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Interrupted versus continuous suturing for vesicourethral anastomosis during radical prostatectomy: protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction Radical prostatectomy is the mainstay of treatment for prostate cancer. The vesicourethral anastomosis is a critical step, which most likely impacts urinary continence and urethral stenosis. To date, it still remains unclear whether interrupted and continuous suturing for the anastomosis have different outcomes. Therefore, the aim of this systematic review and meta-analysis is to compare different suture techniques for vesicourethral anastomosis in terms of surgical and functional parameters.

Methods and analysis A comprehensive literature search will be conducted covering MEDLINE, Embase, Web of Science, the Cochrane Central Register of Controlled Trials and ClinicalTrials.gov. Studies comparing interrupted versus continuous suturing will be included in the analyses. No language restrictions will be applied. Screening, data extraction, statistical analysis and reporting will be done in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Quality assessment will be performed with the help of the Cochrane Collaboration's tool for assessing risk of bias and the Newcastle-Ottawa Scale for assessing quality of non-randomised studies. The quality of evidence will be evaluated with the Grading of Recommendations Assessment, Development and Evaluation. The primary outcome will be the time until removal of the urinary catheter. Secondary outcomes include rate of extravasation, length of hospital stay, time needed to perform the anastomosis, continence level at defined postoperative intervals and development of urethral strictures. Quantitative analysis will be calculated if meaningful.

Ethics and dissemination In order to meet the highest ethical and methodological standards. we followed the PRISMA Protocol 2015 checklist. Each item was answered appropriately. For systematic reviews the ethical issues are strictly methodological as only data that were published earlier will be used. The full manuscript will be submitted to a peer-reviewed journal. Furthermore, the results will be presented on national and international congresses.

Trial registration number International prospective register of systematic reviews PROSPERO CRD42017076126.

Strengths and limitations of this study

- Radical prostatectomy is one of the most commonly performed procedures in urological oncology, thus affecting a tremendous number of patients.
- To our best knowledge, this will be the first systematic review and meta-analysis comparing interrupted versus continuous suturing for vesicourethral anastomosis during radical prostatectomy.
- Subgroup analysis will differentiate between different surgical approaches in order to address a holistic but detailed overview for the individual patient.
- The reporting of outcome parameters might be variable among studies. Therefore, it remains to be determined what outcomes are feasible for pooling of the data.
- Quality assessment of included studies will provide an overview of the strength of evidence for each outcome.

BACKGROUND

Prostate cancer (PCa) is the most frequently occurring cancer among men worldwide,[1 2] with a cancer-specific mortality of about 2%–3% in the Western world.[3 4] The mainstay of curative treatment, besides radiotherapy, is radical prostatectomy (RP). RP is chosen as primary treatment in about 50% of patients, compared with 25% who choose some kind of radiotherapy.[5]

During the last two decades different surgical approaches to RP including open, laparoscopic (LRP) and robotic-assisted prostatectomy (RARP) were established. These have been shown to be comparable with regard to oncological outcome, postoperative complications and continence.[6–8] Despite its effectiveness, RP remains a challenging procedure with a high impact on the patient's life, including continence, erectile function and quality of life.

The vesicourethral anastomosis (VUA) is a crucial and challenging step of RP even in the hands of experienced surgeons.[9 10] Although the quality of the VUA is unlikely to have an impact on oncological outcome, it strongly affects functional outcome and thus quality of life.[11] Notably, VUA leakage was found to be the predominant risk factor for postoperative incontinence.[12] Furthermore, VUA quality possibly influences the development of postoperative vesicourethral anastomotic stenosis (VUAS), which occurs in around 2.1%–7.5% of patients.[13–15]

The suture technique, specifically interrupted (IS) versus continuous suturing (CS), might influence the outcome of the VUA. In general, CS is usually faster and associated with a lower leakage rate.[16 17] On the other side, CS raises concerns for a higher incidence of strictures.[18]

Currently, there is a lack of clear evidence concerning a conceivable superiority of IS or CS for VUA. Therefore, the aim of this systematic review and potential meta-analysis will be to compare different suture techniques for VUA in patients undergoing RP.

METHODS/DESIGN

The protocol of the planned systematic review and potential meta-analysis is written in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol (PRISMA-P) 2015 checklist.[19] Additionally, the systematic review and meta-analysis was registered with the international prospective register of systematic reviews PROSPERO (CRD42017076126).[20]

Search methodology

A systematic literature search will be conducted according to the population, intervention, control and outcomes (PICO) criteria.[21] In order to retrieve as much evidence as possible, the search will include Medical Subject Headings (MESH) terms and free text combined with Boolean operators. The search will include synonyms of the following terms: single suture/continuous suture/vesicourethral/anastomosis/prostatectomy/barbed. A previous screening of relevant articles will help to identify synonyms for suture techniques and further relevant keywords (eg, vesicourethral vs urethrovesical or single suture vs interrupted suture).

The combined search term will be modified for each database and applied to MEDLINE (via PubMed), Embase, Web of Science and the Cochrane Central Register of Controlled Trials and ClinicalTrials.gov. By this approach, published, unpublished and ongoing trials will be detected. After removing all duplicates, the remaining articles will be uploaded to covidence.org.[22] Furthermore, the reference section of all included articles and previous reviews will be searched manually, and experts will be consulted to identify additional literature. In case of missing data, the corresponding authors will be contacted directly.

Study selection and data extraction

Two researchers will independently screen title and abstract of each article. If considered eligible, the full text will be retrieved and reviewed for eligibility again. Potential disagreement in one of those steps will be solved by consensus and, if necessary, with the help of a third reviewer. This process will be documented in detail in order to create a PRISMA flow diagram.

Eligibility criteria

Studies are considered eligible if they compare IS versus CS. All types of studies will be included (randomised controlled trial (RCT), non-RCT, observational studies). No language restrictions will be applied. If needed, studies will be translated by professional translators.

Exclusion criteria

Studies that focus on experiments and operations on animals, models or cadavers will be excluded. Additionally, if a posterior reconstruction was done previously to the VUA in one study group only, these studies or groups will be excluded from analysis. Posterior reconstruction has a potential impact on the operative outcome, which was investigated elsewhere.[23] Furthermore, studies with no comparison group or none of the defined outcome measures analysed will be excluded. Studies reporting a perineal approach for RP, an indication for RP other than PCa, or salvage RP will be excluded.

Data extraction

All extracted data will be filled in a dedicated data sheet (Microsoft Excel, Redmond, Washington, USA). The data sheet will then be tested on five studies to prove its suitability. Two reviewers will extract the data independently from each other. The following information will be retrieved:

1. Methods: authors, year of publication, journal, type of study, country, registration of trial.
2. Patients: mean age, cancer stage, prostata-specific antigen (PSA) level, Gleason score, body mass index.
3. Interventions: intervention technique (open/LRP/RARP), suture technique (continuous/interrupted), suture material (Vicryl/monofilament).
4. Outcome: primary and secondary outcome of each study including but not limited to the following:
   a. Catheterisation time.
   b. Anastomotic time.
   c. Urinary incontinence at reported intervals.
   d. Leakage/extravasation.
   e. VUAS.
   f. Hospital stay.
   g. Prostate size/specimen weight.

Endpoints

The primary endpoint will be catheterisation time. Secondary endpoints will include rate of extravasation, urinary incontinence at 3, 6 and 12 months postoperatively, development of VUAS, length of hospital stay, and time to perform the VUA intraoperatively.

Subgroup analysis

In order to evaluate the best surgical option for VUA, various comparisons of suture techniques and surgical approach will be performed. The following subgroup analysis will be done if the extracted data appear suitable:

1. Interrupted suture versus continuous suture
   a. in minimally invasive approaches.
   b. in LRP.
   c. in RARP.
   d. in open surgery.
   e. in open surgery versus minimally invasive approaches.
   f. in LRP versus RARP.

Quality assessment

Quality assessment of RCTs will be done with the help of the Cochrane Collaboration's tool for assessing risk of bias in randomised trials.[24] This tool incorporates the following seven domains: (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessment, (5) attrition bias, (6) selective reporting and (7) anything else, ideally prespecified (eg, funding). All these domains can be rated as either high, low or unclear.

Quality assessment of all non-RCTs will be done with the Newcastle-Ottawa Scale for assessing quality of non-randomised studies in meta-analyses.[25] Three domains—(1) selection, (2) comparability and (3) exposure—will be rated with a maximum total score of nine stars.

Congress abstracts and further material, which can be considered as 'grey literature', will be rated with the lowest possible quality. This literature will be reported separately and not included in statistical testing.

Quality of evidence

The strength of the body of evidence for relevant endpoints will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool.[26] According to GRADE the quality of evidence can be rated as high, moderate, low and very low.

Statistical analysis

In case the extracted data are appropriate for pooled analyses (eg, similar techniques and patients), a meta-analysis will be performed. Dichotomous data will be analysed using the Mantel-Haenszel model and reported as OR. In case of continuous data, inverse variance models will be used and reported as mean difference. Forest plots will be used for visualisation of the results.

The heterogeneity of studies will be calculated using the I^2 index. An I^2 value of 0%–25% represents insignificant heterogeneity; >25%–50% low heterogeneity; >50%–75% moderate heterogeneity; and >75% high heterogeneity.[27] Insignificant heterogeneity will be calculated using a fixed-effects model and with a low or moderate heterogeneity using a random-effects model. If concerns for high heterogeneity exist, a sensitivity analysis will be performed. In case of a different reporting pattern, mean and SD values (eg, trials reporting median and range/IQR) will be transformed according to Hozo *et al* and Higgins and Green.[28 29] Funnel plots will be used to visualise publication bias. For other bias, a risk of bias assessment figure will be used. For all calculations, the Review Manager V.5.3 (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark) will be used.

A P value of less than 0.05 will be considered as statistically significant.

DISCUSSION

Over 90 000 RPs are performed per year in the USA[30] and about 25 500 in Germany.[31] Due to this high volume, even small differences in surgical outcomes can possibly affect a great number of patients. Therefore, we aim to increase the level of evidence concerning the optimal suture techniques for VUA. Our results might help to further standardise the procedure and to optimise functional outcome of patients undergoing RP for PCa.

In our analyses, the time until removal of the urinary catheter will be used as the primary outcome, as it is also a direct indicator for length of hospital stay and might have a positive influence on continence.[32] Furthermore, it is likely to be stated in the majority of studies, as its assessment is simple and thus little differences between the included studies are expected. In contrast, continence level or quality of life is commonly measured by different scores, making comparison more difficult.[33 34]

Whereas the prevailing aim of the study is to assess differences between IS and CS for VUA in general, subgroup analysis might help to identify the optimal combinations of technique and surgical approach (open vs LRP/RARP). In case of low sample sizes, the studies will be cumulated and subgroup analysis will only be performed if meaningful.

Following the 'best evidence approach' and in order to gather all existing literature, we chose to include RCTs and non-RCTs and observational studies. Whether non-RCTs should be included in systematic reviews and meta-analyses is controversial. Some argue that only RCTs provide the highest scientific quality.[35] Without appropriate randomisation, studies are prone to confounding bias and to overestimate or underestimate the effect of interest.[29] In contrast, randomisation is not feasible for some research questions.[36 37] Besides, observational studies might reflect daily clinical work in a more realistic way.[38] Moreover, grey literature (eg, congress presentations, registered trials) is generally considered to be of poor quality because detailed information on methodology and randomisation is often impossible to reconstruct. Nonetheless, grey literature can be important because it often contains results that were not published since they did not show significant findings and could therefore address publication bias.[39 40] In order to provide a holistic overview, grey literature will be included but marked as such. In addition, it will not be part of the meta-analysis, and conclusions will be drawn extremely carefully. Finally, the comprehensive literature search will

also help to detect alternative surgical strategies that are not commonly used and could be of interest for future research.

In summary, the systematic review and meta-analysis will help to determine if there is any difference in CS or IS for VUA and if one technique is superior to the other. Furthermore, quality assessment of the included studies will yield if further well-designed studies are necessary.

Trial status

- Preliminary searches: started.
- Piloting of the study selection process: started.
- Formal screening: not started.
- Date extraction: not started.
- Risk of bias assessment: not started.
- Data analysis: not started.

Draft of search strategy for MEDLINE

("Prostatectomy"[Mesh]) OR (vesicourethral) OR (vesico AND urethral) OR (urethrovesical) OR (urethro* AND vesical) OR (VUA) OR (prostatectomy))*

AND

((running) OR (running AND sutur*) OR (running* AND knot*) OR (interrupted) OR (interrupted* AND sutur*) OR (interrupted* AND knot*) OR (single) OR (single* AND sutur*) OR (single* AND knot*) OR (velthoven) OR (barbed* AND sutur*) OR (barbed) OR (sutur*) OR (knot*))*

AND

(("Anastomosis, Surgical"[Mesh]) OR (anastomo) OR (re*anastomo*) OR (reanastomo*) OR (reconstruction))*

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