Management of Conduit Ischemia and Necrosis following Esophageal Reconstruction

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Abstract
The stomach is the first digestive organ used to reconstruct the resected esophagus. The colon and jejunal grafts are held in reserve. Graft necrosis is a dreaded and devastating complication which threatens the patient life and affects functional results. It occurs in less than 2% after primary reconstruction. Mortality rate after conduit necrosis exceeds 90%. Multiple methods are used to evaluate graft viability intraoperatively. Various strategies as improvement of graft blood supply and delayed esophageal anastomosis or staged reconstruction are described to deal with intraoperative graft ischemia and necrosis. Early identification and adequate management of delayed graft necrosis is key to achieving a good outcome for patients. Therefore, vigilance is required in postoperative period to detect delayed graft necrosis. Identification of suspicious clinical signs, aggressive investigation to determine viability of potential graft necrosis and timely management are crucial to reduce associated mortality rate. So multidisciplinary approach is key to an adequate management of this complication. The first and best strategy should be the prevention of graft ischemia or necrosis; preoperative identification of high-risk patients, preoperative optimization of patient conditions, careful use of surgical techniques, intraoperative assessment of graft blood supply and use of methods to improve graft vascularity intraperatively are essential to prevent this serious complication.

Key words
Esophagectomy; Reconstruction; Digestive Graft; Necrosis; Diagnosis; Management; Prevention

Introduction
The stomach graft is the most common digestive organ used to restore the intestinal continuity following esophagectomy for benign and malignant diseases. The colon and jejunal grafts are held in reserve. Graft necrosis is a dreaded and devastating complication and it is defined as death of the conduit used to reconstruct diseased esophagus. However, graft ischemia is defined as inadequate blood supply to the graft. Fortunately, the reported incidence of graft necrosis is less than 2% after primary reconstruction [1, 2]. Graft necrosis is a grave complication which threatens the patient life and affects functional results. Mortality rate after conduit necrosis exceeds 90% [3-6]. Various strategies to deal with intraoperative graft ischemia and necrosis are to be considered. Improvements of graft blood supply and delayed esophageal anastomosis or staged reconstruction are described in detail. Vigilance is required in postoperative period to detect delayed graft necrosis. Early identification and adequate management of delayed graft necrosis is key to achieving a good outcome for patients. Identification of suspicious clinical signs, aggressive investigation to determine viability of potential graft necrosis and timely management are crucial to reduce associated mortality rate. Therefore, multidisciplinary approach is key to an adequate management of these patients. The first and best strategy should be the prevention of graft ischemia or necrosis; preoperative identification of high-risk patients, careful use of surgical techniques and intraoperative use of methods to improve graft vascularity are essential to prevent this serious complication.

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Management of acute intraoperative Conduit ischemia or necrosis

Gastric graft

Intraoperative graft ischemia is dreaded and appropriate management is conditioned by the timely intraoperative diagnosis of graft ischemia. The gastric tube is principally based on right gastroepiploic artery (GEA). The causes of ischemia may be the injury to the graft feeding pedicle during dissection and tube creation, right GEA injury caused by previous surgery, patient comorbidities such as arterial disease and intraoperative hemodynamic instability. Graft ischemia can be occult. In such situation, the graft may clinically look hypoperfused and assessed graft perfusion may reveal an inadequate blood flow. The intraoperative clinical impression of conduit perfusion is not particularly accurate [7, 9]. The most used techniques to evaluate intraoperatively graft perfusion are Doppler ultrasound and SPY system (Fluorescence Imaging System) with using an intravenous (IV) fluorescent agent (indocyanine green) which enables visualization of the proposed conduit perfusion [10]. These techniques are easily used in the operating room and reported sensitivity of using these two methods was up to 60% [11]. At this stage of ischemia, if action to improve blood flow is not taken, definite and irreversible graft necrosis will occur. Performing a super charge of graft and enabling adequate arterial supply and venous drainage should be considered if feasible. However gastric conduits are not usually supercharged. As reported by Sekido and colleagues [12], the gastric graft was supercharged when a poor arterial inflow or venous drainage was noted intraoperatively. The authors concluded that both arterial and venous augmentation should be performed to improve graft outcome. If gastric conduit perfusion is improved by performing arterial and venous augmentation, the esophageal anastomosis can be completed. On other hand if there is any doubt as to the viability of the graft, anastomosis reconstruction should not be completed. When this is the case, or in the case of necrosis, a damage-control strategy should be adopted. If patient hemodynamic instability has contributed to or resulted from the graft necrosis, the appropriate attitude is to simply remove the ischemic/necrotic part preserving as much of graft as possible and to drain appropriately the patient before closure by performing venting gastrostomy, cervical esophagostomy and feeding jejunostomy. This approach allows the patient transfer to an intensive care unit for optimization.

Intraoperative graft necrosis in hemodynamic stable patient may be managed differently. If the gastric graft necrosis is a consequence of local anatomy or vascular injury, alternative option of using other conduits should be considered by taking in consideration the patient factors and operative time. If, surgical procedure has taken many hours, it may be better and beneficial to formally defunction patient: cervical esophagostomy, venting gastrostomy, and feeding jejunostomy. If the operative time is relatively short, reconstruction can be performed using alternative conduit at the same time as removal of the ischemic/necrotic part of graft. The authors advocate to preserve as much of gastric graft as possible as it can be used in the second reconstruction. Both colon and jejunum should be assessed for suitability and both conduits are preferred in this situation. Consideration should be given for free graft with supercharging. Always in hemodynamic stable patient, when there is concern for the graft viability, particularly in patient with significant comorbidity factors, an alternative option to delay esophagogastric anastomosis has been described. As described by authors[13], when gastric graft ischemia occurred intraoperatively, an cervical end esophagostomy was performed and the gastric tube was pulled up to the neck either through the posterior mediastinum or the substernal route without performing cervical esophagogastric anastomosis. At 90 days after initial surgery, by reopening the cervical incision, the gastric graft was explored and its viability was verified. When the graft looked healthy and viable, the cervical anastomosis reconstruction was achieved. When substernal approach was used, some authors recommended the widening of the thoracic inlet by performing the resection of the left half of the manubrium, left sternoclavicular joint, and the medial portion of the first rib [14, 20].

Colon graft

The esophageal reconstruction by colon graft should be recognized as a surgical procedure with relatively high risk of surgical complications. The most used colon segments are, the ileocolon and transverse colon both based on the right colic artery graft, and the left colon based on left colic vessels. Author reported a slightly higher ischemia rate of colon graft than that of gastric graft. The cervical portion of transposed colon graft is farthest from the vascular supply and thus is at highest risk of Ischaemia, and the incidence of graft ischemia seems to be less if a short segment colon is used rather...
than long-segment grafting [21]. The reported ischemia incidence is slightly higher in right colon interposition than that in left colon grafting [16, 17, 22]. The causes of graft ischemia are arterial insufficiency or venous stasis of a long-segment graft and intraoperative injury to the arterial supply or venous drainage of the graft [23]. Vascular abnormalities, obstructing atherosclerotic vascular disease and insufficient venous drainage also contribute to graft ischemia [23, 25]. Intraoperative hypotension may also induce an arterial spasm and ischemia. The preexisting comorbidities such as diabetes, hypertension, low cardiac output, and obstructive pulmonary disease are the final risk factors of ischemia [26]. These comorbidity factors carry an increased risk of graft ischemia caused by compromised tissue perfusion and oxygenation. When graft ischemia occurs, it is often identified intraoperatively. As previously reported [10] the handled Doppler ultrasound and SPY system are the most used techniques to evaluate graft perfusion intraoperatively. The ischemia is confirmed by absence Doppler signal of flow in the vascular arcade of graft [24, 27, 28]. At this stage, ischemia is reversible and if blood flow is not improved, definite and irreversible graft necrosis will occur. Adding microvessel anastomosis becomes necessary to salvage the colon graft. Therefore performing a supercharge of graft to optimize arterial and venous blood flow should be considered if feasible. The microvessel anastomosis was mainly performed between the proximal mesenteric vessels of the graft and the internal thoracic vessels namely left internal mammary artery in most cases, or in the cervical vessels in other cases, such as the transverse cervical artery or the branches of the external carotid artery and the internal or external jugular vein. If perfusion of supercharged graft is improved as ascertained by the presence of an adequate pulsatile blood flow in the mesenteric arcade and peristaltic activity, the intestinal anastomosis can be completed. On other hand, if graft supercharge is not feasible, other alternative strategies can be considered. In case of patient with hemodynamic instability, a damage-control strategy should be adopted: Resecting the ischemic or necrotic part of graft, Performig esophageal diversion and a colostomy using remnant graft, inserting a feeding tube-jejunostomy and draining appropriately the patient before closure. This approach permits to transfer patient to an intensive care unit for optimization. In hemodynamically stable patient, the ischemia or necrosis can be managed differently by taking in consideration patient risk factors and operative time. If the operative time is relatively short, reconstruction can be performed using alternative conduit at the same time as remove of the ischemic/necrotic portion of graft. However it is better and beneficial to delay reconstruction if operation has taken many hours. A cervical esophagostomy and feeding jejunostomy are performed, and the ischemic or necrotic colon graft is removed. Stomach, colon (right or left) and jejunum can be used as an alternative graft option for second reconstruction. The substernal approach is preferred in delayed or re-reconstruction. As previously reported, when substernal route is used, authors recommend widening of thoracic to avoid graft compression [14, 20].

Management of delayed graft necrosis

The principal key of successful management of delayed graft necrosis is to early diagnose this disastrous complication. The clinical manifestation of necrosis is broad and may be fulminant but is often nonspecific. Infarction related to venous congestion presents more insidiously. Sepsis, persistent high fevers, unexplained tachycardia, unexplained leukocytosis, hemorrhagic nasogastric tube drainage, lactic acidosis, hemodynamic instability and unexplained clinical deterioration in the absence of pneumonia or an anastomatic leak should prompt an assessment of graft vitality. Therefore when clinical presentation is nonspecific and the necrosis is suspected, investigation is mostly required to determine the graft viability. Because early detection is critical to survival in these patients with such complication. Early diagnosis and appropriate management reduce associated mortality rate. Several investigations have been used to evaluate graft viability including Gastrografin swallow, CT, and Esophagogastrodudodenoscopy (EGD), Upper gastrointestinal contrast swallows have traditionally been used to assess esophageal anastomosis postoperatively [29]. However their use is limited because of associated risk aspiration [30-33]. CT with oral contrast is more sensitive and gives more information with regard to pneumonia, pleural effusion, and other thoracic or abdominal abnormality but as demonstrated normal CT examination does not exclude gastric graft ischemia [34]. The EGD assesses graft by visualizing the subtle mucosal ischemia. There is a concern of risk to disrupt a fresh anastomosis however authors reported that routine endoscopy can safely be performed in the first postoperative week [35]. GD can show necrotic black mucosa throughout the gastric or colon graft with intact anastomosis testifying of the presence of necrosis. If diagnosis of graft necrosis is highly
suspected in unwell patient, it is appropriate to proceed to surgical exploration. An aggressive resuscitation should be undertaken with administration of a broad-spectrum IV antibiotics. When anastomosis is located in the neck, the reopening the cervical incision and exploration of the graft confirm the diagnosis of necrosis. In case of intrathoracic anastomosis, video-assisted thoracic surgery/thoracotomy is required to visualize the graft and verify its viability. In case of gastric graft, if the necrosis is partial, the necrotic part is resected and an end esophagostomy should be performed with venting gastrostomy (if appropriate) and feeding jejunostomy. The graft should be removed if it is completely gangrenous. In case of colon graft, the necrotic graft is resected, an esophageal deunction and feeding jejunostomy or gastrostomy are performed.

Re-reconstruction

Preoperative optimization of Patient

The perioperative risk in these patients is more than those undergoing a primary esophageal reconstruction. After surgical management of graft necrosis and patient has survived to subsequent surgical intervention, it is essential to optimize the patient condition before considering digestive re-reconstruction. During the in-hospital postoperative course, sepsis should be managed appropriately, with IV antibiotics based on culture results and appropriate drainage of collections. Enteral nutrition should be introduced immediately. During this period, dietician and physiotherapy contribution are essential. Patient education with regard to their esophagostomy is critical. Patient should be taught how to care for his/her skin and his/her appliance. He/she should be educated to consult his/her physician if complications as stenosis of the esophagostomy or cellulitis occur. Evaluation of patient’s nutritional status and correction of nutritional disorders should be performed before time of surgery. The most authors advocate to perform esophageal re-reconstruction 3 to 6 months after primary reconstruction [1, 5, 17].

Reconstruction Options

Both Jejunum and colon grafts can be used to restore digestive continuity after failure of first esophageal reconstruction using gastric procedure. Jejunal grafts is preferred to be used for partial reconstruction of resected esophagus (intrathoracic anastomosis) and it can be used in a roux-en-Y fashion if the remnant esophagus is of sufficient length and good vascularity. Free jejunal conduit is used to reconstruct the cervical esophagus after partial esophagectomy. Free jejunal graft, firstly described in 1947 and widely used recently [36], can be used to reconstruct the resected esophagus after failure of primary reconstruction using stomach or colon conduits. In case of partial graft necrosis, combined esophageal re-reconstruction can be performed using free jejunal conduit and the preserved graft (remnant) after resection of necrotic part if remnant graft has a sufficient length. The free jejunal graft is often run on the second jejunal branch of the superior mesenteric artery. The microvascular arterial and venous anastomoses are critical to the graft survival. An indicator flap is left exteriorized so that the blood supply to the conduit can be inferred and monitored in the postoperative course of the surgery. By applying the principles of management of plastic surgical flaps, authors advocate to avoid hypotension and use of vasopressor agents in the postoperative period. Early complications such as pneumonia (30%), anastomotic leak (32%), graft necrosis (5%) and mortality (10%) are important and are related to complex nature of this surgery [13]. Despite the important early morbidity and mortality, the postoperative quality of life and graft function is generally good [37].

Both right and left colon can be used to reconstruct the resected esophagus after gastric graft failure. the left colon is more advocated for esophageal reconstruction because of its smaller diameter which allows less distension and matches well with esophagus lumen, its less variation in the blood supply and the graft ultimately can be a longer length [1, 5, 34]. The right colon graft based on the right or middle colic arteries can be used. After failure of primary colon esophageal reconstruction, the stomach (if available), jejunum and colon (right or left) can be used to establish digestive continuity. As previously [36], free jejunal graft is used in combination with the first graft if it has a sufficient length after removing the necrotic part. The use of left colon graft based on left colic vessels after failure of right colon graft is always possible however the opposite is not always possible if an extended left colon graft is used with ligation of the right colic artery. The substernal approach is often preferred in esophageal re-reconstruction because access to posterior mediastinum after first dissection is technically difficult and is at high risk of operative complications. During substernal approach, the widening the thoracic inlet by resection of the left hemi-manubrium, clavicle, and first
After graft necrosis and survival of patient, acquisition of surgical skills based on preoperative identification of risk factors and procedures. Therefore, the best way is the prevention reconstruction which requires a panel of complex surgical skills. The difficulty is how to complete further digestive re-
tentory factors and high-risk patients is an assessment of key importance to prevent graft ischemia or necrosis. As reported, patients with significant comorbidity have been shown to have an odds ratio (OR) of 2.2 (1.1–4.3, P = .023) for the development of graft ischemia [38]. The risks of graft necrosis and morbidity/mortality from surgery will be prohibitive in some cases, so these patients and their families should be counseled accordingly. Patient factors, such as neoadjuvant therapy, diabetes, low perioperative cardiac output, chronic obstructive pulmonary disease, and peripheral arterial disease are associated with high risk of graft ischemia and necrosis [38]. Preoperative strategies can be used to optimize patient conditions. Therefore preoperative risk assessment of any patient planned for esophageal resection is essential and should include a full history and examination including assessment of cardiorespiratory function, diabetic control, and in the presence of previous abdominal surgery or where colonic interposition is considered mesenteric angiography should be performed[17, 21].

Preoperative evaluation of patient risk

The preoperative identification of risk factors and high-risk patients is an assessment of key importance to prevent graft ischemia or necrosis. As reported, patients with significant comorbidity have been shown to have an odds ratio (OR) of 2.2 (1.1–4.3, P = .023) for the development of graft ischemia [38]. The risks of graft necrosis and morbidity/mortality from surgery will be prohibitive in some cases, so these patients and their families should be counseled accordingly. Patient factors, such as neoadjuvant therapy, diabetes, low perioperative cardiac output, chronic obstructive pulmonary disease, and peripheral arterial disease are associated with high risk of graft ischemia and necrosis [38]. Preoperative strategies can be used to optimize patient conditions. Therefore preoperative risk assessment of any patient planned for esophageal resection is essential and should include a full history and examination including assessment of cardiorespiratory function, diabetic control, and in the presence of previous abdominal surgery or where colonic interposition is considered mesenteric angiography should be performed[17, 21].

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Preoperative evaluation of patient risk

The ischemic preconditioning of the gastric graft before esophageal reconstructive surgery has been proposed in an attempt to reduce graft necrosis and anastomotic leak rates. This technique had firstly been described by Urschel and colleagues in 1997[39, 40]. As demonstrated by Schröder and colleagues [41, 42], the gastric graft microcirculation takes 4 days to return to preoperative levels after surgery. The mechanism is unclear; however, the development of stomach neovascularization and release of humoral factors to improve the blood supply to the fundal region have both been proposed [41, 42]. The basis for this concern is based on the findings of cadaveric specimens studies after esophageal surgery which had shown that 20% of the blood flow to the gastric graft tip is derived from the mucosal capillary network rather than a named vessel [43]. Stomach preconditioning consists of ligation of the left gastric artery and/or short gastric arteries. Preconditioning can be performed by radiological arterial embolization or preresectional laparoscopic [39, 40]. During preresectional laparoscopy, celiac lymph node dissection is performed and omentum, peritoneum and liver are also inspected. The first preoperative arterial embolization use was not successful and was complicated by high rates of pancreatitis and splenic infarction because the splenic and short gastric arteries were embolized in addition to the left gastric artery [44]. Based on obtained results, clinical evidence of studies does not favor preoperative preconditioning of gastric graft [45,45] which is associated with increased cost given the additional surgery and hospital admission.

Intraoperative assessment of conduit blood supply

Many techniques have been described to assess blood supply to the digestive graft (gastric, jejunal, and colon) [47]. However handheld Doppler ultrasound and Fluorescence Imaging System (SPY system) are the most used to evaluate graft perfusion intraoperatively. These two techniques are easily used in the operating room and their reported sensitivity was up to 60% [48]. Murawa and colleagues [48] published the first use of the SPY system to assess the gastric graft and several other studies [47, 49, 50] suggested the utility of using this technique. The SPY system may be particularly useful with considerable contribution when a complex esophageal reconstruction is considered to assess the adequacy of supercharged graft blood supply. Therefore information given by intraoperative assessments can be used to guide intraoperative decision making. As recommended by authors [47, 48, 49, 50], these tools are used in conjunction with clinical acumen to decide whether the conduit blood supply is suitable or whether another conduit must be sought.

Optimizing patient perfusion pressure

Patients undergoing esophageal reconstruction following esophagectomy are predisposed to hemodynamic changes, secondary to fluid shifts, intraoperative blood loss, epidural anesthesia, IV fluid administration, and the potential use of vasopressor agents. Thoracic epidural

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analgesia, which is commonly used in patients undergoing esophagectomy, causes increased blood flow in the gastric graft by way of sympathetic block. This increased graft blood flow occurs 1 hour and 18 hours following thoracic epidural anesthesia [51]. As demonstrated in animal models, the administration of vasopressors, noradrenaline, has been associated with reduced perfusion to the conduit [52]. Many surgeons have reservations with regard to the intraoperative administration of vasopressor agents and are concerned about reducing perfusion to the conduit. On other hand and as shown recently, uncommon use of intraoperative vasopressor during free tissue transfer flaps in plastic surgery did not seem to adversely affect patient outcomes [53]. By extrapolation of these results, the judicious use of vasopressors during pediced gastrointestinal reconstructions following esophagectomy is not always harmful.

Aggressive fluid resuscitation is an alternative strategy to maintain perfusion pressure to the distal part of graft. This strategy needs the intraoperative administration of a large volume of fluid which allows maintaining both patients’ blood pressure and grafting perfusion pressure. As observed, restrictive intraoperative fluid regimen coupled with norepinephrine to maintain a mean arterial pressure of 65 mm Hg or greater reduced the incidence of pneumonia and respiratory complications with no increase in graft ischemia incidence [54]. With regard to graft perfusion, current evidence [52, 53] does not support the superiority of one approach over the other when fluid resuscitation or vasopressor administration are used to correct the decrease in blood pressure seen in 40% to 60% with general anesthetic agent administration. In fact, hypotension with concomitant reduced graft perfusion is not benign [54, 55, 56]. Therefore clear communication between the surgical and anesthetic team is required to adopt a management strategy tailored to each patient.

Operative technique

Vascular augmentation techniques to optimize arterial and venous blood flow to the graft should be considered [12, 17]. Therefore patients who showed intraoperative graft ischemia, adding microvessel anastomosis became necessary to salvage the graft [12, 17, 21]. So in comorbid patients a strategy to deal with graft ischemia this is to perform delayed graft creation, or delayed esophageal reconstruction, or supercharge of graft [17, 21]. Careful handling and passage of the graft through the reconstruction route is highly required, particularly when the substernal route is employed. When pulling up the graft to the neck, constant checking of the vessels position is required. Even minimal twisting may represent a significant obstacle to the venous flow. Venous drainage is very sensitive to a mechanical obstacle [21]. In substernal esophageal reconstruction, it is important to ensure there is no compression on the transposed graft at the thoracic inlet level. We feel so it is essential to enlarge the thoracic inlet in order to avoid any cervical compression on the transposed graft [15].

Conclusion

Conduit necrosis is a dreaded and devastating complication during esophageal reconstruction. Necrosis is associated with high mortality rate in absence of early diagnosis and adequate management. Specialized techniques as Doppler fluorescence may be useful to assess intraoperatively conduit ischemia. Various Strategies described to deal with intraoperative graft ischemia may be useful. Identification of suspicious clinical signs, aggressive investigation to determine graft viability and timely management are crucial in delayed necrosis. So vigilance is required in postoperative period. Early identification and adequate management of delayed graft necrosis is key to achieving a good outcome for patients. Multidisciplinary approach is essential to an adequate management of necrosis. The best way is the prevention of this complication. Therefore preoperative identification of patient risk factors, perioperative optimization of patient conditions, careful use of surgical techniques are the best defenses against conduit ischemia and necrosis.

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