with \( P < 0.05 \) considered statistically significant. The proportion of heterogeneity across studies was tested by the \( \chi^2 \) and \( I^2 \) tests with significance level set at \( P < 0.1 \) or \( I^2 > 50\% \) [15]. If heterogeneity existed, the data were analysed using a random effects model (Mantel-Haenszel method, M-H). In the absence of heterogeneity, a fixed effects model was used (Mantel-Haenszel method, M-H). Sensitivity analysis was also performed to assess the effect of each study on the combined ORs by omitting each study in each turn. Besides, subgroup analyses and meta-regression would be used to dig the reason of heterogeneity if it's necessary, because the included studies could be stratified by different factors. Potential publication bias was checked by Begg’s funnel plots [16] and Egger’s regression test [17]. An asymmetric plot and the \( P \) value of Egger’s test less than 0.05 was considered a significant publication bias. All statistical analyses were conducted using Stata software (version 12.0, StataCorp, College Station, TX, USA). A two-tailed \( P < 0.05 \) was considered significant except for specified conditions, where a certain \( P \) value was declared.

Results

Characteristics of studies

The article selection process was shown in Figure 1 according to the PRISMA Statement. Five studies were recruited to the analysis including 434 (46.6%) with and 498 (53.4%) without BNR. They, respectively, were defined as intervention group and control group (Table 3). Four studies were case-control studies (LE:3b) [6, 11, 12, 18], and one RCT (LE:2b) [19]. The methodological quality of included studies was relatively high for three nonrandomized studies (NOS: 6 of 9 points) [6, 12, 18] and medium for one (NOS: 5 of 9 points) [11], whereas the one RCT were also relatively high quality (modified Jadad scale: 6.5 of 8 points) [19]. There are two types of operative techniques available in the studies included in the meta-analysis, the RARP [12, 19] and the ORP [11, 18, 20]. Recovery from incontinence at 1, 3, 6 and 12 months was analyzed, respectively. The details of studies included in different month were shown in Table 4.
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At 3 month, we identified five studies reporting on recovery from incontinent postoperatively into the meta-analysis. The fixed-effect model pooled OR was 1.57 (95% CI, 1.19-3.38, \( P = 0.030 \)), suggesting that the effect of the intervention group is statistically superior to control group. However, the heterogeneity statistic \( P \) value was 0.03, indicating the nonhomogeneity of the studies (\( I^2 = 62.8\% \)). Using the random effect model, the pooled OR was 1.59 (95% CI: 1.19-2.13, \( P = 0.002 \)) for the overall effect. In the statistical heterogeneity analysis, \( P = 0.177 \) and \( I^2 = 0\%. \) These data suggest that continent rate at 1 month are not associated with BNR.

At 1 month, by including a total of 262 patients with BNR and 302 controls from three eligible studies, meta-analysis demonstrated no significant difference in the continence rate between the two groups. The fixed-effect model pooled OR was 1.31 (95% CI: 0.85-2.20, \( P = 0.216 \)) for the overall effect. In the statistical heterogeneity analysis, \( P = 0.377 \) and \( I^2 = 0\% \). These data suggest that continent rate at 1 month are not associated with BNR.

Overall analysis at different month

Meta-analysis was applied depending on different postoperative month points to identify if the continence rate difference exists between intervention group and control group (Figure 2 and Table 4).

At 3 month, we identified five studies reporting on recovery from incontinent postoperatively into the meta-analysis. The fixed-effect model pooled OR was 1.57 (95% CI, 1.19-3.38, \( P = 0.030 \)), suggesting that the effect of the intervention group is statistically superior to control group. However, the heterogeneity statistic \( P \) value was 0.03, indicating the nonhomogeneity of the studies (\( I^2 = 62.8\% \)). Using the random effect model, the pooled OR was 1.59 (95% CI: 1.19-2.13, \( P = 0.002 \)).
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0.98-2.59, \( P = 0.062 \)), indicating that the two groups is not statistically significant. The reason of greater heterogeneity at 3 month will be investigated in the ensuing paragraphs.

At 6 and 12 month, we identified two studies into meta-analysis, respectively. Because of the different heterogeneity, the fixed model and the random model were used respectively. The pooled OR was 0.89 (95% CI: 0.45-1.75, \( P = 0.729 \)) at 6 month and 1.31 (95% CI: 0.52-3.28, \( P = 0.563 \)) at 12 month. No significant association was found either.

The meta-analysis demonstrated no significant difference in the continence rate at 1, 3, 6 and 12 month.

Investigation about the reason of heterogeneity at 3 month

Although the result at 3 month and 12 month was not statistically significant, i.e. there was no difference between the two methods' influence on early postoperative incontinence recover, it is worthwhile to note that the results were of greater heterogeneity, and the reason is supposed to be investigated. As the result at 3 month included more studies in terms of quantity, we take the recovery situation from incontinent at 3 month as an object.

Sensitivity analysis: Sensitivity analysis was performed to examine the influence set by the individual study on the pooled ORs for continence rate at 3 month by excluding each study once from the five identifying studies. The pooled estimates of the remaining four studies showed no significant association in any attempt (Figure 3).

Subgroup analysis and meta-regression: There are two types of operative techniques available in the studies included in the meta-analysis, the RARP [12, 19] group and ORP [6, 11, 18] group. Subgroup analysis was conducted according to the operative techniques (Figure 4). No significant statistical heterogeneity were identified in both two subgroups (RARP group: \( I^2 = 58.7\%, \ P = 0.120 \); ORP group: \( I^2 = 27.2\%, \ P = 0.253 \)), so that the factor, different operative techniques, was not the reason of heterogeneity. Neither was study design factor (RCT group: 1 study; non-RCT group: \( I^2 = 38.2\%, \ P = 0.183 \)).

Figure 4. Subgroup analysis.
We also managed to conduct Monte Carlo permutation test for meta-regression to testify the result above (Permute = 10000). The adjusted P value of the two regression factors, operative techniques and study design, are 0.499 and 0.352, respectively.

Publication bias

No publication bias for the continent rate between the surgery with and without BNR at 3 month was identified by Begg’s funnel plot (P = 1) or Egger’s regression test (P = 0.812). Symmetrical Begg’s funnel plot and Egger’s bias plot were shown in Figure 5. No funnel plot or Egger’s test were performed for the rate at other month owing to the limited number of included studies.

Discussion

There have been several disagreements about the role of BNR. To summarize the results of and to overcome small sample sizes of existing individual studies, we performed this meta-analysis. To the best of our knowledge, this is the first meta-analysis to assess the association of postoperative continence with BNR.

Our meta-analysis involves a total of 434 patients with BNR and 498 controls from five eligible studies. This meta-analysis resulted in the following findings. Firstly, the operative techniques of RARP and ORP were consistent, and the result of their combination did not affect meta-analysis outcomes. Secondly, there was no significant difference in the earlier postoperative recovery of continence.

Our findings of the association of the recovery rate and BNR have no statistical significant at all selected months. However, the result should be interpreted with caution due to the reason that only few studies at 1, 6, and 12 month was included and the heterogeneity at 12 month was as high as I² = 76.9% (P = 0.038). The outcome at 3 month includes 5 studies, and its highest quantity of studies guaranteed a more reliable conclusion.

We made a further investigation about the resource of heterogeneity at 3 month for two reasons as below. Firstly, the meta-analysis outcome at 3 month was with a higher heterogeneity, hence it was supposed to dissect the reliability of its conclusion; secondly, as the included studies concerned two kinds of operative techniques, it was supposed to verify whether the difference between two kinds of operative techniques and study design affect ed the heterogeneity, if so, their comparison meta-analysis outcome was inappropriate. With reference to above analysis conclusions, sensitivity analysis result eliminated the influence set by one single individual study; subgroup analysis and meta-regression result proved that neither different operative techniques nor different study design was the rea-
son of heterogeneity (i.e., the RARP and ORP studies combined meta-analysis outcome and the RCT and non RCT studies combined meta-analysis outcome were both of reliability); Begg’s funnel plot and Egger’s regression test indicated that no publication bias were identified to affect meta-analysis outcome. Consequently, we considered the reason of heterogeneity at 3 month stem from the inherent heterogeneity of individual studies.

Walsh et al [11] firstly reported the intussusception of the bladder neck improve earlier restoration of continence after retropubic radical prostatectomy. In that study, 82% men were continent 3 months after the intussusception of the bladder neck compared with only 54% men who underwent retropubic radical prostatectomy without intussusception. The precise mechanism by which intussusception of the bladder neck promotes earlier recovery from postoperative incontinence remains unclear, although two possibilities were suggested: (1) buttressing sutures may prevent the bladder neck from pulling apart as the bladder fills; and (2) functional residual urethral length may be increased by preventing the proximal end of urethral stump from opening. Two subsequent comparative studies of intussusception of the bladder neck yielded contradictory findings. Wille et al [18] found that intussusception of the bladder neck during retropubic radical prostatectomy resulted in a significantly greater continence rate of (77% vs 60%) after 3 months although continence rates at 12 months were similar. By contrast, Sakai et al [6] found that continence rates at 1, 3, and 6 months were no significant between-group differences at any time point.

A modification of the intussusception stitch technique led to the development of the bladder neck plication stitch in RARP [12]. This method involved anterior stitching only after urethrovesical anastomosis because posterior bladder neck stitching is technically difficult to perform robotically. The bladder neck plication stitch causes the bladder neck to become more funneled in appearance, likely decreasing the degree of stretch on the bladder neck and urinary sphincter at rest. Furthermore, this funneling may lengthen the functional length of the urethra. That study reported total continence rates in patients with and without bladder neck plication stitching were higher at 1 month (16% vs 8.9%, \( P = 0.097 \)) and 3 months (36.3% vs 31.3%, \( P = 0.63 \)), and were significantly higher at 12 months (85.7% vs 74.4%, \( P = 0.042 \)). By contrast, Choi et al [19] found that the percentages of continent patients with and without bladder neck plication stitching after RARP similar at 1 month (27.8% vs 29.1%), 3 months (53.2% vs 59.5%), and 6 months (72.2% vs 74.7%).

These disagreement can be explained by the theory that the mechanism of regulating continence was affected by many factors including age, BMI, prostate volume, MUL, shape of the prostatic apex, nerve-sparing surgery [7-10]. Choi et al [19] conclude the percentage of patients with non protruding prostatic apex on preoperative magnetic resonance imaging was slightly higher in patients who did not undergo bladder neck plication stitching.

Meta-analysis is a powerful statistical method and has the capability to increase the sample size and thus potentially to improve the power to assess the association of the recovery rate with BNR. However, there are some limitations to its use in the present study. Firstly, the main limitation of this meta-analysis is that only a small number of studies were retrieved, and thus they may not represent sufficient diversity of the patient populations. Secondly, the inherent heterogeneity of the included studies, in terms of study population and design, detection method, and data interpretation, rendered it difficult to integrate results across studies. Particularly, some of the included studies did not provide details about the patient basic-line characteristics. The lack of analysis of these confounding factors may weaken the results.

In conclusion, our meta-analysis suggests that the surgery technique, BNR, could not improve the earlier recovery rate from urinary incontinence after prostatectomy. Well-designed studies with larger sample size are required to validate the risk identified in the current meta-analysis.

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Disclosure of conflict of interest

None.
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References