



Stoma closure and reinforcement (SCAR): A study protocol for a pilot trial

Jenaya L. Goldwag^a, Lauren R. Wilson^{a,c}, Srinivas J. Ivatury^{a,c}, Eric M. Pauli^d,
Michael J. Tsapakos^{b,c}, Matthew Z. Wilson^{a,c,*}

^a Department of Surgery, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA

^b Department of Radiology, Dartmouth Hitchcock Medical Center, Lebanon, NH, USA

^c Geisel School of Medicine at Dartmouth, Hanover, NH, USA

^d Department of Surgery, Penn State Milton S. Hershey Medical Center, Hershey, PA, USA

ARTICLE INFO

Keywords:

Colorectal cancer
Incisional hernia
Ileostomy

ABSTRACT

A quality metric for centers performing rectal cancer surgery is a high percentage of sphincter sparing procedures. These procedures often involve temporary bowel diversion to minimize the complications of an anastomotic leak. The most common strategy is a diverting loop ileostomy which is then closed after completion of adjuvant therapy or the patient recovers from surgery. Loop ileostomy is not without complications and the closure is complicated by a one in three chance of incisional hernia development. Strategies to prevent this problem have been designed using a variety of techniques with and without mesh placement. This proposed pilot study will test the safety and efficacy of a novel stoma closure technique involving permanent mesh in the retro rectus position during ileostomy closure. The study will prospectively follow 20 patients undergoing ileostomy closure using this technique and evaluate for safety of the procedure, quality of life, and feasibility for a larger randomized controlled trial. Patients will be followed post procedurally and evaluated for 30-day complications, as well as followed up with routine cancer surveillance computed tomography every 6 months in which the presence of stoma site incisional hernias will be evaluated. The results of this pilot study will inform the design of a multiple center, blinded randomized controlled trial to evaluate the utility of permanent mesh placement to decrease the incidence of prior stoma site incisional hernias.

1. Introduction

Survival from colorectal cancer is continually increasing due to advances in multi-modality therapies leading to a growing cohort of patients with a history of the disease [1,2]. Technologic improvements have allowed sphincter preserving surgery to be offered to a greater proportion of patients [3]. However, temporary ostomies are often used as part of sphincter preserving surgery to minimize the consequences of complications at downstream anastomosis and are closed when clinically appropriate [4]. The most common ostomy used for temporary diversion for colon and rectal cancer is the loop ileostomy, which is an ostomy fashioned from the terminal segment of the small intestine. Eventual restoration of intestinal continuity and closure of the ostomy puts patients at risk of developing a hernia at that site – a complication that occurs in approximately one third of patients [5–9]. These prior stoma site incisional hernias can reduce quality of life through chronic pain and disfigurement, and at worst require emergency surgery for

intestinal obstruction [10–15].

Risk factors for incisional hernias include obesity, malnutrition, immunosuppression, connective tissue disorders, and previous abdominal surgery [10,16–19]. Prior stoma site incisional hernias have similar risk factors, but have also been shown to be more prevalent in patients with a history of malignancy, surgical site infections, preoperative radiotherapy, ASA>3, hypertension, and duration of stoma in situ [7,8,20,21]. While some of these general hernia risk factors, such as smoking, may be modifiable, others, such as the level of wound contamination, are not [22]. Since providers cannot address all risk factors for stoma site hernias, research has been focused on alternative ways to address this clinical problem.

Recently, attention has focused to ileostomy site closure technique in order to address the high rate of prior stoma site incisional hernias. Although the fascia of stoma sites are routinely closed primarily, primary repair of abdominal wall hernias have an unacceptably high recurrence rate of up to 43% [23]. In addition, nearly all ostomy sites

* Corresponding author. Department of Surgery, Dartmouth-Hitchcock Medical Center, 1 Medical Center Drive, Lebanon, NH, 03766, USA.

E-mail address: Matthew.Z.Wilson@hitchcock.org (M.Z. Wilson).

<https://doi.org/10.1016/j.conctc.2020.100582>

Received 21 November 2019; Received in revised form 21 May 2020; Accepted 7 June 2020

Available online 9 June 2020

2451-8654/© 2020 The Authors.

Published by Elsevier Inc.

This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

will have a fascial defect greater than 2 cm, which is where most surgeons would consider using mesh for ventral hernia repair, as incorporating mesh, whether biologic or synthetic, has been shown to decrease the failure rate of repair for incisional hernias [23,24]. Thus the idea of incorporating mesh at the time of stoma site closure in order to prevent future stoma site hernia has been proposed.

Previous efforts to reduce formation of these hernias by placing mesh at the time of closure have been described as having fair success, however they are limited by heterogeneity in both patient selection and procedure [25–29]. These studies have used suboptimal anatomic positioning of the mesh reinforcement and are further limited by lack of technique consistency between surgeons and consideration of associated resource costs. Our goal is to evaluate the safety and feasibility of our technique for closure of ostomy sites, designed to minimize the potential for hernia formation, in addition to evaluating post procedure quality of life. We aim to provide baseline information for the design of a larger trial aimed at evaluating the superiority of the technique over the current standard.

2. Methods

2.1. Study aims

Aim 1: To test our hypothesis that our technical procedure of mesh implantation at the time of ileostomy closure is safe and does not increase the risk of wound occurrences, including those requiring procedural intervention, compared to historical controls of primary fascial closure only.

- (a) Our closure technique as compared to institutional historical control will result the same or fewer surgical site infections such as superficial, deep, and organ space infections at 30 days
- (b) Our closure technique as compared to control will result the same or fewer surgical wound complications requiring procedural intervention: such as dehiscence, seroma formation, or chronic wound infection at 30 days

Aim 2: To test the hypothesis that our technical procedure of mesh implantation at the time of ileostomy closure will be associated with key secondary outcomes:

- (a) Our closure technique will decrease the incidence of stoma site incisional hernia site occurrences compared to historical controls of primary fascial closure only evaluated at 30 days after surgery and every 6 months after, until two years from date of closure.
- (b) Our closure technique as compared to control result in higher quality of life scores after surgery

Aim 3: We will evaluate our study protocol for the feasibility of performing a larger trial by measuring recruitment, retention of patients, adherence to the study protocol, and process assessment.

- (a) By the completion of this pilot study, our expected outcomes are to have demonstrated a high level of procedural fidelity among the operating surgeons of the modified ostomy closure technique and comparable costs to the standard procedure
- (b) By the completion of this pilot study, our expected outcomes are to have demonstrated greater than 80% recruitment and retention of eligible participants
- (c) By the completion of this pilot study, our expected outcomes are to have demonstrated greater than 90% adherence to the study protocol.

2.2. Approach

This is a pilot study evaluating the feasibility of a novel modification

to an established surgical procedure. We will use a modification of Simon's Two stage approach, whereby we will use a initial cohort monitoring each patient through the primary end point before enrolling subsequent patients in the expansion cohort [30]. The first phase will include five patients, if there are 1 or fewer major wound occurrences within 30 days including those requiring return to the operating room, then the study will proceed to the second phase which will include a total of 15 patients followed concurrently. All patients will be seen in clinic where eligibility for the study and voluntary consent will take place, undergo the mesh placement at the time of ileostomy reversal, and then have follow up appointments 30 days post operatively and then every 6 months as part of routine colorectal cancer surveillance. At each of the appointment's patients will fill out both the quality of life and bowel function questionnaires which will provide both a baseline and many post-operative evaluations. Computed tomography imaging will be obtained every 6 months per National Comprehensive Cancer Network (NCCN) guidelines and the stoma site evaluated for hernia formation. Other pertinent patient data will be obtained through chart review through the electronic health record.

2.3. Preliminary data

The research team performed a retrospective study of our institutional cohort in order to evaluate the natural history of post stoma closure incisional hernias in patients diagnosed with colorectal cancer by examining the prevalence, as well as changes of the abdominal wall over time at previous stoma sites. The study was performed at our academic tertiary referral center of adult patients diagnosed with colorectal cancer, identified by ICD9/10 codes, who underwent stoma reversal, identified by CPT codes, from 2011 to 2018 and had at least one post-operative CT scan performed. Our main outcome measure for this work was fascial defect identified on post stoma reversal CT scan.

Of 92 patients that were included, 52 (57%) were male, with mean age of 58 years at stoma reversal. A total of 81 (87%) were diagnosed with rectal cancer, and 11 (12%) with colon cancer. Fascial defects were noted in 45 (49%) patients, with stoma site hernias present in 24 (26%) patients on CT imaging. Our institutional prior stoma site hernia prevalence is consistent with rates of prior stoma site hernias of 30% in other studies [5–9]. In addition, we found that the radiologic stoma site incisional hernia incidence was much higher than the rate of clinical diagnosis. The clinical rate of hernia detection was only 6 (25%) of patients with radiologic hernias. Of these, three were electively repaired. There were no differences in stoma duration to type of defect development after stoma reversal ($p = 0.133$). Most hernias occurred within two years.

In terms of risk factors a BMI >30 was associated with significantly increased risk of stoma site hernia on multivariate analyses (OR 11.9, 95% CI 2.41–58.94, $p = 0.002$), though smoking, hypertension, stoma type, pathologic stage, and chemotherapy within 90 days were not found to be significant. It is possible that our analysis for this review was not powered to identify these risk factors as significant given our sample of 92 patients. Our preliminary study was also limited by the retrospective nature and inconsistencies in clinical documentation which did not allow us to specify stoma closure technique. Since our preliminary work showed similar rates of prior stoma site incisional hernias at our institution to the literature, we wanted to further evaluate a potential solution to this problem, starting with our population, to reduce the burden of these hernias.

2.4. Participants and procedures

Participants will be 20 adult patients diagnosed with left sided colon and rectal cancer treated with resection and diverting loop ileostomy who plan to undergo closure of their loop ileostomy. Participants must be evaluated by a qualified surgeon and found to be a suitable candidate for surgery. Participants will be excluded from the pilot study if they

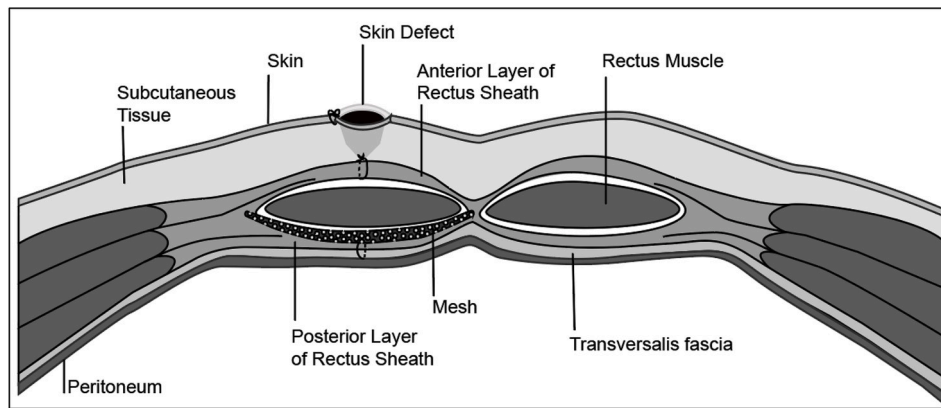


Fig. 1. Retro-rectus placement of mesh in abdominal wall.

have a pre-existing systemic infection at the time of their scheduled ileostomy closure, have severe medical comorbidities or take medications that can affect tissue healing such as: cirrhosis, chronic renal failure requiring dialysis, collagen disorder, or on immunosuppression (anti-TNF agents, chemotherapy, or prednisone >10 mg/day). Patients will also be excluded if they have undergone a previous abdominal hernia repair with mesh placement, are scheduled to undergo concurrent procedures in addition to closure of diverting loop ileostomy, and those who's ileostomy closure is not performed through the previous stoma site (those requiring exploratory laparotomy for closure). The study has been reviewed and approved by Dartmouth Hitchcock Medical Center Institutional Review Board (00030952) and is registered on [ClinicalTrials.gov](https://clinicaltrials.gov) (NCT03750461).

Participants will be recruited from the Dartmouth Hitchcock Department of Surgery, Division of Colon and Rectal Surgery clinical practice. The three operating surgeons and patient recruiters are faculty members of the Division of Colon and Rectal Surgery in the Department of Surgery at DHMC. The anticipated number of patients included (20) represents an attainable number within the planned study period (1 year) based on the clinical volume of colon and rectal surgery clinical practice.

All patients will undergo the following encounters; For encounter 1 patients will be assessed for ileostomy closure based upon completion of any applicable therapy after primary resection of their malignancy. Appropriate candidates will be determined at the operating surgeon's discretion based on customary evaluation of clinical status. The informed consent process will be initiated, and the patient recruited into the study. Encounter 2 is the operative procedure. The procedure for closing the ileostomy (i.e. bowel anastomosis) will be at the discretion of the surgeon, provided it is performed through the ileostomy site without additional laparotomy incisions. In accordance with SCIP guidelines, pre-operative intravenous antibiotic and subcutaneous pharmacologic venous thromboembolism prophylaxis will be administered. Patients with a history of MRSA infection will also receive a dose of intravenous vancomycin prior to the procedure.

The abdominal wall reconstruction portion of the procedure will be standardized to ensure consistency between surgeons. The posterior rectus sheath is closed with native tissue either primarily, using hernia sac if present, or bridged with polyglactin-type mesh and a quickly absorbing suture material. This is done to isolate the mesh from the peritoneal cavity. The retrorectus plane is developed using electrocautery and blunt dissection to provide adequate placement of mesh such that it overlaps the posterior sheath defect by a minimum of 3 cm on all sides (Fig. 1). The mesh used will be a Bard™ Soft Mesh which is a light weight, woven, large pore mesh made of polypropylene, which is an FDA approved product indicated for use in the reconstruction of soft tissue defects.

The mesh is placed in this plane and secured in place with slowly

absorbable monofilament (0-polydioxanone preferred) sutures placed through the anterior fascia or with application of fibrin sealant at the surgeon's discretion. This space is then irrigated with 250 mL of bacitracin/neomycin/polymixin antibiotic solution, patients with a history of MRSA will have vancomycin added to this solution. The anterior rectus sheath is then closed in a running fashion with slowly absorbing monofilament suture (0-polydioxanone preferred). Again, 250 mL of antibiotic solution are used as irrigation. A closed suction drain may be left in the retrorectus space at the discretion of the surgeon. Scarpa's layer is closed if possible and then skin closed with a circumferential purse string absorbable suture and the subcutaneous cavity packed with iodoform gauze. This gauze is then removed on post-operative day 2. Post operatively the patient will receive standard care.

For encounter 3 and beyond the patients will be seen at 30 days following discharge from hospitalization for stoma closure for a clinical examination and then will undergo standard follow-up for their cancer surveillance. Patients will be evaluated for complications within 30 days, including surgical site infections, the definition of which was taken directly from the CDC criteria and was categorized into superficial, deep, and organ space infections. Cancer surveillance will proceed in accordance with National Comprehensive Cancer Network (NCCN) guidelines which include computed tomography imaging every 6 months. Concurrently, clinical cancer surveillance evaluation by the operating surgeon (in conjunction with surveillance visits by medical oncology) will be performed on the same schedule with evaluation of clinical evidence of hernia formation as well as assessment of patient experience with the stoma site as part of regular cancer surveillance visit. These images will be subsequently evaluated for radiographic evidence of hernia formation by a radiologist blinded to the presence of the mesh, which is radiolucent. All radiographs will be reviewed by a single faculty of the Department of Radiology. Patients will be undergoing computed tomography evaluation primarily as part of their cancer surveillance, and the imaging is not obtained expressly for the purposes of this study and are only secondarily utilized to screen for hernia occurrence. These visits occur on a prescribed schedule for a period of 5 years after cancer treatment has concluded, after which no further follow-up is required.

During each appointment with their surgeon patients will fill out both a quality of life assessment questionnaire as well as a bowel function questionnaire. The Promis SF 2.0 8a Ability to Participate in Social Roles and Activities instrument was chosen to assess quality of life because it has been used prior to evaluate quality of life in patients diagnosed with cancer [31]. To assess bowel function the Colorectal Functional Outcome (COREFO) instrument was chosen due to its ability to appropriately assess bowel function in colorectal cancer patients who have undergone surgery, including those with severe bowel function like those patients suffering from low anterior resection syndrome [32]. Both questionnaires will be administered via tablet both prior to their procedure and at every post-operative visit to the colon and rectal surgery

Table 1
Study measures

Table 1: Study Measures	Post-operative period						
	Baseline	Operation	30 days	6 months	1 year	1.5 years	2 years
Demographic information	X						
Promis SF 2.0 8a questionnaire	X		X	X	X	X	X
COREFO questionnaire	X		X	X	X	X	X
Intraoperative data		X					
Complications		X	X				
CT Scans				X	X	X	X
Surgeon fidelity		X					
Retention and recruitment	X	X	X				
Adherence to study protocol	X	X	X	X	X	X	X

clinic.

The primary concern is for surgical site infections. In the absence of mesh, the incidence of infection in ileostomy closures is estimated between 6 and 18% [33–35]. This rate is minimized with the use of a purse string skin closure with iodine impregnated gauze packing vs partial closure with an open ended drain (Penrose type) or primary skin closure [36]. Prospective trial data estimates the overall incidence of infections when bioabsorbable mesh is placed in Class II and III ventral hernia repairs at 18%. None required mesh explantation and all wounds eventually healed [37]. Other reports of macroporous polypropylene mesh in clean-contaminated and contaminated wounds suggest an infection rate of 7.1% for clean contaminated and 19% for contaminated cases [38]. Surgical site occurrences will be treated on an individual patient basis determined by the clinical consequences of the occurrence. Infection may potentially be treated with antibiotics, local wound care, operative debridement, radiographically guided drainage procedures, vacuum assisted wound closure devices, or mesh removal at the discretion of the study team. Other potential adverse events are those inherent to intestinal surgery; anastomotic leak, peritoneal abscess formation, bowel obstruction, or ileus, in addition to the risks associated with general anesthesia. Any adverse event will be reported to the IRB of record and handled appropriately according to the accepted standard of care.

2.5. Assessment measures

We will collect measures of our primary, secondary, and tertiary outcomes (see Table 1 below).

2.6. Data analysis

Initially descriptive statistics will be calculated to summarize the demographic and baseline characteristics of the participants using appropriate univariate tests.

The results of aim 1 of this study will be compared using a univariate analysis to historical control data obtained from the DHMC ACS-NSQIP database, with emphasis on surgical site occurrences including all types of SSI, and unplanned return to the operating room data points. The preliminary safety and feasibility data obtained from this study will be used to inform design of a larger study to test the hypothesis that the procedure can obtain a 50% reduction in the incidence of hernia formation at previous ileostomy sites compared to rates reported in the literature. The aim 2 secondary objectives have not been previously reported in the literature either for patient reported outcomes or prospective evaluation of hernia formation so these results will be compared to historical controls from our institutional database. Future work, based on the data gained from this study, will attempt to show the superiority of the technique over currently used closure techniques as well as patient satisfaction with the procedure in a blinded, randomized trial. For aim 3 we will evaluate our study protocol for the feasibility of performing a larger trial by measuring recruitment, retention of patients, adherence to the study protocol, and process assessment.

2.7. Power

This is a pilot study and therefore the anticipated number of patients included (20) represents an attainable number within the planned study period (1 year) based on the clinical volume of our group. Our group treats approximately 35–40 patients per year who would likely meet inclusion criteria for this trial. We estimate a cohort of 200 patients in a randomized controlled trial will be required to demonstrate superiority of the technique by demonstrating a 50% reduction in the prevalence of hernias from 30% to 15%. We then estimated that a 10% sample of that cohort will be sufficient provide preliminary safety data as well as to demonstrate feasibility of a future trial.

3. Discussion

Survival from colorectal cancer is continually increasing leading to a growing cohort of patients with a history of the disease. Quality of life after sphincter sparing surgery in colorectal cancer is highly variable and correlates to the proximity of the anastomosis to the anal canal, which is inversely proportional to amount of rectum removed [39]. Technologic advances has allowed more patients to undergo sphincter-preserving surgery than has previously been possible [4]. Given that most patients undergoing sphincter-preserving surgery for distal colorectal cancer will also undergo temporary proximal diversion, minimizing complications of this portion of the procedure is imperative. It is well known hernias are associated with a reduced quality of life [11]. Since many of these patients are receiving temporary fecal diversion as part of their treatment more patients will be at risk for prior stoma site hernias, research should focus on how to prevent these hernias from forming.

Historically, the data for repairing hernias argues against utilizing mesh in a contaminated or clean contaminated field, such as during ileostomy closure, due to concerns of significant complications such as infections, mesh erosion, bowel adhesions, fistula formation, and pain [30–42]. Biologic meshes have been used in these situations, with the prevailing theory being that biologics are more resistant to infection [43,44]. More recent data suggests that sublay placement of a macroporous mesh of lightweight permanent or bioabsorbable synthetic materials are relatively resistant to chronic infection challenge this notion, perhaps indicating the design and plane of implantation, rather than material of the mesh, are most important [38,44–46]. Multiple reports have indicated intraperitoneal placement of mesh is associated with a higher recurrence rate compared to sublay or onlay techniques, with the sublay associated with the most favorable long term outcomes [47–49]. The cost advantages of macroporous and bioabsorbable mesh have also been reported as superior to biologic mesh [50,51].

Our ileostomy closure technique incorporates a permanent mesh in the retrorectus position for which we expect to preliminarily demonstrate safety and similar quality of life compared to historical controls on short term follow-up. These results are expected to inform development of an appropriately powered, multiple center, and randomized controlled trial comparing the effectiveness of our novel modification of

ostomy closure technique to the standard technique.

Disclosures

The authors have no financial disclosures.

Funding

This pilot project is funded by The Hitchcock Foundation.

Author contributions

All authors have substantial contributions to the conception or design of the work. Specifically all authors were responsible for the acquisition, analysis, and interpretation of data for the work. JLG, LRW, SJI, and MZW contributed to the design and collection of data. JLG, MZW drafted the work and all authors revised it critically for important intellectual content including final approval of the version to be published. All authors are in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Acknowledgements

The authors would like to thank The Hitchcock Foundation for their support of this work. In addition the authors would like to thank Julia Kelly for her help as study coordinator.

References

- [1] S. Fujii, M. Tsukamoto, Y. Fukushima, et al., Systematic review of laparoscopic vs open surgery for colorectal cancer in elderly patients, *World J. Gastrointest. Oncol.* 8 (7) (2016) 573–582.
- [2] E.N. Butler, N. Chawla, J. Lund, et al., Patterns of colorectal cancer care in the United States and Canada: a systematic review, *J. Natl. Canc. Inst. Monogr.* (46) (2013) 13–35, 2013.
- [3] R. Ricciardi, B.A. Virnig, R.D. Madoff, et al., The status of radical proctectomy and sphincter-sparing surgery in the United States: diseases of the colon, & Rectum 50 (8) (2007) 1119–1127.
- [4] T.J. Ridolfi, N. Berger, K.A. Ludwig, Low anterior resection syndrome: current management and future directions, *Clin. Colon Rectal Surg.* 29 (3) (2016) 239–245.
- [5] M.T. Nguyen, U.R. Phatak, L.T. Li, et al., Review of stoma site and midline incisional hernias after stoma reversal, *J. Surg. Res.* 190 (2) (2014) 504–509.
- [6] G. De Keersmaecker, R. Beckers, E. Heindryckx, et al., Retrospective observational study on the incidence of incisional hernias after reversal of a temporary diverting ileostomy following rectal carcinoma resection with follow-up CT scans, *Hernia* 20 (2) (2016) 271–277.
- [7] B.S. Oriol, Q. Chen, K.M.F. Itani, Incidence, recurrence and risk factors of hernias following stoma reversal, *Am. J. Surg.* 214 (2) (2017) 232–238.
- [8] M.H. Schreinemacher, G.H. Vijgen, P.C. Dagnelie, J.G. Bloemen, B.F. Huijzinga, N. D. Bouvy, Incisional hernias in temporary stoma wounds: a cohort study, *Arch. Surg.* 146 (1) (2011) 94–99.
- [9] S.P. Sharp, J.K. Francis, B.T. Valerian, J.J. Canete, A.D. Chismark, E.C. Lee, Incidence of ostomy site incisional hernias after stoma closure, *Am. Surg.* 81 (12) (2015) 1244–1248.
- [10] B. de Goede, H.H. Eker, P.J. Klitsie, et al., Incisional hernia after liver transplantation: risk factors and health-related quality of life, *Clin. Transplant.* 28 (7) (2014) 829–836.
- [11] D.R. Urbach, Measuring quality of life after surgery, *Surg. Innovat.* 12 (2) (2005) 161–165.
- [12] E.Y. Ah-Kee, T. Kallachil, P.J. O'Dwyer, Patient awareness and symptoms from an incisional hernia, *Int. Surg.* 99 (3) (2014) 241–246.
- [13] V. Shubinets, J.P. Fox, M.A. Lanni, et al., Incisional hernia in the United States: trends in hospital encounters and corresponding healthcare charges, *Am. Surg.* 84 (1) (2018) 118–125.
- [14] G.H. van Ramshorst, H.H. Eker, W.C.J. Hop, et al., Impact of incisional hernia on health-related quality of life and body image: a prospective cohort study, *Am. J. Surg.* 204 (2) (2012) 144–150.
- [15] S. Ravn, H.V. Thaysen, S. Harsløf, et al., Incisional hernia and its impact on health-related quality of life after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy: a national prospective cohort study, *World J. Surg. Oncol.* 16 (1) (2018).
- [16] K. Itatsu, Y. Yokoyama, G. Sugawara, et al., Incidence of and risk factors for incisional hernia after abdominal surgery, *Br. J. Surg.* 101 (11) (2014) 1439–1447.
- [17] N.A. Henriksen, F. Helgstrand, K.C. Vogt, L.N. Jorgensen, T. Bisgaard, Risk factors for incisional hernia repair after aortic reconstructive surgery in a nationwide study, *J. Vasc. Surg.* 57 (6) (2013) 1524–1530, 1530.e1521–1523.
- [18] M. Nakayama, K. Yoshimatsu, H. Yokomizo, et al., Incidence and risk factors for incisional hernia after open surgery for colorectal cancer, *Hepato-Gastroenterology* 61 (133) (2014) 1220–1223.
- [19] T.M. Connelly, R. Tappouni, P. Mathew, J. Salgado, E. Messaris, Risk factors for the development of an incisional hernia after sigmoid resection for diverticulitis: an analysis of 33 patients, operative and disease-associated factors, *Am. Surg.* 81 (5) (2015) 492–497.
- [20] F.J. Amelung, L.E.V.M. de Guerre, E.C.J. Consten, et al., Incidence of and risk factors for stoma-site incisional herniation after reversal, *BJS Open* 2 (3) (2018) 128–134.
- [21] T. Kaneko, K. Funahashi, M. Ushigome, et al., Incidence of and risk factors for incisional hernia after closure of temporary ileostomy for colorectal malignancy, *Hernia* Aug; 23 (4) (2019) 743–748, <https://doi.org/10.1007/s10029-018-1855-4>.
- [22] J.M. Weissler, M.A. Lanni, J.Y. Hsu, et al., Development of a clinically actionable incisional hernia risk model after colectomy using the healthcare cost and utilization project, *J. Am. Coll. Surg.* 225 (2) (2017) 274–284, e271.
- [23] R.W. Luijendijk, W.C. Hop, M.P. van den Tol, et al., A comparison of suture repair with mesh repair for incisional hernia, *N. Engl. J. Med.* 343 (6) (2000) 392–398.
- [24] M.W. Christoffersen, F. Helgstrand, J. Rosenberg, H. Kehlet, T. Bisgaard, Lower reoperation rate for recurrence after mesh versus sutured elective repair in small umbilical and epigastric hernias. A nationwide register study, *World J. Surg.* 37 (11) (2013) 2548–2552.
- [25] A. Bhangu, K. Futaba, A. Patel, T. Pinkney, D. Morton, Reinforcement of closure of stoma site using a biological mesh, *Tech. Coloproctol.* 18 (3) (2014) 305–308.
- [26] D.S. Liu, E. Banham, S. Yellapu, Prophylactic mesh reinforcement reduces stomal site incisional hernia after ileostomy closure, *World J. Surg.* 37 (9) (2013) 2039–2045.
- [27] L. Maggiori, D. Moszkowicz, M. Zappa, C. Mongin, Y. Panis, Bioprosthetic mesh reinforcement during temporary stoma closure decreases the rate of incisional hernia: a blinded, case-matched study in 94 patients with rectal cancer, *Surgery* 158 (6) (2015) 1651–1657.
- [28] Reinforcement of Closure of Stoma Site C, the West Midlands Research C, Feasibility study from a randomized controlled trial of standard closure of a stoma site vs biological mesh reinforcement, *Colorectal Dis.* 18 (9) (2016) 889–896.
- [29] K.W. van Barneveld, R.R. Vogels, G.L. Beets, et al., Prophylactic intraperitoneal mesh placement to prevent incisional hernia after stoma reversal: a feasibility study, *Surg. Endosc.* 28 (5) (2014) 1522–1527.
- [30] R. Simon, Optimal two-stage designs for phase II clinical trials, *Contr. Clin. Trials* 10 (1) (1989) 1–10.
- [31] R.E. Jensen, A.L. Potosky, C.M. Moinpour, T. Lobo, D. Cella, E.A. Hahn, B.B. Reeve, United States population-based estimates of patient-reported outcomes measurement information system symptom and functional status reference values for individuals with cancer, *J. Clin. Oncol. : Off. J. Am. Soc. Clin. Oncol.* 35 (17) (2017) 1913–1920, <https://doi.org/10.1200/JCO.2016.71.4410>.
- [32] A. Liapi, C. Mavrantonis, P. Lazaridis, E. Kourkouni, A. Zevlas, G. Zografos, G. Theodoropoulos, Validation and comparative assessment of low anterior resection syndrome questionnaires in Greek rectal cancer patients, *Ann. Gastroenterol.* 32 (2) (2019) 185–192, <https://doi.org/10.20524/aog.2019.0350>.
- [33] A. Sharma, A.P. Deeb, A.S. Rickles, J.C. Iannuzzi, J.R. Monson, F.J. Fleming, Closure of defunctioning loop ileostomy is associated with considerable morbidity, *Colorectal Dis.* 15 (4) (2013) 458–462.
- [34] M. Mengual-Ballester, J.A. Garcia-Marin, E. Pellicer-Franco, et al., Protective ileostomy: complications and mortality associated with its closure, *Rev. Esp. Enferm. Dig. : organo oficial de la Sociedad Espanola de Patologia Digestiva* 104 (7) (2012) 350–354.
- [35] N. Mirbagheri, J. Dark, S. Skinner, Factors predicting stomal wound closure infection rates, *Tech. Coloproctol.* 17 (2) (2013) 215–220.
- [36] J.T. Lee, T.T. Marquez, D. Clerc, et al., Pursestring closure of the stoma site leads to fewer wound infections: results from a multicenter randomized controlled trial, *Dis. Colon Rectum* 57 (11) (2014) 1282–1289.
- [37] M.J. Rosen, J.J. Bauer, M. Harmaty, et al., Multicenter, prospective, longitudinal study of the recurrence, surgical site infection, and quality of life after contaminated ventral hernia repair using biosynthetic absorbable mesh: the COBRA study, *Ann. Surg.* 265 (1) (2017) 205–211.
- [38] A.M. Carbonell, C.N. Criss, W.S. Cobb, Y.W. Novitsky, M.J. Rosen, Outcomes of synthetic mesh in contaminated ventral hernia repairs, *J. Am. Coll. Surg.* 217 (6) (2013) 991–998.
- [39] L.M. Jimenez-Gomez, E. Espin-Basany, L. Trenti, et al., Factors associated with low anterior resection syndrome after surgical treatment of rectal cancer, *Colorectal Dis.* (2017).
- [40] A.E. Park, J.S. Roth, S.M. Kavac, Abdominal wall hernia, *Curr. Probl. Surg.* 43 (5) (2006) 326–375.
- [41] D.R. Baillie, S.P. Stawicki, N. Eustance, D. Warsaw, D. Desai, Use of human and porcine dermal-derived bioprostheses in complex abdominal wall reconstructions: a literature review and case report, *Ostomy/Wound Manag.* 53 (5) (2007) 30–37.
- [42] K. Breuing, C.E. Butler, S. Ferzoco, et al., Incisional ventral hernias: review of the literature and recommendations regarding the grading and technique of repair, *Surgery* 148 (3) (2010) 544–558.
- [43] N.K. Burns, M.V. Jaffari, C.N. Rios, A.B. Mathur, C.E. Butler, Non-cross-linked porcine acellular dermal matrices for abdominal wall reconstruction, *Plast. Reconstr. Surg.* 125 (1) (2010) 167–176.
- [44] F.E. Primus, H.W. Harris, A critical review of biologic mesh use in ventral hernia repairs under contaminated conditions, *Hernia* 17 (1) (2013) 21–30.

- [45] A. Majumder, J.S. Winder, Y. Wen, E.M. Pauli, I. Belyansky, Y.W. Novitsky, Comparative analysis of biologic versus synthetic mesh outcomes in contaminated hernia repairs, *Surgery* 160 (4) (2016) 828–838.
- [46] N. Argudo, J.A. Pereira, J.J. Sancho, E. Membrilla, M.J. Pons, L. Grande, Prophylactic synthetic mesh can be safely used to close emergency laparotomies, even in peritonitis, *Surgery* 156 (5) (2014) 1238–1244.
- [47] F.P. Albino, K.M. Patel, M.Y. Nahabedian, M. Sosin, C.E. Attinger, P. Bhanot, Does mesh location matter in abdominal wall reconstruction? A systematic review of the literature and a summary of recommendations, *Plast. Reconstr. Surg.* 132 (5) (2013) 1295–1304.
- [48] L. Timmermans, B. de Goede, S.M. van Dijk, G.J. Kleinrensink, J. Jeekel, J. F. Lange, Meta-analysis of sublay versus onlay mesh repair in incisional hernia surgery, *Am. J. Surg.* 207 (6) (2014) 980–988.
- [49] J.L. Holihan, I. Bondre, E.P. Askenasy, et al., Sublay versus underlay in open ventral hernia repair, *J. Surg. Res.* 202 (1) (2016) 26–32.
- [50] B.K. Poulouse, J. Shelton, S. Phillips, et al., Epidemiology and cost of ventral hernia repair: making the case for hernia research, *Hernia* 16 (2) (2012) 179–183.
- [51] J.P. Fischer, M.N. Basta, N.M. Krishnan, J.D. Wink, S.J. Kovach, A cost-utility assessment of mesh selection in clean-contaminated ventral hernia repair, *Plast. Reconstr. Surg.* 137 (2) (2016) 647–659.