A systematic review on reporting outcomes and outcome measures in trials on synthetic mesh procedures for pelvic organ prolapse. Urgent action is needed to improve quality of research.

Abstract

The use of synthetic mesh in pelvic organ prolapse surgery is being closely scrutinized because of serious concerns regarding life-changing complications such as erosion, pain, infection, bleeding, dyspareunia, organ perforation and urinary problems. Randomized trials and their syntheses in meta-analysis offer a unique opportunity to assess efficacy and safety. However, outcomes and outcome measures need to be consistently selected, collected, and reported across randomized trials to be effectively combined in systematic reviews.

Aims

We evaluated outcome and outcome measure reporting across randomized controlled trials on surgical interventions using synthetic mesh for pelvic organ prolapse.

Methods

Systematic review of randomized controlled trials using synthetic mesh for the treatment of pelvic organ prolapse. The selected studies were evaluated using Jadad and MOMENT criteria. Outcomes and outcome measures were systematically identified and categorized.

Results

Seventy-one randomized trials were included. Twenty-four different types of mesh were identified. Included trials reported 110 different outcomes and 60 outcome measures. Erosion (40 trials, 78,43%), pain (29 trials, 56,86%), bleeding (31 trials, 60,78%) and dyspareunia (25 trials, 49,02%) were the most frequently reported outcomes. The longest follow up was 74 months.

Conclusions

Most randomized trials evaluating surgical interventions using synthetic mesh for pelvic organ prolapse failed to report on clinically important outcomes and to evaluate efficacy and safety over the medium- and long-term. Developing and implementing a minimum data set, known as a core outcome set, in future vaginal prolapse trials could help address these issues.

Keywords:
Core outcome sets
Efficacy
Outcome variation
Pelvic organ prolapse
Randomized controlled trials
Safety
Synthetic mesh
Systematic reviews

Introduction

Surgical interventions for the treatment of pelvic organ prolapse have been performed extensively . The International Urogynecological Association and the International Continence Society have defined mesh as ‘a (prosthetic) network fabric or structure used in general for prolapse surgery with synthetic materials’. [1] The Food and Drug Administration has recently reclassified synthetic mesh as a high-risk device. [2] Our specialty has failed many women with pelvic organ prolapse and has not lived up to one of the oldest medical principles “above all, do no harm”.

Randomized controlled trials and their syntheses in meta-analysis should offer a unique opportunity to assess the efficacy and safety of synthetic mesh for pelvic organ prolapse procedure. Although there is often no hypothesis concerning harms in trials, safety outcomes should be collected and reported as secondary outcomes. Unfortunately, the collection and reporting of safety has drawn limited attention: for example, the Consolidated Standards of Reporting Trials (CONSORT) statement published an extension for harm reporting, five years after the original statement. Without high-quality data relating to the trade-offs between benefits and harms suboptimal decisions may have been made.

The International Urogynecologial Association and the International Continence Society has engaged with standardizing the mesh complication definitions:

1. Exposure: Condition of displaying, revealing, exhibiting or making accessible;
2. Extrusion: Passage gradually out of a body structure or tissue; and
3. Perforation: Abnormal opening into a hollow organ or viscus [1]

The next challenge is to address unwarranted, unhelpful and often confusing variation in outcome selection, collection and reporting. The development and use of a core outcome

set would help to address this challenge. The first step in core outcome set development requires an evaluation of outcome and outcome reporting across published randomized trials. CHORUS is an International Collaboration for Harmonizing Outcomes, Research and Standards in Urogynaecology and Women's Health (http://i-chorus.org), aiming to address such issues in all areas of urogynaecology/female pelvic medicine and reconstructive surgery. We have recently published relevant papers on childbirth trauma and anterior prolapse surgery. [3, 4]

Therefore, the aim of the present study was to assess the consistency in outcome and outcome measure reporting among randomized trials evaluating surgical interventions using synthetic mesh for pelvic organ prolapse.

Material and methods

This systematic review has been undertaken by CHORUS: An International Collaboration for Harmonizing Outcomes, Research and Standards in Urogynecology and Women's Health and has been registered with the Prospective Register of Systematic Reviews (PROSPERO), registration number CRD42017062456. A protocol including explicitly defined objectives, study selection criteria, and data extraction methods was developed. Ethical approval for this study was not required.

Search strategy

The search strategy was performed in accordance to PRISMA criteria. The review was undertaken by searching the Cochrane Central register of Controlled Trials (CENTRAL), EMBASE and MEDLINE, from their inception to June 2018 using MeSH words pelvic organ prolapse, vaginal prolapse, bladder prolapse, cystocele, bowel prolapse, rectocele, enterocele, uterine prolapse and vault prolapse. Two researchers independently screened

each potentially relevant record on the basis of its title and abstract, and subsequently reviewed the full text of each selected study to assess eligibility. Discrepancies in initial screening between the two researchers were resolved by consensus.

We included randomized controlled trials evaluating surgical interventions using synthetic mesh for pelvic organ prolapse in English language. Non-randomized studies, observational studies, and case reports were excluded.

Two researchers independently extracted study characteristics, including methodological quality and quality of outcomes, interventions and reported outcomes. Again, any discrepancies between the researchers were resolved by consensus among the authors.

The methodological quality of the selected studies was evaluated according to modified Jadad score. This is a 5-point scale that scores 1 point for each description: randomisation; adequate method for randomisation; blinded trial described; adequate method for blinding and if the trial accounts for the patients selected. [5] The outcome quality was scored according to the MOMENT criteria (Management of otitis media with effusion in cleft palate score system), in a 6-point scale. It sums 1 point for the state of a primary outcome; if the primary outcome is defined for reproducible measures; the state of a second outcome; if the second outcome is defined as for reproducible measures; if the choice of outcome is explained and if the methods used are designed to improve appropriately the quality of measures. [6] High quality was determined for studies that reached score 4 or more in these criteria.

An inventory of outcomes reported in each study was developed. They were then organized into thematic domains by the researchers.

Articles that used the same population and intervention (secondary analyses) were defined as follow up studies and duplicated outcomes for the same population were considered only once. Year and Journal of publication were also listed and Journal impact factor was reported according to Thomson Reuters' (NY, USA) citation reports for obstetrics and gynecology. Descriptive statistics were used to characterize the trials included in the review, mapping outcomes and their methods of definition or measurement across included trials. These data were managed in Excel 2013 (Microsoft Corporation, WA, USA)

Results

In total, 2567 titles and abstracts were screened, and 234 potentially relevant studies were examined in detail (Figure 1). Fifty-one randomized trials met the inclusion criteria. Twenty published follow-up studies were included. Quality of studies and outcomes are presented in Table 1. Year of publication ranged from 2000-2017 in vaginal and 2003-2015 in abdominal studies. The mean JADAD and MOMENT score among all studies were 3.59 and 4.63 respectively. (Table 1) Description of interventions and mesh used are displayed in Tables 2 and 3. The longest patient follow up was reported as 74 months. The mean follow up was 19.34 months.

Reported outcomes

In total, 110 different outcomes were identified. They were divided into domains (adverse events, clinical effectiveness, efficacy and cost effectiveness) and described in Table 4. The most common outcomes were mesh exposure (40 studies, 78.43%), operative time (38 studies, 74.50%), blood loss and hospital stay (32 studies each, 62.74%).

Twenty-four different meshes were described in the included studies. Studies on vaginal

meshes reported more voiding symptoms and dysfunction (21 times documented in the studies) than the ones on abdominal approach (6 times). Stress urinary incontinence was the most frequently reported outcome for urinary incontinence (26 studies, 50.98%), 3 times more in vaginal than abdominal route. Also, vaginal studies presented more on sexuality in women after the procedure, and dyspareunia was 4.2-fold more cited in vaginal than in abdominal mesh studies (21 and 5 studies, respectively).

Mesh-related outcomes

In relation to mesh, there were 20 different outcomes. Mesh related outcomes were much more frequently reported in studies on vaginal mesh compared to those on abdominal insertion of mesh (87 times and 25 times respectively). Emphasis on mesh excision, mesh exposure and mesh removal were much more often observed in studies evaluating prolapse repairs using mesh via vaginal route.

A high number of studies presented data as length of hospital stay (32 studies, 62.74%) and operative time (38 studies, 74.50%). These outcomes were more frequently reported than bladder injury (20 studies, 39.21%) and abdominal and pelvic pain (30 studies, 58.82%).

Variations in outcomes measures

Sixty outcome measures are listed in Table 5. Visual Analogue Scale (VAS) was used in 32% of the studies for different purposes (pain, patient satisfaction, degree of bother). Only 72.54% of the studies reported POP-Q measurement for treatment effectiveness evaluation. Baden-Walker scale was reported in 2 studies. Eighteen studies described physical examination as a part of the evaluation (35.29%).

A few studies reported on the amount of intraoperative bleeding, but there was no variation on this measurement. Only in one study the weighing of towels was used to measure bleeding, while 6 studies used hemoglobin or haematocrit.

Efficacy outcomes

Outcomes reported efficacy as “cure” or “success” (27 studies, 52.94%) or “failure” (10 studies, 19.60%). Some studies evaluated success or failure only anatomically, while others included patient satisfaction. Some used the term ‘cure’ to show optimal results, making the anatomical evaluation variable between optimal and satisfactory success outcome. POP-Q assessment was used in all studies to evaluate outcome of surgery (success if POP-Q < stage 2, failure if POP-Q ≥ stage 2). A reported measure of success was the lack of prolapse recurrence indirectly evaluated as no need for operation.

Quality of life evaluation

Quality of life was assessed by validated questionnaires and scores in the majority of studies. All the questionnaires used are listed in Table 4. We identified 34 different tools, and questionnaires being part of another questionnaire (as CRADI belongs to PFDI). The most commonly used questionnaire was the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12), featured 14 times (28%), followed by Pelvic Floor Distress Inventory (PFDI) and Pelvic Floor Impact Questionnaire (PFIQ), identified in 11 (22%) and 10 (20%) studies, respectively.

Discussion

Summary of main findings

Our systematic review demonstrated a wide variation both in reported outcomes and outcome measures in most trials on POP surgery. Among the reported outcomes, mesh-related, intraoperative data and complications and anatomic results were the most variable ones. Post-operative urinary symptoms and functional outcomes were more extensively presented in studies on vaginal procedures.

Interpretation

It is clear that the identified variations in outcomes would preclude comparisons and combinations of the findings in a meta-analysis. In addition, these wide variations may be responsible at least partly for the inconsistent and often conflicting evidence and controversies around mesh research evidence.

Variations in outcomes may be secondary to several inherent methodological factors in surgical trials, including surgical techniques, surgeon's skills, type of instruments and material used as well as demographic characteristics of the patients. However, superimposing these often unavoidable variations with additional heterogeneity based on the selection of outcomes and outcome measures, will inevitably result in an unnecessarily compounded overall heterogeneity of the primary trials.

Certainly, the results may also be somehow affected by the significant and rapid changes in reconstructive pelvic surgery which have occurred in the last two decades, moving towards minimally invasive surgery (laparoscopic/robotic). The outcomes reflect also surgical routes and techniques. Studies on laparoscopic procedures may report outcomes related to length of hospitalization more than those on open abdominal techniques.

Strengths and limitations

To our knowledge, this is the first systematic review evaluating the quality of randomized controlled trials and analyzing these outcomes and outcome measures. We followed a rigorous search strategy and the assessment of the studies was as standardized as possible following the methodology of previous publications in this field. [3, 7]

However, as most studies of this type, we acknowledge the limitation of missing out reported outcomes from non-randomized trials which were excluded from our study. The rationale for analyzing outcomes of randomized and non-randomized studies separately follows the conventional approach of performing meta-analysis and systematic reviews of randomized and non-randomized studies separately. Moreover,only studies in English language were included as this criterion was predefined in the present systematic review. One of the main reasons involves possible complexities arising from terminology and definitions in the area of pelvic medicine across different languages, which would possibly influence the taxonomy and classifications of outcomes in thematic groups, without adding much essential weight into our findings given that the vast majority of randomized controlled trials would be in English language.

Categorization of outcomes and outcome domains can be undertaken through different approaches and therefore interpretation of the different groups of outcomes may vary. We did not differentiate specific outcomes to studies on specific anatomical compartment as our aim was to have a uniform approach to all prolapse trials using mesh and ideally focus on mesh related outcomes rather than creating smaller subsets with limited weight of evidence.

Recommendations

While the development of Core Outcome sets in the area of POP is still under way, we would recommend as an interim consensus the use of a short list of the most commonly reported outcomes based on our findings as a minimum set. These outcomes and outcome measures could be the three or four most commonly reported ones in each domain, including a separate domain specific for mesh. Future studies should use validated questionnaires for Quality of Life, such as Pelvic Floor Distress Inventory (PFDI), Pelvic Floor Impact Questionnaire (PFIQ) and Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ). All patients after a prolapse surgery with mesh augmentation should undergo physical examination and POP-Q measurement ideally in a long-term follow up assessment, which would facilitate the establishment of the definition of anatomical success or failure of each procedure.

Long term follow-ups for prolapse interventions using mesh have been recommended. The post-operative interval to law suits is 5.3 years for prolapse treatment with synthetic mesh. In patients treated with sling tapes concomitantly to prolapse the interval is 4.8 years. [2]

The establishment of an interim minimum set of core outcomes and outcome measures based on this review may well differ from the final set as patient involvement as well as a wider stakeholder participation is essential in this development and may influence the agreed core outcome sets.

Conclusion

Interventions for pelvic organ prolapse using synthetic mesh require additional attention for

complications and postoperative symptoms and outcomes. They are not free from failure and recurrence. Vaginal and abdominal procedures may have different success and failure rates. Their outcomes should be comparable. The development of core outcome sets for these procedures will facilitate the design of future studies and promote high quality evidence that will advise patient centered clinical practice.

Conflicts of interest: the authors report that they have no conflicts of interest

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