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Review Article

Anastomotic leaks following gastrointestinal surgery: updates on diagnosis and interventions

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Abstract: Gastrointestinal surgery-associated anastomotic leaks and luminal perforations can be life-threatening events with high mortality and morbidity rates. In order to get a favorable outcome, early diagnosis and prompt therapy are necessary. In these conditions, the 'gold standard' approach to treatment in the past was surgery. However, surgical procedures are associated with higher re-intervention mortality and morbidity. Non-surgical mode of treatment comes as a reasonable and attractive approach with the recent developments in endoscopic devices and techniques in the management of fistulae, perforations and leaks. Although these upcoming and recently developed techniques have found wide acceptance, comparative data involving the various techniques are yet to be obtained. In this review, we outline in detail the pros and cons of the various available options in the treatment of patients with gastrointestinal (GI) anastomotic leaks. The available literature has also been assessed for the potential of these techniques in treating other GI tract defects including fistulae and perforations; besides, highlighting the suitable diagnostic tests for detecting anastomotic leaks. This information can be highly useful in getting an insight into the current options in the management of GI anastomotic leaks and in improving the treatment outcomes.

Keywords: Anastomotic leaks, gastrointestinal surgery, endoscopy, non-surgical, computed tomography

Introduction

Gastrointestinal surgery-associated anastomotic leaks have been a major reason behind post-operative morbidity and mortality irrespective of the continual improvements in surgical procedures [1-3]. Varying rates of leaks are found based on the anastomosis site involved: rectum (8%-41%) [4], colon (3%-29%) [5, 6], small intestine (1%-3%) [7, 8], bile ducts (10%-16%) [7, 9], pancreas (9%-16%) [10, 11], stomach (1%-9%) [12-14] and esophagus (2% to 16%) [15]. Following specific gastrointestinal procedures, post-operative, intra- operative and pre-operative anastomotic leak risk factors have been identified [1, 16-18]. Patients with anastomotic leaks show poorer long-term functional results; reduced 5-year survival, and increased local recurrence rates [19, 20]. Anastomotic leak-associated clinical manifestations would often require hospital re-admission. This can put significant burden on the healthcare providers and patients, besides the possible negative clinical outcomes [21].

Post-operative mortality rate and high complications associated with anastomotic leaks could be reduced with the continual optimization of surgical techniques. Among the post-operative complications, anastomotic leakage is still the most feared [22-24]. The initial technical problems associated with surgical techniques were almost eliminated with the introduction of mechanical staplers [25, 26]. Today, the major issues concerning anastomotic leakage are early detection and their best possible treatment. Radiological control of anastomases in combination with water soluble contrast used to be the main diagnostic procedure for anastomotic leakage [27-29]. Two other reliable means of diagnosis: computed tomography (CT) and endoscopy, are also available nowadays [30, 31]. The possibility of significant reduction in anastomotic leaks-related mortality and morbidity require not only an understanding of the factors influencing the condition but also the selection of right therapeutic strategy [32, 33].

Previously, surgery was thought to be the 'gold standard' for tackling these conditions. However, the high rate of mortality and morbidity associated with surgical interventions has urged the surgeons to look for other available options in treating GI anastomotic leaks [34]. A number of devices and techniques have been developed and undertaken so as to close the GI leaks. In this regard, endoscopic interventions come up as a reasonable and important alternative. The critical factors determining the choice of approach in closing the GI defects include state of health of the patient concerned, characteristics of the leaks, site of leak, and overall prognosis [32-34]. The major goals of treatment are: drainage of collection, nutritional support, prevention of further contamination and infection, and returning of continuity of digestive tract [35]. The development of several devices and techniques (suturing devices, stents, endoscopically placed tubes, through the scope clips, over the scope clips, glues and adhesives, vacuum therapy and omentoplasty) in the past few years have taken place that have shown promise in the closure of GI anastomotic leaks. The ideal device for closure should be easy to deploy, inexpensive, robust, safe and durable so that it can provide rapid and stable closure [32]. In addition, it should be successfully able to close larger defects and have low rate of complications. Reviews that deal about the diagnosis of gastrointestinal anastomotic leaks by comparing the advantages and limitations of the various non-surgical methods of combating the problem are very scanty and not updated. Existing reviews on the subject do not discuss all the available non-surgical options.

In this review, we detail the pros and cons of the various available options in the treatment of patients with anastomotic leaks; besides, highlighting the diagnostic options available in detecting the condition. This information can be highly useful for getting an insight into the current options in the management of GI anastomotic leaks and in improving the treatment outcomes.

Causes

There can be two categories of anastomotic gastric leaks based on their cause: ischemic or mechanical. Direct tissular injury or stapler misfiring has been categorized under 'mechanical-tissular' causes by Baker *et al* [36]. Such leaks usually appear within 2 days following surgery and are hence also referred to as 'early'. Generally, the 'ischemic causes' appear 5-6 days after surgery and are called 'intermediate'. In a multicenter experience, leaks post laparoscopic sleeve gastrectomy (LSG) included aggressive dissection-mediated improper vascularization which took place within 2 days after surgery, especially of the upper sleeve posterior attachments, orogastric tube stapling, stapler device misfiring, and ultrasonic device-led thermal injuries to the gastric tube (Ligasure, harmonic) [37]. Owing to impairment in gastric emptying, which leads to decreased gastric tube compliance and increased intraluminal pressure, proximal leaks are more common in patients with distal stenosis [13, 38]. More elaborate mechanism concerning anastomotic leaks following gastrointestinal surgery is still elusive, except for case report that demonstrated a 16 months post surgery occurrence of leakage [39].

Symptoms and diagnosis

There are longstanding debates regarding the most specific and sensitive diagnostic modality for detecting gastrectomy leakage. However, most authors agree that better outcome is associated with early detection. Also, the cornerstone in the diagnosis and detection of leaks is a high suspicion index [37, 40].

The clinical presentations of an asymptomatic patient (who can be diagnosed with common imaging techniques post-operatively) [41] vary greatly to that of septic shock signs and symptoms that include abdominal pain, fever, hypotension, tachycardia, leucocytosis and peritonitis [42]. The suspicion index for a potential complication should be raised with unexplainable tachycardia and fever. Subsequently, the surgeon should confirm the presence of the leak with further radiological investigations [13]. A number of authors have indicated fever as the most important clinical factor for detecting gastric leak [13, 39]. But tachycardia is considered to be the earliest and most constant, significant clinical finding that indicates the presence of an anastomotic gastric leak [34]. A strong indication for systemic compromise and leak is indicated by a tachycardia > 120 beat/min [43]. In most cases, fever and tachycardia along with sudden abdominal pain are presented by early leaks, on the other hand late leaks present with fever associated insidious abdominal pain [44]. Laboratory studies including CRP, CBCD, etc rarely contribute to the diagnosis, since they are neither specific nor sensitive [37]. Transrectal contrast-enhanced ultrasonography (CEUS) and transrectal ultrasonography (TRUS) are able to provide insights about the vesicourethral anastomosis integrity [45].

Abdominal computed tomography (CT) with water soluble contrast for patients with suspected leak is considered to be an important part of the diagnostic set-up [46]. At present, gastric leak is best detected and confirmed through CT and hence has been considered as the best non-invasive modality available [30, 44]. In a multicentre experience, it was found that the detection rate of gastric leaks was highest with CT in about 86% of the patients [47]. However, some investigators question the superiority of CT scan over other available non-invasive and invasive modalities. This has to do with the fact that large body dimensions (BMI over 50) and obesity can produce artifacts that lead to reduction in quality of the image. Thus, they recommended endoscopy or upper gastrointestinal (UGI) radiography that may overcome the technical difficulties imposed by the larger dimensions and body weight [48]. Also, the gastrografin swallow test performed routinely 24-72 hours post-operatively opens up an area of large debate. A retrospective review by Wahby *et al* [41] involving 712 patients suggests that it is unable to detect post-operative leakage. However, performing this procedure is still recommended, owing to the fact that it can detect other complications such as anatomical sleeve consequences and strictures. Routine post-operative methylene blue test is also recommended at the same time. It should be kept in mind that a normal test cannot distinguish between a fistula and a leak and therefore can lead to delay in diagnosis of a leakage when employed [49]. An upper gastrointestinal swallow can be of great help in identifying the gravity and level of a leak even in the context of positive diagnosis of a leak with CT scan [44].

Interventions

Most of the literature concerning the management and prevention of GI defects including anastomotic leaks following surgery consists of retrospective reviews and small case series. Till date, no randomized controlled trials have been conducted to compare and evaluate the efficiency of different techniques in this regard. In order to achieve improved outcomes in patients with anastomotic leaks, early diagnosis and treatment is essential [47]. Evidence of chronic defects is given by established fistulae to tubular structures or to the skin and/or contained fluid collections. The success and available options in the treatment of longstanding leaks has been more limited. A number of procedures have been contemplated in the management of gastrointestinal surgery-mediated anastomotic leaks which we will discuss in the following sections.

Conservative treatment

Micro-perforations with localized extravasation or small leaks that are diagnosed early can be treated with the help of conservative management strategies. The conservation approach is also favored by thoracic esophagus or cervical location, absence of sepsis syndrome and lack of malignancy [35, 50]. The conservative therapy elements consist of fluid reconstitution, intravenous broad spectrum antibiotics, nasogastric suction, nothing by mouth and proton pump inhibitor therapy [35]. Medication related to pain should only be administered on demand. A surgical consultation and frequent radiologic and clinical assessment are considered prudent. The efficacy of conservative therapy was evaluated by Hasan et al retrospectively, reporting a mortality of 15% [51].

Suturing devices

An endoscopic suturing platform allows for full thickness non-absorbable or absorbable suture placements. It is a device attached to a double channel endoscope's therapeutic end. There is no need to remove the scope from the patient in using the device multiple times. Application of sutures can be done in interrupted or running fashion that includes figure of 8 or simple sutures. Following its introduction, the suturing device has been used successfully in closing acute GI perforations, fistulae, anastomotic leaks and endoscopic resection sites [25, 26]. The device has been found to exhibit effective and safe suturing. In a related study in humans, it was found that suturing with the device was consistent at a subserosal depth in colon without injury to adjacent structures or full thickness penetration [52]. It has been successful in closing staple-line and anastomotic leaks, gastrogastric fistulae and aid in preventing migration [53, 54]. But mixed results have been achieved when long-term success is considered [55].

Stents

Full thickness GI defect diversion with the use of stents (non-FDA approved) has been widely accepted by endoscopists and surgeons alike as a defect management strategy. The deployment of stent at the defect site works by diverting the enteric contents away from the defect. Different types of stents have been in use that include plastic (expandable, covered), metallic (completely or partially covered) and biodegradable materials. In case of larger defects (> 1.5 cm), stent placement can be of particular interest as it permits continued enteral nutrition [56, 57]. Notwithstanding the success achieved with the use of stents in the management of GI defects, they require frequent radiographic monitoring since they are prone to migration; nearly 20-30% of the cases have shown such migrations [57, 58]. The issue has been addressed with the use of techniques such as endoscopic suturing devices and through the scope clips that can be useful in anchoring the stent in place. In addition, a complete seal is not achievable with stents within the GI tract; often leaks of varying extent appear around the stent sites. In patients with high output EC fistulas, percutaneous enteric stent placement has been found to be useful where they lead to decreased fistula output, TPN requirements, improvement in oral diet tolerance and wound [59]. The use of stents in treating GI tract defects is well supported by available literature. A meta-analysis involving stent placement in cases of acute leak following bariatric surgery demonstrated a successful closure rate of 87.8% after stent removal as suggested through radiographic evidence [60]. It was also found that 16.9% of the patients showed migration while reoperation was needed in only 9% of the patients. In order to prevent migration, some authors suggest for the placement of clips to anchor the stents. In one such study where endoscopic clips were used to anchor stents, rate of migration was found to be 34% without the clips and 13% with clips [61].

Endoscopically placed tubes

One of the well known strategies in combating GI leaks without defect repairing is making use of the hole for other therapeutic modalities. Formation of such 'tube ostomy' is considered as a standard maneuver in surgical processes for countering difficult-to-deal perforations in retroperitoneal organs such as duodenum and colon. 'PEG rescue' is performed in patients with a leaking gastrotomy and an acutely dislodged PEG tube. Here, the defect is used for endoscopically entering the abdominal cavity and replacing the tube correctly [62]. A similar procedure was used in an esophagostomy tube dislodged patient where without any further surgical intervention a new esophagostomy tube was placed. In this process, a wire was passed from the skin cutaneous opening, endoscopically secured in the esophagus and drawn out through the patient's mouth [63]. Such examples demonstrate the possibilities of endoscopic management of cases which would have been managed traditionally through surgical means.

Through the scope clips

Endoscopic clips initially designed for endoluminal marking and hemostasis are now used in managing GI leaks. They are deployed within the GI tract lumen by passing through the endoscopic working channel. They are also known as endoclips, hemoclips or through the scope clips (TTSC). Reports explaining their use as a means of closing colonic and gastric perforations started emerging in the late 1990's [64, 65]. Although this method has been found efficient in the closure of smaller defects, the small size of the clips makes it difficult to close larger defects; which has to do with their inability in grasping deeper tissues [64]. Straight regular edged surgically incised tissues are more effectively closed as compared to bluntly perforated tissues with gaping, striated and irregular edges. The ability of these clips in the closure of surgically incised mucosal edges is well documented [66, 67]. Clinically, the success rate of TTSC in closing GI tract iatrogenic defects range between 59%-83% [68]. The major limitations to the success of TTSC are small size, mucosa-only tissue apposition and small closing force. However, when applied in the right context, i.e., in the closure of small defects they can be very effective. These limiting factors concerning the use of endoclips have introduced some bias into the initial clinical experience with them. Therefore, the surgeons may receive biased reviews about the success rate of commonly applied endoscopic interventions in the management of GI tract leaks.

Over the scope clips

Over the scope clips (OTSC) are popular as a means of choice when it comes to the closure of the GI tract leaks and defects. The short learning curve, large capacity caps, and ease of use, associated with them are all responsible in their surge of use. They are made of biocompatible, elastic nitinol and have the ability to close full thickness leaks that measure 2 cm in diameter [69]. In conjunction with OTSC, two more devices are usually used: a 3-pronged tissue anchor and a twin grasper; that help in tissue apposition before firing and used to secure the edges of the defect. Prior to OTSC deployment, they can be passed through the working channel and drawn up into the cap. As compared to the TTSC, they have the ability to close larger defects owing to their larger size and ability to make full-thickness tissue bites. In addition, their design provides them with a larger closure force.

The Padlock device consists of a clear applicator cap (present at the endoscope end) and a nitinol ring. When applied, a 360-degree tissue approximation and compression is provided by the ring. Available literature suggests that OTSC is successful in closing acute leaks, fistulae and perforations with long-term success rates [70-72]. In a recent study, where OTSC was used in the closure of leaks, fistulae and perforations, success rates of 73.3%, 42.9% and 90% could be achieved respectively [73]. There are also reports suggesting for nearly 100% closure rates of leaks with OTSC [74].

Vacuum therapy

Anastomotic dehiscence following gastrointestinal surgery can be closed with the aid of a device called endo-sponge that uses the technique of endoscopic vacuum-assisted closure (VAC). Effective and continuous drainage of fistulae and abscess in the pelvic region is provided by the sponge when combined with topical negative pressure. Lavage of the cavity and leak and endoscopic debridement is required before the start of treatment [75]. It is a well tolerated and highly successful technique; however, frequent changing of the sponge every 48-72 hours is required; necessitating multiple endoscopies for a period between 15 to 45 days. The major disadvantage of using the endo-sponge is the possibility of the exposure of the major vessel to the sponge. Also, the sponge may be in direct contact with parts of colon or small bowel owing to risk of erosion. As the cavity is totally covered by granulation tissue and nearly closed, endo-sponge treatment is stopped [76, 77]. Deep cavities and even larger defects can be efficiently closed using such an approach [77]. Defunctioning stoma may be avoided if systemic infections are not associated with the anastomotic leak [76]. Endo-sponge application does not face any problem from radio-chemotherapy [78, 79]. However, most of the studies involving this technique consisted of small number of patients and none of them compared it with other existing techniques in closing anastomotic leaks.

Omentoplasty

Anastomotic leaks can be re-enforced by omentoplasty and hence in the first few days following surgery it can provide additional support when the risk for anastomotic leak is the greatest. Besides, neovascularization at the anastomotic site is greatly increased by omentoplasty thereby further reducing the risk of leak [80]. However, during gastrointestinal anastomosis, omentoplasty is not so popular mainly due to the concerns of possible omental necrosis [81]. In case of esophageal surgery, there are also concerns since the omental pedicle vascular supply is contributed by the right gastro-epiploic artery, thereby supply from this artery to the gastric conduit may be theoretically affected. In gastrointestinal anastomosis, no confirmed evidence for or against omentoplasty use could be found. Therefore, more detailed studies are needed in order to accurately assess the effectiveness of omentoplasty in gastrointestinal anastomosis.

Glue and adhesives

Defects in GI tract including anastomotic leaks have been managed with varying degree of success with the use of hemostatic agents and tissue adhesives, including fibrin sealants. The use of tissue adhesives in such cases is indicated from the experience of their usage in skin closure in surgery. Tissue adhesives of different types are available with varying properties. These adhesives ensure strong adhesion through a balance of adhesive and cohesive forces as they form physical or chemical bonds with the substrate. Tissue adhesives have been broadly distinguished into two categories: sealants that protect and cover anastomosis and glues that connect different structures [82]. Their preference in surgical procedures has to do with their ability to distribute forces across the wound in a non-invasive manner. They are also flexible and strong and don't interfere with the process of healing [82]. The use of adhesives in the treatment of anastomotic leaks following bariatric surgery has been reported by a number of case series. Fibrin glue and/or vicryl plug have been used by some authors in this regard [83, 84]. A vicryl mesh was used by Bohm *et al* [84], which worked as a net, allowing for quick healing of larger defects owing to rapid cell growth, eventually leading to early oral feeding [84]. Others used a combination of topical application of vicryl, fibrin or aloderm along with the use of debridement intra-fistulous and sometimes followed by placement of stents with a success rate of 78-87%; the patients required no re-operation, neither was there any procedure-related mortality [83, 84]. Although this technique shows enough promise, further prospective studies are necessary for their evaluation and routine application.

Discussion

The possible fatal consequences of an anastomotic leak following a gastrointestinal surgery are well known to the surgeons. Classically, the patients with this condition develop high fever, tachycardia, failure to thrive, prolonged ileus, rigid abdomen, agonizing abdominal pain, and hemodynamic instability in most occasions [42]. In most cases, the patient may require rehospitalization often requiring prolonged hospital stay. Furthermore, diminished survival and increased local recurrence have been linked with anastomotic leakage after surgery [85, 86]. The anastomotic leak in a large number of patients ultimately leads to a more insidious presentation. In such cases, greater difficulty may be faced in making the diagnosis since the clinical presentation may be quite similar to other forms of post-operative infections [42]. The diagnosis may be uncertain or elusive even when radiologic imaging is used.

CT scanning appears to be an important method of detecting anastomotic leaks [30]. In comparison, contrast enemas could not identify 60% of the leaks. However, there have been instances where contrast enema could successfully diagnose the leak even when CT scan result was negative thereby indicating the complementary nature of the tests in detecting the complication. Under the circumstances of insufficient clinical findings, many surgeons do not prefer CT scan as the method of choice in the diagnosis of gastrointestinal surgery-associated anastomotic leak; however, the number of studies suggesting such preferences is very small. The elementary anastomotic leak management principles include adequate drainage, anastomotic viability assessment, control of sepsis and resuscitation. In some cases, conservative mode of management including antibiotics, avoiding oral feeds, and nutrition delivery through jejunostom/nasojejunal tube has been found to be useful [13]. Well localized, smaller leaks may be intervened with fibrin glue/endoscopic clips or over the scope clips. Endoscopic vacuum-assisted therapy, in combination or alone can be highly beneficial in certain cases [77]. Surgery in combination with any of these non-surgical methods can thus be successful in limiting anastomotic leaks.

Anastomotic leaks following gastrointestinal surgery have grabbed the attention of the surgeons, as it implies prolonged hospital stay, mortality and morbidity. With no standard algorithm to follow, the management and prevention of the complication becomes difficult and variable. However, data in the available literature suggest that the planning of interventions should concentrate on the time of diagnosis, clinical evaluation and most importantly on the location and type of leak. Non-surgical interventions have become popular in recent times owing to the lower level of associated risk of mortalities as compared to surgical means. Besides, having knowledge about the anatomical aspects of the leak can be of great help in deciding the method of treatment. A greater understanding of the advantages and limitations of the various available devices and techniques in use in the prevention and treatment of anastomotic leaks can help in selecting the right technique in a specific context which would eventually improve the overall outcomes.

Disclosure of conflict of interest

None.

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