Pathophysiology of Seroma Formation and Its Preventive Measures in Cases of Ventral Hernia

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Abstract

Background: Seroma is an abnormal collection of serous fluid in the dead space of the wound. The origin of this serous fluid remains unclear. Seroma formation can be seen as a consequence of the inflammatory foreign body reaction with monocytes and macrophages involved at the interface of connective tissue and implant. These cells produce a variety of cytokines, which regulate the local immune response, wound healing and scar formation. Seroma causes discomfort to the patient, prolonged hospital stay, and infection at the operation site and re-operations. Seroma is of one the most common complications following open techniques and is particularity likely to occur when large skin flaps are developed during the surgical procedure so closure of the dead space may reduce the risk of seroma formation. Though the risk for seroma formation increases when mesh is used for repair, little is known about the genesis of seroma formation. Alloplastic mesh prosthesis led to a multitude of tissue reactions, including the postoperative release of cytokines.

Background

Abdominal Wall Hernia Repair

The best surgical technique for the repair of umbilical and paraumbilical hernias remains controversial. A simple primary suture repair can be used for small defects. Umbilical and paraumbilical hernias have historically been repaired without mesh. The technique of overlapping abdominal wall fascia in a “vest-over-pants” maneuver was described by Mayo and remained the most renowned surgical technique for a long time. The Mayo repair has been shown to be associated with high recurrence rates of up to 28% (1).

Open hernioplasty

The open repair of PUH was also done under general anaesthesia with a transverse skin incision over the bulge near the umbilicus. With blunt dissection the rectus sheath was cleared of fatty tissue and the defect containing the hernia contents was identified. With a small nick of knife the defect was opened along with sac and a small piece of omentum usually popped out. The circumferential incision was enlarged, the contents were removed and the margins of the defect were held by Ellis forceps. The sac was separated and contents were reduced into the abdominal cavity. A non-absorbable suture was used to close the defect in the linea alba and a proline mesh of adequate size was placed in the preperitoneal space and fixed with few stitches. Homeostasis was secured and wound was closed over a drain placed in the depths of the wound to avoid haematoma (2).

The mesh was 5-10 cm larger than the actual size of the defect in all directions in order to overlap a wider area than the actual defect in the abdominal wall. One suture was placed in each corner of the mesh and abdomen was marked for the position of mesh (2).

Pathophysiology of Seroma
A seroma is a collection of liquefied fat, serum, and lymphatic fluid in a closed space. The fluid is usually clear, yellow, and somewhat viscous and is found in the subcutaneous layer of the skin. Seromas represent the most benign complications after an operative procedure and are particularly likely to occur when large skin flaps are developed in the course of the operation, as is often seen with mastectomy, axillary dissection, groin dissection, and large ventral hernias (3).

There has been no consistent definition of chronic seroma in the literature, although it has been documented most frequently when it is symptomatic, bothersome to the patient, palpable, fluctuant, tense, and requires at least one needle aspiration (3).

In contrast, in a published study, seroma was documented only when multiple aspirations were required, or if insertion of a new drain was necessary in persistent cases. Similarly, other studies used the term seroma if a verified volume of more than 5–20 ml of fluid was obtained by puncture and aspiration, whereas some studies have used ultrasonography to verify seroma (4).

Seroma formation is one of the most commonly reported complications after laparoscopic and open hernia surgery. It occurs early after operation in virtually all patients, to some extent. Virtually all seromas resolve spontaneously over a period of weeks to months, with fewer than 5% persisting for more than 8 weeks. Because of this, seromas are rarely clinically significant (4).

**Physiology**

Postoperative fluid collections represent sequelae of events that ultimately contribute to negative soft tissue healing events. It has been demonstrated that seroma is not merely an accumulation of serum, but exudate resulting from an acute inflammatory reaction, and concluded that seroma formation reflects an increased intensity and prolongation of the first phase of wound repair (4).

Mc Cauel et al., 2000 have also demonstrated that drainage fluid has a composition different from that of lymph but similar to that of inflammatory exudate. Seroma formation can be seen as a consequence of the inflammatory foreign body reaction with monocytes and macrophages involved at the interface of connective tissue and implant (4).

These cells produce a variety of cytokines, which regulate the local immune response, wound healing, and scar formation (5).

On the other hand, **Wu et al., (5)** have reported an increase of vascular endothelial growth factor (VEGF) and a decrease of Endostatin in drainage fluid immediately after surgery. VEGF is a known mediator of angiogenesis, vascular proliferation, and permeability, and Endostatin is a potent inhibitor of angiogenesis (6).

Therefore, these changes may not only reflect induction of angiogenesis as a physiologic response to operative trauma but also enhanced accumulation of fluid. Heidemann et al. showed that stabilizing the pH value in the environment of implants for several weeks improves the biocompatibility by reducing adverse tissue reactions (6).

Though the risk of seroma formation increases when mesh is used for repair, little is known about the genesis of seroma formation. Alloplastic mesh prosthesis leads to a multitude of tissue reactions, including the postoperative release of cytokines and the formation of seroma sometimes persistent for months (7).

The pathogenesis of seroma has not been fully elucidated. Seroma is formed by acute inflammatory exudates in response to surgical trauma and acute phase of wound healing. **Oertli et al., (8)** believed that the fibrinolytic activity contributes to seroma formation.
However, Gonzalez et al., (9) and Hashemi et al., (10) reported that the only statistically significant factor influencing the incidence of seroma formation was the type of surgery. They reported higher seroma rate in modified radical mastectomy than following wide local excision and axillary dissection. Factors such as age of the patient, obesity, tumour size, and neoadjuvant therapy did not influence the incidence of seroma formation in the three mentioned studies.

Extensive dissection in mastectomy and axillary lymphadenectomy damages several blood vessels and lymphatics and the subsequent oozing of blood and lymphatic fluid from a larger raw surface area when compared with breast-conserving procedures leads to seroma (11). Seroma accumulation elevates the flaps from the chest wall and axilla thereby hampering their adherence to the tissue bed. It thus can lead to significant morbidity such as wound haematoma, delayed wound healing, wound infection, flap necrosis, wound dehiscence, prolonged hospitalization, delayed recovery and initiation of adjuvant therapy (12).

Nature of seroma fluids:
The term “seroma” suggests that the fluid originates from ultrafiltration of blood. But, the term “lymphocele” or “lymphocyst” can also be used. In support of this, a laboratory analysis of fluid aspirated from two patients with protracted seroma revealed characteristics of lymph, with a low protein concentration compared to serum and a cell content that was limited to lymphocytes. The occurrence of chylous leakage may be consistent with this assumption of lymph leakage (13). Akinci et al., (14) have also demonstrated that drainage fluid has a composition different from that of lymph, but similar to that of inflammatory exudates.

On the other hand, Gong et al., (15) have reported an increase of vascular endothelial growth factor (VEGF) and a decrease of endostatin in drainage fluid immediately after surgery. VEGF is a known mediator of angiogenesis, vascular proliferation and permeability, and endostatin is a potent inhibitor of angiogenesis. Therefore, these changes may not only reflect induction of angiogenesis as a physiological response to operative trauma, but also enhanced accumulation of fluid. There was good evidence for a large dead space causing seroma, although it was obscure whether seroma is composed of lymph-like fluid or exudates (3).

Risk factors for seroma formation:

1) Patients characteristics:
Age, anemia, body mass or obesity index, body weight, diabetes mellitus, hypertension, size, smoking (16).

Several studies had found a positive association between body weight and seroma formation and also had found that hypertension is associated with an increase of seroma formation (3).

Similarly, no individual study found a significant association with other factors such as presence of anemia or diabetes mellitus, smoking (16).

On the other hand, existing evidence was inconclusive for age, body mass index or obesity index (16).
2) Surgical factors:

a) Wound drainage:
Intensity of negative suction pressure, no drainage, number of drains, type of drainage (closed suction versus passive drainage), type of drainage unit (evacuated bottle type versus bellow type) and type of drainage tube (multiple hole type versus multiple channel type) were assessed. As for no drainage, studies had reported that this policy increases seroma formation. However, seroma formation was not influenced by the intensity of negative suction pressure, by the number of drains, or by the choice of closed suction drainage or passive drainage. These findings were consistent among studies. Similarly, in an RCT choice of evacuated bottle type or bellow type did not affect the number of aspirations required (17).

In contrast, a flat-type drain with multiple channels running the length of the drain reduced seroma formation as compared with a flat-type drain with multiple holes. It was speculated that the holes might clog more easily than the channels, which could lead to premature removal of drains. However, this study was not primarily planned to assess drain type, and the drain was selected according to the attending surgeon's preference (3).

b) Surgical devices:
Several surgical devices including electrocautery, laser scalpel, argon diathermy, ultrasonic scalpel and ultrasonic scissors have been investigated in an effort to achieve better hemostasis and to reduce seroma formation. However, there is no a significant effect on seroma formation with or without use of argon diathermy, a laser scalpel or an ultrasonic scalpel (13).

On the other hand, the use of electrocautery was significantly associated with increased seroma formation in an RCT by Porter et al., (18). In this study, the flap and fascia were dissected either by electrocautery or by scalpel, while control of small bleeding vessels with electrocautery (3).

c) Suture flap fixation:
Suture flap fixation is a surgical technique for securing flaps to underlying tissues to close the dead space with sutures. Although this technique is not commonly performed, it reduced seroma formation in patients (19).

d) Miscellaneous surgical factors:
Moreover, several factors such as blood loss, blood transfusion, operation time, skin incision, surgeon and type of anesthesia have been assessed, and individual study has demonstrated that a longer operation time increase seroma formation (15).

On the other hand, no association was found for type of anesthesia (local or general) or blood transfusion. Available evidence was inconclusive for whether or not skill or experience of the surgeon influences seroma formation, for quantity of blood loss (15).

PREVENTION OF SEROMA
Mesh repairs of ventral hernias result in lower rate of recurrence but comes with wound complications such as clinically significant seroma formation requiring intervention in 3–17% of laparoscopic ventral hernia repair cases (20).

Seroma is defined as a collection of fluid detected in the subcutaneous space through clinical or radiographical investigation and is most common following surgery that involves extensive tissue dissection resulting in a “dead space” (20).
While clinically significant seroma is reported in up to 17% of hernia repairs, studies have reported that the rate of seroma detection approaches 100% when diagnosed based on radiological criteria alone (21). This is clinically relevant as all seroma can lead to postoperative wound infection and potentially increase recurrence rate. Seroma formation results in patient dissatisfaction, poor aesthetic outcome and serious surgical site infections (21).

Therefore, many surgeons are exploring perioperative strategies that aid to minimize the rate of seroma occurrence. These interventions include suture or tack for mesh fixation and use of electrical cauterization (22).

Massey has performed a systematic review to evaluate adjuncts to reduce seroma formation in open incisional hernia repairs but there are no studies to our knowledge that compares strategies employed in laparoscopic ventral hernia repairs (22).

**Method of mesh fixation**
A variety of strategies have been demonstrated to fix the mesh to close the hernia defect. The methods include use of glue, tacks and sutures.

**Primary defect closure and bridged repair**
Primary defect closure describes the approximation of the fascial defect before the placement of the mesh. Bridged repair is when a piece of mesh is placed intraperitoneally in an underlay position to achieve circumferential overlap of the fascial defect (23).

Primary defect closure is performed with the primary approximation of the fascial edges of the hernia defect with sutures before placing the mesh. Three trocars are used for the procedure, one as a central optical trocar and two for lysis of adhesions, defect closure and mesh positioning. This is followed by the lysis of the adhesions to the abdominal wall surrounding the hernia. The defect is then either closed with a needle and laparoscopic needle driver, an Endo Stitch (Covidien) suturing device or closed percutaneously using a suture passer. After the defect closure, an appropriately sized intraperitoneal mesh is placed to overlap the margins of the defect by 5–7 cm (23).

**Types of mesh**
Different types of mesh for fixation are available for laparoscopic repair of ventral hernias. The characteristic of an ideal mesh should prevent adhesions and promote fibrous ingrowth (23). The commonly used types of mesh include composite mesh with monofilament polyester textile on one side and a hydrophilic absorbable collagen film on one side (Parietex) and non-coated synthetic polyvinylidene fluoride and polypropylene mesh (DynaMesh-IPOM) (23).

Other choices of mesh include a nitinol frame on the mesh to keep the mesh well positioned against the abdominal wall and reduce the incidence of mesh shrinkage (24).

**Electrical cauterization**
Cauterization of the hernia sac destroys the serosal surface of the hernia subcutaneous cavity and creates adhesions immediately in the burned sac close to the dead space (25).

**Single-incision laparoscopy**
Single-port laparoscopy has been introduced to minimize abdominal wall trauma by performing the hernia repair through a minimal single fascia incision (26).

**Fibrin sealant**
This describes the percutaneous application of a heterologous fibrin sealant with the intention of collapsing the dead space where the seroma settles (26).

**Pre-peritoneal placement of mesh**
The placement of mesh in the pre-peritoneal/retro-muscular space instead of the standard intraperitoneal location to avoid direct contact of mesh with abdominal contents (27). Laparoscopic ventral hernia repair is being performed more commonly with about 20–27% of ventral hernia repairs performed laparoscopically (27). Massey et al. first performed a Table review on the adjuncts to reduce seroma in open incisional hernia repair and we believe that as LVHR becomes increasingly popular, it would be imperative to study the factors contributing to seroma formation in laparoscopic repair as well.

Seroma formation is a common complication after LVHR with incidence ranging from 3 to 100% depending on whether clinical or radiological criteria are used to define seroma. This is important as seromas can be detected through radiological imaging in almost all patients after a LVHR and is generally regarded as an expected outcome (28). Morales-Conde (26) proposes the adoption of a seroma classification to categorize seromas into clinically insignificant, asymptomatic collections to those with complications such as infection so as to allow data to be interpreted and compared more meaningfully across studies.

In our review, we identified the recurring themes and strategies in seroma prevention and propose a logical recommendation based on the current available literature and limitations on this topic below.

**Primary fascial closure of defect**
The necessity of primary fascial closure (PFC) of the hernia defect in laparoscopic ventral hernia repair (LVHR) continues to be controversial. This is further supported by a recent meta-analysis in 2016 by Tandon et al. which found PFC in LVHR to be associated with fewer recurrences, mesh eventration and/or bulging as well as a lower incidence of seroma formation (29).

However, our study has found five new studies in addition to the meta-analysis by Tandon. Four of the studies did not associate PFC with lower incidences of seroma formation while one study found statistically lower seroma formation rate (29).

This highlights that emerging new studies with conflicting results continue to add on to the existing debate regarding this intervention.

Nevertheless, most large analysis supports the use of PFC in reducing seroma formation. The purported benefits of this intervention could lie in the reduction of effective dead space between the mesh and overlying tissue (23).

Proponents of PFC also cite its importance through the restoration of abdominal wall function which is achieved by the realignment of the abdominal muscle and fascial layers which restores normal anatomy. There is also decreased incidence of infection after seroma formation as the mesh is physically separated from the skin by the abdominal wall muscle and fascia (30). However, the downside of performing
routine PFC will be that it is time consuming, has a learning curve and fascia may be under tension for larger defects.

**Cauterization of hernia sac**

Our systematic review found that in the small number of studies published thus far, the intra-operative maneuver of cauterizing the hernia sac appears to be associated with lower rates of seroma formation. The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) currently provides a weak recommendation for the routine cauterization of the hernia sac in reducing seroma formation, largely based on Tsimonyiannis’s 2001 prospective study on 51 patients (25).

We have only found two new retrospective studies to further support SAGES’s weak recommendation. The pathophysiological basis of such a maneuver is well described by Prassas et al. who postulate that the inflammatory response is mitigated by destroying the mesothelial cells (which produce cytokines and chemokines to form an inflammatory exudate) and eliminates dead space by forming adhesion between the mesh and cauterized surface (25).

The obliteration of dead space to reduce seroma formation is an important theme for several other different intra-operative maneuvers such as PFC in LVHR as well as quilting sutures in abdominoplasties and mastectomy (31).

Currently, the evidence for routine sac cauterization is weak and based on small studies. We recommend interpretation of the results with caution. Nevertheless, cauterization of the hernia sac is a relatively intuitive and safe intra-operative maneuver with no added cost that may prove promising if future multicenter studies can confirm its benefit (31).

**Mesh types**

There remains a lot of controversy on the indications of using a synthetic versus biologic mesh. The sheer volume of different types of meshes available on the market can be overwhelming, with subtypes within each different mesh groups. The categories of mesh types can be largely classified into synthetic and biologic mesh. There remains little high-quality evidence to suggest the choice of mesh in LVHR and this largely depends on its institutional availability, costs as well as the surgeon’s preference. Older studies conducted that used ePTFE (expanded tetra-fluoro-ethylene)-based meshes for hernia repair have found high rates of seroma, postulated to be due to the low porosity of the material that prevented adequate drainage of fluid (32).

Our systematic review found two studies comparing different mesh types and their risk of developing seromas, but in these studies’ seroma formation was measured as secondary outcomes. There also exists much variability in surgical techniques, mesh positions as well as surgeon’s experience which can all influence the patient’s seroma formation incidence independent of the mesh alone. This makes it extremely difficult to directly compare these studies and conclude that a certain mesh type is superior due to the numerous confounders. As such we are unable to recommend any particular type of mesh to be used in LVHR that may particularly decrease seroma formation, but it is probably worthy to note that PTFE meshes may potentially increase rates of seroma due to its inherent mesh property (32).
Mesh fixation methods
Fixation of meshes to the abdominal wall is an important step in LVHR. However, there exists controversy over the type of fixation method. Mesh fixation methods can be widely categorized into tacks and sutures, both in absorbable and non-absorbable (permanent) forms. Meshes can be secured purely with tacks, sutures or a combination of both (33). Mesh fixation to the abdominal wall must be able to withstand shear forces created by the abdominal musculature such that it will not break loose and cause mesh migration within the abdomen. There have been various studies including a meta-analysis evaluating for the optimal fixation technique. However, no single-mesh fixation method has proven to be the superior option (33). There still exists conflicting evidence in hernia recurrence as well as postoperative pain in individuals receiving suture versus tack fixation (33).

There are many series published using these fixation methods but there appears to be a lack of review studies specifically looking at seroma incidence. Our systematic review found a total of five studies, two of which are randomized control trials and they generally do not find any fixation method to be more superior to the other in terms of seroma incidence (33).
Muysoms et al. (34) compared mesh fixation with double rows of permanent tacks versus trans-fascial sutures with a single row of tacks and reported that trans-fascial sutures caused more postoperative pain at 3 months.

Furthermore, although absorbable tacks do not have any significantly greater adverse outcomes, they are also associated with increased healthcare cost and no apparent benefit in primary outcomes such as postoperative pain and patient satisfaction (33).

It is important to note that the primary outcome of these studies looked into hernia recurrence rate, postoperative quality of life and the incidence of abdominal wall pain with seroma formation being a secondary outcome (34).

As such, we do not recommend any particular type of mesh fixation and suggests interpreting the data with caution as none of these studies is powered to detect primary difference in seroma formation and any positive findings may likely be an incidental secondary finding rather than a true effect from the type of fixation.

Mesh placement location
There is a growing interest in alternative mesh placement locations in LVHR. The intraperitoneal on-lay mesh (IPOM) technique is widely used in clinical practice and is the equivalent of the underlay method in open ventral hernia repair (34).

Single-site laparoscopy
Our study identified one prospective comparative study on the use of single incision versus conventional laparoscopy. There is inconclusive evidence to recommend such a surgical procedure due to the paucity of such studies and the intrinsic challenges in performing single-site laparoscopy compared to standard laparoscopy, as acknowledged by the authors in this study (34).

Fibrin sealant
Our study identified one prospective comparative study on the use of injection of fibrin sealant into the hernia sac to reduce seroma incidence via the reduction of dead space seroma with the use of fibrin sealant, this remains an isolated study and use of fibrin sealant is also associated with increased cost. Until future studies confirm its benefit, we are currently unable to recommend its usage based on a single study (34).
Hernia sac excision
Although there we are unable to identify any specific study looking at the effect of hernia sac excision, we are aware that some surgeons routinely excise the sac in an attempt to decrease seroma formation. This may be the subject of future research (34).

References


