Biological OviTex versus synthetic graft in robotic prolapse surgery: a multicentre, phase II-III, partially randomized patient preference trial

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Main study parameter/endpoint phase II- Post-operative morbidity measured by reoperations, reinterventions, re-admissions, serious adverse events, Clavien Dindo classification and CTS classification. - The rate of rectal prolapse recurrence and…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON54397

Source
ToetsingOnline

Brief title
ProTex

Condition

- Gastrointestinal therapeutic procedures

Synonym
intussusception, Rectal prolapse

Research involving
Human

Sponsors and support

Primary sponsor: Meander Medisch Centrum

Source(s) of monetary or material Support: Health Holland PPP allowance ,TelaBio,Universitair Medisch Centrum Groningen

Intervention

Keyword: Biologic mesh, OviTex, Pelvic Floor Prolapse, Ventral rectopexy

Outcome measures

Primary outcome

Study parameters/endpoints

Main study parameter/endpoint phase II

- Post-operative morbidity measured by reoperations, reinterventions, re-admissions, serious adverse events, Clavien Dindo classification and CTS classification.

- The rate of rectal prolapse recurrence and complications (complaints, physical examination, addition research, re-operation and readmission).

Main study parameter/endpoint phase III

Constipation, incontinence and urogenital functioning (questionnaire, validated scoring system: Fecal Incontinence Severity Index (FISI), Altomare obstructive defecation score (ODS)) and Pelvic Floor Distress Inventory-20 (PFDI-20).

Secondary outcome

Secondary study parameters/endpoints

- Quality of life (QoL) pre- and postoperatively objectified primarily by the Patient Assessment of Constipation-Quality of Life Questionnaire (PAC-QoL), Fecal Incontinence Quality of Life Scale (FIQL), Pelvic Floor impact Questionnaire (PFIQ-7), Patient Global Impression of Improvement (PGI-I),

Patient Global Impression of Severity (PGI-S) and European Quality of Life Five Dimension (EQ-5D).

- Post-operative morbidity measured by reoperations, reinterventions, re-admissions, and serious adverse advents.

- Anatomic recurrence of the prolapse, measured by defecogram or MR defecography in rest and during Valsalva maneuver.

- Rate of rectal prolapse recurrence and complications (complaints, physical examination, addition research, re-operation and readmission).

- Anatomic recurrence of pelvic organ prolapse (POP) using the simplified Pelvic Organ Prolapse Quantification (sPOPQ)

- Sexual functioning pre- and postoperatively by the questionnaire Prolapse Incontinence Sexual Inventory Questionnaire (PSIQ-12).

- Length of hospital stay, peri-operative and post-operative in hospital mortality and morbidity.

- Rate of extra outpatient visits because of complaints.

Study description

Background summary

Minimal-invasive ventral mesh rectopexy (VMR) and sacrocolporectopexy (SCRP) are widely accepted treatments for patients suffering from pelvic prolapse.Choice of material used in VMR or SCRP - synthetic or biologic surgical mesh - remains subject of debate. Recent developments in usage of transvaginal mesh to repair pelvic organ prolapse (POP) in April 2019, with the Food and Drug Administration (FDA) ordering a direct stop in selling and distributing this type of mesh products, have negatively influenced the perception on surgical mesh for VMR. Currently, the most widely used mesh in VMR is synthetic and has shown good results regarding recurrence, mesh exposure and functional outcome. Although complication rates are low, the serious

complications of fistulation, erosion and dyspareunia are reasons to opt for a more expensive biological mesh. High-quality evidence of synthetic versus biological mesh is lacking, but does not stop resistance against synthetic mesh from growing. This has even led to concerns and questions about synthetic mesh use from the Dutch government addressed at the medical professionals and options for alternatives are being asked.

Biologic grafts are characterized by degradation of the implant and regeneration of host tissue. It is assumed that this process of degradation and remodeling decreases the risk of erosion and infection. However, this transformation may possibly lead to a higher chance of recurrence in the long term. Rate of recurrence, but also mesh-related complications to a lesser extent, largely depends on duration of follow-up. Since biologic graft implementation in VMR is relatively new and its usage is restricted due to higher costs, literature on biologic mesh with long term follow-up is limited. In addition, there is a significant difference in various described biological meshes. This is important to keep in mind when comparing outcome of VMR or SCP with synthetic versus biologic mesh.

In VMR there are no randomized controlled trials on synthetic versus biologic mesh. The biologic meshes studied thus far are Biodesign and Permacol. Erosion rates after VMR with Biodesign and Permacol have both been studied in three studies in total (N = 349 and N = 425 in total respectively) and show low erosion rates of 0 to 0.1%.8,9,10. In comparison, mesh related complications after VMR with synthetic non-resorbable mesh (like polypropylene) are around 2%.
2,3,5,8 Recurrence rates after synthetic mesh in VMR range between 2% and 14% after a median follow-up of 12-61 months. When comparing studies on biologic implants that report on recurrence rates there seems to be a slight difference in favor of Biodesign. Studies on Biodesign in VMR with a median follow-up ranging between 12 and 47 months show a recurrence rate around 5%. Literature on Permacol shows higher recurrence rates ranging between 5 to 14% after a median follow-up of 12 to 29 months.

In SCP allografts and xenografts have been investigated as an alternative for polypropylene. A randomized controlled trial compared SCP using polypropylene mesh with solvent cadaveric fascia lata.16 After one year of follow-up, polypropylene mesh had a higher anatomical cure rate than cadaveric fascia lata (91 percent versus 68 percent; p=0.007). Two mesh-related complications occurred in patients who received polypropylene mesh, while none occurred in the allograft group (p= 0.5). Another RCT with the same comparison and a follow-up of 5 years showed similar results, with considering cadaveric fascia not as strong of a support. Deprest et al. compared polypropylene mesh with porcine grafts in a prospective study and found xenografts to be associated with more apical failures and reoperations than with a polypropylene mesh (21 percent versus 3 percent; p = 0.01). However, there was no significant difference in functional outcomes between the two groups. An erosion rate of 11

percent was described in both groups. A more recent study showed more positive results for xenograft use.

Although Biodesign (Surgisis), Permacol and other are all grouped under the common denominator *Biologic mesh*, each of these products is unique. There are differences in tissue source, differences in the processes used to decellularize the tissue and differences in the final processing steps such as sterilization and preservation. As a result, there are significant variations in biological and clinical performance between these products. Permacol, which is purposely cross-linked pig dermis, behaves like a synthetic material in-vivo and induces a permanent foreign body response, leading to encapsulation.This prevents integration with and in the surrounding tissue. Consequently, high rates of erosion occurwith Permacol implants. Biodesign, one of the early biologics, is derived from small intestinal submucosa and is a non-cross-linked mesh. Likely due to its (proprietary) processing, Biodesign in practice often dissolves before healing and remodeling can take place.

A novelty on the surgical mesh market is OviTex. It is produced by GD medical and exist of sterile sheep extracellular matrix (ECM) interwoven with a (absorbable or non-absorbable) synthetic fiber. OviTex comes with a grid of absorbable polyglycolic acid (PGA) or permanent polypropylene. Unique to OviTex is its composition, which consists of essential components required for regeneration of host tissue. Additionally, the coupling of an ECM with a (absorbable) synthetic carrier ECM ensures that cross-linking is avoided but mechanical strength is maintained. Moreover, OviTex is lower in costs than any other biological mesh on the market. Preliminary results of a recent pilot study at Meander MC showed that the use of an OviTex PGA (with absorbable grid) mesh in the pelvic floor is feasible and safe. Nevertheless, 2 out of 11 patients who completed follow-up of 6 months showed an early anatomical recurrence. This suggests that the use of permanent synthetic fiber may be necessary for a more durable repair and fewer recurrences than using OviTex PGA. Although resistance against synthetic grafts is growing, OviTex Permanent contains 96% sheep ECM and only 4% polymer, compared to the standard Prolene mesh which is 100% polymer (polymer areal density 16g/m2 OviTex 1S vs. 76g/m2 prolene). Furthermore, the polymer is embedded in the ECM which further attenuates any inflammatory response. Observations in primates show that the minimized amount of embedded synthetic reinforcement results in an implant that, histologically, behaves like a biologic mesh yet maintains its functional structure.

There are no studies comparing OviTex to the current standard (Prolene, PMN3, Ethicon Inc Johnson & Johnson, The Netherlands) Therefore, a comparative study should be conducted before OviTex is used as a biologic alternative for polypropylene in VMR on a larger scale. Following the OviTex pilot study, we aim to conduct a follow-up study (ProTex trial) in which, both in the short and longer term, the efficacy of the OviTex mesh in pelvic floor surgery will be assessed in comparison with the current standard polypropylene, by means of a

non-inferiority test.

Study objective

Main study parameter/endpoint phase II
- Post-operative morbidity measured by reoperations, reinterventions, re-admissions, serious adverse events, Clavien Dindo classification and CTS classification.
- The rate of rectal prolapse recurrence and complications (complaints, physical examination, addition research, re-operation and readmission).

Main study parameter/endpoint phase III
Constipation, incontinence and urogenital functioning (questionnaire, validated scoring system: Fecal Incontinence Severity Index (FISI), Altomare obstructive defecation score (ODS)) and Pelvic Floor Distress Inventory-20 (PFDI-20).

Secondary Objective(s):
- Quality of life (QoL) pre- and postoperatively objectified primarily by the Patient Assessment of Constipation-Quality of Life Questionnaire (PAC-QoL), Fecal Incontinence Quality of Life Scale (FIQL), Pelvic Floor impact Questionnaire (PFIQ-7), Patient Global Impression of Improvement (PGI-I), Patient Global Impression of Severity (PGI-S) and European Quality of Life Five Dimension (EQ-5D).
- Post-operative morbidity measured by reoperations, reinterventions, re-admissions, and serious adverse advents.
- Anatomic recurrence of the prolapse, measured by defecogram or MR defecography in rest and during Valsalva maneuver.
- Rate of rectal prolapse recurrence and complications (complaints, physical examination, addition research, re-operation and readmission).
- Anatomic recurrence of pelvic organ prolapse (POP) using the simplified Pelvic Organ Prolapse Quantification (sPOPQ)
- Sexual functioning pre- and postoperatively by the questionnaire Prolapse Incontinence Sexual Inventory Questionnaire (PSIQ-12).
- Length of hospital stay, peri-operative and post-operative in hospital mortality and morbidity.
- Rate of extra outpatient visits because of complaints.

Study design

This study aims to investigate the efficacy of the OviTex mesh in pelvic floor surgery in comparison with the currently used polypropylene mesh, by means of a multi-center, phase II-III, partly randomised patient-preference, non-inferiority study.

In the phase II study, in the experimental arm 10 patients for each operation indication (30 in total) will be included:

- Full thickness external rectal prolapse (ERP) (n=10);
- Internal rectal prolapse (IRP) Oxford grade 3 or 4 with symptoms (n=10);
- Any of the above indications combined with a sPOPQ stage >= 2 for which concomitant surgery is required (SCR or cervicopexy) (n=10).

After the total of 30 participants completed a follow-up of 90 days, an interim analysis takes place. (see chapter 9)

In the subsequent phase III follow-up of the patients will be performed according to routine postoperative follow-up with some minor adjustments. After the standard 6 weeks follow-up visit at the outpatient visit, the patients will be asked to fill in a questionnaire after 90 days. Recurrence, complications and pelvic floor function will be assessed at 6, 12 and 24 months post-operatively by means of an outpatient visit and questionnaires. Compared to standard care, the last visit has been added in relation to the study. If symptoms persist or recur the responsible physician may be decided to carry out additional imaging.

Intervention

The primary aim of this study is to compare prolapse surgery with OviTex instead of the current standard polypropylene mesh (Prolene, Ethocin Inc, Johnson & Johnson, Hamburg, Germany; weight 80-85 g/m2) in adult patients with a rectal prolapse and/or pelvic prolapse performed by experienced surgeons. Study participants will have 2 additional follow-up moments (each including the questionnaire and outpatient visits) in addition to standard practice. Further treatment will be the same for patients undergoing current VMR or SCR with polypropylene mesh.

Study burden and risks

In VMR and SCR a mesh implant is used to reinforce weakened tissue of the pelvic floor (the rectovaginal septum). Ovitex is a CE certified surgical mesh and its usage in VMR and SCP falls under the intended use. A recent pilot study on safety and feasibility concluded that the usage of Ovitex in VMR is safe.

Disadvantages of participating in the study are:
- The participant will spend extra time filling in the questionnaires during follow-up (usually 10-30 minutes).
- The participant has two extra outpatient visits to which he or she must attend as much as possible.
- The participant may find the questionnaires confronting.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Indication for ventral mesh rectopexy with or without sacrocolpopexy
Informed consent for OviTex or Polypropylene
Age of 18 years or older
Able to complete questionnaires and outpatient visits

Exclusion criteria

Mental incompetence
Allergy to ovine rumen

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-12-2023
Enrollment:	184
Type:	Actual

Medical products/devices used

Generic name:	OviTex reinforced bioscaffold
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	01-08-2023
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL79184.100.22