Multi-institutional Experience Using Human Acellular Dermal Matrix for Ventral Hernia Repair in a Compromised Surgical Field

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Background: A complex ventral hernia repair (CVHR) involves a compromised surgical field where gastrointestinal, biliary, and genitourinary procedures are performed. Complex ventral hernia is a significant problem in trauma, emergency, and elective general surgery in which prosthetic material is contraindicated. In this clinical scenario, primary fascia closure carries a 50% risk of developing a hernia. The other option is a planned ventral hernia with delayed repair.

Hypothesis: Human acellular dermal matrix is a suitable implant for CVHR in a compromised surgical field.

Design: Multi-institutional, 5-year retrospective review.

Setting: Four academic medical centers.

Patients and Methods: Each center obtained institutional review board approval. Patients included in the review had undergone CVHR with human acellular dermal matrix. Data collected included age, body mass index (calculated as weight in kilograms divided by height in meters squared), comorbidities, size of fascial defect, wound classification, hospital length of stay, length of follow-up, and mortality. Primary outcomes were surgical site infection, fistula recurrence, and hernia recurrence. Both $\chi^2$ and logistic regression analyses were performed.

Results: Two hundred forty patients met the study criteria. Their mean (SD) age was 52.2 (15.0) years, and 132 (55.0%) were men. The most common comorbidity was hypertension (115 patients [47.9%]), and the mean defect size was 201 cm$^2$. The mean hospital length of stay was 17.2 days, and the mean follow-up was 317 days. The overall mortality was 2.9%. The hernia recurrence rate was 17.1% (41 patients). Repair of a fistula or stoma was associated with hernia recurrence ($P = .03$) and with fistula recurrence ($P < .0011$). Logistic regression analysis demonstrated surgical site infection and body mass index of greater than 30 to be independent risks of hernia recurrence.

Conclusions: Human acellular dermal matrix is a suitable alternative for CVHR in a compromised surgical field. The hernia recurrence rate with human acellular dermal matrix in a compromised surgical field is less than that seen with primary repair, offering additional and improved surgical options for CVHR in this group of patients. Stoma or fistula takedown at the time of CVHR continues to be associated with significant complications.


Repair of a ventral hernia is one of the most common general surgical procedures. A prosthetic mesh repair during a clean case (ie, with no bacterial contamination) remains the standard of care for optimal long-term results.\textsuperscript{1,5} Patient selection and comorbidities are important factors in identifying patients who may be at risk of a recurrent hernia or a complication.\textsuperscript{6,7} Ventral hernia repair on a patient with significant comorbidities or in conjunction with another surgical procedure, with the potential for bacterial contamination, makes the use of a prosthetic mesh contraindicated.\textsuperscript{8,9} An infected prosthetic mesh usually needs to be removed and may result in a hernia defect.\textsuperscript{10,11}

An increasing number of patients are surviving surgery performed after trauma or peritonitis that occurs as a result of general surgery.\textsuperscript{12-15} This patient population is at a higher risk of the development of a complex ventral hernia (CVH). There are no classification systems that define a CVH, which can be described as a ventral hernia in a patient with a significant comorbidity or comorbidities or multiple previous operations or hernia repairs; in a

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patient with a planned ventral hernia after trauma with or without a split-thickness skin graft; or in a patient with a compromised surgical field in which gastrointestinal tract, biliary, or genitourinary procedures might contaminate the surgical field. Patients with an anastomosis, infected prosthetic mesh, or an enterocutaneous fistula with or without a hernia represent a surgical dilemma.

The clinical options for treating a patient with actively infected mesh, an ostomy takedown, or repair of an intestinal fistula are limited in terms of performing gastrointestinal tract procedures and a hernia repair during the same operation. One option is to stage the procedures. Initially, the contamination procedure, such as a colostomy takedown, would be performed. One accepts the planned ventral defect to be repaired at a later date. The patient must return 6 to 12 months later to undergo a clean ventral hernia repair. Staging the procedure requires that the patient undergo a temporary hernia repair, undergo 2 anesthetic procedures, and incur the risk involved with 2 surgical procedures. During the recovery period in a patient with a planned ventral hernia, the abdominal muscles begin to contract laterally and that results in the extrusion of the viscera out of the abdominal cavity. This causes the abdominal cavity to get smaller, resulting in loss of abdominal domain. The patient may be unable to return to work or care for his or her family.

Surgical site infection (SSI) remains a serious problem in this patient population. The biomedical industry has introduced biologic mesh that might be better able to tolerate bacterial contamination and have a lower incidence of SSI. Several companies have produced either porcine or human biologic mesh. Most are dermal matrices that have been engineered so that only the biologic scaffolding remains and all of the cellular and immunologic elements have been removed. We choose to study human acellular dermal matrix (HADM) (LifeCell Corporation, Branchburg, New Jersey) because this product has demonstrated the greatest success in the limited single-site studies to date. Our hypothesis was that HADM is a suitable implant for complex ventral hernia repair (CVHR) in a compromised surgical field.

METHODS

We performed a multi-institutional, 5-year (December 17, 2002, to January 27, 2006) retrospective study at 4 academic medical centers. Researchers at each center obtained institutional review board approval before beginning the study. Vanderbilt University Medical Center was the lead site, and all data analyses were performed there.

DEFINITIONS AND PATIENTS

A CVH was defined as a recurrent ventral hernia in a compromised surgical field in which gastrointestinal tract, biliary, and/or genitourinary procedures are performed. Removal of infected mesh and a plan to later repair the ventral hernia with or without a split-thickness skin graft represented a CVH in a compromised surgical field. Ostomy repair was defined as a formal ostomy takedown with a bowel anastomosis. Fistula repair was defined as a formal fistula takedown with a bowel resection and anastomosis.

Patients were included if they underwent a CVHR with HADM. Patients were excluded if they did not undergo repair of a midline, ventral fascial defect, or were prisoners. Human acellular dermal matrix is derived from the dermis of human donors and is harvested at tissue and organ banks. Preparation involves a multistep process in which the epidermis is separated from the dermis and all the cellular and immunologic elements are removed. This leaves a 3-dimensional matrix with all the mucopolysaccharides and vascular channels intact. Via a proprietary process, the matrix is cryopreserved with a shelf-life of 2 years.

DATA COLLECTION

The data collected included age, sex, body mass index (calculated as weight in kilograms divided by height in meters squared), comorbidities, hospital length of stay, length of follow-up, and mortality. The cumulative size of the implants was used to estimate the size of the ventral defect. The clinical scenario during the procedure was divided into trauma, emergency general surgery, and elective general surgery.

From a procedural standpoint, wound classification, suture type, and repair type were recorded. There were 4 types of repair performed: (1) interpositional (the edge of the mesh was sewn directly to the edge of the fascia), (2) onlay (mesh was laid onto the fascia with 3-5 cm of overlap), (3) inlay (mesh was placed under the fascia with 3-5 cm of underlay from the fascial edge), and (4) component separation. Component separation was performed using either a separation of parts or an open book technique of the myofascial component and advancement of the components medially. Human acellular dermal matrix was used for additional support as an onlay repair of the fascial relaxing incisions and/or an underlay. If a fascial defect remained, the repair type was then a bridge technique (interposition, onlay, or underlay). Closed suction drains were universally used in potential spaces. The clinical examination at follow-up was used to determine hernia recurrence (HR).

PRIMARY AND SECONDARY OUTCOMES

Primary outcomes were SSI, fistula recurrence, and HR. Secondary outcomes included other infectious complications (urinary tract infections, bloodstream infections, and ventilator-associated pneumonia), wound dehiscence, seroma formation (a sterile postoperative fluid collection in the subcutaneous layers), and days receiving ventilator support. Surgical site infections included only wound infections. Intra-abdominal abscesses were recorded separately. The Centers for Disease Control and Prevention National Nosocomial Infections Surveillance definitions for SSI, urinary tract infection, bloodstream infection, and ventilator-associated pneumonia were used.

A complete data set of study variables was not available for all patients owing to the retrospective nature of the study and the multiple study sites.

STATISTICAL ANALYSIS

Data analysis was performed using χ² test. Statistical significance was considered at P < .05. Logistic regression analysis was performed to identify the independent risk of HR for comorbidities. Multivariate logistic regression models were performed to determine the odds of HR, SSI, and fistula using PROC LOGISTIC in SAS version 9.1 (SAS Institute Inc, Cary, North Carolina). All intra-abdominal procedures were grouped and compared with ventral hernia repair only. Point estimates and 95% confidence intervals for odds ratios were reported. Confidence intervals not crossing unity were considered statistically significant.
RESULTS

There were 240 patients who met study criteria. Their mean (SD) age was 52.2 (15.0) years, and 132 (55.0%) were men. Of the 240 patients, 190 (79.2%) underwent an additional surgical procedure (Table 1). In this study population, none of the comorbidities were statistically significant in terms of risk for HR or SSI. Fifty-one (21.3%) of the 240 patients underwent removal of old mesh, and 40 (16.7%) underwent removal of a split-thickness skin graft. The mean (SD) hospital length of stay was 17.2 (20.9) days. There were 165 patients (68.7%) who had follow-up data, with a mean follow-up of 317 days (range [SD], 9-1161 [269] days).

The overall mortality was 2.9% (7 of 240). Four deaths occurred in patients who underwent emergency general surgery, 2 deaths occurred after elective surgery, and 1 death occurred in a trauma patient. Mortality during elective surgery occurred in patients who underwent successive attempts at repair of multiple atmospheric enterocutaneous fistulas (Table 2).

The mean (SD) defect size was 201 (155) cm² (median, 168; range, 21-896). When the defect size was divided into quartiles, there was no statistical significance in the rate of HR or SSI (Table 3).

The overall HR rate for the study was 17.1% (41 of 240). Most of the HRs occurred in patients in whom an additional procedure was performed (33 of 41 [80.5%]). Hernia recurrence was associated with a body mass index of greater than 30 (P = .02), mesh removal (P = .048), or ostomy or enterocutaneous fistula repair (P = .03). Postoperative factors associated with HR were SSI (P = .003) and fistula formation (P = .005). Component separation repair type had the lowest HR (2 of 31 [6.5%]), and inlay (17 of 91 [18.7%]), onlay (4 of 28 [14.3%]), and interpositional mesh repairs had the highest recurrence (18 of 89 [20.2%]), but these results did not reach statistical significance (P = .46). There was 1 patient for whom the repair type was unknown (Table 4).

Surgical site infections occurred in 96 of the patients (40.0%). Surgical site infection was associated with the repair type (interpositional mesh repair; P = .003) and wound classification (clean-contaminated; P = .01) (Table 5).

There were 28 postoperative fistulas (11.6%) among the 240 study patients. The fistulas occurred in the setting of ostomy or enterocutaneous fistula repairs (18 patients), bowel procedures (5 patients), and ventral hernia repair only (5 patients). Of the 5 cases of ventral hernia repair only, 1 patient underwent removal of old mesh. Fistula formation was associated with an ostomy or enterocutaneous fistula repairs (P < .001) and with removal of a split-thickness skin graft (P = .048) (Table 6).

Regarding other complications, postoperative ileus (34 of 240 [14.2%]) and wound seroma (31 of 240 [12.9%]) were the most common. Twenty-three of the 240 patients (9.6%) developed an intra-abdominal abscess, with 18 of the 23 abscesses (78.3%) occurring in cases in which a bowel procedure was performed. If an intra-abdominal abscess and a fistula developed, they were only counted as fistulas. There were 38 patients (24.2%) who required more than 1 day of ventilator support, with a mean (SD) of 4 (13) days receiving ventilator support. All of the pneumonia complications occurred in patients who required mechanical ventilation, except for 1 case (Table 7).
Logistic regression analysis was used to identify risk factors for HR. Body mass index greater than 30, SSI, and ostomy or fistula repair were independently associated with the development of an HR. Wound classification was associated with SSI. Ostomy or fistula repair and removal of a split-thickness skin graft during a planned ventral hernia were independent risk factors for fistula formation (Table 8).

The repair of a CVH has baffled surgeons for many years, and the standard of care continues to require the use of prosthetic mesh.1-3,20-22 Prosthetic mesh in a compromised surgical field is considered by many surgeons to be a contraindication.10,11 The wound infection rate is higher, and infection of a prosthetic mesh is a serious clinical problem.10,11 The clinical options when faced with such a scenario are to stage the procedures by initially per-
forming the bowel procedure and then, at a later date, to repair the hernia defect. Others have had success with the use of polypropylene mesh in ventral hernia repairs with an elective bowel procedure.21,22 However, polypropylene mesh is known to have the highest fistula formation of any prosthetic mesh, and the formation of a fistula can occur many years later.23,24

Recently, the biomedical industry has developed several biologic meshes for the repair of a ventral defect. Human and porcine matrixes have been the most common sources. We choose to study HADM because it most closely resembles the properties of native fascia. Once the matrix is implanted, it becomes revascularized into the wound with angiogenesis, bringing in the necessary fibroblasts to begin the incorporation process.26-28 The process of early angiogenesis is thought to provide the matrix with the abilities to clear local bacterial contamination and to resist infection.

Only HADM has been demonstrated in animal models to allow adequate fibroblast infiltration with resultant angiogenesis into the matrix.29 Other porcine matrix demonstrates higher fibroblast proliferation but limited infiltration into the matrix.27,28 This seems to be more specific to the porcine matrixes that have been permanently cross-linked.30 There is still concern that a xenograft dermal matrix implant will elicit an antibody response, which could result in rejection.31

Our study population reflects an extremely complex group of patients; only 5.6% of the cases were clean cases (ie, no bacterial contamination), 50% of the study group had at least 1 comorbidity, and 70% underwent an additional surgical procedure other than the hernia repair. Yet, the mortality was only 2.9%. In our study population, comorbidity did not demonstrate increased risk of HR or SSI, but patients with diabetes mellitus and morbid obesity are known to carry an increased risk of complications.5,6,32

The SSI rate in this population was 40%, which is high. The most recent Centers for Disease Control and Prevention National Nosocomial Infections Surveillance Report (1999-2004) of infection rates in elective ventral hernia repairs without bowel procedures gives a range of 1% to 3.8%, and colorectal procedures are listed in the range of 3.98% to 11.25% for SSIs, although dirty cases (with gross bacterial contamination) or infected cases historically have infection rates well above 50%. Recently, antibiotic studies for SSIs have provided more reliable data. For example, the PREVENT trial had an SSI rate, in elective colorectal surgery, in the range of 18% to 30%.33 Yet, even with our high infection rate for the study, the HR rate was only 17%. Our regression analysis demonstrated that SSI was an independent risk factor for HR. In general, SSI is a known risk factor of the development of a hernia in all laparotomies.6

The fistula recurrence for this population is high (12%). The study was not designed to tell if a biologic mesh contributed to the development of a fistula. Most of the fistulas (18 of 26 [69.2%]) occurred during an ostomy or a fistula repair. The group of concern is the 5 patients with postoperative fistula formation who underwent a hernia repair only. In review of the cases, 2 were trauma cases and 1 was an emergency general surgery case. The 2 elective cases in which a fistula occurred could be attributable to either a missed enterotomy or technical problem.

The HR rate for the study was 17%. These results are similar to the recently published reports with HADM.17-19 The short follow-up period and the low follow-up rate for this patient population do not allow for an accurate assessment of long-term success. The study did confirm that like prosthetic mesh repairs, ostomy, fistula repair, SSI, and obesity (body mass index of >30) are independent risk factors for early HR.6,32

The ability to combine a ventral hernia repair and a “contaminated” procedure into 1 anesthetic procedure and a single hospital stay is extremely attractive. From the patient’s perspective, recovering from 1 procedure, as opposed to 2, and returning to functional status are much more attractive. The study demonstrated that 123 of the 240 patients (51.2%) did not have an SSI, postoperative fistula, or HR in this complex patient population.

The question that has arisen from our study is, “Is there a subpopulation of patients for whom staging the repair of contaminated procedures and, at a later date, performing a ventral hernia repair is the better option?” Our study was not designed to answer this question, but clearly, owing to the high SSI and fistula formation rates, there is a group of patients for whom one should consider a staged approach.

**STUDY STRENGTHS**

There are several strengths to our study. It is a multi-institutional study with the study sites selected for their academic focus, large clinical experience with this complex patient population, and clinical expertise using the various available biologic mesh implants other than HADM for hernia repair. Our study is, to our knowledge, the largest series to date to study a complex patient population and the use of HADM for hernia repair. In addition, the results in this study parallel those seen in earlier single-site reports using HADM.17-19

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**Table 8. Multivariate Logistic Regression Analysis of Hernia Recurrence, Surgical Site Infection, and Fistula Formation**

<table>
<thead>
<tr>
<th>Effect</th>
<th>No.</th>
<th>P Value</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logistic Regression Analysis of Recurrent Hernia (n=41)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI &gt;30</td>
<td>240</td>
<td>0.02</td>
<td>0.374 (0.162-0.864)</td>
</tr>
<tr>
<td>SSI</td>
<td>96</td>
<td>0.003</td>
<td>0.969 (0.268-3.529)</td>
</tr>
<tr>
<td>Ostomy or fistula repair</td>
<td>81</td>
<td>0.03</td>
<td>0.276 (0.097-0.782)</td>
</tr>
<tr>
<td>Logistic Regression Analysis of SSI (n=96)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wound classification</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clean</td>
<td>50</td>
<td></td>
<td>6.164 (0.266-13.529)</td>
</tr>
<tr>
<td>Contaminated</td>
<td>113</td>
<td></td>
<td>7.099 (1.35-37.215)</td>
</tr>
<tr>
<td>Contaminated</td>
<td>13</td>
<td>0.01</td>
<td>7.201 (1.162-44.617)</td>
</tr>
<tr>
<td>Contaminated</td>
<td>49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contaminated</td>
<td>28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Logistic Regression Analysis of Fistula (n=28)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ostomy or ECF takedown</td>
<td>81</td>
<td>&lt;.001</td>
<td>5.670 (2.181-14.741)</td>
</tr>
<tr>
<td>STSG</td>
<td>40</td>
<td>0.048</td>
<td>5.606 (0.713-44.057)</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; ECF, enterocutaneous fistula; SSI, surgical site infection; STSG, split-thickness skin graft.
STUDY LIMITATIONS

There are several weaknesses to our study. This is a retrospective review with all the inherent associated problems. The multiple sites, multiple surgeons, and heterogeneity of the patient population make it difficult to accurately classify the results. In addition, the repair types and the suture used vary to the degree that HR rates are difficult to analyze. The trauma and emergency general surgery patient populations are known to have poor follow-up and resulted in incomplete study data capture. The clinical examination for defining an HR may have resulted in bias. Some of these ‘recurrences’ could have been better defined as laxity of the repair vs a true hernia.

The study was not designed to examine the issue of laxity of the abdominal wall repair. Laxity of the abdominal repair has been described in the literature. Many of the early series of ventral hernia repairs with HADM were performed during an acute illness. At this point, the patient has gained a significant amount of weight owing to the volume resuscitation and lost domain of the abdominal cavity. Laxity of the repair can later develop into a problem when the patient has improved clinically and loses the weight. Human acellular dermal matrix does not elicit as significant an inflammatory response as do other porcine or prosthetic implants because minimal wound contracture occurs. Laxity of the repair should be an almost expected result. Also, during the implantation, HADM must be placed on a great deal of tension. This is contrary to ventral hernia repair with a prosthetic mesh. If the elasticity in HADM is inadequately addressed during the repair, laxity of the repair may occur.

This study describes the early 5-year history of HADM for the repair of CVHR. Patient selection, operative techniques, postoperative complications, and follow-up assessments have continued to be refined. Yet, in a field where the available data are severely lacking, this study begins to define the scope of the problem and the areas of future study.

In conclusion, HADM is a suitable alternative for the CVHR in a compromised surgical field. The HR rate with HADM in a compromised surgical field is less than that seen with primary repair, offering additional and improved surgical options for CVHR in this group of patients. Ostomy or fistula takedown at the time of CVHR continues to be associated with significant complications. A randomized, multi-institutional study is needed to help define the patient who would best benefit from the use of HADM for the repair of a CVH and the best operative technique to use.

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Author Contributions: Drs Diaz, Conquest, and Miller had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Diaz and Vargo. Acquisition of data: Conquest, Ferzoco, Vargo, and Miller. Analysis and interpretation of data: Diaz, Conquest, Ferzoco, Wu, and Donahue. Drafting of the manuscript: Diaz, Conquest, Wu, and Donahue. Critical revision of the manuscript for important intellectual content: Diaz, Conquest, Ferzoco, Vargo, and Miller. Statistical analysis: Wu and Donahue. Administrative, technical, and material support: Diaz, Conquest, Vargo, and Miller. Study supervision: Diaz and Ferzoco.

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REFERENCES


