**Scientific title** PREVENTION OF INCISIONAL HERNIA AFTER STOMA CLOSURE USING A SYNTHETIC BIO-ABSORBABLE TISSUE REINFORCEMENT

**Simple title S**TOMA **C**LOSURE **U**SING **B**IO-**A**BSORBALE **R**EINFORCEMENT (SCUBAR)

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**BACKGROUND**

A temporary stoma maybe formed in a number of clinical scenarios including defunctioning of a distal anastomosis or diverting faecal flow away from a diseased segment of bowel. Once the indication for the temporary stoma no longer exists, surgery to restore intestinal continuity can be performed. The rate of incisional hernia (IH) formation following closure of a temporary stoma is approximately 30% (range 0-48%)(1-3). Similarly, a stoma site may be closed due to a requirement to reposition or resite a stoma away from its initial location, usually due to the occurrence of local complications arising from the stoma. IHs following abdominal surgery are a significant cause of morbidity and may adversely affect a patient’s quality of life (4-6). Symptomatic hernias will often require surgical repair, sometimes emergently.

Existing techniques for preventing the formation of IH include the use of either synthetic non-absorbable meshes or biological tissue grafts to reinforce the primary closure of the fascia. It is well established that prophylactic use of these materials to reinforce a primary suture closure of a midline laparotomy wound can significantly reduce the IH rate(7,8) and may be more cost effective than primary suture repairs alone (9). There are only a limited number of studies in the literature examining the use of prophylactic mesh at the time of stoma closure to reduce the high IH rate following this procedure. There have been just over 200 participants in these trials combined, over half are single arm studies and as yet, there are no randomised trials (Table 1).

**Table 1 Summary of studies on prophylactic mesh placement at the time of primary stoma wound closure for the prevention of incisional hernias.**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Publication author** | **Year** | **Total no.** | **IH rate** | | **F-up (m)** | **Stoma type** | **Mesh type** | **Mesh position** | **Study results** |
|  |  |  | **Mesh** | **No mesh** |  |  |  |  |  |
| Ramanujam (10) | 2012 | 28 | 0/14 | 3/14 | 24 | Mixed | Synthetic bio-absorbable  (Gore BioA) | Retro-rectus | IH rate reduced in mesh group |
| Pandey (11) | 2013 | 50\* | 0/50\* | - | 6 | Mixed | Synthetic bio-absorbable  (Gore BioA) | Retro-rectus | No IH |
| Liu (12) | 2013 | 47 | 3/47 | 16/36 | 18 | Ileostomy | Synthetic non-absorbable (Ultrapro) | Onlay | IH rate reduced in mesh group |
| Bhangu (13) | 2014 | 7 | 0/7 | - | 1 | Ileostomy | Biological tissue graft  (Strattice) | Intra-peritoneal | No early IH |
| Van Barneveld (14) | 2014 | 10 | 0/10 | - | 26 | Ileostomy | Dual synthetic absorbable and non-absorbable  (Parietex composite) | Intra-peritoneal | No IH |
| Maggiori  (15) | 2015 | 94 | 1/30 | 12/64 | 12 | Ileostomy | Biological tissue graft (Meccelis) | Retro-muscular | IH rate reduced in mesh group |
| Lalezari  (16) | 2017 | 6 | 0/6 | - | 11-25 | Mixed | Synthetic bio-absorbable  (Gore BioA) | Retro-muscular | No IH |

IH: incisional hernia, F-up: follow-up, m: months, \* publication by same authors/institution and uncertain if same patients in later study.

Placement of prophylactic mesh at the time of stoma closure or resiting is not routine for most surgeons and mostly primary suture closure of the fascia is performed. This is due to concerns of a high rate of surgical site infections (SSIs) especially for synthetic prosthetic meshes in clean contaminated (Class 2) wounds. This can lead to prolonged length of stay, prolonged antibiotic use, reoperation for mesh explantation and IH formation. In the largest analysis of post-operative outcomes following ventral hernia repair with and without mesh in clean (Class 1), clean contaminated (Class 2) and contaminated (Class 3) wounds there were significantly greater infective complications (superficial SSI, deep SSI, organ/space SSI, sepsis) when mesh was used in clean contaminated and contaminated wounds compared to clean wounds(17). Furthermore, when compared to no mesh (primary suture repair), the use of mesh in clean contaminated wounds was associated with an increased odds of any post-operative complication (OR 3.56 versus 2.52, P < 0.001) (17). Table 2 summarises the reported rates of wound infection in existing studies which have evaluated the use of mesh following stoma reversal. These studies are non-randomised and retrospective in nature and for many the definition of wound infection was not defined nor blinded by study authors. Taking this into account, the rates of wound infection are similar for patients who received mesh (4 – 14%) and those who did not (2 – 14%).

**Table 2 Summary of infective complications after prophylactic mesh placement at the time of primary stoma wound closure for the prevention of incisional hernias.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Publication author** | **Year** | **Total no.** | **Infective complications** | | **F-up (m)** | **Stoma type** | **Mesh type** | **Mesh position** |
|  |  |  | **Mesh** | **No mesh** |  |  |  |  |
| Ramanujam (10) | 2012 | 28\* | 2/14 | 2/14 | 24 | Mixed | Synthetic bio-absorbable  (Gore BioA) | Retro-rectus |
| Pandey (11) | 2013 | 50\* | 4/50 | - | 6 | Mixed | Synthetic bio-absorbable  (Gore BioA) | Retro-rectus |
| Liu (12) | 2013 | 47 | 2/47 | 1/36 | 18 | Ileostomy | Synthetic non-absorbable (Ultrapro) | Onlay |
| Bhangu (13) | 2014 | 7 | 1/7 | - | 1 | Ileostomy | Biological tissue graft  (Strattice) | Intra-peritoneal |
| Van Barneveld (14) | 2014 | 10 | 1/10 | - | 26 | Ileostomy | Dual synthetic absorbable and non-absorbable  (Parietex composite) | Intra-peritoneal |
| Maggiori  (15) | 2015 | 94 | 2/30 | 1/64 | 12 | Ileostomy | Biological tissue graft (Meccelis) | Retro-muscular |
| Lalezari  (16) | 2017 | 6 | 0/6 | - | 11-25 | Mixed | Synthetic bio-absorbable  (Gore BioA) | Retro-muscular |

F-up: follow-up, m: months, \* publication by same authors/institution.

Newer surgical materials to reinforce fascial closure have recently emerged and have shown promise in their abilities to reduce IH formation and tolerate bacterial contamination. Gore™ BioA™ is a 100% synthetic, 100% bio-absorbable tissue scaffold formed from a copolymer of 66% polyglycolic acid (PGA) and 33% trimethylene carbonate (TMC). This material is gradually reabsorbed over 6 – 7 months and replaced by native collagen. As summarised in Table 1, it has been used in case series and cohort studies to prevent IH formation after stoma closure. The largest prospective longitudinal trial using Gore™ BioA™ was for reinforcement in contaminated ventral hernia repairs which showed an IH recurrence rate after 24 months 17%(18). The estimated incidence of IH recurrence after primary suture repair alone is up to 50% (19). SSI occurred in 18% of these patients, but there was no requirement for mesh explantation over the 24-month follow-up period (18). Mesh explantation or indefinite antibiotic treatment are the usual outcomes for patients who have wound infections in the setting of synthetic mesh. It has become routine in some centres to use this mesh to reinforce the abdominal wall after stoma closure but there is no randomised clinical trial to demonstrate its efficacy at reducing incisional hernia development above that of simple suture repair.

**STUDY OBJECTIVES**

**Aim**

The primary objective of this study is to determine whether placement of a synthetic bioabsorbable material (Gore™ BioA™) to reinforce fascial closure at the time of closing or resiting a stoma reduces the incidence of IH formation at the site of the stoma when compared to standard fascial closure 3 years after surgery. The secondary outcomes of this study will be to determine if the intervention is associated with differences in post-operative pain scores, SSIs and quality of life compared to routine closure.

**Hypothesis**

Synthetic bioabsorbable tissue reinforcement of the abdominal fascia at the time of temporary stoma reversal reduces the incidence of IH formation when compared to routine primary suture closure of the abdominal fascia.

**RESEARCH PLAN**

**Study type:** A prospective single centre randomised clinical trial.

**Location:** Westmead Hospital Western Sydney Local Health District (WSLHD)

**Duration:** 5 years

**Methodology**:

Patient population: Any adult patients presenting for elective ileostomy or colostomy closure or re-siting.

Inclusion criteria:

1. Age > 18 years
2. Patient with a temporary stoma that has met criteria for stoma reversal or a permanent or temporary stoma that requires resiting.
3. Patient capable of participating in informed consent for the study
4. Patient willing to complete follow-up over the study period (3 years).

Exclusion criteria:

1. Pregnancy
2. Pre-existing placement of synthetic non-absorbable mesh in the region of the stoma site.

Sample size: Anticipating a 30% incidence of IH formation in the control group and a reduction of IH formation in the intervention group of 50% with a 1:1 allocation of patients to the treatment groups and an 80% power to detect a difference the sample size is 120 patients in each arm of the study. Allowing for a 20% dropout or lost to follow-up rate, this equates to a total of 288 patients (144 patients in each arm of the study).

Operative procedure (All patients): All study participants will have routine pre-operative planning and investigations in preparation for general anaesthesia and stoma reversal or resiting as per the treating surgeon and anaesthetist. All patients undergoing elective stoma closure or resiting will be asked for informed consent to participate in the trial at the time of completing their operating theatre booking paperwork with their treating surgeon or in the hospital on the day of surgery. Patients who consent to enrolment in this study will be randomised with the aim of allocating patients to the intervention and control groups on a 1:1 ratio. The process of randomisation will be achieved using a computer based random number generator. Heterogeneity will be dealt with by the randomisation process and post-hoc analyses will be undertaken to deal with any potential confounding variables. Randomisation will occur once the patient is anaesthetised. This will assist in blinding the study participant. It will also allow for confirmation that, in the case of stoma reversal, that surgery is to proceed once flexible sigmoidoscopy and examination under anaesthesia (routine assessments performed immediately prior to stoma reversal once the patient has been anaesthetised) have confirmed that the anastomosis is intact or that bowel lesions have been excluded.

All patients will undergo surgery under general anaesthesia with prophylactic intravenous antibiotics in accordance with the WSLND Surgical Antibiotic Prophylaxis Guideline – Adult (Appendix 1). Patients will have skin preparation with topical povidone-iodine USP 10% or chlorhexidine gluconate 4% aqueous solation if allergic to iodine in accordance with routine operating theatre protocols. Surgical dissection and mobilisation of bowel and bowel anastomosis will be performed in the manner determined by the operating surgeon. Both peri-stomal or elliptical skin excisions will be accepted. Prior to closure the fascia the wound is to be irrigated with normal saline until clear return and the size of the fascial defect is to be formally measured with a sterilised ruler and recorded in the operation report. The need to extend the wound to perform the procedure is to be recorded. The skin is to be closed in the manner determined by the operating surgeon and suture material and method of closure recorded on the operation report. Post-operative cares including diet, deep venous thrombosis prophylaxis are to be determined by the operating surgeon. If post-operative antibiotics are to be given, the type, duration and indication for these are to be recorded in the online database.

Control: At the time of stoma reversal or resiting, the control group will have routine mass suture closure of the fascia performed with interrupted 0 polydioxanone sutures.

Intervention: The closure of the abdominal wall in the intervention group will be identical to that in the control group. The only difference will be the placement of the Gore BioA synthetic absorbable tissue reinforcement (Gore™ BioA™ FS0808 (8 x 8cm)), at the site of the stoma reversal. The recto-rectus position is preferred, however if this is not achievable, the mesh can be placed deep to the anterior fascia of the abdominal wall and above the rectus muscle. Ideally the space created should be adequate to place the. Suture closure of the fascia will be performed with interrupted 0 polydioxanone sutures in the same manner as for the control group.

**Outcomes**

Primary outcome: The development of an incisional hernia at 30 days, one, two and three years after surgery. This will be assessed clinically at post-operative follow-up (4-6 weeks), 1, 2 and 3 years after surgery in either the treating surgeon’s rooms or in the outpatient department. An incisional hernia will be defined according to the European Hernia Society definition as “any abdominal wall gap with or without a bulge in the area of post-operative scar perceptible or palpable by clinical examination or imaging” (20). Classification of incisional hernias will be by size, location and reducibility of the contents. The details of clinical examination will be recorded in the Data Sheet for Clinical Examination in (Appendix 2).

Patients will also have an ultrasound of the abdominal wall performed at 1 and 3 years after surgery to evaluate the stoma site. If the patient receives a computed tomography (CT) scan for another indication at around 1 or 3 years post-operatively this can be used in lieu of an ultrasound. CT scans will not form part of the routine follow-up for patients in this study. The radiologists reporting the ultrasound or CT scan will be blinded to the intervention.

See the Data Sheet for Ultrasound Examination in Appendix 3 for the outcomes to be recorded from the ultrasound or CT examination.

Secondary outcomes:

1. Postoperative outcomes 30-days after surgery including SSI, wound haematoma, wound dehiscence (superficial or deep), readmission within 30 days, length of stay (LOS) and reoperation. SSI will be defined according to the Centre for Disease Control (CDC) definitions for surgical site infection surveillance(21). Superficial wound dehiscence will be recorded if a previously closed wound opens spontaneously and may not necessarily be associated with the presence of a SSI. Deep wound dehiscence will be recorded if there is clinical evidence of dehiscence of the abdominal wall fascia defined as visualisation of separation of the abdominal wall fascia either at clinical examination or at reoperation. The identification of abdominal viscera in the wound base also equates to deep wound dehiscence.

These outcomes will be evaluated on discharge or between Day 5 and Day 7 whichever comes later by the stoma therapy nurses whom are blinded to the intervention. They will also be assessed at a routine post-operative visit at 4 – 6 weeks after surgery by the consultant surgeon. These outcomes will be recorded on the Data Sheet in Appendix 4.

1. Pain at the previous site of the intestinal stoma will be measured on a 10-point visual analogue scale (on discharge, 1, 2 and 3 years after surgery). See Data Sheet in Appendix 5.
2. Health related quality of life as measured by the Carolinas Comfort Sale and the 36 item Short Form Health Survey (SF-36) at 1, 2 and 3 years after surgery. The Carolinas Comfort Scale (22) is an internationally validated quality of life tool for post-operative hernia (umbilical, ventral and inguinal) patients. It is available in 24 languages. SF-36 is also an internationally validated health related quality of life score measuring patient reported outcomes and is available in 170 languages. See Quality of Life Questionnaire in Appendix 6.

**Data and statistical analysis**

The outcomes in addition to pre-operative demographics and operative details (Appendix 7) will be tabulated in a secure password protected electronic database (REDCAP). Descriptive statistics will include median and interquartile range for continuous variables, and absolute numbers (with %) for categorical variables. The two randomised groups will be compared in post-hoc analyses to assess for any group differences that may have arisen due to chance. Analysis will be by intention-to-treat basis. Differences between randomised groups will be tested with appropriate statistical methods, including t-tests or Mann-Whitney tests for continuous variables and Fischer exact tests for categorical variables. The primary outcome (incisional hernia) will be analyzed with Kaplan-Meier analysis and a Cox regression analysis, to adjust for any loss to follow up. Quality of life data will be analyzed by paired T-tests, comparing immediate post-operative outcomes with longer term follow-up measurements, and repeated measures analysis. A two-sided p < 0.05 will be taken to indicate statistical significance for all calculations. An interim analysis will be performed after halfway through patient recruitment to assess the post-operative outcomes. If either arm of the study proves to be inferior, we will stop study recruitment.

**Significance**

IH form in approximately a third of all patients who undergo stoma reversal and can have a negative effect on a patient’s quality of life. Symptomatic hernias will often require surgical repair, sometimes emergently. This study aims to determine if IH formation is significantly reduced by using a bio-absorbable material.

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