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Review – Prostate Cancer

Preservation of the Neurovascular Bundles Is Associated with Improved Time to Continence After Radical Prostatectomy But Not Long-term Continence Rates: Results of a Systematic Review and Meta-analysis

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Abstract

Context: The aetiology of urinary incontinence following radical prostatectomy (RP) is incompletely understood. In particular, it is unclear whether there is a relationship between neurovascular bundle (NVB) sparing and post-RP urinary continence.
Objective: To review systematically the association of NVB sparing in RP with postoperative urinary continence outcomes and synthesise the results in a meta-analysis.
Evidence acquisition: This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement. PubMed, Medline, and Cochrane Central Register of Controlled Trials were searched (December 2013), yielding 3413 unique records. A total of 27 longitudinal cohort studies were selected for inclusion. Studies were evaluated using a predefined criteria adapted from the Cochrane Tool to Assess Risk of Bias in Cohort Studies.
Evidence synthesis: Data from 13 749 participants in 27 studies were synthesised in a meta-analysis. An assessment of the study methodology revealed a high risk of bias due to differences in baseline characteristics, outcome assessment, and the likely presence of unreported confounding factors such as meticulous apical dissection. Meta-analysis demonstrated that nerve sparing (NS) compared with non–nerve sparing (NNS) resulted in improved early urinary continence rates up to 6 mo postoperatively. Beyond this time, no significant difference was observed. This effect was seen most clearly for bilateral NS compared with NNS. A sensitivity analysis of prospective cohort studies revealed consistent results.
Conclusions: This analysis demonstrates an association between NS and improved urinary continence outcomes up to 6 mo postoperatively. NS in men with poor preoperative erectile function should be considered in the context of oncologic risk stratification because it may improve time to continence recovery. The underlying cause of the relationship between NS and continence is unknown. It may represent preservation of the intrapelvic somatic nerves supplying the rhabdosphincter or the influence of other confounding factors. Future research should be directed towards improving understanding of the anatomy of urinary continence and the pathophysiology of post-RP incontinence.
Patient summary: We found that avoiding damage to the nerves around the prostate improves urinary continence in the first 6 mo after surgery. After this time, there is no difference in continence between men who had these nerves removed and those who had them saved. This finding could be due to a true effect of saving these nerves or to a number of other factors affecting the research.

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1. Introduction

For most men with localised prostate cancer (PCa), radical prostatectomy (RP) provides excellent oncologic outcomes [1]. The trifecta of optimal outcomes following RP includes preservation of continence and potency in addition to oncologic control [2] but is only achieved by 62–70% of patients in centres of excellence [2,3]. Despite improvements in surgical technique, urinary incontinence and erectile dysfunction, in particular, significantly affect quality of life (QoL) in many men. Reported 12-mo potency rates following robot-assisted RP are highly variable, ranging from 54% to 90% [4]. Post-RP incontinence also remains a devastating problem for many men. On average, 16% of men are incontinent at 12 mo (using a no-pad definition) [5]. Post-RP incontinence is associated with a decreased QoL [6] that may manifest as a preoccupation with leakage avoidance and/or location of bathrooms, and feeling dirty, helpless, and embarrassed [7].

Since Walsh and Donker's description of the pelvic course of the cavernous nerves [8] and the subsequent development of the NS RP, postoperative potency outcomes have improved dramatically. Whether or not there is also an association between sparing the neurovascular bundle (NVB) and urinary continence outcomes is a controversial but important clinical question that previous systematic reviews have not addressed. If sparing the NVB has a true effect on postoperative urinary continence, then preservation of continence should be an independent indication for nerve sparing (NS). This question is particularly contentious because there is no clear anatomic basis for such a relationship [9]. The classical view is that nerve supply to the external striated rhabdosphincter comes from the somatic pudendal nerve [10–13], which takes its course caudal to the levator ani and therefore should be protected from operative injury and not influenced by NVB sparing. However, some authors have posited the existence of an intrapelvic somatic supply to the rhabdosphincter [14–16].

The primary objective of this study was to conduct a systematic review and meta-analysis to evaluate if in men having RP, sparing the NVB is associated with postoperative urinary continence outcomes. The secondary objective was to assess if NS is associated with the timing of urinary continence return postoperatively.

2. Evidence acquisition

This systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement [17]. A study protocol was written a priori (Supplement 1) defining the search strategy (based on the patient, problem, or population; intervention; comparison, control, or comparator; and outcomes [PICO] framework), study eligibility criteria, data collection, and a synthesis process.

2.1. Search strategy and eligibility criteria

A search of the PubMed, Medline, and Cochrane Central Register of Controlled Trials electronic databases was conducted (December 2013) to identify potentially relevant studies. The search was limited to studies published from 1982 onwards, given that NS surgery was not formally described before that time.

Studies reporting urinary continence outcomes in men who had an NS RP (intervention) for PCa compared with non–nerve-sparing (NNS) RP (control) were included. Subcategories evaluated included bilateral nerve sparing (BNS), unilateral nerve sparing (UNS), or nerve sparing (NS unspecified). This study did not attempt to evaluate more specific or alternative types of NS such as the effects of intra/interfascial versus standard, risk-stratified NS, or sural nerve grafting. If these classifications were used in studies, results were included if they could be pooled to evaluate one of the intervention groups of this systematic review (ie, UNS, BNS, or unspecified NS). Studies were not selected or excluded based on surgical approach.

The following terms were searched: [“prostatic neoplasms” OR “prostate” OR “prostate cancer”] AND [“prostatectomy OR “radical prostatectomy”] AND [“urinary incontinence” OR “postoperative complications” OR “continence”].

Relevant original longitudinal cohort studies identified that had adequate data for meta-analysis were included. Authors were contacted if missing data were identified for high-quality studies only. Observational studies with no comparison group (ie, single-cohort studies) and cross-sectional studies were excluded. Studies in languages other than English were excluded. Manual searching of reference lists of relevant publications including reviews was performed to identify additional potentially relevant studies.

When multiple publications were identified from the same institution and overlapping data sets were used, the publication with the most recent data was included in the meta-analysis.

2.2. Outcome

The primary outcome of this systematic review was postoperative urinary continence. Continence rates from individual studies were pooled in a meta-analysis.

We initially aimed to also review results from studies reporting urinary domain health-related quality of life (HRQoL) results. Seven relevant studies were identified that reported HRQoL [18–24]. However, they were significantly heterogeneous, and it was deemed unsuitable to combine their results.

The secondary outcome for this review was to investigate the effect of NS on the timing of urinary continence return after RP.

2.3. Study selection and data extraction

Two independent authors screened all search results (titles and abstracts). The full text of any potentially relevant publications was retrieved for review, and studies were selected based on the selection criteria previously outlined.

Data were extracted and studies analysed independently by two authors using a standardised data collection form