**pRophylactic utErosacral suspension AT Total lAparoscopiC Hysterectomy and the risk of prolapse occurrence – a randomised controlled trial**

**(REATTACH)**

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1. **Introduction**

Hysterectomy is one of the most commonly performed gynaecological surgical procedures for many reasons such as malignancy as well as benign conditions such as heavy menstrual bleeding. One of the long-term risks associated with hysterectomy is the occurrence of pelvic organ prolapse (POP), which has a prevalence of 0-39%, and may affect the wellbeing of women adversely.1,2 Pelvic organ prolapse may adversely affect physical, sexual and emotional health, and results in an increasing economic burden on the health system. Based on data from the United States, annual direct costs on the health care system are estimated to exceed $1 billion for prolapse surgeries, and the number of women who will undergo prolapse surgery is projected to double by the year 2050.3,4

1. **Background**

There is currently minimal published data on the literature to the effect of prophylactic uterosacral suspension on the prevention of prolapse in the future. It is currently not routine practice for uterosacral suspension to be done laparoscopically, especially at time of laparoscopic hysterectomy when performed for non-prolapse reasons. There has only been one retrospective Australian study performed in 2009 which showed a 1% rate of vault prolapse post total laparoscopic hysterectomy with uterosacral suspension with 2 out of 102 patients requiring further surgery for prolapse reasons.5 Data on surgical methods and procedures performed at time of hysterectomy to prevent de novo vault prolapse are scarce, with only 1 published RCT included in a systematic review published in 2020 and since then a McCall-type procedure has been suggested at time of hysterectomy in order to prevent subsequent apical pelvic organ prolapse.2

Laparoscopic hysterectomy is the preferred minimally invasive route of hysterectomy especially where there is presence of adnexal pathology, severe endometriosis, adhesions or an enlarged uterus, and has been performed increasingly more commonly due to its multiple patient benefits such as shorter admission to hospital, a quicker return to baseline function as well as reduced opioid requirements.6 Additionally, when compared to a vaginal route, performing a concurrent uterosacral suspension at time of laparoscopic hysterectomy also has the benefit of a lower risk of ureteric injury due to better visualisation, considering the anatomical proximity of the ureter to the uterosacral ligaments.2

A systematic review of recent evidence has shown that laparoscopic sacrocolpopexy for the management of vault prolapse had the best anatomical results and highest patient satisfaction rates.7 However, this also creates a challenging problem for the pelvic constructive surgeons given the removal of synthetic pelvic mesh from the health industry recently by the Therapeutic Goods Administration (TGA).1,8 With concerns of mesh related complications, total laparoscopic hysterectomy with concurrent laparoscopic uterosacral ligament vaginal vault suspension provides a safe, effective and low cost alternative technique with similar efficacy rates when compared to laparoscopic sacrocolpopexy without the use of synthetic mesh. The uterosacral ligaments are able to provide a strong level 1 support as supportive tissue for vaginal vault suspension that spans through the 3 levels of pelvic organ support as initially described by DeLancey.9,10 A small cohort study looked at prophylactic uterosacral ligament suspension with no evidence of ureteric or nerve injury and it is considered a safe procedure with minimal complications.11 The addition of a similar vault suspension procedure (McCall’s culdoplasty) from a pilot study in the United States did not find an increase in operative time, estimated blood loss or surgical complications and longitudinal results regarding sexual function was reassuring.12 The use of a permanent suture for uterosacral ligament suspension has been associated with a lower rate of apical prolapse with a 2-year mean follow up.13

As per the recommendations from AAGL practice report, uterosacral ligament suspension may be performed during laparoscopic hysterectomy to reduce the risk of post-hysterectomy vaginal vault prolapse.14 Hence, ongoing research into the most effective method of preventing prolapse is warranted, this study aims to evaluate the effect of prophylactic uterosacral suspension at time of laparoscopic hysterectomy on reducing the risk of developing prolapse in the future.

1. **Aims**

**3.1 Primary aim**

The aim of the study is to determine the effects of prophylactic uterosacral suspension at time of total laparoscopic hysterectomy in the prevention of prolapse in the future.

**3.2 Secondary aim**

To determine the impact of prophylactic uterosacral suspension on operative time, and associated complications such as urinary tract infection, visceral injuries (urinary tract, bowel, bladder), urinary retention, hospital readmissions, neuropathies, and sexual function when compared with routine vault closure.

1. **Objectives**
	1. **Primary objective**
* To compare the preoperative C point at immediately postoperative, followed by 6 and 12 months post surgery.
* To assess if there was a difference in prolapse, urinary and faecal incontinence symptoms as well as sexual function through obtaining a patient filled survey (PISQ-12 and PFDI-20) at pre and 3 months post surgery.16,17
	1. **Secondary objective**
* To compare the length of operative time among patients receiving the uterosacral suspension when compared with the routine vault closure.
* To describe and compare the postoperative complications profile related to the uterosacral suspension when compared to the routine vault closure at 3 months postoperatively.
1. **Hypotheses**

**5.1 Primary hypothesis**

The primary hypothesis of the project will demonstrate that in patients who received the uterosacral suspension, they would see a better improvement in their postoperative C point and be less likely to develop prolapse at 6 and 12 months when compared to routine vault closure. It will also demonstrate that patients will notice an improvement in their prolapse symptoms through the patient filled questionnaire at pre surgery and in the 3 months postoperative period.

**5.2 Secondary hypothesis**

The secondary hypotheses of the project will demonstrate that patients who are randomised to receive the uterosacral suspension are not at an increased risk of complications such as urinary tract infection, visceral injuries (urinary tract, bowel, bladder), urinary retention, hospital readmissions, neuropathies, and impaired sexual function when compared with routine vault closure. The length of operative time between the 2 arms will be comparable.

1. **Project design**

The project will be a RCT with two arms: intervention and control.

**Intervention arm**: the patient will receive uterosacral suspension at time of total laparoscopic hysterectomy in addition to the routine 2-layer vault closure.

**Control arm**: the patient will receive routine 2-layer vault closure at time of total laparoscopic hysterectomy.

**Randomisation:** the patient and clinician will be blinded to their arm of the study. Randomisation will occur via permuted block randomisation.

1. **Project setting/locations**

The project will be conducted at Townsville University Hospital, Douglas.

1. **Project duration**

The project is expected to run from June 2022 till March 2024 (Table 1).

**Table 1. Timeline of the project**

|  |  |  |  |
| --- | --- | --- | --- |
|   | 2022  | 2023  | 2024  |
|   | F  | M  | A  | M  | J  | J  | A  | S  | O  | N  | D  | J  | F  | M  | A  | M  | J  | J  | A  | S  | O  | N  | D  | J  | F  | M  |
| **Ethics & SSA applications** | x  | x  | x  | x  |  X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| **Participant recruitment** |   |   |   |   |  | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  |   |   |   |   |   |   |   |   |   |   |
| **Database entry and checking** |   |   |   |   |   |   | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  | x  |  x |   |   |   |   |   |   |   |   |
| **Data cleaning & analysis** |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  | x  | x  |  x |   |   |   |   |   |
| **Preparation of publication** |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  | x  | x  |  x |   |   |
| **Dissemination of findings** |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | x  | x  | x  |

1. **Project population**

Women who are scheduled to undergo a total laparoscopic hysterectomy for benign indications and non-prolapse reasons will be invited to participate in the study at their pre-operative visit by a member of the study team. Patients that are interested in participating in the study will receive additional information (including an information sheet) about the study from a doctor who is independent of the study team at pre-admission. This doctor will ask the patients to sign the informed consent should they wish to participate in the study. This is to ensure that participation has been voluntary and that there has been no coercion. At this point, the patients will provisionally be included in the study and final inclusion of these patients will be determined pre-operatively.

**Inclusion criteria**

* Patients must be 18 years of age or older
* Patients must be able to provide informed consent
* Preoperative inclusion criteria include: C point not past the hymenal remnant, i.e., C point at point 0 at Valsalva
* Patients with no prolapse symptoms
* A Pelvic USS in the last 6 months from booking of procedure to show that size of uterus is less than or equal to 300cc

**Exclusion criteria**

* Women undergoing a total laparoscopic hysterectomy for malignancy
* Women with a history of pre-existing pelvic organ prolapse, patients with cervical apical descent past the hymen, grade 2 uterocervical pelvic organ prolapse will be excluded
* Women with serious medical conditions who are unable to perform a Valsalva manoeuvre
* Non-English-speaking patients (unless access to a qualified interpreter is available during the full duration of the study)
* Size of uterus on ultrasound scan greater than 300cc
* Age greater than 75 years old
* BMI greater than 45
* Pathology obliterating the pouch of Douglas
* Stage 4 endometriosis
* Anticipated geographic relocation within the first 12 months following surgery
1. **Project outcomes**

**10.1 Primary outcomes**

* + The primary outcome will be the quantitative C point that will be recorded at prior to surgery, immediately post-surgery, and at 6 and 12 months, the relevant change in c point post uterosacral suspension will be measured at each time point.
	+ It will also be the quantitative survey scores as generated by the PFDI-20 and PISQ12 prior to surgery and 3 months following surgery.16,17 (See appendix)

**10.2 Secondary outcomes**

* + The secondary outcome will be the length of operative time.
	+ Other secondary outcome is also to ascertain the presence of complications such as rates of urinary retention, urinary tract infection, bladder injury, paraesthesia, changes to sexual function such as dyspareunia. will be the length of operating time, as well as the presence of complications such as rates of urinary retention, urinary tract infection, bladder injury, paraesthesia, changes to sexual function such as dyspareunia.
1. **Project procedures**

**11.1 Informed consent**

Patients invited to participate in the study will be provided with an information sheet and will be asked to provide written informed consent to participate in the study. Information regarding the study will be provided at the initial point of consultation, but patients will also be asked to consent again at time of surgery and clinical measurements of Pelvic Organ Prolapse Quantification system (POPQ) dimensions by each clinician.

A patient is able to withdraw from the study at any time. Should a patient wish to withdraw from the study, they are able to inform the research team, however, as will be explained in the consent form, their data will continue to be used for data evaluation.

**11.2 Randomisation**

Randomisation will occur via permuted block randomisation, to the intervention or control group. The 66 patients will be randomised to their study allocation prior to surgery. It will be double blinded.

**11.3 Preoperative procedures**

Following induction of anaesthesia, the C point will be measured using traction of the cervix with a vulsellum mimicking the Valsalva manoeuvre, along with other domains of POPQ measurements. Once this is recorded, then an envelope revealing assignment of the patient to which intervention will be revealed.

**11.4 Intraoperative procedures**

All patients will have a 10mm port either at the umbilicus or supraumbilically for the camera and 3x further 5mm ports placed. Operating pneumoperitoneum pressure will be 15mmHg, after initially placing the ports at a higher pressure of 22mmHg.

Consistent with our standard technique of hysterectomy, we commence the exposure of the uterosacrals by developing the medial pararectal space of Okabayashi. By this stage the lateral pararectal space of Latzko already has already been developed, ureters identified and lysed if necessary, and uterine vessels secured at the origin of the internal iliacs. The ureter is identified separating these two potential spaces, with the medial dissection carried to expose the uterosacral through its entire extent, especially the junction of the upper and middle thirds. The inferior hypogastric nerve is identified and preserved whenever possible. If excision of deep infiltrating endometriotic deposits make the preservation of parts of the uterosacrals untenable, a proximal anchor towards the upper third of the ligament is chosen. A marking stitch may be appropriate in such cases for easy identification. The hysterectomy will then proceed per usual methods, including possible removal of associated adnexae. Uniformity of surgery will be ensured by a single surgical team performing all surgeries.

For patients that are randomised to the high uterosacral suspension arm, following the hysterectomy ensuring adequate “pedicalisation” of the uterine vessels, the assistant places the uterosacral ligament ligament under stretch by lifting the vaginal angle. A 0 Prolene D7580 on a 26 mm CT2 needle is cut to 30 cm length (shorter if 2 separate suture packs used). The uterosacral ligament is plicated in an inside-out, outside-in fashion, always commencing within the medial rectal space with the ureter coursing laterally in view. This suture is then driven through the bulky attachment of the uterosacral to the peri-cervical ring. The next bite is taken lateral to the vaginal edge and medial to the uterine pedicle ensuring that the Prolene does not enter the vaginal mucosa throughout its entire course. This also prevents bunching or infolding of the vault edges which can make vault closure tricky. The suture carried anteriorly is then robustly anchored to the pubovesical fascia and then makes it way posteriorly past the anchor point to the uterosacral at the pericervical ring to incorporate a robust bite through the rectovaginal fascial attachment to this structure. Following this, the suture is tied intracorporeally with 5 squared knots. The procedure is then repeated on the other side. This will then be followed by vaginal closure of the vault is carried out using V-Loc 90 suture (Covidien, Dublin, Ireland) in 2 layers taking care to incorporate the pubovesical fascia and the rectovaginal fascia which is contiguous with the vaginal vault.

For patients that are randomised and assigned to the standard cuff closure group without the high uterosacral suspension, they will undergo a standard 2-layer laparoscopic closure of the colpotomy incorporating the pubovesical fascia, the rectovaginal fascia and distal ends of the uterosacral ligaments using a continuous 2-0 V-Loc 90 suture.

**11.5 Postoperative assessment**

Following completion of hysterectomy, an independent clinician not part of the operating team will be performing the post operative C point.

**11.6 Data collection and measurement tools**

A clinician blinded to the study intervention will be performing the pre and post objective clinical measurements of POPQ, with a POP Stix for objective clinical measurements. Patients undergoing total laparoscopic hysterectomy will have their Ba, Bp, C and D point measured under Valsalva (i.e., with traction on those points under GA with a vulsellum) with a popstix. The reason for this measurement is to ensure objective clinical assessments for comparison. Post-surgery at 6 and 12 months, when patients come back for their post operative measurement, they will be asked to perform a Valsalva manoeuvre and their Ba, Bp, C and D points will be measured with the POPstix respectively. The PISQ12 and PFDI-20 Questionnaire will also be filled out by patients pre-operatively and postoperatively at 3 months. (See appendix)

**11.7 Data management and safety monitoring**

Study data collected will be populated into REDCap electronic data capture tools hosted at Townsville Hospital. REDCap (Research Electronic Data capture) is a secure, web-based software platform about the study.15 Patients will be reassured that their participation is voluntary, and they may withdraw from the study at any point without any impact on their routine standard of care.

1. **Sample size and statistical analysis**

Postoperative change in c point was used in the sample size calculation as the primary end point. The sample size was calculated based on a pilot study12 where there was a total of 50 patients recruited, in accounting of 30% attrition rate, the number of patients needed to be recruited in each arm was calculated to be 33. Statistical analysis will be performed using STATA (version 16; StataCorp LP; College Station, Tx). Continuous variables will be summarized using mean and standard deviation with parametric data and using median and interquartile range with non-parametric data. Categorical variables will be summarized using frequencies and percentages. Continuous variables were tested for normal distribution and subsequently analysed using either the unpaired Student’s *t* test or Mann-Whitney *U* test where appropriate. Categorical variables were analysed using the chi-square test or Fisher’s exact test, where appropriate. Values of p<0.05 were considered statistically significant.

1. **Ethical considerations**

There are several ethical considerations in this study.

**13.1 Risk of coercion to participate as the medical team providing the treatment is performing the study**

This will be mitigated by a doctor, who is independent of the study team, obtaining consent for participation. At the time of consenting, this doctor will inform patients about the study in person and via information sheets they will be given about the study. Patients will be reassured that their participation is voluntary and they may withdraw from the study at any point without any impact to their treatment. Existing patients on the waiting list, and new patients seen at the Gynae clinics will be considered for recruitment. Patients currently on the waiting list will be contacted telephonically after their surgery date has been allocated to be invited to join the study, with written information emailed. They will still be consented at their pre-admission visit.

**13.2 Risk of inconveniencing patients**

There is a risk of inconvenience to the patient as the study requires them to answer questions as a pre operative survey, and to be contacted by study staff to answer the post operative survey as well as return for POPQ measurements post operatively at the 6- and 12-month postoperative period.

**13.3 Risk of disclosure of personal information**

This will be mitigated by all personal information being de-identified for publication and identified storage of the database on REDCap.15

**13.4 Risk of patient attrition**

There is a risk of attrition as some patients may not answer their phone for the 3 month follow up survey or turn up for their 6 months and 12 months follow up. This will hopefully be mitigated by offering the participants regular follow up with our clinicians as deemed appropriate.

1. **Dissemination of results**

The results of the study will be published in a peer reviewed journal and presented both within the hospital and at national Obstetrics/Gynaecology conferences shortly after study completion. Participants of the study will have the option to be informed of the study findings upon request. Specifically in the field of Gynaecology, we would like to publish our findings at the Journal of Minimally Invasive Gynaecology, as well as present our findings at an AGES (Australian Gynaecology and Endoscopic Society) conference. If the uterosacral suspension is shown to prevent prolapse, it would be prudent to generate research hypotheses for larger scale studies and discuss potential changes to existing practice by surgeons for patients moving forward.

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**Appendix**



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