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Systematic review of reported outcomes and outcome measures in randomized controlled trials on apical prolapse surgery

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Synopsis: We reviewed variations on reported outcomes and outcome measures in apical prolapse interventions. Development of a core outcome set is warranted based on our results.

Abstract

Background: Evidence on efficacy and safety of pelvic organ prolapse interventions is variable, and methodological flaws preclude meaningful synthesis of primary research data.

Objective: To evaluate variations in reported outcomes and outcome measures in randomized controlled trials (RCTs) on apical prolapse surgical interventions.

Search strategy: We searched Cochrane, EMBASE, MEDLINE, and Scopus for English-language articles published from inception to September 30, 2017, using the terms “management”, “repair”, “operation”, and “pelvic organ prolapse”.

Selection criteria: RCTs on apical prolapse surgical treatment.

Data collection and analysis: Outcomes and outcome measures were identified and categorized into domains. Studies were evaluated for quality of outcomes. Descriptive statistics were used to calculate frequencies.

Main results: Forty-three RCTs were included. Seventy-six outcomes and 66 outcome measures were identified. Bladder and ureteric injury were the most commonly reported intraoperative complications (19/31 studies; 61%). Quality of life was assessed by 19 different instruments and questionnaires. Fourteen (45%) of 31 studies used recurrence of prolapse as a postoperative anatomical outcome.

Conclusions: Substantial variation in reported outcomes and outcome measures was confirmed, precluding comparisons across trials and synthesis of the results. Development of a core outcome set will enable high-quality meta-analyses to be performed in the future.

PROSPERO registration: CRD42017062456.

1 INTRODUCTION

Surgical procedures for the treatment of apical prolapse (vault or uterine) can be undertaken vaginally or abdominally, open or laparoscopically. The vaginal route is more commonly used [1,2] as it is associated with quicker recovery and shorter operative time and hospitalization.[3]

Apical prolapse is often accompanied by anterior or posterior vaginal wall prolapse.[4] Surgical techniques for its treatment include hysterectomy, sacrospinous fixation (uni- or bilaterally), uterosacral ligament suspension and sacrocolpopexy, and variations.[5] Selection of the procedure can depend on the surgeon’s experience, the patient’s symptoms and history (including age, the woman’s clinical status and/or desire, prolapse recurrence or none), and anatomical considerations.

Heterogeneity in methodology and specifically in reported outcomes in randomized trials prohibits the use of data in systematic reviews and meta-analyses, thus preventing firm conclusions and consensus in the clinical application of the research evidence. Variation in outcome measures renders this task even more challenging.[6,7]

We aimed to identify and classify all the reported outcomes and outcome measures in randomized controlled trials on apical prolapse interventions.

2 MATERIALS AND METHODS

This systematic review is part of the work of CHORUS: An International Collaboration for Harmonising Outcomes, Research and Standards in Urogynaecology and Women's Health (https://i-chorus.org/). Ethical approval was not required.

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline to report the search and selection of studies. Cochrane, EMBASE, MEDLINE, and Scopus databases were searched from inception to September 30, 2017, using the Medical Subject Headings (MeSH) "management", "repair", "operation", and "pelvic organ prolapse". We included English-language randomized controlled trials of apical (vaginal vault, cervix, or uterine) prolapse. Exclusion criteria were ecological studies, retrospective studies, non-randomized studies, and case reports. Studies of pelvic organ prolapse that did not specify apical or uterine prolapse in their methods were also excluded. Secondary analysis studies or studies that used the same population to the initial intervention were added, but duplicate outcomes were described only once. For calculations of the frequencies of some outcomes, we considered only the primary trials as denominators, as these outcomes may not be relevant in secondary studies.

Two researchers (CD, AE) performed the study selection. Discrepancies were resolved by the senior author (SKD). Selected studies were classified for methodological and outcomes quality independently by two authors (CD, AE) using the Management of Otitis Media with Effusion in Cleft Palate (MOMENT) score system [8]. This score evaluates the presence of a primary outcome, clear definition of the primary outcome for reproducible measures, the presence of secondary outcomes and its definition for reproducible measures, the rationale behind the definition of outcomes, and whether the methods that were used are designed to improve appropriately the quality of measures. An arbitrary decision was made to define studies of high quality as those scoring at least 4 points.

This review was registered with the International Prospective Register of Systematic Reviews (PROSPERO; registration number CRD42017062456).

3 RESULTS

We included 43 articles (File S1), of which 31 were primary studies and 12 were follow-up studies (Table S1) (Fig. 1). Quality of outcomes among the studies are described in Figure 2, according to MOMENT score. Seventy-six reported outcomes and 66 outcome measures were identified (Table 1).

Mesh/graft prostheses were used in 22 (71%) of 31 trials and erosion was the most frequently reported outcome/complication in studies that used mesh for the correction of apical prolapse. (15/22 studies; 68%) Bladder and ureteric injury was overall the most frequently reported intraoperative complication (19 studies; 61%). Estimated blood loss was reported in 16 trials (51%), but only four studies (13%) quantified the loss, and two used a decrease in hemoglobin level to measure it.

Abdominal pain was reported in 14 (45%) of the 31 primary studies, dyspareunia in 13 (42%), and vaginal pain in four (13%). Being sexually active was the most frequently reported sexual outcome (10 studies; 32%). Urinary incontinence was evaluated in six (19%) studies and specifically stress urinary incontinence in 15 (48%) and urgency incontinence in 11 (35%). De-novo urinary incontinence and de-novo urgency incontinence were reported in 10 (32%) and six (19%) studies, respectively. Voiding dysfunction was found in 18 (58%) studies and de-novo voiding dysfunction in one (3%) study. Only one study reported on obstructed defecation.

Efficacy of the procedure was evaluated by recurrence of prolapse (14 studies; 45%) and the need for reoperation for prolapse (17 studies; 55%). Patient satisfaction was evaluated in eight (26%) studies. On the other hand, the surgeon's satisfaction was mentioned in only one (3%) study. The most common questionnaire for quality of life was the Pelvic Floor Distress Inventory (PFDI) (8 studies; 26%), followed by the Urinary Distress Inventory (UDI) (6 studies; 19%).

4 DISCUSSION

This systematic review identified a wide variation in outcomes and outcome measures for apical prolapse in the selected trials. Urinary tract-related outcomes were extensively reported.

Different studies are designed based on variable research priorities and objectives. The choice of outcomes to study will therefore depend on these priorities. Furthermore, the selected outcomes may depend on the intervention and a number of related characteristics, the population, and the researcher's interest.

A wide range of interventions will inevitably be associated with wide variation in reported outcomes and outcome measures, especially considering that prolapse of the anterior and posterior vaginal wall are usually accompanied by a concomitant apical defect. Concomitant procedures and multicompartmental surgery are also likely to have variable reported outcomes when evaluated in a trial. Pain may be underreported in some trials as, in our review, pain-related outcomes featured in only half of the studies by comparison with mesh-related outcomes. We noted that outcomes tend to be more associated with the procedure itself than overall quality of life parameters.

Different instruments for measuring outcomes have been used, resulting in a variation of terms for the same outcome. The selected outcome measures also resulted in a difficulty to compare outcomes. Blood loss was measured by visual analysis, hematocrit count, and weight of towels, and the cut-off between normal and heavy bleeding ranged from 300 mL to 500 mL.

We followed a rigorous and previously applied methodology to ensure that our systematic review provides robust findings. Our study included randomized controlled trials only and certainly could not identify all outcomes that may be present in excluded studies. Other types of studies may report outcomes with even wider variation. Inherent publication bias or selective reporting bias in the primary

studies can be challenging to identify and weigh in a systematic review. Another challenge has been the variety of ways to classify and categorize outcomes in groups. Although such categorization facilitates the process of prioritization and selection of outcomes to be included in future Delphi surveys, we believe that any misclassifications would not limit the overall value of our findings.

The aim of this study was to identify previously reported outcomes and create a “bank” of outcomes to be considered in a future Delphi survey for a consensus in establishing core outcome sets in apical prolapse studies. This may help limiting research waste by setting priorities, based on important questions for studies with high methodological quality.[9] We would propose an interim list of outcomes to be included in studies while our work on establishing consensus is still underway. This may facilitate comparisons of studies and meta-analysis and reduce methodological bias in trials. Until a core outcome set has been developed, we propose use of the two most frequently reported outcomes of each category as a minimum: operative (operating time, number of sutures); intraoperative adverse events (bladder or ureteric injury, estimated blood loss); postoperative adverse events (infection, hematoma); morbidity management (length of stay, blood transfusion); success and failure (reoperation for prolapse, recurrence of prolapse); mesh-related complications (mesh erosion, mesh excision); urinary tract function (voiding dysfunction, stress incontinence); sexual outcomes (sexually active, sexual function); and pain (abdominal pain, dyspareunia). Patient-reported outcomes (patient satisfaction, return to daily activities) and validated questionnaires for quality of life assessment (PFDI, UDI) are also recommended for use as core outcome sets. Beyond this minimum of proposed outcomes, researchers are encouraged to evaluate and report on additional outcomes.

Given the wide variety of interventions for the treatment of apical prolapse and the associated variable outcomes that our systematic review identified and evaluated, establishing a minimum set of core outcomes for such studies is of paramount importance to enable comparisons and synthesis of findings from different studies.

The findings of this review and a series of similar studies will form the basis for further evaluation of the currently used outcomes and outcome measures in studies in this area as well as development of a consensus on core outcome sets that will be proposed for use in future trials. Harmonization of outcomes and outcome measures will enable research evidence to better inform clinical practice.

Author contributions

TRdML contributed to data collection, data analysis, and manuscript writing. VP contributed to data analysis, manuscript writing, and critical review. CD and AE performed the study selection and contributed to data collection, data tabulation, and manuscript writing. JMH, CB, and GF contributed to data analysis, manuscript writing, and critical review. SKD was responsible for project development and contributed to data tabulation, manuscript writing, manuscript editing, and critical review. All authors approved the final version for publication.

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Conflicts of interest

The authors have no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

File S1. Selected studies for systematic review on apical prolapse intervention.
Table S1. Description of studies.

TABLE 1 Outcome and outcome measure reporting.

Outcome	Trials (n)	Outcome measures	Trials (n)
Operative			
Operating time	22	Surgical records	12
		Unclear/not reported	10
Number of sutures	2	Unclear/not reported	2
Surgeon satisfaction	1	Visual Analogue Scale (0–10)	1
Intraoperative adverse events			
Bladder or ureteric injury	19	Unclear/not reported	18
		Cystoscopy	1
Estimated blood loss	16	Unclear/not reported	12
		Fall in hemoglobin	2
		Estimated by anesthetist	1
		Volumetry and weight of swabs	1
Bowel injury	14	Unclear/not reported	14
Hemorrhage	7	Unclear/not reported	5
		Need for transfusion	2
Nerve injury	3	Unclear/not reported	3
Levator muscle avulsion	1	Translabial ultrasound	1
Vascular injury	1	Unclear/not reported	1
Postoperative adverse events		Clavien-Dindo II classification	3
		Adverse events forms	1
		ICS/IUGA prosthesis complication chart	1
		Interviews	1
Infection	20	Unclear/not reported	20
Hematoma	9	Unclear/not reported	9
Bowel obstruction	4	Unclear/not reported	4
Abscess	3	Unclear/not reported	3
Granulation tissues	3	Unclear/not reported	3
Incisional hernia	3	Unclear/not reported	3

Suture cutting/erosion/exposure	3	Unclear/not reported	3
Vaginal bleeding	3	Unclear/not reported	3
Vaginal erosion	2	Unclear/not reported	2
Fistula	1	Unclear/not reported	1
Seromas	1	Unclear/not reported	1
Vaginal cuff laceration	1	Unclear/not reported	1
Vaginal stricture	1	Unclear/not reported	1
Additional interventions to manage morbidity			
Length of stay	22	Unclear/not reported	15
		Administrative data	7
Blood transfusion	12	Unclear/not reported	12
Reoperation for complications	5	Unclear/not reported	5
Conversion to alternative route	4	Unclear/not reported	4
Cystotomy	4	Unclear/not reported	4
Readmission	4	Unclear/not reported	4
Admission to intensive care unit	1	Unclear/not reported	1
Success and failure			
Reoperation for prolapse	17	Unclear/not reported	17
Recurrence of prolapse	14	Pelvic Organ Prolapse Quantification System	14
		Baden-Walker scale	2
		Ring forceps	2
		Standardized questions	2
		Halfway International Continence Society system	1
		Magnetic resonance imaging	1
		Ultrasound assessment	1
		Visual Analogue Scale (0–10)	1
		International Consultation on Incontinence Questionnaire–Vaginal Symptoms	1
		Prolapse Symptom Inventory	1
		Urinary Distress Inventory	1
Mortality			

Mortality	3	Unclear/not reported	3
Mesh related complications			
Mesh erosion	15	Unclear/not reported	14
		Pelvic examination	1
Mesh resection	10	Unclear/not reported	10
Mesh infection	3	Unclear/not reported	3
Mesh contraction	1	Unclear/not reported	1
Mesh extension	1	Unclear/not reported	1
Mesh rejection	1	Unclear/not reported	1
Neurological			
Stroke	1	Unclear/not reported	1
Respiratory			
Pulmonary embolism	2	Unclear/not reported	2
Pneumonia	1	Unclear/not reported	1
Gastrointestinal			
Irritative colorectal symptoms	11	Unclear/not reported	3
		Colo-Recto-Anal Impact Questionnaire	2
		Ano-rectal function tests	1
		Constipation severity score	1
		Defecation diary	1
		Defecography	1
		International Consultation On Incontinence Questionnaire	1
		Wexner score	1
Fecal incontinence	3	Unclear/not reported	3
Digital assistance to defecate	1	Unclear/not reported	1
Obstructed defecation	1	Unclear/not reported	1
Rectal prolapse	1	Unclear/not reported	1
Urogenital			
Voiding dysfunction	18	Unclear/not reported	11
		Urodynamic study	3
		Standard questions	2

		Urinary Impact Questionnaire	1
		Voiding diary	1
Stress incontinence	15	Stress test	4
		Urodynamic study	3
		Incontinence Severity Index	2
		Urinary Distress Inventory	2
		Birmingham Bowel and Lower Urinary Tract Symptoms Questionnaire	1
		International Consultation On Incontinence Questionnaire	1
		Sandvik Index	1
		Standard questions	1
Urge incontinence	11	Unclear/not reported	10
		Urodynamic study	1
De-novo stress incontinence	10	Unclear/not reported	10
De-novo urge incontinence	6	Unclear/not reported	6
Urinary incontinence	6	Unclear/not reported	6
Urinary frequency	2	Unclear/not reported	2
De-novo voiding dysfunction	1	Unclear/not reported	1
Heaviness sensation	1	Unclear/not reported	1
Mixed incontinence	1	Unclear/not reported	1
Nocturia	1	Unclear/not reported	1
Occult stress incontinence	1	Urodynamic study	1
Sexual outcomes			
Sexually active	10	Unclear/not reported	10
Sexual function	8	Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire	6
		Female Sexual Function Index	1
		Questionnaire for screening sexual dysfunction	1
Sexual dysfunction	3	Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire	3
Pain			
Abdominal pain	14	Visual Analogue Scale (0–10)	7

		Analgesic/opiate requirement	3
		Urinary Distress Inventory	2
		Visual face scale	2
		Surgical Pain Scales	1
		Visual Analogue Scale (0-–00)	1
Dyspareunia	13	Unclear/not reported	12
		Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire	1
Buttock pain	4	Unclear/not reported	4
Vaginal pain	4	Unclear/not reported	3
		Vaginal electrostimulation	1
Back pain	3	Unclear/not reported	3
Neurologic pain	2	Unclear/not reported	2
Patient-reported outcomes			
Patient satisfaction	8	Patient Global Impression Of Improvement	4
		Visual Analogue Scale (0–100)	3
		Interview	1
Return to daily activities	8	Patient interview	2
		Activity Assessment Scale	2
		Convalescence And Recovery Evaluation	1
		Recovery index-10	1
		Short-form health survey	1
		Standard questionnaire	1
Nausea and vomiting	2	Unclear/not reported	2
Body image	1	Unclear/not reported	1
Fear of incontinence	1	Unclear/not reported	1
Resource utilization			
Costs	5	Administrative data	3
		Unclear/not reported	2
Number of medical visits	1	Unclear/not reported	1
Quality of life	51		
		Pelvic Floor Distress Inventory	8

		Urinary Distress Inventory	6
		Incontinence Impact Questionnaire	5
		Pelvic Floor Impact Questionnaire	5
		Short-Form Health Survey	5
		Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire	4
		Prolapse quality of life	4
		Euroqol-5 Dimensions	3
		Australian Pelvic Floor Questionnaire	1
		Defecatory Distress Inventory	1
		General and disease-specific quality of life questionnaire	1
		Hunskaar Severity Index	1
		King's College pelvic organ prolapse quality of life	1
		Pelvic Organ Prolapse Impact Questionnaire	1
		Prolapse-Specific Surgical Satisfaction Questionnaire	1
		Rand-36 Item Health Survey	1
		10-item Short-Portable Mental Status Questionnaire	1
		Telephone interview	1
		Visual Analogue Scale (0–10)	1

Abbreviations: ICS, International Continence Society; IUGA, International Urogynecological Association.

FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta- Analyses (PRISMA) flow diagram. Abbreviations: POP, pelvic organ prolapse.

FIGURE 2 Quality of outcomes among the included studies (n=43).