



Management Strategies for the Open Abdomen Following Damage Control Laparotomy

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Abstract

Purpose of Review The resultant open abdomen following damage control laparotomy can present a challenging clinical scenario. Management strategies remain critically important to optimize patient recovery and mitigate long-term morbidities.

Recent Findings The summation of recent data is largely limited to low-quality evidence, case series, and expert opinions on the optimal treatment strategies for patients with an open abdomen. Although a myriad of techniques have been studied in elective patients, there remains a paucity of data surrounding open abdominal closure. Recent guidelines from the European Hernia Society and the World Society of Emergency Surgery are limited based on the lack of high-quality data available.

Summary High-quality data surrounding optimal treatment strategies for the open abdomen is lacking. Early primary fascial closure represents the strategy of choice; however, when not possible, temporary abdominal closure with negative pressure therapy should be performed. Sequential dynamic closure techniques allow for improved outcomes when complete abdominal closure is not possible.

Keywords Open abdomen · Damage control laparotomy · Abdominal closure · Temporary abdominal closure · Trauma laparotomy

Introduction

Damage control laparotomy for traumatically injured patients represents a life-saving advancement in trauma care. Following the initial insult, this concept focuses on prompt open surgical exploration, control of ongoing hemorrhage, and gastrointestinal spillage plus resection

of damaged viscera without definitive repair or abdominal closure [1–4]. Rapid damage control interventions mitigate the effects of life-threatening disease processes and aid in stabilizing patients for further resuscitative efforts. Any evidence of decompensation during the acute period following the initial laparotomy is suggestive of ongoing ischemia, hemorrhage, or sepsis and requires an urgent

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evaluation. If this occurs, patients are returned to the operating room for repeated exploration in efforts to achieve control over the ongoing disease process. Following damage control surgery, the timing for re-exploration should occur following demonstration of adequate resuscitation no later than 24–48 h from the primary surgery. Definitive repair and/or closure of the abdominal fascia should be conducted once the patient is physiologically stable [5]. Although the principles governing damage control laparotomy decrease the overall operative time per procedure and allow for corrections in physiologic status prior to more complex repairs, patients often remain with an open abdomen for multiple days. Those who remain open for prolonged periods of time are at increased risk for loss of abdominal wall domain, dehiscence, ventral hernia, prolonged ileus, infections, fistula formation, and electrolyte disturbances [6–8, 9••]. Accordingly, all efforts to close the abdominal wall fascia in an expedient fashion should be made due to a reported 1.1% decrease in primary closure rates for every hour after the first 24 h with an open abdomen [10].

The management of the open abdomen can be challenging depending on the clinical situation present. Temporary abdominal closures are typically utilized in order to provide a protective seal between the underlying viscera and the outside environment. Initial reports during World War II describe the use of a Vaseline-covered piece of light canvas sutured to the edges of the rectus muscle to bridge the fascial defect in efforts to prevent retraction of the edges and allow the abdominal wall to help with respiration [11]. Advances in technology have largely altered the aforementioned approach; however, the principles of early strategies remain analogous to current-day techniques. A variety of commercially available temporary abdominal closure devices are on the market; however, many centers utilize a “homemade” approach using standard products found within the operating room. In fact, adoption of damage control laparotomy and the subsequent open abdomen has ventured beyond trauma cases and has been readily described for use within emergency general surgery, abdominal compartment syndrome, vascular surgery, and intraabdominal sepsis [12•, 13]. This article intends to describe the principles surrounding the management of the open abdomen, highlight various strategies to help aid in definitive closure, and describe various treatment strategies for loss of abdominal wall domain.

To Close or Not to Close?

The intraoperative decision to leave an abdomen open should be dictated by the patient’s underlying pathophysiology [3, 5]. Although primary closure at the end of each case should be considered, ineffective source control, ongoing concerns for malperfusion, hemodynamic instability, and loss of abdominal

wall domain may dictate otherwise. A multitude of approaches have been used for temporary abdominal closure, all of which focus on controlling fluid loss and providing a barrier to the outside environment to minimize injury and infection. Prior to the development of negative pressure wound dressings for open abdomens, Feliciano and Borraez Gaona [14] developed the “Bogata Bag.” This technique utilizes a sterile plastic 3-l bag of irrigation fluid to act as a protective barrier between the bowel and the outside environment so the bowel does not extrude from the peritoneal cavity. The irrigation bag is opened, drained, and cut into an oval. It is then sutured to the surrounding skin or fascial edges [14, 15]. This technique requires very little resources and provides a window to the intraperitoneal contents. However, when sutured in an air-tight fashion that does not allow for drainage of the intraabdominal ascites, it may increase intraabdominal pressures and result in an increased risk for abdominal compartment syndrome when left unchecked. Following stabilization of the physiologic insult, the bag must be removed in hopes for abdominal wall closure. If sutures were used to secure the bag to the fascial edge, the fascial integrity may be compromised from these sutures and can place the patient at increased risk for future hernia development due to the previously perforated fascia. This technique remains the potentially most viable option in low-resource and austere settings lacking more sophisticated and dedicated devices designed for the management of the open abdomen. Despite the paucity of large-scale data on clearly defining the optimal temporary closure technique, utilization of negative pressure wound therapy systems has become the most commonly employed technique in the USA [13].

Barker et al. [16, 17], Brock et al. [18], and Smith et al. [19] subsequently described their experience using a homemade vacuum pack as an alternative temporary abdominal closure technique that utilizes readily available materials found within the operating room. Similar in its complexity to the Bogata Bag, this approach uses negative pressure therapy and may help remove some of the pro-inflammatory cytokines found within the intraperitoneal fluid [20]. First, a sterile polyethylene sheet is placed into the intraperitoneal cavity and used to cover the bowel. Prior to placing the barrier, it is perforated to allow drainage of the abdominal fluid. The barrier should have wide coverage of the underlying bowel and wrap around the paracolic gutters to minimize the risk of evisceration. Moist sterile surgical towels are placed over the newly placed barrier with two 10-French flat silicone drains on top. The cavity is then covered in a large sheet of sterile drape (e.g., Ioban) that serves as a barrier from the surrounding environment. The drains are then connected to a suction source at 100 to 150 mm Hg of continuous negative pressure [16]. This approach has the benefit of providing suture-free negative pressure therapy to promote drainage of the intraperitoneal fluid. It does not, however, allow for direct visualization of the intraperitoneal contents.

A multitude of variations have been proposed to this technique to include the use of chest tubes to allow for improved negative pressure and wound vac sponges and canisters, as well as commercially available negative pressure temporary abdominal wall closure products (e.g., ABTHERA) [21]. Although most commonly associated with temporary abdominal closure, these techniques can also be used in the chest following resuscitative thoracotomy or median sternotomy during damage control settings (Fig. 1). Whether using commercially available systems or a combination of readily available resources from the operating room, the techniques that utilize negative pressure wound therapy represent the most commonly utilized approach for temporary abdominal wall closure following damage control laparotomy in both military and civilian settings (Fig. 2).

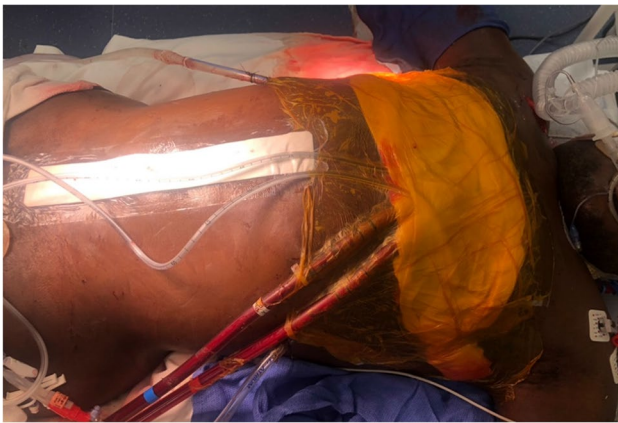
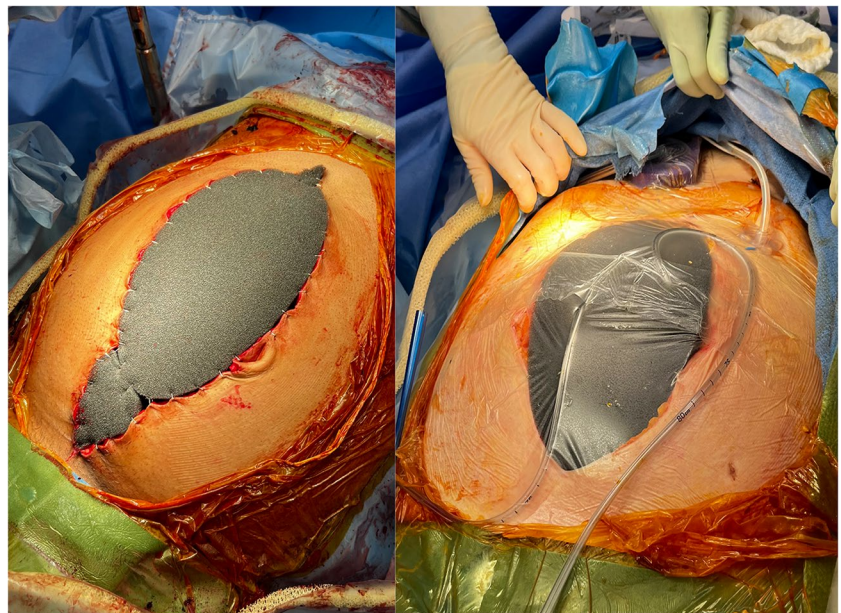


Fig. 1 Application of “homemade” negative pressure temporary closure following a resuscitative clamshell thoracotomy

Fig. 2 Application of wound vac sponge for negative pressure temporary abdominal closure



Resuscitation to Optimize Closure?

Following improvements in a patient’s physiologic status, prompt closure of the abdominal wall is critical. Nevertheless, failure to achieve primary closure is not uncommon. While negative pressure therapy as described above has demonstrated overall improvements in closure rate compared to other techniques, this does not completely address underlying visceral edema that may persist from the ongoing inflammatory state. This visceral edema, whether from the small bowel, colon, mesentery, or retroperitoneum, may prevent the abdominal wall from being physically closed or lead to increased intraabdominal hypertension that precedes abdominal compartment syndrome. In either case, retroperitoneal, intraperitoneal, and visceral edema represent a major component driving this pathophysiology and need to be addressed prior to successful closure.

Resuscitation strategies have evolved tremendously over the last 20 years. The previously accepted large-volume crystalloid-based resuscitations have become replaced with blood product-based strategies [22]. Moreover, whole blood is becoming increasingly utilized and accepted as the ideal resuscitation fluid for trauma patients [23, 24]. Fortunately, efforts to mitigate early crystalloid administration in trauma patients have decreased the rates of dilutional coagulopathy, acute respiratory distress syndrome, and visceral organ edema leading to multiorgan dysfunction. While changes in resuscitation patterns may have improved the overall visceral edema rates, there is a substantial inflammatory burden created by traumatic injuries. This inflammatory burden predisposes patients to capillary leak resulting in intravascular

depletion and increased interstitial edema. As such, morbidities due to the efflux of volume into the interstitial space persist, albeit at a seemingly lower rate than in previous eras.

The use of hypertonic saline is one intervention that takes aim at reducing endothelial leak within the bowel. Harvin et al. [25] were the first to describe their experience utilizing 3% hypertonic saline for maintenance intravascular fluid therapy following damage control laparotomy as an adjunct to help decrease the time to primary fascial closure. This protocol utilized 30 ml/h of 3% hypertonic saline for the first 3 days following the initial laparotomy or until primary fascial closure was obtained, whichever came first. When compared to their standard controls, the group receiving intravenous hypertonic saline demonstrated a decreased total volume of crystalloid administration within the first 72 h. Furthermore, the administration of intravenous hypertonic saline was associated with a 100% fascial closure rate and a reduction in time to fascial closure [25]. The idea of utilizing hypertonic saline to promote fascial closure was further evaluated by Loftus et al. [26]. This study demonstrated that hypertonic saline administration was associated with decreased intravenous fluid requirements and a non-statistically significant increased primary fascial closure rate, despite a potentially clinically significant 15% improvement in closure rates (92% vs 77%, $P=0.06$) [26]. Following the adoption of a standardized hypertonic saline protocol within their institution, Loftus et al. [27•] later demonstrated statically significant improved rates in primary fascial closure (93% vs 81%, $P=0.045$) without any adverse effects following their hypertonic protocol implementation. Basic science work has also demonstrated that the hypertonic osmotic gradient following hypotonic saline administration may decrease bowel wall edema within numerous animal models [28–30]. Despite the conglomerate of data from these studies displaying a near 100% primary fascial closure rate, the overall limited data currently available restricts the widespread inclusion of using intravascular hypertonic saline as an open abdomen adjunct into any current guidelines.

An alternative approach geared toward mitigating acute tissue edema acutely following damage control laparotomy is the utilization of direct peritoneal resuscitation (DPR). This process involves instilling a hypertonic glucose-based dialysis formula into the peritoneal cavity and has demonstrated promising results within the current trauma literature. Beyond mitigating tissue edema, DPR has demonstrated improvements in visceral perfusion, downregulation of the inflammatory response, normalization of internal body water ratios, mitigation of ischemia–reperfusion injury, improvements in intestinal barrier breakdown, and restoration of the endothelial glycocalyx in animal models [31–34]. This was extrapolated into the clinical setting by Smith et al. [35]. In this study, the authors demonstrated a significantly decreased time to abdominal wall closure, higher rates of primary closure, and a decreased rate of ventral hernia formation at 6 months in

hemorrhagic shock trauma patients who underwent damage control laparotomy with DPR compared to case-matched controls [35]. Single-center randomized control data assessing DPR in trauma patients subsequently demonstrated improved time to definitive closure, an increased primary fascial closure rate, and decreases in total intraabdominal complications [36]. DPR has further demonstrated similar benefits for intraabdominal sepsis, as well as improved organ donation rates when used in brain-dead organ donors [37, 38]. This technique is performed by inserting the tubing of a 19-French Jackson-Pratt drain through the abdominal wall, wrapping it around the base of the mesentery, and applying a negative pressure temporary abdominal closure device. Warmed hypertonic 2.5% glucose-based peritoneal dialysate is then infused through the Jackson-Pratt drain at 800 ml/h for the first hour, followed by 400 ml/h or 5 ml/kg/h until definitive closure [37]. The limited data utilizing DPR is promising with its effects on restoration of the microcirculation, downregulation of inflammatory mediators, and decreased visceral edema. However, similar to intravenous hypertonic saline, continued study in larger populations to determine its true efficacy is required prior to widescale implementation.

Augmenting the Definitive Closure

Once it is determined that the abdomen is ready to be closed, careful planning should go into the closure in order to optimize the patient's chances of success. Fistula formation and dehiscence are early complications that harbor significant morbidity, while ventral hernias represent late complications often requiring complex surgical repair [7]. To mitigate these risks, fascial closure should be performed as soon as possible [39, 40]. Abdominal wall closure should be carefully performed in accordance with the adage “approximate, don't strangulate” in order to mitigate ischemia at the fascial edges during closure. That said, proper tissue apposition remains critical for healing. This concept becomes increasingly important as there is often a high degree of intraabdominal swelling that may result in early evisceration if the defect is closed too loosely, whereas too tight of a closure may tear through the fascia or result in localized ischemia leading to early dehiscence or evisceration. Well-known data from a recent randomized controlled trial found the use of small bites (5 mm bites spaced 5 mm apart) of fascia with a 2–0 polydioxanone (PDS) suture on a 31 mm needle to be more effective than large bites of fascia (1 cm bites spaced 1 cm apart) with a #1 looped PDS suture on a 48 mm needle in preventing incisional hernias at 1-year follow-up. However, the patient population and inclusion criteria for this trial are not translatable to the urgent and emergent surgical scenarios that often result in open abdomens [41]. While the concepts from this trial may have benefits within the

trauma population (use of smaller needles, minimizing bites of muscle, use of non-looped sutures, etc.), there remains a paucity of high-quality data within the literature regarding the optimal closure technique for open abdomens.

Debates surrounding the use of interrupted versus continuous sutures for the closure of high-risk abdomens remain prevalent amongst trauma and acute care surgeons. Proponents for interrupted sutures suggest that failure of one stitch may not result in evisceration and can be managed with local wound care if needed. This suggests that failure of a continuous suture line will result in a complete breakdown of the fascial closure resulting in a need for surgical intervention. Conversely, proponents for continuous suture closure argue that the running nature of the stitch more evenly distributes tension along the fascia and minimizes localized areas of increased pressure. Peponis et al. [42] recently evaluated the use of interrupted versus continuous suture for fascial closure in emergent laparotomy and failed to demonstrate any differences between the two techniques in rates of dehiscence, infection, or incisional hernia. During their study, Peponis et al. [42] utilized #0 non-looped PDS sutures with a tapered needle (size not mentioned) and 1 cm bites of fascia spaced 1 cm apart from each other; however, trauma patients and those with open abdomens were excluded. Similarly, Tolstrup et al. [43] assessed the incorporation of a standardized protocol that utilized a running 2–0 PDS suture on a 36 mm CT-1 needle for fascial closure performed with 5 mm bites of fascia spaced 5 mm apart following emergency laparotomy and demonstrated that this newly incorporated standardized protocol significantly decreased the rate of dehiscence when compared to their historic controls (3.8% vs 6.6%, $P=0.03$). Although these studies do not directly represent patients with open abdomens, when taken together, the data suggests that the use of slowly adsorbing suture with smaller bites of the fascia may provide an optimal closure. The European Hernia Society (EHS) clinical practice guidelines for the management of the open abdomen endorses the use of a continuous monofilament suture with small bites that is at least 4 times greater than the wound length, albeit their recommendation is based on expert opinion and is supported by very low-quality evidence [44]. To date, there are no high-quality definitive guidelines for the optimal suture technique toward closing an open abdomen; however, multiple approaches such as simple interrupted, figure of eight, horizontal mattress, and running continuous sutures have been proposed. Proper surgical technique focusing on quality tissue handling, appropriate utilization of the curve of the needle, and assuring adequate bites of the proper fascia are likely the most critical components of closing an open abdomen.

Beyond the primary closure techniques discussed above, efforts have been made to augment the strength of the midline repair in hopes to mitigate dehiscence and prevent future hernias. Of these approaches, the utilization of retention

sutures and mesh augmentation have seemingly garnered the most attention. Retention sutures typically involve large sutures that are passed through the skin, subcutaneous tissue, abdominal wall fascia, and rectus muscles on either side of the fascial closure in efforts to take tension off the midline. Khorgami et al. [45] assessed the use of prophylactic retention sutures following midline laparotomy closure in patients at high risk for dehiscence. They demonstrated an overall decreased rate of dehiscence compared to their controls (4% vs 13.3%, $P<0.01$) and similar rates of evisceration (0.7% vs 2.7%, $P=0.37$) [45]. Despite these findings, the routine use of retention sutures has not been readily accepted amongst trauma surgeons. This is thought to be by in large due to their associated discomfort for the patient, potential for skin breakdown with associated wound complications, and fear of further fascial compromise resulting in increased risks for hernia development [46]. Variations in surgical teaching and practice patterns have continued to promote their use within various institutions; however, there remains a paucity of high-quality data following damage control laparotomy assessing their role.

Mesh augmentation with midline closure remains a debated topic within trauma communities (Fig. 3). Implantable mesh has become the standard of care in elective settings for hernia repair for reducing recurrence. Select studies in elective surgical populations have used this idea and applied mesh in a prophylactic manner following midline laparotomy in order to decrease incisional hernia rates [47]. In a recent systematic review, Burns et al. [48••] assessed the use of prophylactic mesh for emergency laparotomy closure and found that implantation of mesh during these scenarios may reduce the rate of future incisional hernia development. However, following exclusion criteria, this review only assessed two articles. Both studies displayed high degrees of selection bias and neither focused on closure of the already open abdomen [48••]. The European Hernia Society (EHS) clinical guidelines on the open abdomen support the use of mesh during fascial closure based on expert opinion; however, they recognize that the studies supporting this displayed a high degree of heterogeneity with very low quality of data [44]. Regardless, prior to any formalized definitive guidelines, questions regarding the type of mesh, location of mesh placement, and risk profile of prophylactic mesh to bolster fascial closures will need to be addressed.

When the Abdomen Just Won't Close

Despite early efforts to close the abdomen, visceral edema and loss of domain create scenarios where abdominal closure is sometimes not possible within the first 10–14 days. Fortunately, due to the widely accepted advances in trauma resuscitation protocols, these morbid scenarios are becoming

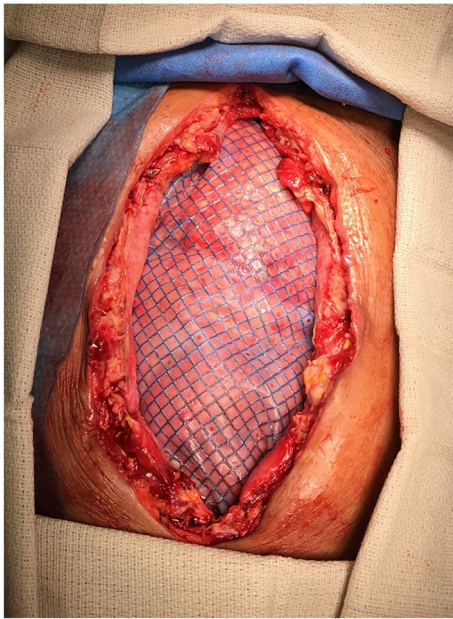


Fig. 3 Use of sublay mesh to help augment closure of midline incision prior to fascial sutures

more infrequent. When they do occur, however, a number of management strategies have been described with each resulting in their own clinical challenges. Due to the lack of high-quality guidelines for this patient population, critical thought regarding the pros and cons of each closure technique must be considered by the operating surgeon.

Sequential closure of the abdomen may be an option when the abdomen cannot be completely closed. During this process, as described by Burlew et al. [49], a network of white wound VAC sponges are stapled together and placed over the bowel, but under the open fascial layer to act as a protective barrier. The fascia is then placed under tension using simple interrupted #1 PDS sutures spaced 5 cm apart roughly 1–2 cm from the fascial edge over the white sponges. A black wound VAC sponge is then placed on top of the traction sutures and white sponge barrier, covered with an occlusive dressing, and placed on suction. At each scheduled take-back, the superior and inferior edges of the wound are assessed and sequentially placed simple interrupted fascial sutures are used until the midline is closed. This is repeated every 48 h; however, the white sponges are not removed at each take-back, nor is the abdomen explored unless clinically indicated. In doing so, constant tension can be maintained on the fascial edges in order to mitigate the risk of retraction and loss of domain. During their initial description, the authors reported a 100% fascial closure rate when strictly adhering to the aforementioned protocol [49, 50]. Although this process was not the first to describe the benefits of sustaining fascial traction through a dynamic closure, it was the first to describe the simultaneous incorporation of negative pressure wound vac therapy.

Dynamic closure represents a process that aims to prevent fascial retraction and loss of domain through applying fascial tension toward the midline. This tension counteracts the natural tendency of the external oblique, internal oblique, and transversus abdominus muscles to contract. Contraction of these muscles results in retraction of the rectus abdominus muscles away from the midline, creating a less compliant abdominal wall, and a larger open defect. Recognizing the benefits of dynamic closure techniques, the European Hernia Society strongly recommended the use of these techniques as opposed to a static closure approach in their guidelines on various management strategies for the open abdomen [44]. Common types of dynamic closure approaches consist of the Wittmann patch, Abdominal Re-approximation Anchor (ABRA) System, and mesh-mediated fascial traction. Transitioning from the static approaches, such as the previously discussed Bogota Bag, homemade vacuum pack temporary abdominal dressing, or ABthera device, to one of the more dynamic methods following clinical stability helps to prevent fascial retraction and ultimately facilitate closure if primary closure is not initially feasible.

The Wittmann patch consists of two self-adhering Velcro-type sheets of mesh that are sewn to the fascial edges and sequentially tightened to prevent retraction and promote primary closure over time [51]. ABRA uses transfascial button anchors and elastomers to slowly pull the wound edges together. This has to be placed intraoperatively, but has the unique advantage of being able to be managed and tightened at the bedside [52–54]. Finally, mesh-mediated fascial traction uses inlay mesh sutured to the fascial edges to counteract fascial retraction (Fig. 4). A wound vac is then placed over the mesh in order to create a negative pressure environment. Patients are taken back to the operating room every 48–72 h to change the wound vac system and sequentially tighten the mesh [55–57, 58•]. Although these approaches have readily demonstrated improved rates of fascial closure, they potentially come at the expense of tissue compromise from the fascial sutures.

Aside from dynamic traction on the fascial edges, the use of botulinum toxin injected into the transversus abdominus, internal oblique, and external oblique muscles has recently been described as a “chemical component separation.” While a traditional component separation of the abdominal wall layers is not recommended for coverage of an open abdomen, botulinum toxin creates a temporary flaccid paralysis of these muscles in order to prevent lateral muscle contraction and decrease midline abdominal wall tension [6, 59, 60•]. Onset has been reported as early as 48 h following injection and typically displays lasting effects up to 9 months. Due to the delay in onset, Zielinski et al. [59] recommend injection as soon as possible following hemodynamic stabilization. Importantly, this technique can be utilized in combination with any static or dynamic temporary abdominal closure technique.

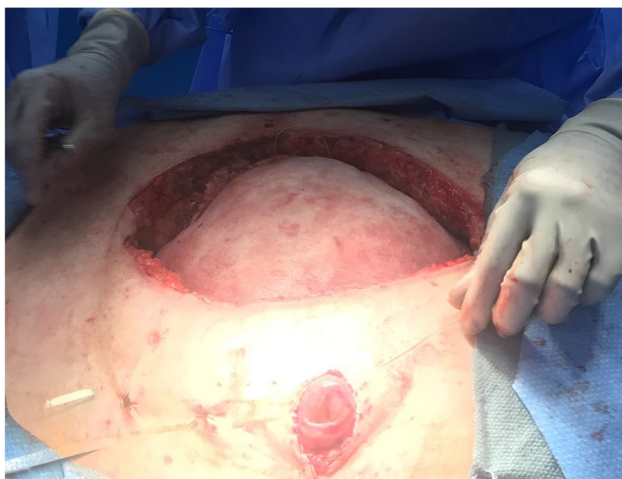


Fig. 4 Mesh-mediated fascial traction performed using inlay mesh to counteract fascial retraction

When primary closure of the fascia cannot be achieved, the creation of a planned ventral hernia remains a final option to provide coverage of the abdominal contents [61, 62••]. This is accomplished either via the creation of skin flaps with sutured closure at the skin level or the placement of inlay mesh and granulation tissue formation for future skin grafting. Both approaches allow for future elective repair and abdominal wall reconstruction following recovery from the initial insult. Importantly, if split-thickness skin grafting is utilized over the granulated defect, reconstruction should be delayed until there is complete separation of the graft from the underlying bowel. This is accomplished via the pinch test, where the skin graft is pinched between the index finger and thumb and lifted off the underlying bowel. If the graft is freely lifted, this suggests there is a safe plane between the abdominal wall graft and the underlying bowel in order to perform definitive reconstruction. While these planned ventral hernia techniques previously were the standard of care prior to advancements in dynamic closure and tension augmentation, they still have their place and remain a safe option when all other options fail. However, the morbidity and patient discomfort following this approach remains high. Based on the current World Society of Emergency Surgery guidelines for the open abdomen, planned ventral hernia via skin grafts or skin closure should remain an option only for the complicated open abdomen or in settings non-amenable to other options [62••].

Conclusion

In conclusion, the utilization of damage control surgery has provided a life-saving approach to trauma patients. These life-saving strategies are not benign and come with

a cost. Basic principles of blood product resuscitation can help avoid many of the complications associated with prolonged open abdomens; however, the unpredictable nature surrounding trauma patients lends way to unplanned abdominal catastrophes. Understanding the concepts of temporary abdominal closure remains critical for all surgeons. The preponderance of data is limited by low-quality evidence that is lacking in head-to-head trials; therefore, definitive statements regarding optimal practices cannot be made. In our experience, the utilization of a homemade vacuum pack offers the benefits of negative pressure therapy for temporary abdominal closure and remains our preference when the patient's physiology has yet to normalize. This provides a less expensive, yet similar, alternative to the commercially available products. Following stabilization, it remains rare in our practice to have patients with prolonged open abdomens. However, when needed, dynamic closure using mesh-mediated fascial traction with negative pressure therapy remains our method of choice when primary closure is not an option. While we do not routinely practice direct peritoneal resuscitation, hypertonic saline, or botulinum toxin injections at our institution, these techniques remain appealing as potential future avenues to incorporate into practice due to their potential benefits. Finally, once the midline is ready to close, we prefer to utilize small bites of the fascia using a non-looped PDS suture in either a continuous or interrupted fashion depending on the perceived degree of intraabdominal pressure by the operating surgeon. While the ideal size of the suture varies between the authors and ranges from 2–0 PDS to #1 PDS, we believe smaller-sized needles mitigate damage to the fascia and decrease the risk of future hernia formation. Prophylactic mesh has not been incorporated into our practice at this time; however, its use remains intriguing as an option to further mitigate the risk of future incisional hernias. The open abdomen remains a clinically difficult problem that comes with a high degree of associated morbidity. Although many strategies have been suggested, future well-planned studies need to be performed in order to develop optimized management strategies within this notoriously challenging patient subset.

Author Contribution I, Daniel Lammers, have reviewed and edited the submission to omit any identifying information.

Declarations

Conflict of Interest Daniel Lammers, Jeff Conner, Ronald Hardin, and Steven Gillis are active-duty members of the US Army. Richard Betzold is an active-duty member of the US Air Force. Omar Rokayak is a member of the US Air Force Reserves. The views expressed here are those of the authors and do not reflect the views of the US government, Department of Defense, US military, US Army, or US Air Force. The authors have no relevant conflicts of interest to report.

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- Of importance
- Of major importance

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