Evaluating the Impact of Technique and Mesh Type in Complicated Ventral Hernia Repair: A Prospective Randomized Multicenter Controlled Trial

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BACKGROUND: To our knowledge, there is an absence of prospective randomized multicenter controlled trials evaluating both the impact of technique and mesh type on outcomes in complicated ventral hernia repair.

STUDY DESIGN: A prospective randomized multicenter controlled trial of 120 patients at 3 sites was conducted in which patients were randomized to either overlay (anterior component separation) or underlay mesh placement (posterior component separation) and mesh type (human acellular dermis [HADM] vs porcine acellular dermis [PADM]). Key inclusion criteria included hernia size (>200 cm^2), BMI < 40 kg/m^2, hemoglobin A1C < 7%, tobacco free > 6 weeks and primary fascial closure. Primary outcome was hernia recurrence at 1 year, determined by independent examiner/imaging. Secondary outcomes included complications and patient satisfaction (short form [SF]-36v2). Standardized investigator training included a porcine model followed by a proctored first case by the lead investigator.

RESULTS: There were no significant differences in demographics between the 4 groups (age 60 ±12 years, BMI 32 ± 5 kg/m^2, 51% female). The overall 1-year recurrence rate was 10.8%. There was no significant difference in recurrence rate by location of mesh placement (overlay 9.8%, underlay 11.9%) or mesh type (HADM 10.3%, PADM 11.3%). Overlay patients had a significantly lower surgical site infection rate (1.6% vs 11.9% $p = 0.03$), reported better physical functioning ($p = 0.001$) and role limitation scores ($p = 0.04$) in the early postoperative period, and achieved the highest physical functioning score during the 12-month period ($p < 0.03$).

CONCLUSIONS: Recurrence rates were not affected by either anatomic location or type of mesh used. To our knowledge, this represents the first prospective randomized multicenter controlled trial that demonstrates similar clinical outcomes using HADM vs PADM (not inferiority, contrary to previously published literature), with several advantages identified using the overlay technique. (J Am Coll Surg 2019;228:377−390. © 2019 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Large complicated abdominal wall hernias are extremely challenging in this patient population due to comorbidities such as obesity, diabetes, and surgical complications related to the repair because of the size and complexity of the hernia.[1,2] For decades, surgeons performing abdominal wall reconstruction have continued their attempt to find the perfect technique and prosthetic to achieve the best outcome for these patients.[3-21] As with any

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Abbreviations and Acronyms

HADM = human acellular dermis
PADM = porcine acellular dermis
SF-36v2 = Medical Outcomes Study 36-Item Short Form Survey version 2

complicated procedure, experts continue to debate which technique is superior and which mesh is best or optimal for the repair, especially because recurrence rates continue to be reported to be as high as 30%.[1]

Abdominal wall reconstruction continues to evolve with advancements in surgical techniques. Plastic and reconstructive surgeons were the first to introduce component separation as a means to advance tissue (both muscle and fascia) to the midline to allow for midline abdominal wall closure.[22] Ramirez and colleagues[22] originally described techniques of medial fascial advancement to aid in reconstruction. This included both posterior release of the rectus sheath and creation of large skin flaps and release of the external oblique muscles in cases in which posterior release was insufficient. There are ongoing modifications of these techniques in an attempt to decrease recurrence rates and complications. This modification continuum extends to the Rives-Stoppa–Wantz retrorectus repair, in which the 6 to 8 cm wide potential space between the posterior sheath and the rectus muscle is opened to allow for insertion of mesh.[23,24] Methods to extend this potential space are described to include the release of the transversus abdominis muscle (TAR).[25-27] Despite these recent advancements, debate continues between the various surgical disciplines regarding whether one technique is clearly superior to the other and whether this difference affects outcome.[28]

The type of mesh to be used in complicated abdominal hernia repair is also undecided. It has been clearly shown that some type of reinforcement is needed because tissue repair alone is associated with a higher recurrence rate.[16,17] The other key factor is that large complex repairs tend to be recurrent in nature and therefore have significant adhesive disease, which typically is associated with numerous enterotomies and/or intra-abdominal contamination. Therefore, the surgeon is often faced with the dilemma to avoid a permanent synthetic mesh. In these settings, the safest option usually involves the use of a biologic mesh, which acts as a tissue-conductive scaffold allowing for cellular infiltration and remodeling into host tissue or "neofascia."[8,29] This neofascia acts as a new and additional supportive layer to the patient's own native tissue. There is no consensus about which biologic mesh is superior; several reports have demonstrated conflicting results regarding the efficacy of these meshes derived from various sources such as human cadaveric or porcine dermis in complicated hernia repair.[8,29,30] Most recently, porcine acellular dermis (PADM or Strattice [Allergan]) has gained favor in regard to market share in abdominal reconstruction as compared with human acellular dermis (HADM) when an acellular dermal mesh is chosen for hernia repair. This is most likely related to several reports regarding the high failure rate of highly processed human cadaveric dermis such as Alloderm (Allergan) as it is believed that HADM is more likely to stretch as compared with PADM.[8,30] We previously reported greater success with a less processed HADM (Flex-HD, Musculoskeletal Transplant Foundation) in abdominal wall reconstruction because our experience with it has shown that it is less likely to stretch and is associated with a significantly lower recurrence rate compared with Alloderm.[8]

There is a lack of prospective randomized trials evaluating techniques of repair and comparison of different biologic mesh. The main objective of our study was to determine which technique (overlay/anterior component separation vs underlay/posterior component separation [sublay/retrorectus]) and which biologic mesh (HADM [Flex-HD] or PADM [Strattice]) is most effective in complicated abdominal hernia repair.

METHODS

Patients and oversight

We conducted a prospective randomized double-blinded controlled trial at 3 centers in the United States. Before study initiation, all surgeon investigators were required to complete a proctored animal lab, where all study procedures and mesh insertion techniques were supervised by the study's principal investigator. In addition, the first study patient enrolled at each site was proctored by the principal investigator to assure that all study procedures and techniques were understood and followed. Strict inclusion/exclusion criteria are listed in Table 1. Most notably, we included adult patients with ventral hernia defects ≥ 200 cm^2, a BMI ≤ 40 kg/m^2, and a known hemoglobin A1C < 7. We excluded moribund patients, patients unlikely to survive more than 1 year, those unwilling to return for follow-up, and patients with infected prosthetic material (Fig. 1). Before enrolling patients, institutional review board approval was obtained at all sites. All study procedures were performed in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki.

Procedures and randomization

Patients who met inclusion and exclusion criteria were approached to participate in the informed consent

Table 1. Complete List of Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
≥18 years of age; have a BMI ≤40 kg/m^2; have a preoperative estimate of a hernia defect of ~ 200 cm square **or** multiple hernia defects whose combined area is ≥ an estimated 200 cm^2. Patients whose defects do not meet these criteria intraoperatively will be withdrawn from the study and will be considered an intraoperative screen failure; have no contraindications to test material(s); have a life expectancy > 1 year in the opinion of the investigator; able to provide informed consent; able and willing to return for scheduled study visits during 1-year postoperative period.	<18 years of age; subject is determined to have an America Society of Anesthesiologists physical class of 4, 5, or 6; have a BMI > 40 kg/m^2; have an estimated hernia size of < 200 cm^2; have abdominal loss of domain such that the operation would be impractical or adversely affect respiratory or cardiovascular function to an unacceptable degree; inability to close the fascia primarily without abdominal wall mobilization or component separation; participation in an investigational drug or device study within the past 6 weeks before enrollment; have active necrotizing fasciitis or any other known active local or systemic infection; have a known collagen metabolism disorder or any medical condition that could interfere with normal tissue healing process, as determined by the investigator; have a known active malignancy present and/or had chemotherapy 12 weeks before screening or planned chemotherapy within 12 weeks of enrollment; have known moderate to severe cirrhosis, which, in the opinion of the investigator, would affect the outcome of this trial; have a life expectancy < 1 year; be unable to participate in the informed consent process or unwilling to return for scheduled study visits during 1-year postoperative period.

process. Those who provided informed consent were randomized by a central randomization system at the lead study site and maintained centrally by the study statistician. Enrolled subjects were randomly assigned in a 1:1 ratio in regard to technique (anterior component separation with mesh overlay vs posterior component separation with mesh inserted in the retrorectus space or as a sublay if the retrorectus space was not available). In addition,

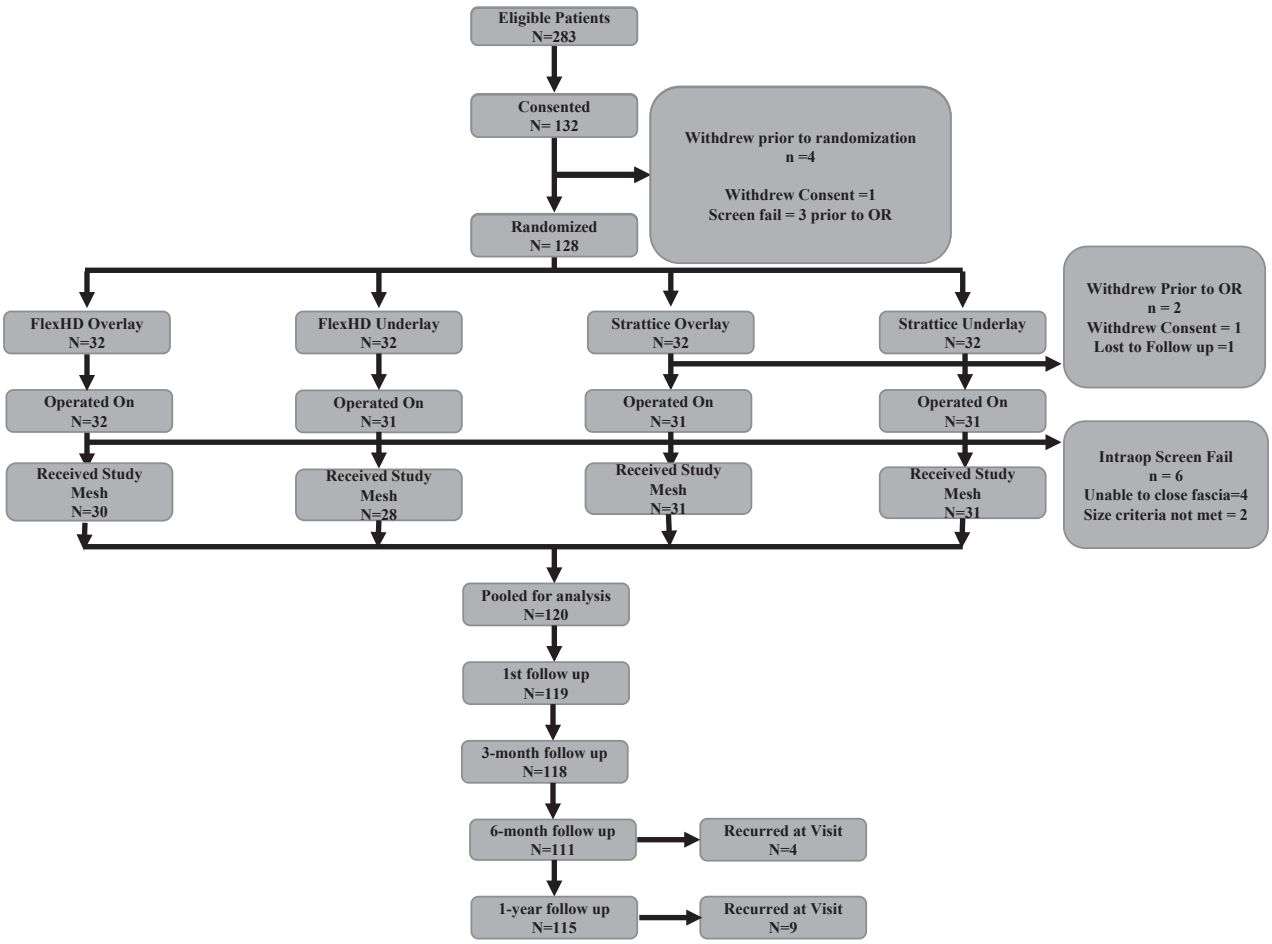

Figure 1. CONSORT diagram.

patients were randomly assigned in a 1:1 fashion to mesh type (human acellular dermis or porcine acellular dermis). Computer-generated randomization in blocks of 8, stratified by study center, were used to create a 1:1:1:1 protocol assignment. Cohort assignments were communicated to investigators immediately before surgery.

Our methods of anterior component separation are similar to that described by Ramirez and colleagues,[22] as the external oblique is released 2 cm lateral to its insertion at the linea semilunaris. The fascia is primarily closed, restoring the linea alba. The overlay mesh is sutured on tension to the fascia to create a "compressive" effect on the anterior abdominal wall. Regarding posterior component separation, the rectus sheath is released approximately 1 cm lateral to the linea alba, and careful dissection is performed, preserving the intercostal nerves. The posterior sheath is incised just lateral to the semilunaris and medial to the nerves, allowing exposure of the transversus abdominis muscle. If needed, dissection is continued and the transversus abdominis muscle is released, allowing entry to the retromuscular preperitoneal space. After the posterior rectus sheaths are reapproximated in the midline, the mesh is placed in the retrorectus space and secured with transfascial sutures. The linea alba is then restored by reapproximation of the anterior rectus sheaths. The key factor for each case was that the hernia defect was required to be too large for primary closure, as determined by the surgeon investigator, and component separation was indicated and needed in order to obtain midline closure of the hernia defect. If after the component separation was performed and midline fascial closure could not still be obtained, the patient was withdrawn from the study and considered a screen failure. These withdrawn patients were not included in the analysis.

All products were prepared in accordance with the manufacturer's instructions for use. Use of other mesh products and fibrin sealants were excluded. After repair, drains were inserted in the retrorectus and/or subcutaneous spaces. The number of drains placed was at the discretion of the investigator performing the surgery.

Outcomes and follow-up

Primary outcomes were the incidence of true hernia recurrence, fluid collections, surgical site infections, enterocutaneous fistulas, systemic infections, mesh failures, and adverse events at or before 1 year. Secondary outcomes included incidence of functional hernia recurrence or laxity and patient satisfaction ratings via the Medical Outcomes Study 36-Item Short Form Survey version 2 (SF-36v2) evaluation.

Data were collected at the patient's preoperative visit, intraoperatively, immediately in the postoperative period, at the 1- to 6-week postoperative visit, at a 3-month telephone follow-up, and at 6- and 12-month follow-ups. Demographics, medical history, a physical exam, and preoperative sitting and standing lateral and frontal photographs were captured at the preoperative visit.

Intraoperatively, duration of the surgery, size and location of the hernia defect, details of the operative procedure, and information regarding complications of the surgery were collected by study staff in real time. In addition, intraoperative photos delineating the size of the hernia as well as confirmation of mesh placement were performed. Hernia recurrence was assessed at the immediate postoperative visit and at the 3- 6-, and 12- month follow-up visits. Photos were taken at all study visits and recurrence was assessed by physical exam by a blinded investigator. If there was any concern for hernia recurrence, a CT scan of the abdomen and pelvis was performed. Patient well-being, as measured by the SF-36v2 was collected preoperatively, at the postoperative visit, and at 3-, 6-, and 12-month follow-ups.[31]

Analysis

We planned to enroll 120 patients based on an 80% power to detect differences at the 95% significance level with a 1-sided test. This assumed recurrence rates of 35% and 15% for HADM and PADM, respectively.

Data from each site were pooled for analysis. We performed univariate analysis comparing the demographics, medical history, and outcomes for all 4 study arms. We then performed univariate analysis to assess for possible predictors of recurrence. After this, binary logistic regression for all factors of $p < 0.200$, mesh used, and mesh location was performed to assess for independent risk factors for hernia recurrence. The SF-36v2 surveys were converted to their 8 functional domains, as previously described.[31] Finally, we performed further analysis of HADM vs PADM and overlay vs underlay placement. Continuous variables were analyzed by *t*-test and 1-way ANOVA. Chi-square test was used to analyze categorical variables. The Cochran-Armitage Ordinal test and Jonckheere-Terprstra tests were used for trends. All analyses were performed using SAS version 9.4.

RESULTS

Enrollment

Of 283 patients screened, 137 met inclusion criteria; 120 patients were consented, randomized, and then underwent the study procedure. Thirty patients received HADM in an overlay position, 28 received HADM in an underlay position; 31 received PADM in an overlay and 31 received PADM as an underlay.

Demographics

The average age of study participants was 60.6 years (±12.23 years); 61 (50.8%) were women and 89 (74.2%) were Caucasian. The average BMI was 31.7 kg/m^2 (±5.37 kg/m^2) and 100 patients (83.3%) were identified as having had their hernia for more than 1 year at time of enrollment. The majority of patients, 117 (97.5%) had at least 1 previous abdominal wall hernia repair. After randomization, there were no significant differences in demographics, past medical history, or patient characteristics (hernia size) between patients allocated to different study arms, including hernia defect size at time of randomization. Complete demographics and patient characteristics are shown in Table 2. We then re-evaluated for any significant differences based on specific randomization group. When comparing the overlay vs underlay groups alone, the only differences identified were that underlay patients were slightly older (63 vs 58 years, p = 0.03) and were more likely to be female (p = 0.03) (Table 3)

Outcomes of patients by randomization group

Regarding the primary outcome, there were a total of 13 recurrences (10.8%) in the entire study cohort (Table 4).

Table 2. Demographics by Randomization Group

Variable	Overall	HADM over	HADM under	PADM over	PADM under	p Value
n	120	30	28	31	31	N/A
Age, y, mean (SD)	60.64 (12.23)	56.33 (11.20)	64.86 (9.48)	60.06 (14.03)	61.52 (12.58)	0.06
BMI, kg/m^2, mean (SD)	31.73 (5.37)	32.19 (5.55)	32.69 (5.08)	30.48 (5.40)	31.68 (5.45)	0.42
Sex, n (%)						0.11
Male	59 (49.17)	20 (66.67)	11 (39.29)	16 (51.61)	12 (38.71)	
Female	61 (50.83)	10 (33.33)	17 (60.71)	15 (48.39)	19 (61.90)	
Race, n (%)						0.84
White	89 (74.17)	22 (73.33)	21 (75.0)	24 (77.42)	22 (70.97)	0.95
Black or African American	12 (10.0)	3 (10.0)	1 (3.57)	3 (9.68)	5 (16.13)	0.47
Hispanic or Latino	13 (10.83)	3 (10.0)	3 (10.71)	3 (9.68)	4 (12.90)	1.000
Native Hawaiian or Pacific Islander	1 (0.83)	0 (0.0)	1 (3.57)	0 (0.0)	0 (0.0)	0.23
Other	5 (4.17)	2 (6.67)	2 (7.14)	1 (3.23)	0 (0.0)	0.45
Duration of current hernia, n (%)						0.49
<6 wk	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	N/A
6 wk to 1 y	15 (12.5)	3 (10.0)	5 (17.86)	2 (6.45)	5 (16.13)	0.50
>1 y	100 (83.33)	26 (86.67)	22 (78.57)	26 (83.87)	26 (83.87)	0.87
Unknown	5 (4.17)	1 (3.33)	1 (3.57)	3 (9.68)	0 (0.0)	0.29
Alcohol use, n (%)						0.82
Yes	39 (32.50)	10 (33.33)	11 (39.29)	9 (29.03)	9 (29.03)	
No	81 (67.50)	20 (66.67)	17 (60.71)	22 (70.97)	22 (70.97)	
Tobacco use, n (%)						0.89
Past	59 (49.17)	16 (53.33)	13 (46.43)	17 (54.84)	13 (41.94)	0.75
Never	58 (48.33)	13 (43.33)	15 (53.57)	13 (41.94)	17 (54.84)	0.66
Diabetes, n (%)	33 (27.5)	6 (20.0)	8 (28.57)	8 (25.81)	11 (35.48)	0.59
Hypertension, n (%)	69 (57.5)	15 (50.0)	19 (67.86)	16 (51.61)	19 (61.29)	0.47
Obesity, n (%)	69 (57.5)	17 (56.67)	20 (71.53)	14 (45.16)	18 (58.06)	0.25
HIV/AIDS, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	N/A
COPD, n (%)	15 (12.5)	2 (6.67)	4 (14.29)	5 (16.13)	4 (12.90)	0.73
Collagen vascular disorder, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	N/A
Drug addiction, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	N/A
Additional medical history, n (%)	5 (4.17)	0 (0.0)	2 (7.14)	2 (6.45)	1 (3.23)	0.56
Previous surgical history, n (%)	117 (97.5)	30 (100.0)	28 (100.0)	29 (93.55)	30 (96.77)	0.62
Hernia defect size, cm^2, mean (SD)	297.15 (179.87)	287.78 (169.33)	296.45 (129.01)	258.05 (128.79)	345.96 (254.80)	0.28

HADM, human acellular dermis; PADM, porcine acellular dermis.

Table 3. Demographics Stratified by Mesh Type and Technique/Location

Variable	Overall	HADM	PADM	p Value	Over	Under	p Value
n	120	58	62		61	59	
Age, y, mean (SD)	60.64 (12.23)	60.45 (11.18)	60.79 (13.23)	0.8791	58.23 (12.75)	63.1 (11.25)	0.03*
BMI, kg/m^2, mean (SD)	31.73 (5.37)	32.43 (5.29)	31.08 (5.41)	0.1691	31.32 (5.5)	32.16 (5.26)	0.39
Sex, n (%)				0.3642			0.03*
Male	59 (49.17)	31 (53.45)	28 (45.16)		36 (59.02)	23 (38.98)	
Female	61 (50.83)	27 (46.55)	34 (54.84)		25 (40.98)	36 (61.02)	
Race, n (%)				0.3943			0.96
White	89 (74.17)	43 (74.14)	46 (74.19)	0.9945	46 (75.41)	43 (72.88)	0.21
Black or African American	12 (10.0)	4 (6.9)	8 (12.9)	0.273	6 (9.84)	6 (10.17)	0.95
Hispanic or Latino	13 (10.83)	6 (10.34)	7 (11.29)	0.8677	6 (9.84)	7 (11.86)	0.72
Native Hawaiian or Pacific Islander	1 (0.83)	1 (1.72)	0 (0)	0.4915	0 (0)	1 (1.69)	0.49
Other	5 (4.17)	4 (6.9)	1 (1.61)	0.196	3 (4.92)	2 (3.39)	1.00
Duration of current hernia, n (%)				0.9296			0.18
<6 wk	0 (0.0)	0 (0.0)	0 (0.0)	N/A	0 (0.0)	0 (0.0)	N/A
6 wk to 1 y	15 (12.5)	8 (13.79)	7 (11.29)	0.6787	5 (8.2)	10 (16.95)	0.15
>1 y	100 (83.33)	48 (82.76)	52 (83.87)	0.8702	52 (85.25)	48 (81.36)	0.56
Unknown	5 (4.17)	2 (3.45)	3 (4.84)	0.7033	4 (6.56)	1 (1.69)	0.18
Alcohol use, n (%)				0.4017			0.7
Yes	39 (32.50)	21 (36.21)	18 (29.03)		19 (31.15)	20 (33.9)	
No	81 (67.50)	37 (63.79)	44 (70.97)		42 (68.85)	39 (66.1)	
Tobacco use, n (%)				1.0000			0.44
Past	59 (49.17)	29 (50)	30 (48.39)	0.8598	33 (54.1)	26 (44.07)	0.27
Never	58 (48.33)	28 (48.28)	30 (48.39)	0.9903	26 (42.62)	32 (54.24)	0.20
Diabetes, n (%)	33 (27.5)	14 (24.14)	19 (30.65)	0.4250	14 (22.95)	19 (32.2)	0.25
Hypertension, n (%)	69 (57.5)	34 (58.62)	35 (56.45)	0.8102	31 (50.82)	38 (64.41)	0.13
Obesity, n (%)	69 (57.5)	37 (63.79)	32 (51.61)	0.1774	31 (50.82)	38 (64.41)	0.13
HIV/AIDs, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA	0 (0.0)	0 (0.0)	NA
COPD, n (%)	15 (12.5)	6 (10.34)	9 (14.52)	0.4899	7 (11.48)	8 (13.56)	0.73
Collagen vascular disorder, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA	0 (0.0)	0 (0.0)	NA
Drug addiction, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA	0 (0.0)	0 (0.0)	NA
Additional medical history, n (%)	5 (4.17)	2 (3.45)	3 (4.84)	1.0000	2 (3.28)	3 (5.08)	0.67
Previous hernia surgery, n (%)	117 (97.5)	58 (100)	59 (95.16)	0.2445	59 (96.72)	58 (98.31)	1.00
Hernia defect size, cm^2, mean (SD)	297.15 (179.87)	272.7 (149.6)	322.5 (204.8)	0.1323	302 (205.1)	292 (150)	0.75

*Significant.
HADM, human acellular dermis; PADM, porcine acellular dermis.

There were no significant differences in recurrence rates at 1 year overall and when compared by both technique (overlay, 9.84% vs underlay, 11.86%) and mesh type (HADM, 10.3% vs PADM, 11.29%). As expected, seroma rates were significantly higher in the overlay group (26% vs 8.5%, p = 0.01); however, surgical site infections were higher in the underlay group (11.86% vs 1.64%, p = 0.03). When we performed further analysis stratified by mesh type and technique, the HADM overlay group had the lowest rates of surgical site infection (p = 0.05) and infection rate (p = 0.02) of all 4 groups (Table 5).

Risk factors of hernia recurrence

Finally, we sought to determine risk factors of hernia recurrence. On univariate analysis, patients with recurrence at 1 year were more likely to have had numerous previous abdominal hernia repairs compared with those who did not have hernia recurrence (p = 0.03). Although there were no other significant risk factors when evaluated by univariate analysis, the p value of BMI, race, duration of current hernia, tobacco use, and hernia size were < 0.200 and thus included in multivariate analysis along with mesh type and location. Complete univariate analysis is shown in Table 6.

Table 4. Outcomes by Mesh Type and Location

Variable	Overall	HADM	PADM	p Value	Overlay	Underlay	p Value
n	120	58	62		61	59	
Recurrence, n (%)	13 (10.83)	6 (10.34)	7 (11.29)	0.8677	6 (9.84)	7 (11.86)	0.72
Time to recurrence, d, mean (SD)	327.38 (89.61)	320.2 (83.11)	333.6 (101.0)	0.8010	329.7 (115.0)	325.4 (70.87)	0.93
Mortality, n (%)	1 (0.83)	0 (0)	1 (1.61)	1.0000	0 (0)	1 (1.69)	0.49
Wound dehiscence, n (%)	13 (10.83)	6 (10.34)	7 (11.29)	0.8677	7 (11.48)	6 (10.17)	0.81
Seroma, n (%)	21 (17.50)	10 (17.24)	11 (17.74)	0.9425	16 (26.23)	5 (8.47)	0.01
Hematoma, n (%)	6 (5.00)	3 (5.17)	3 (4.84)	1.0000	5 (8.2)	1 (1.69)	0.20
Enterocutaneous fistula, n (%)	1 (0.83)	0 (0)	1 (1.61)	1.0000	0 (0)	1 (1.69)	0.49
Max laxity, n (%)				0.6299			0.95
None	79 (68.70)	39 (69.64)	40 (67.8)	0.7531	41 (67.21)	38 (70.37)	0.74
Mild	21 (18.26)	10 (17.86)	11 (18.64)	0.9425	12 (19.67)	9 (16.67)	0.52
Moderate	8 (6.96)	5 (8.93)	3 (5.08)	0.4807	5 (8.2)	3 (5.56)	0.71
Severe	7 (6.09)	2 (3.57)	5 (8.47)	0.4409	3 (4.92)	4 (7.41)	0.71
Infection, n (%)	34 (28.3)	13 (22.41)	21 (33.87)	0.164	13 (21.31)	21 (35.59)	0.08
SSI, n (%)	8 (6.7)	2 (3.45)	6 (9.68)	0.2745	1 (1.64)	7 (11.86)	0.03
Contaminated procedure, n (%)	18 (15)	10 (17.24)	8 (12.9)	0.5060	7 (11.48)	11 (18.64)	0.27

HADM, human acellular dermis; PADM, porcine acellular dermis; SSI, surgical site infection.

Finally, to evaluate independent risk factors for hernia recurrence at 1 year, we performed binary logistic regression. All variables with $p < 0.0200$ as well as mesh location and mesh type were considered in this model. There were no statistically significant independent predictors of hernia recurrence except for BMI, number of previous abdominal operations, hernia size, and smoking history (Table 7).

Quality of life outcomes

We sought to determine the impact of study procedures on patient quality of life using the SF-36v2. We assessed changes in health in the year after hernia repair by analyzing change in health over the previous year at the 1-year visit between groups and by computing the 8 functional SF-36v2 health scores. Complete analysis of all 8 functional SF-36v2 measures are available in Table 8.

Table 5. Outcome Analysis by Both Mesh Type and Technique

Variable	Overall	HADM over	HADM under	PADM over	PADM under	p Value
n	120	30	28	31	31	120
Recurrence, n (%)	13 (10.83)	2 (6.67)	4 (14.29)	4 (12.90)	3 (9.68)	0.82
Time to recurrence, d, mean (SD)	327.38 (89.61)	291.5 (129.4)	334.5 (71.48)	348.75 (122.54)	313.33 (83.77)	0.91
Mortality, n (%)	1 (0.83)	0 (0.00)	0 (0.00)	0 (0.00)	1 (3.23)	1.0
Wound dehiscence, n (%)	13 (10.83)	5 (16.67)	1 (3.57)	2 (6.45)	5 (16.13)	0.24
Seroma, n (%)	21 (17.50)	8 (26.67)	2 (7.14)	8 (25.81)	3 (9.68)	0.08
Hematoma, n (%)	6 (5.00)	2 (6.67)	1 (3.57)	3 (9.68)	0 (0.00)	0.38
Enterocutaneous fistula, n (%)	1 (0.83)	0 (0.00)	0 (0.00)	0 (0.00)	1 (3.23)	1.0
Maximum laxity, n (%)						0.89
None	79 (68.70)	20 (66.67)	19 (73.08)	21 (67.74)	19 (67.86)	0.95
Mild	21 (18.26)	7 (23.33)	3 (11.54)	5 (16.13)	6 (21.43)	0.65
Moderate	8 (6.96)	2 (6.67)	3 (11.54)	3 (9.68)	0 (0.00)	0.29
Severe	7 (6.09)	1 (3.33)	1 (3.85)	2 (6.45)	3 (10.71)	0.83
SSI, n (%)	8 (6.7)	0 (0)	2 (7.14)	1 (3.23)	5 (16.13)	0.05*
Infection, n (%)	34 (28.3)	2 (6.67)	11 (39.29)	11 (35.48)	10 (32.26)	0.02*
Contaminated procedure, n (%)	18 (15)	4 (13.33)	6 (21.43)	3 (9.68)	5 (16.13)	0.65

*Significant.
HADM, human acellular dermis; PADM, porcine acellular dermis; SSI, surgical site infection.

Table 6. Univariate Analysis of Risk Factors for Hernia Recurrence

Variable	Recurrence	No recurrence	p Value
n	13	107	N/A
Age, y, mean (SD)	60.08 (18.13)	60.69 (11.43)	0.90
BMI, kg/m^2, mean (SD)	29.76 (5.96)	31.97 (5.28)	0.16
Sex, n (%)			1.00
Male	6 (46.15)	53 (49.53)	
Female	7 (53.85)	54 (50.47)	
Race, n (%)			0.09
White	9 (69.23)	80 (74.77)	
Black or African American	0 (0.0)	12 (11.21)	
Hispanic or Latino	2 (15.38)	11 (10.28)	
Native Hawaiian or Pacific Islander	1 (7.69)	0 (0.0)	
Other	1 (7.69)	4 (3.74)	
Duration of current hernia, n (%)			0.19
<6 wk	0 (0.0)	0 (0.0)	
6 wk to 1 y	3 (23.08)	12 (11.21)	
>1 y	9 (69.23)	91 (85.05)	
Unknown	1 (7.69)	4 (3.74)	
Alcohol use, n (%)			0.76
Yes	5 (38.46)	72 (67.29)	
No	8 (61.54)	35 (32.71)	
Tobacco use, n (%)			0.14
Past	4 (30.77)	54 (50.47)	
Never	8 (61.54)	50 (46.73)	
Diabetes, n (%)	4 (30.77)	29 (27.1)	0.75
Hypertension, n (%)	6 (46.15)	63 (58.88)	0.38
Obesity, n (%)	5 (38.46)	64 (59.81)	0.23
HIV/AIDS, n (%)	0 (0.0)	0 (0.0)	N/A
COPD, n (%)	2 (15.38)	13 (12.15)	0.66
Collagen vascular disorder, n (%)	0 (0.0)	0 (0.0)	N/A
Drug addiction, n (%)	0 (0.0)	0 (0.0)	N/A
Additional medical, n (%)	0 (0.0)	5 (4.67)	1.0
Previous hernia repair, n (%)	11 (84.62)	106 (99.07)	0.03*
Mesh used, n (%)			1.0
HADM, n (%)	6 (46.15)	52 (48.60)	
PADM, n (%)	7 (53.85)	55 (51.40)	
Repair location, n (%)			0.72
Overlay	6 (46.15)	55 (51.40)	
Underlay	7 (53.85)	52 (48.60)	
Hernia defect size, cm^2, mean (SD)	350.6 (336.8)	290.7 (151.9)	0.53
Contaminated procedure, n (%)	1 (7.69)	17 (15.89)	0.68

*Significant.
HADM, human acellular dermis; N/A, not applicable; PADM, porcine acellular dermis.

Patients who underwent overlay mesh placement had better physical functioning (49.44 ±27.24 vs 33.33 ± 24.30, p = 0.0013) and role limitation subscores (36.64 ± 28.74 vs 26.18 ± 24.05, p = 0.0409) at the immediate postoperative visit than patients in the underlay group. In addition, the maximum physical functioning score was significantly higher in the overlay group over the 12-month period ($p < 0.030$).

DISCUSSION

Ventral hernia repair with abdominal wall reconstruction has become a commonly performed procedure and has

Table 7. Multivariate Analysis of Recurrence

Variable	Odds ratio	95% CI		p Value
BMI	0.769	0.636	0.931	0.007
Race				
White	reference			
Black or African American	0.002	<0.001	>999.999	0.94
Hispanic or Latino	0.829	0.037	18.754	0.97
Native Hawaiian or other Pacific Islander	>999.999	<0.001	>999.999	0.97
Other	3.609	0.251	51.959	0.99
Hernia duration				
Unknown	Reference			
6 wk to 1 y	0.134	0.004	4.95	0.53
>1 y	0.09	0.002	3.418	0.29
Previous hernia repair	0.014	<0.001	0.392	0.012*
Tobacco use				
Never	reference			
Former	0.25	0.045	1.386	0.022*
Hernia size	1.005	1.002	1.009	0.01*
Mesh				
PADM	reference			
HADM	2.049	0.419	10.019	0.38
Repair				
Underlay	reference			
Overlay	0.773	0.164	3.632	0.74

*Significant.
HADM, human acellular dermis; PADM, porcine acellular dermis.

evolved over the past several decades. Although there continues to be debate regarding which procedure is best and which mesh to use, there has been a general consensus that primary closure of the hernia defect is of the utmost importance and that mesh reinforcement decreases hernia recurrence.[8,13,16,17] In addition, mandating the modification of preoperative risk factors such as smoking cessation, weight loss (BMI < 40 kg/m^2), and glucose control (hemoglobin A1C < 7) have become widely accepted by most hernia experts in order to decrease recurrence rates and other complications in this high risk population.[1-4] Hernia specialists, however, continue to search for the most optimal technique and prosthetic for these complicated patients. A large number of different techniques stem from the fact that no single technique has stood out as being significantly better.[32]

The evolution of component separation stems from the desire to advance muscle/fascia tissue flaps to the midline for closure of large abdominal wall defects. As first described by Ramirez and colleagues,[22] anterior component separation in which the overlying fascia above the external oblique was divided became widely adapted. As with any procedure, surgeons began to attempt to modify this procedure in order to decrease complications and improve patient outcomes. Many surgeons believed that by performing a posterior component separation, they would avoid creating large abdominal wall soft tissue flaps, decreasing seroma and recurrence rates due to the positioning of mesh under the rectus muscle.[27]

This leads to the first question of whether there is a significant difference between anterior component separation with overlay mesh placement vs posterior component separation with retrorectus or underlay mesh placement in hernia recurrence. In our trial, there was no significant difference in hernia recurrence at 1 year when comparing anterior component separation with overlay mesh placement to posterior component separation with mesh underlay. This suggests that appropriate tension-free midline closure (with mesh support) is the most important factor in preventing hernia recurrence. In a comparative, retrospective review of more than 400 operations over a 25-year period, Langer and coauthors[33] concluded that the most important prognostic factor for good outcome was the experience and skill of the operating surgeon. It stands to reason, therefore, that any general surgeon contemplating abdominal wall reconstruction must have expertise in all of the following: knowledge of prosthetic materials to include both

Table 8. Analysis of the Eight Functional Subgroups by Randomized Group, Mesh Type, and Mesh Location

Variable	Preoperative	Postoperative	3-mo follow-up	6-mo follow-up	12-mo follow-up
Physical functioning					
n	115	112	110	96	86
Overlay (SD)	53.43 (27.07)	49.44 (27.24)	63.75 (24.67)	69.26 (22.43)	72.31 (23.17)
Underlay (SD)	47.07 (24.39)	33.33 (24.3)	59.77 (27.72)	59.36 (30.73)	61.96 (30.65)
p Value	0.189	0.001*	0.427	0.076	0.080
PADM (SD)	49.8338 (24.83)	40.69 (26.43)	63.77 (24.37)	63.54 (27.68)	68.71 (26.55)
HADM (SD)	50.9053 (27.25)	42.59 (27.69)	60.16 (27.68)	65.29 (26.8)	65.93 (28.43)
p Value	0.826	0.713	0.471	0.754	0.641
HADM over (SD)	55.32 (27.47)	50.63 (27.01)	66.72 (23.4)	67.29 (24.76)	72.27 (21.2)
HADM Under (SD)	46.15 (26.73)	30 (21.54)	60.05 (25.59)	59.79 (30.38)	64.59 (31.76)
PADM over (SD)	51.73 (27.05)	48.33 (27.86)	60.78 (25.96)	71.16 (20.28)	72.35 (25.5)
PADM under (SD)	47.87 (22.6)	36.43 (26.63)	59.54 (29.74)	58.91 (31.76)	59.78 (30.24)
p Value	0.562	0.011*	0.712	0.330	0.341
Role limitation due to physical health					
n	116	111	111	96	85
Overlay (SD)	48.94 (30.27)	36.64 (28.74)	64.66 (28.35)	67.52 (28.55)	71.83 (25.98)
Underlay (SD)	47.3 (29.98)	26.81 (24.05)	59.43 (27.72)	66.36 (27.91)	63.31 (34.62)
p Value	0.769	0.041*	0.330	0.841	0.201
PADM (SD)	48.74 (29.75)	31.96 (28.34)	66.86 (23.53)	69.44 (28.01)	64.94 (30.74)
HADM (SD)	47.46 (30.55)	31.36 (25.95)	57.83 (31.21)	64.45 (28.25)	70.31 (30.53)
p Value	0.821	0.908	0.088	0.387	0.421
HADM over (SD)	50.45 (33.33)	40.18 (29.87)	68.53 (25.14)	69.1 (29.38)	69.22 (23.2)
HADM under (SD)	44.37 (27.67)	22.75 (23.86)	64.84 (21.79)	69.79 (27.19)	59.98 (37.72)
PADM over (SD)	47.58 (27.7)	33.33 (27.73)	60.78 (31.2)	66 (28.25)	74.43 (28.8)
PADM under (SD)	49.93 (32.17)	29.24 (24.24)	54.96 (31.49)	62.77 (28.79)	66.19 (32.31)
p Value	0.874	0.118	0.299	0.825	0.503
Role limitation due to emotional problem					
n	116	111	111	96	86
Overlay (SD)	64.41 (31.78)	63.51 (33.98)	78.59 (27.13)	74.32 (28.91)	80.3 (25.86)
Underlay (SD)	66.16 (31.97)	62.26 (35.6)	78.77 (29.76)	82.27 (23.22)	76.69 (29.35)
p Value	0.768	0.851	0.973	0.142	0.546
PADM (SD)	64.55 (32.06)	61.32 (33.26)	83.02 (24.78)	79.17 (25.21)	77.74 (28.47)
HADM (SD)	66.06 (31.67)	64.37 (36.03)	74.71 (30.83)	77.26 (27.86)	79.26 (26.92)
p Value	0.799	0.645	0.123	0.726	0.800
HADM over (SD)	66.37 (33.14)	63.99 (30.6)	82.47 (24.43)	74.65 (27.85)	80.3 (22.35)
HADM Under (SD)	65.74 (30.69)	58.33 (36.4)	83.68 (25.71)	83.68 (21.91)	74.78 (34.65)
PADM over (SD)	62.63 (30.95)	63.06 (37.38)	74.71 (29.5)	74 (30.46)	80.3 (29.5)
PADM under (SD)	66.53 (33.59)	65.77 (35.16)	74.71 (32.62)	80.8 (24.93)	78.26 (24.84)
p Value	0.961	0.886	0.497	0.516	0.914
Energy/fatigue					
n	115	111	111	96	86
Overlay (SD)	50.95 (23.12)	47.13 (19.83)	60.45 (21.47)	61.35 (21.97)	62.45 (21.31)
Underlay (SD)	48.33 (20.41)	42.22 (21.68)	60.73 (19.04)	60.42 (23.41)	57.64 (26.77)
p Value	0.520	0.215	0.943	0.840	0.358
PADM (SD)	49.72 (21.35)	42.26 (20.94)	62.62 (20.82)	62.11 (22.6)	61.13 (25.27)
HADM (SD)	49.62 (22.45)	47.09 (20.55)	58.73 (19.73)	59.68 (22.72)	59.17 (23.26)
p Value	0.980	0.223	0.315	0.601	0.709

(Continued)

Table 8. Continued

Variable	Preoperative	Postoperative	3-mo follow-up	6-mo follow-up	12-mo follow-up
HADM over (SD)	50.45 (24.53)	40.92 (18.91)	60.99 (23.9)	59.9 (22.19)	62.41 (22.5)
HADM Under (SD)	48.77 (20.51)	43.75 (23.32)	64.58 (16.66)	64.32 (23.27)	59.65 (28.71)
PADM over (SD)	51.41 (22.17)	52.92 (19.19)	59.91 (19.16)	62.75 (22.13)	62.5 (20.59)
PADM under (SD)	47.92 (20.67)	40.85 (20.45)	57.54 (20.55)	56.34 (23.36)	55.98 (25.6)
p Value	0.9279	0.083	0.6578	0.6424	0.7838
Emotional well-being					
n	115	111	111	96	86
Overlay (SD)	68.71 (23.24)	67.5 (18.29)	75.78 (18.8)	72.76 (22.57)	76.11 (19.9)
Underlay (SD)	65.2 (22.17)	66.42 (21.09)	80.38 (17.86)	78.4 (19.62)	78.57 (17.92)
p Value	0.410	0.772	0.190	0.195	0.549
PADM (SD)	65.46 (21.36)	67.17 (20.32)	81.23 (17.78)	78.96 (18.91)	78.78 (19.07)
HADM (SD)	68.68 (24.1504)	66.81 (19.07)	75 (18.64)	72.08 (23.06)	75.97 (18.83)
p Value	0.449	0.924	0.075	0.114	0.494
HADM over (SD)	71.38 (25.02)	65 (18.1)	78.79 (19.71)	74.79 (22.77)	76.36 (20.36)
HADM under (SD)	65.88 (23.35)	69.6 (22.68)	84.17 (15.01)	83.13 (13.25)	81.58 (17.56)
PADM over (SD)	66.29 (21.64)	69.83 (18.45)	72.76 (17.66)	70.8 (22.67)	75.85 (19.89)
PADM under (SD)	64.57 (21.4)	63.57 (19.52)	77.24 (19.62)	73.48 (23.9)	76.09 (18.21)
p Value	0.694	0.534	0.162	0.209	0.747
Social functioning					
n	116	111	111	96	86
Overlay (SD)	65.89 (27.93)	53.02 (27.74)	74.35 (26.12)	76.53 (26.1)	83.24 (21.72)
Underlay (SD)	57.68 (28.71)	46.7 (28.71)	72.17 (28.13)	76.86 (25.67)	76.49 (30.14)
p Value	0.121	0.241	0.672	0.950	0.239
PADM (SD)	60.45 (28.25)	51.65 (29.01)	78.77 (23.2)	80.21 (24.71)	82.62 (23.37)
HADM (SD)	63.41 (28.95)	48.49 (27.71)	68.32 (29.36)	73.18 (26.55)	77.5 (28.65)
p Value	0.580	0.559	0.041*	0.182	0.369
HADM over (SD)	67.86 (28.95)	55.36 (27.09)	78.88 (24.34)	76.56 (28.39)	84.09 (18.17)
HADM under (SD)	58.8 (28.76)	47.5 (31.04)	78.65 (22.26)	83.85 (20.35)	80.92 (28.68)
PADM over (SD)	64.11 (27.34)	50.83 (28.61)	69.83 (27.45)	76.5 (24.29)	82.39 (25.2)
PADM under (SD)	56.67 (29.13)	45.98 (27.01)	66.81 (31.57)	69.57 (28.91)	72.83 (31.45)
p Value	0.438	0.622	0.229	0.309	0.490
Pain					
n	116	111	111	96	86
Overlay (SD)	57.42 (24.69)	40.82 (22.22)	69.91 (23.05)	72.81 (28.11)	70.4 (24.56)
Underlay (SD)	49.47 (28.53)	35.94 (22.43)	67.45 (27.28)	68.67 (24.86)	68.04 (28.77)
p Value	0.111	0.253	0.608	0.448	0.683
PADM (SD)	49.84 (28.09)	39.91 (21.86)	72.31 (24.81)	73.39 (25.4)	68.96 (25.6)
HADM (SD)	57.59 (24.98)	37.2 (22.9)	65.47 (25.08)	68.18 (27.6)	69.5 (27.71)
p Value	0.121	0.526	0.152	0.339	0.926
HADM over (SD)	60.8 (24.27)	41.88 (24.2)	71.55 (24.86)	71.04 (30.46)	66.93 (24.04)
HADM under (SD)	54.26 (25.72)	37.7 (19.16)	73.23 (25.24)	75.73 (19.47)	71.32 (27.77)
PADM over (SD)	54.35 (25.07)	39.83 (20.56)	68.28 (21.39)	74.5 (26.18)	73.86 (25.14)
PADM under (SD)	45.17 (30.63)	34.38 (25.24)	62.67 (28.39)	61.3 (28.02)	65.33 (29.92)
p Value	0.17	0.636	0.421	0.236	0.702
General health					
n	116	112	111	96	86
Overlay (SD)	58.45 (23.28)	61.72 (17.21)	63.51 (19.1)	66.07 (20.3)	66.28 (22.07)
Underlay (SD)	53.3114 (23.13)	62.31 (21.63)	64.93 (16.91)	66.12 (19.88)	62.2 (23.38)
p Value	0.235	0.873	0.681	0.991	0.408

(Continued)

Table 8. Continued

Variable	Preoperative	Postoperative	3-mo follow-up	6-mo follow-up	12-mo follow-up
PADM (SD)	54.28 (22.64)	63.33 (19.28)	67.38 (18.09)	67.08 (18.73)	64.7 (22.97)
HADM (SD)	57.75 (23.98)	60.78 (19.55)	61.27 (17.6)	65.1 (21.32)	63.92 (22.66)
p Value	0.425	0.488	0.074	0.630	0.875
HADM over (SD)	57.72 (24.57)	61.43 (18.65)	67.41 (20.03)	63.75 (21.58)	62.73 (24.38)
HADM under (SD)	57.78 (23.82)	65.38 (20.1)	67.34 (15.86)	70.42 (15.1)	66.97 (21.64)
PADM over (SD)	59.11 (22.44)	62 (16.06)	59.61 (17.6)	68.3 (19.16)	69.83 (19.4)
PADM under (SD)	49.29 (22.11)	59.46 (22.95)	62.93 (17.75)	61.63 (23.37)	58.26 (24.48)
p Value	0.342	0.735	0.301	0.412	0.351

*Significant.
HADM, human acellular dermis; PADM, porcine acellular dermis.

synthetic and biologic, when and where to use them, anterior and posterior separation of components, vacuum-assisted closure devices, and when to involve plastic surgeons.[32]

In this study, experienced surgeons were chosen as investigators to avoid having experience and skill level affect the results of the study. In addition, we held a training lab to standardize the procedures and ensure proper technique. Finally, the first case of each site was proctored by the lead investigator, and he determined if the site was ready to independently enroll study participants.

As expected, sterile seromas were more common in the anterior component separation/overlay approach (26% vs 8.5%, $p < 0.01$). Most interesting, there was a significantly higher surgical site infection rate in the underlay arm (11.8% vs 1.64%, $p < 0.01$). This was not expected because there was no significant difference in the number of "contaminated" cases, defined as patients having any gastric or bowel enterotomy during the procedure. We believe that this difference may stem from the fact that in the anterior/overlay approach, drains are placed widely above the mesh and are more effective in protecting the mesh from bacteria and consequently, surgical site infection. Another potential factor may be related to bacteria proliferating more in the underlay position as compared with the overlay position. We have considered this as a possible explanation for this finding, as we previously reported this outcome in animal models in which we infected rabbits with various pathogens and randomized them in a similar fashion to this study. A significantly lower surgical site infection rate was observed in the overlay technique, but it is worth mentioning that the animal model did not include placing drains.[34]

The next question we sought to answer was whether there was a difference in outcomes between human acellular dermis vs porcine acellular dermis when used as a reinforcement in complicated hernia repair with midline fascial closure. Ngo and colleagues[29] reported that HADM, compared with PADM, had significantly greater tensile strength and significantly faster tissue ingrowth at both 4 and 20 weeks in a rabbit model. In this study, there was no significant difference in hernia recurrence when comparing the 2 mesh types, regardless of anatomic mesh placement (overlay vs underlay/retrorectus). As mentioned earlier, there was a significantly greater seroma rate in both HADM and PADM overlay patients; however, there was no significant difference between the 2 meshes themselves. Again, we saw a significantly lower surgical site infection rate in the overlay arm (regardless of type of mesh); however, the lowest rate was seen in patients who received overlay mesh with HADM ($p < 0.05$). This may be due to the faster tissue ingrowth, as reported in animal models, as well as the local tissue environment and drain protection.[29,34]

We evaluated numerous factors that have previously been shown to be associated with higher recurrence rates. As expected, increasing defect size was associated with a higher recurrence rate. This study was focused on recurrence rates in large hernias (>200 cm^2); however, there may be a threshold at which the size of the hernia places one at an additional higher risk category that is only clearly delineated at the time of surgery, when a definitive intraoperative measurement is made (which was a study-related procedure in this study). In addition, a history of smoking was associated with a higher recurrence rate. One of the exclusion criteria was smoking cessation at a minimum of 6 weeks before surgery. There may be a subset of patients who do not benefit from only a 6-week period of smoking cessation before and after surgery.

Physical function is extremely important after abdominal reconstruction. Patients who underwent overlay mesh placement reported significantly higher satisfaction physical performance scores early in the postoperative period, regardless of mesh type. In addition, the overlay performance scores remained higher throughout the 1-year period, and patients with overlay placement reported a significantly higher score over the 12-month period. Further research is needed to better understand this

finding and to evaluate the long-term impact of surgical technique on improvement in physical performance.

CONCLUSIONS

In summary, to our knowledge, this represents the first prospective randomized trial that has evaluated clinical outcomes comparing both mesh type (HADM vs PADM) as well as surgical technique (anterior component separation/overlay vs posterior component separation [underlay]). We found no significant difference in recurrence rates at 1 year between groups. In addition, the overlay group did have advantages including lower surgical site infection rates and improved physical functioning over the 12-month study period. As expected, the overlay group did have a higher seroma rate. Further research is needed to better understand the nature of these differences.

Author Contributions

Study conception and design: G Bochicchio, Garcia, Kaufman, K Bochicchio

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REFERENCES

1. Vidović D, Jurisić D, Franjić BD, et al. Factors affecting recurrence after incisional hernia repair. Hernia 2006;10:322–325.
2. Anthony T, Bergen PC, Kim LT, et al. Factors affecting recurrences following incisional herniorrhaphy. World J Surg 2000; 24:95–100.
3. Santora TA, Rosylin JJ. Incisional hernia. Surg Clin North Am 1993;73:557–570.
4. Pollock AV, Evans M. Early prediction of late incisional hernia. Br J Surg 1989;76:953–954.
5. Mudge M, Hughes LE. Incisional hernia: a 10 year prospective study of incidence and attitudes. Br J Surg 1985;72:70–71.
6. Cassar K, Munro A. Surgical treatment of incisional hernia. Br J Surg 2002;89:534–545.
7. Paul E, Rosen M. Open ventral hernia repair with component separation. Surg Clin North Am 2013;93:111–113.
8. Bochicchio GV, De Castro GP, Bochicchio KM, et al. Comparison study of acellular dermices in complicated hernia surgery. J Am Coll Surg 2013;217:606–613.
9. Bluebond-Langner R, Keifa ES, Mithani S, et al. Recurrent abdominal laxity following interpositional human acellular dermal matrix. Ann Plast Surg 2008;60:76–80.
10. Rodriguez ED, Bluebond-Langner R, Silverman RP, et al. Abdominal wall reconstruction following severe loss of domain: the R Adams Cowley Shock Trauma Center algorithm. Plast Reconstr Surg 2007;120:669–680.
11. Jin J, Rosen MJ. Laparoscopic versus open ventral hernia repair. Surg Clin North Am 2008;88:1083–1100.
12. Paul A, Korenkov M, Peters S, et al. Unacceptable results of the Mayo procedure for repair of abdominal incisional hernias. Eur J Surg 1998;164:361–367.
13. Flum DR, Horvath K, Koepsell T. Have outcomes of incisional hernia repair improved with time? A population-based analysis. Ann Surg 2003;237:129–135.
14. Korenkov M, Sauerland S, Arndt M, et al. Randomized clinical trial of suture repair, polypropylene mesh or autodermal hernioplasty for incisional hernia. Br J Surg 2002;89:50–56.
15. Wheeler AA, Matz ST, Bachman SL, et al. Retrorectus polyester mesh repair for midline ventral hernias. Hernia 2009; 13:597–603.
16. Burger JW, Luijendijk RW, Hop WC, et al. Long-term follow-up of a randomized controlled trial of suture versus mesh repair of incisional hernia. Ann Surg 2004;240: 578–583.
17. Luijendijk RW, Hop WC, van den Tol MP, et al. A comparison of suture repair with mesh repair for incisional hernia. N Engl J Med 2000;343:392–398.
18. Koller R, Miholic J, Jakl RJ. Repair of incisional hernias with expanded polytetrafluoroethylene. Eur J Surg 1997;163: 261–266.
19. de Vries Reilingh TS, van Goor H, Charbon JA, et al. Repair of giant midline abdominal wall hernias: "components separation technique" versus prosthetic repair: interim analysis of a randomized controlled trial. World J Surg 2007;31:756–763.
20. Usher FC, Ochsner J, Tuttle LL Jr. Use of marlex mesh in the repair of incisional hernias. Am Surg 1958;24:967–974.
21. Klinge U, Conze J, Krones C, et al. Incisional hernia: open techniques. World J Surg 2005;29:1066–1072.
22. Ramirez OM, Ruas E, Dellon AL. "Components separation" method for closure of abdominal-wall defects: an anatomic and clinical study. Plast Reconstr Surg 1990;86:519–526.
23. Rives J, Pire JC, Flament JB, et al. Treatment of large eventrations. New therapeutic indications apropos of 322 cases. Chirurgie 1985;111:215–225.
24. Stoppa RE. The treatment of complicated groin and incisional hernias. World J Surg 1989;13:545–554.
25. Carbonell AM, Cobb WS, Chen SM. Posterior components separation during retromuscular hernia repair. Hernia 2008; 12:359–362.
26. Novitsky YW, Elliott HL, Orenstein SB, et al. Transversus abdominis muscle release: a novel approach to posterior component separation during complex abdominal wall reconstruction. Am J Surg 2012;204:709–716.
27. Krpata DM, Blatnik JA, Novitsky YW, et al. Posterior and open anterior components separations: a comparative analysis. Am J Surg 2012;203:318–322.
28. Reid CM, Brandel MG, Gosman AA. Comparison of surgeon specialty in open ventral hernia repair. Ann Plast Surg 2017; 78:S212–S216.
29. Ngo M, Aberman H, Hawes M, et al. Evaluation of human acellular in an in vivo model for incisional hernia repair. Cell Tissue Bank 2011;12:135–145.

30. Janis J, O'Neill A, Ahmad J, et al. Acellular dermal matrices in abdominal wall reconstruction: a systematic review of the current evidence. Plast Reconstr Surg 2012;130:183–193.
31. Ware JE Jr, Sherbourne CD. The MOS 36-Item Short-Form Health Survey (SF-36): I. Conceptual framework and item selection. Med Care 1992;30:473–483.
32. Stylianides N, Slade D. Abdominal wall reconstruction. Br J Hosp Med 2016;77:151–158.
33. Langer C, Schaper A, Lierch T, et al. Prognosis factors in incisional hernia surgery: 25 years of experience. Hernia 2005;9:16–21.
34. Nohra E, Turnbull I, Fuchs A, et al. Overlay placement of mesh compared to underlay is associated with greater bacterial clearance and lower intra-abdominal infection in a contaminated ventral hernia repair model. Surg Infections 2016;17:38.

Discussion

DR BRENT MATTHEWS (Charlotte, NC): Surgical literature is littered with low-impact preclinical studies and retrospective, prospective uncontrolled, or single-armed longitudinal clinical trials evaluating similar biologic meshes. Ventral hernia repair is primed for disruption in a value-based delivery model based on clinical outcomes, cost of care, and patient-reported outcomes such as functionality and physical and/or mental well-being.

This study facilitates our understanding of how mesh use, either human acellular dermis or porcine acellular dermis, and surgical technique, anterior component with overlay vs posterior component with sublay, alter outcomes.

This study can be criticized for minor methodologic concerns, such as transaxial imaging, to be performed at the discretion of the blinded observer vs all patients undergoing imaging to determine recurrences, not testing the patients the day of operation for urine nicotine and metabolites to verify smoking cessation, and a follow-up period of 1 year that is likely not enough time to evaluate recurrence. Nevertheless, the study was otherwise extremely well controlled.

The patients enrolled in this prospective randomized trial had CDC Class 1 wounds. Eighteen patients had conversion to a contaminated wound more in the human acellular dermal matrix and sublay groups. What were the CDC wound classifications of the contaminated cases, and were they distributed equally among the cohorts? Did the difference in the number of those converted to a contaminated case potentially influence outcomes such as surgical site infection and recurrence?

Truly, a little bit more thought provoking, in patients who have a BMI < 40 kg/m^2, a hemoglobin A1C < 7, have stopped smoking 6 weeks before operation, and have a CDC Class 1, is synthetic mesh the more appropriate choice of biomaterial, and how did that affect informed consent for the trial?

One of the inclusion criteria was a ventral hernia > 200 cm^2. Although similar in terms of inclusion criteria for this study, the technical challenge of a patient with a ventral hernia 20 cm in vertical length and 10 cm in width is completely different than that of a patient with a ventral hernia 10 cm in vertical length and 20 cm in width. If recurrence rates in the cohorts were evaluated based on width alone, do you anticipate similar outcomes would be reported?

There is not any reference in the paper to the size of biomaterials used for repair or the need to suture any of the biologic meshes together due to limitations in size, as shown in the past. Can the authors comment about this and if there were any potential effects on the outcomes of the study in respect to recurrence?

A total of 97.5% of patients enrolled in the trial had undergone previous ventral hernia repair. It is likely that there was significant heterogeneity of techniques used for repair during these index procedures. If patients had undergone a previous myofascial release or had lipocutaneous flaps develop during the previous operations, did you anticipate this to be a confounding variable?

Lastly, the overlay patients who had large lipocutaneous flaps had a significantly lower surgical site infection rate than the patients with retrorectus/posterior component repairs. This is a very unusual finding in comparison to previous published clinical literature. Intuitively, based on principles of blood supply, you would not expect that as an outcome. What is the reasoning for the increased surgical site infection rate in the sublay patients?

DR PHILIP S BARIE (New York, NY): Abdominal wall reconstruction for large ventral incisional hernia is commonplace, yet relatively uninformed by prospective clinical data compared with other abdominal operations of similar frequency or complexity. Laparoscopic vs open, which mesh to use, how to mitigate the numerous complications that befall patients and their surgeons, are all valid questions and all are largely unanswered. Nonstandardized terminology is an important cofounder. The literature, as mentioned, is replete with anecdotes and nonrigorous investigations and specifically, with respect to mesh choice, with marketing claims that can be gossamer thin and sometimes seem to defy logic.

This randomized clinical trial presented by Bochicchio and colleagues is welcome indeed. By power analysis, assuming 15% and 35% recurrence rates for patients with, respectively, porcine and human dermis, 120 patients were enrolled from 283 screened and 137 eligible and randomized to 1 of 4 groups to receive either human or porcine dermal matrix, placed either as an overlay or in the retromuscular space in the manner of Rives-Stoppa, popularized in the US by one of my mentors, Dr George Watts.

This was a small study with 4 groups of 30 patients each, essentially. Included hernias were large in patients with morbid obesity and diabetes mellitus, and cases of infected mesh from a previous repair were excluded. The primary endpoint was hernia recurrence at 1-year follow-up, although seromas, surgical site infection (SSI), fistula, systemic infection, mesh failure, and other adverse events were tabulated. The technical descriptions in the manuscript are sufficiently clear to allow the reader to understand the surgical approaches. Statistical analysis was appropriate.

With respect to outcomes, seroma formation was significantly higher among the overlay patients; SSI was higher after retromuscular mesh placement. The lowest SSI rate was observed when human dermal matrix was used in an overlay position. By multivariable analysis, the factors that were independent predictors of 1-year hernia recurrence were higher BMI, higher number of previous