



## Case report

## Long term outcome of a subcutaneous colonic interposition after pharyngo-laryngectomy for strictures of the larynx and hypopharynx resulting from caustic ingestion: A case report

Orlino C. Bisquera Jr.<sup>a</sup>, Anthony R. Perez<sup>a,\*</sup>, Neresito T. Espiritu<sup>b</sup>, Ma. Katrina B. Guillermo<sup>b</sup>, Mary Ellen Chiong Perez<sup>b</sup>

<sup>a</sup> University Of The Philippines Manila College Of Medicine, Philippines

<sup>b</sup> University Of The Philippines Manila Philippine General Hospital, Philippines

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## ABSTRACT

**Introduction:** Caustic agents, also called corrosive agents, could be acids or alkali in nature. If ingested, these agents can injure any part of the aerodigestive tree. Extent of injury depends on the type, concentration, duration of exposure and volume of caustic agent ingested. Serious complications after caustic agent ingestion can occur both in the short term such as hollow viscus perforation and death and in the long term such as stricture formation causing obstruction and lifetime risk of development of carcinoma.

**Presentation of a case:** This is a case of a 25-year-old female who ingested an unknown substance resulting to a severe stricture of the larynx, hypopharynx, esophagus and pyloroantral region of the stomach. Six months after her tracheostomy and tube jejunostomy, she sought further medical attention in our institution due to inability to swallow food and saliva. She underwent pharyngolaryngectomy (PL) with the strictured esophagus and stomach left in-situ due to extensive adhesions. The subcutaneous colonic interposition reestablished the alimentary continuity by providing enough length for tension-free anastomosis and a more direct route for cervical anastomosis.

**Discussion:** Stricture formation is one of the most challenging late complication of corrosive injury. It results from scar formation in response to inflammation of the aerodigestive tract. Key factors in managing caustic strictures include safety of strictured segment resection, choice of replacement organ for reconstruction and route of conduit.

**Conclusion:** Timing of surgery and proper selection the surgical procedure for complications of caustic ingestion can result in excellent long term outcomes.

### 1. Introduction

Caustic agents, also called corrosive agents, are substances which could be acids or alkali in nature. Strong alkali are agents with pH > 12 while strong acids have pH of <2 [1]. If ingested, these agents can injure any part of the aerodigestive tree. Extent of injury is variable depending upon the type, concentration, duration of exposure and volume of caustic agent ingested [2]. Alkali-containing caustic agents, like household bleaches, toilet cleaners and drain openers, cause liquefactive necrosis resulting in deep penetration and perforation. Acid-containing agents, like toilet bowl cleaners, anti-rust compound and swimming pool cleaners, cause coagulative necrosis that result in the formation of a

coagulum or eschar limiting the depth of tissue injury [3]. Furthermore, alkali agents tend to injure more on the esophagus rather than the stomach, whereas acidic agents injure more on the stomach rather than the esophagus. It is not uncommon, however, for acid agents to also cause extensive esophageal injury and sometimes perforation [2]. Larynx, trachea and bronchi may likewise get injured by both acidic and alkaline substances. Serious complications after caustic agent ingestion can occur both in the short term such as hollow viscus perforation and death and in the long term such as stricture formation causing obstruction and lifetime risk of development of carcinoma [4]. The risk of stricture formation becomes higher with increasing severity of acute injury based on Zargar's endoscopic grading (Table 1) [5]. Grade 2B and

\* Corresponding author at: University Of The Philippines Manila College Of Medicine And Philippine General Hospital, Department Of Surgery, Philippines.  
E-mail address: [Arperez1@up.edu.ph](mailto:Arperez1@up.edu.ph) (A.R. Perez).

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**Table 1**  
Zargar's classification and its corresponding endoscopic description.

Grade	Description
Grade 0	Normal mucosa
Grade 1	Edema and hyperemia of the mucosa
Grade 2a	Superficial localized ulceration, friability, and blisters
Grade 2b	Grade 2a plus circumferential ulceration
Grade 3	Multiple and deep ulcerations and small scattered areas of necrosis
Grade 3b	Extensive necrosis
Grade 4	Perforation

Grade 3 will have risks of stricture formation of about 71% and 100% respectively [6]. Stricture usually develops within 8 week after ingestion in 80% of patients, but it can happen as early as 3 week and as late as 1 year [7].

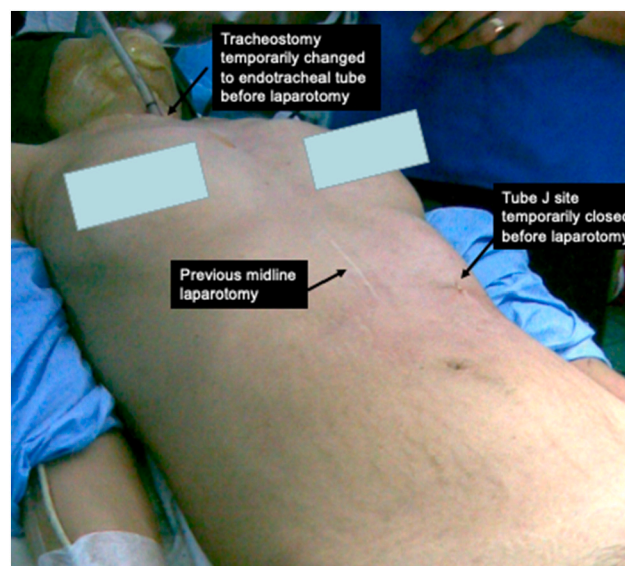
Stricture formation is one of the most challenging late complication of corrosive injury. It results from scar formation in response to inflammation of the aerodigestive tract. This can start as early as second week, and can lasts for about six months for a full fibrosis to develop after injury [8]. Timing of operation is one of the key factors to consider in surgical management. A too early operation, when the scar has not completely formed, can promote the risk of anastomotic stenosis. Thus, operation is usually carried out at least six months after injury. Treatment depends on the length of stricture and number of areas with stricture. Endoscopic dilatation is effective for short strictures, less than 2 cm in length. Long strictures or multiple site strictures, on the other hand, are usually non-dilatable strictures. For these types of stricture, surgery is the only option to reestablish gastrointestinal continuity [3].

This paper aims to describe the conduct of surgery, technical highlights and key factors considered in the definitive surgical management of caustic strictures. It also aims to discuss the nuances in performing subcutaneous colonic interposition and modifications adopted in this case to address its common pitfalls. This case is being reported according to the SCARE guidelines [9].

### 1.1. Presentation of the case

A 25 year old female was admitted at our institution for further evaluation and management of her upper gut stricture secondary to previous caustic acid ingestion. Six months prior, she was admitted at a hospital abroad where she worked as a baby sitter. With no available clinical records, she claimed to have been forced for unknown reason by her employer to drink approximately 1 glass of unknown colorless and odorless fluid which turned out eventually as caustic agent most likely a strong base. This caused her to manifest abdominal pain, vomiting and difficulty of breathing. She was brought to a hospital where tracheostomy and tube jejunostomy were done. She was discharged after 1 week as improved and advised regular follow up to monitor her condition. She continued to gain weight through jejunostomy feeding but was unhappy in her progressive inability to tolerate solid and liquid diet hence decided to go back to the Philippines.

She arrived at our institution ambulatory and breathing per tracheostomy with tube jejunostomy in place. Her only pertinent symptom is immediate regurgitation of solid and liquid foods whenever she attempt to ingest including her saliva. She was coherent with normal vital signs and a Body Mass Index (BMI) of 18. Her abdomen was flat with 7 cm midline laparotomy scar and tube jejunostomy placed at the left upper quadrant (Fig. 1). No voice was elicited even with an externally closed fenestrated tracheostomy tube. Flexible nasopharyngoscopy under local anesthesia revealed normal oropharynx but with stricture resulting to complete obliteration of the opening of the laryngeal inlet and the hypopharynx precluding visualization of the vocal cords. Because of this, assessment of the status of the esophagus and stomach through barium swallow and upper GI endoscopy as initially planned were not done. With the clinical diagnosis of complete hypopharyngeal and laryngeal obstruction secondary to stricture from caustic agent ingestion, she



**Fig. 1.** Patient shown just before surgery with tube jejunostomy site closed and tracheostomy temporarily changed to endotracheal tube for general anesthesia.

consented for surgery for definitive management.

The surgical plan was pharyngolaryngoesophagectomy (PLO) with gastric pull-up possible colonic interposition. Colonoscopy revealed normal result. Cardiopulmonary assessment was low risk with normal pulmonary function test. Two day bowel preparation was done and preoperative intravenous antibiotic was given.

### 1.2. The surgical technique

Patient was placed on supine position and neck extended with rolled pad placed transversely behind the shoulders. Induction of general anesthesia was commenced through the tracheostomy tube then changed to endotracheal tube to allow better neck exposure. Tube jejunostomy was removed and the site closed with purse string skin suture to prevent intraoperative wound contamination. Standard anti-septic wound preparation was done.

Initial approach was through the abdomen with a supraumbilical midline laparotomy. Findings revealed a thickened and contracted distal 2/3 of the stomach that is fixed to the retroperitoneum. The proximal 3rd of the stomach was distended due to cicatricial obstruction at the antral area. The hiatus was dissected to expose and assess the distal esophagus which likewise revealed to be thickened and markedly adherent to the thoracic aorta and pericardium. No further proximal dissection of the esophagus was attempted. The initial plan to use the stomach, which was left in-situ, as esophageal substitute was changed to colonic interposition. Proceeded with mobilization of the colon extending from distal ileum about 10–15 cm from ileocecal valve to the sigmoid colon for a left colic artery-based colonic interposition. After marking for the approximate length of colon that can be anastomosed to the neck without tension, the sufficiency of the left colic artery as the future blood supply of the interposed colon was checked with temporary placement of vascular clamps to occlude the main trunk of the right colic artery, middle colic artery, and the marginal artery of Drummond proximally at ascending colon and distally at the descending colon area. Intestinal clamps were also placed at the proposed ascending and descending colon transection sites to prevent submucosal blood supply. This completely isolated the ascending colon, transverse colon and descending colon from all possible sources of blood supply leaving only behind an intact left colic artery. The isolated segment of colon was viable after 10 min of occlusion. Proceeded with transection and ligation of the right colic and middle colic arteries close to its origin from the

superior mesenteric artery to preserve the bifurcation branches supplying the colon graft. Colonic resection was done proximally at the junction of cecum and ascending colon and distally at the junction of descending and sigmoid colon. The left colic artery and inferior mesenteric vein were carefully preserved to supply and drain respectively the isoperistaltic colon graft. The colonic graft was temporarily laid over the chest up to the neck area for further observation for any changes in its color and pulsation (Fig. 2A) while anastomosing the cecum to the sigmoid colon using 2-layer colonic suturing technique. Because of the eventual anatomic change in the location of the appendix, appendectomy was done preceding the cecum-sigmoid anastomosis. A Roux-en-Y gastrojejunostomy was also done to drain the dilated gastric fundus (Fig. 2B).

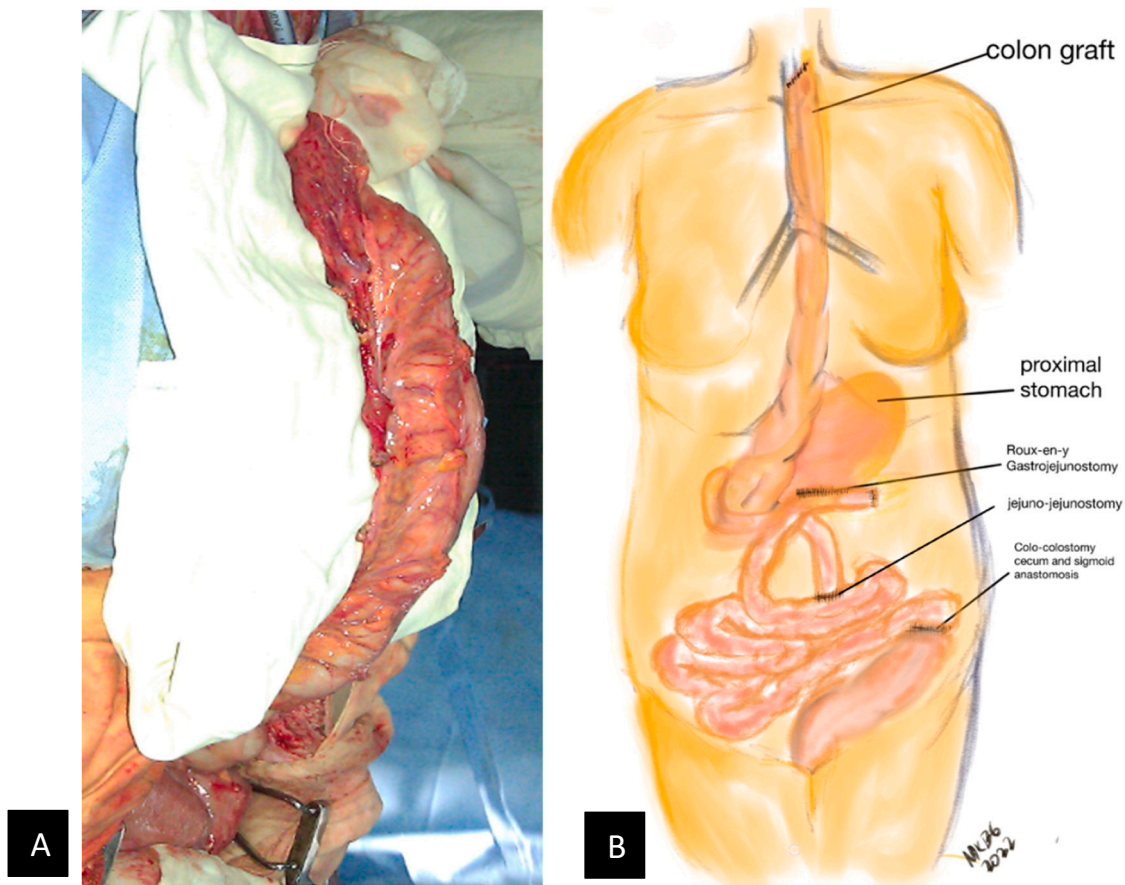
Next approach is on the neck through an apron skin incision down to the platysma. Subplatysmal flap superiorly up to the mandible and inferiorly down to the clavicle was created. Mobilization of the larynx and hypopharynx was done with care to preserve the right and left thyroid lobes, parathyroid glands and the inferior thyroid vessels. Inferiorly, strap muscles were transected to expose the trachea which was circumferentially cut at the 2nd tracheal ring. The endotracheal tube was then replaced to the distal trachea which was secured through an anchoring suture to the skin to maintain its position preventing endobronchial tube migration. The cervical esophagus revealed to be markedly stenotic and adherent to the prevertebral fascia and to the surrounding structures. Because of this, the initial plan to perform a PLO was abandoned and instead did only a pharyngo-laryngectomy (PL). The strictured esophagus was transected at the level of tracheal transection and suture-ligated with silk 2-0. Dissection continued upwards to fully mobilize the larynx and the hypopharynx. Superior thyroid artery, middle thyroid vein and recurrent laryngeal nerve were transected

bilaterally. Suprahyoid muscles released to expose the body and greater horn of the hyoid bone and the pyriform mucosa, which was opened, to circumferentially transect the hypopharynx at this level. Pharyngo-laryngectomy was then completed (Fig. 3). Histology report of pharynx and larynx showed diffuse fibrosis with stenosis, congestion and chronic inflammation. Margins were morphologically viable.

The isolated segment of isoperistaltic colonic graft was tunneled subcutaneously at the left anterior chest to reach the neck area. Anastomosis between the oropharynx and the proximal colon (ascending colon part) was done using 2-layer suturing technique. The distal colon (descending colon part) was anastomosed to the Roux limb of jejunum about 40 cm distal to the gastrojejunostomy and 40 cm proximal to the Jejunum-jejunostomy (Fig. 4). Tube jejunostomy was placed distal to the jejunojejunostomy. Subphrenic tube (Jackson-Pratt) drain placed and abdominal incision closed in layers. A circular opening along the lower part of the neck skin incision was created to anchor the trachea creating a permanent tracheostoma. Neck incision closed using absorbable suture after tube drain was placed at the subplatysmal area (Fig. 5). The operative time was 5 h with the patient tolerated well the procedure. Postoperatively, immediate extubation was done. The surgical team consisted of attending surgeons and three fellows.

### 1.3. Postoperative course

The postoperative course was uneventful with the patient breathing well through the tracheostoma. Tube jejunostomy feeding started on 1st postoperative day and progressed to regular diet per orem on the 6th postoperative day after a normal barium swallow (Fig. 6). Tube drains were removed and was discharged on the 8th postoperative day. Tube jejunostomy was removed one month after the surgery.



**Fig. 2.** A. Abdominal phase showing prepared isoperistaltic colonic graft temporarily laid over the chest for further observation while anastomosing cecum and sigmoid colon. B. cecum to sigmoid anastomosis and Roux-en-Y gastrojejunostomy.

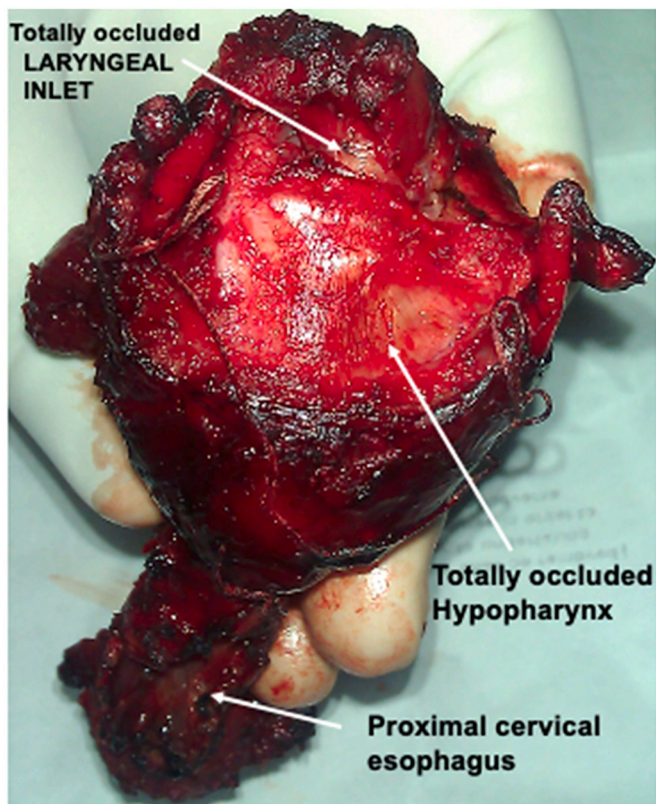


Fig. 3. Pharyngolaryngectomy specimen showing the totally occluded laryngeal inlet and hypopharynx.

On her 10th year follow-up, she continued to report no dysphagia, able to eat 2–3 times a day, without postprandial symptoms such as regurgitation or pain. Her weight and BMI were 60 kg and 24, respectively. Contrast enhanced Chest CT scan showed no mass on the residual esophagus and stomach. The colonic interposition placed subcutaneously at the left anterior chest had normal gas pattern with no signs of obstruction (Fig. 7).

## 2. Discussion

Surgical management of non-dilatable caustic stricture can pose a technical challenge. Several factors that need to be addressed are: (1) safety of strictured segment resection, (2) the choice of replacement organ after resection—stomach, jejunum and colon and (3) route of conduit—posterior mediastinum (previous location of esophagus), retrosternal (anterior mediastinum) or antesternal (subcutaneous area).

The removal of the strictured segment is usually difficult and dangerous due to the development of extensive inflammation and scarring. Adhesiolysis can be bloody. Difficulty in dissection can also cause concomitant pneumothorax, mediastinitis and other morbidities. Some may even require opening the chest. Given that the reconstruction after corrosive injury is usually delayed, extensive inflammation and scarring of the posterior mediastinum are common reasons for not proceeding with resection [10].

The choice of organ for reconstruction depends on the length of the tract that needs replacement. Jejunum may be used for short segment involvement but long segment is usually reconstructed using either the stomach or colon. One feature of corrosive injury is the likelihood of concomitant gastric involvement specifically at the pyloric area. Marked scarring of the stomach such as found in this case can make mobilization difficult and unsafe. This leaves the colon as the most likely best replacement for severe corrosive injury reconstruction. It can provide long segment conduit, can be mobilized easily, and acid regurgitation

with anastomotic ulceration or stricture formation rarely occurs [11].

Preoperative workup prior to utilizing colon as conduit may include (1) colonoscopy, (2) barium enema and (3) angiography [12]. A thorough history must first be elicited for any chronic colonic symptoms that might suggest anatomic pathology like inflammatory bowel disease, telangiectasia, polyposis, extensive diverticulosis (severe constipation esp. in elderly) or even synchronous neoplasm of the colon. Questions on prior colonic resection or vascular/abdominal aortic aneurysm repair, which could suggest possible vascular pedicle compromise, must also be sought. These conditions are contraindications in selecting colon as conduit.

At a minimum an air contrast barium enema should be obtained but colonoscopy is preferred and standard in practice since it allows direct examination of colonic mucosa [13]. The utility of CT colonoscopy prior colonic interposition in lieu of colonoscopy was also proposed due to its minimally invasive nature and reliability in evaluating the colon for patients with average colorectal cancer risk [14]. There is no significant difference in rates of complications secondary to ischemia in patients who undergo routine preoperative angiography as compared to those who do not [15]. Certain population however absolutely needs preoperative colonic arterial evaluation via arteriography. These patients are those expected to have extensive limiting atherosclerosis (i.e. elderly, lower extremity claudication, diabetic, cardiac disease, peripheral arterial disease) or those suspected to have had previous bowel resection and vascular surgery. Particularly, patency and robustness of superior and inferior mesenteric arteries, ileocolic, right, middle and left colonic arteries are of great interest.

The location for conduit placement is also a unique challenge for caustic injury. Previous acute inflammation of the thoracic esophagus in response to prior caustic ingestion may result to extensive scarring at the posterior mediastinum. This will prevent safe dissection and removal of the strictured esophagus. As a consequence, this route cannot be utilized to pull-up the colonic graft to reach the neck area. In such situation, the next best route will be through a substernal tunnel provided that no future tracheostoma creation is planned. Otherwise when pharyngolaryngectomy is also performed, subcutaneous placement of the colonic graft at the left anterior chest can serve as the alternative location because the subcutaneous tunnel towards the neck can be created in a manner avoiding the future site of tracheostoma. The first colonic interposition technique described by Kelling and Vuilet in 1911 utilized subcutaneous placement because of its simplicity and safety. The shift towards retrosternal or posterior mediastinum placement is mainly from its poor cosmesis. Preoperative investigation on inflammatory conditions in esophageal bed, pleural space (i.e. thoracotomy, infectious lung disease), anterior mediastinum, previous thoracic surgery (i.e. sternotomy, coronary artery bypass grafting) may render the retrosternal and posterior mediastinal route unsuitable for esophageal reconstruction.

The case showcases key points discussed in introduction. The patient presented 6 months after her injury, an optimal time for reconstruction. She was unable to tolerate oral intake, severity was further cemented by her inability to ingest her saliva. The extensiveness of her disease preclude pre-operative evaluation via upper gastrointestinal endoscopy and barium swallow. The proximal extent of pathology, strictured hypopharynx and laryngeal inlet, was confirmed using flexible nasopharyngoscopy. Initial surgical plan discussed with the patient was pharyngolaryngoesophagectomy (PLO) with gastric pull-up possible colonic interposition. The suitability of the stomach as possible conduit will be made intraoperatively, while the colon was evaluated to be normal with preoperatively performed colonoscopy. Upon exploration, the proximal stomach was dilated due to obstruction at the antral area from markedly adherent stricture formation resulting to thick and contracted distal stomach fixed to the retroperitoneum. The cervical and thoracic esophagus was difficult to mobilize and adherence to the adjacent structures (i.e. prevertebral fascia, aorta and pericardium) were noted.

Taking all these into account, we address the factors that need to be

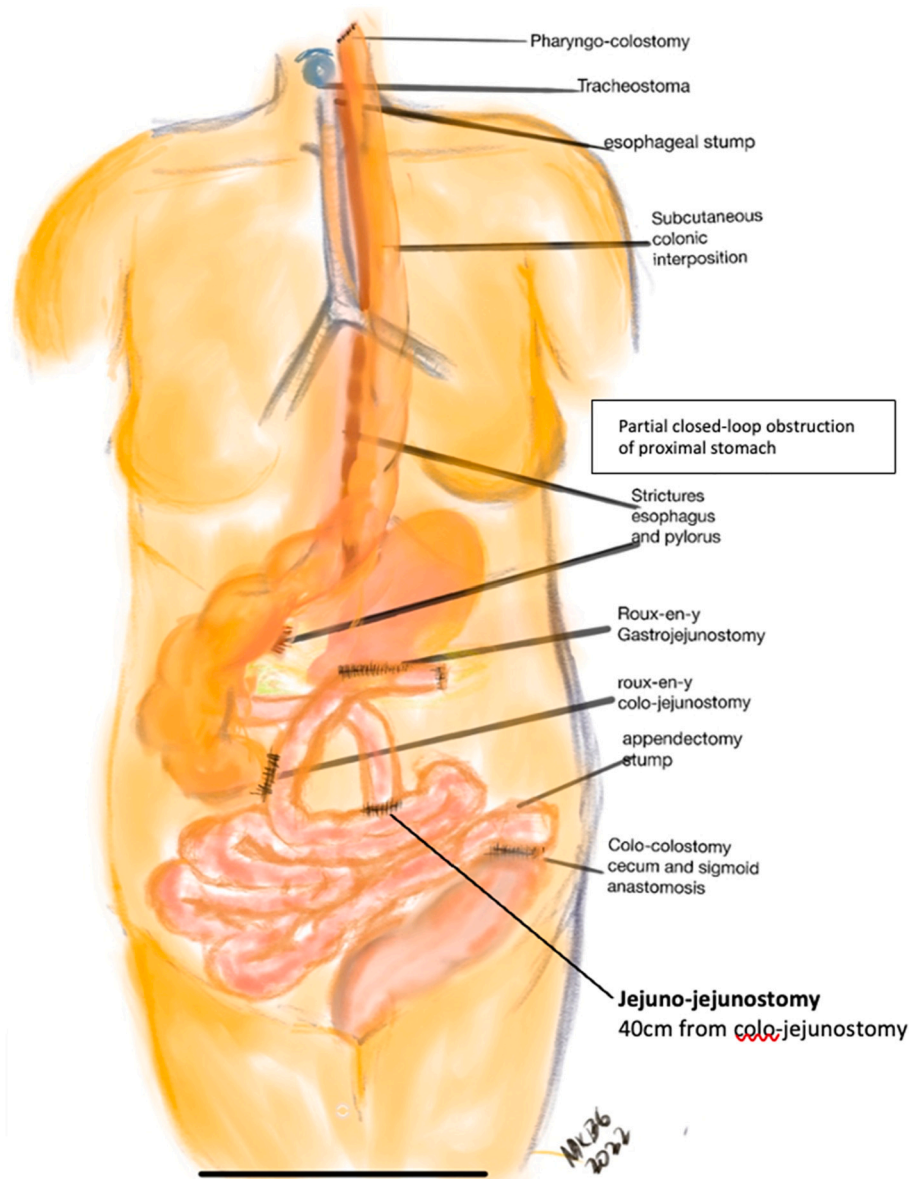


Fig. 4. Illustration of the complete extent of reconstruction to restore gastrointestinal continuity.

answered during the surgical restoration of intestinal continuity. First, the diseased esophagus was not further dissected and removed due to safety. Pharyngolaryngectomy (PL) was safely done in the strictured hypopharynx and larynx providing adequate area for anastomosis of the colon conduit to the healthy part of oropharynx. Second, a Roux-en-Y gastro-jejunostomy was established to drain the obstructed proximal stomach. Third, colon was utilized as conduit due to the long segment disease and unsuitability of the stomach as replacement. And lastly, the conduit was placed subcutaneously due to the residual thoracic esophageal disease at the posterior mediastinum and presence of tracheostoma obstructing the substernal route.

The nuances involved in the surgical technique presented include three key aspects. These are (1) conduit preparation, (2) tunneling technique and (3) cervical anastomosis.

The conduit harvested was a left colic artery based colonic graft. Careful attention on determining the sufficient length for tensionless anastomosis and absence of redundancy was determined. The technique on temporary occlusion to test vascular integrity were also crucial during the conduit preparation. And lastly, the graft was allowed to sit on the chest to allow enough time for observation and evaluation of its

viability (Fig. 2A). Recent advances in intraoperative real-time fluorescence angiography using Indocyanine green (ICG) would have been a useful adjunct in assessing objectively intestinal viability. During the surgery of this case, this modality was not yet available in our institution, hence, was not utilized. ICG fluoresces well vascularized tissue within a minute using infrared-sensitive charge-coupled device (CCD) camera system [16]. Tissues that did not light up after such time may be objectively judged as non-viable.

Subcutaneous tunnel for the interposed colon was created at the left anterior chest going up to the cervical area for anastomosis with the oropharynx. This avoided the anterior obstruction of cervical tracheostoma placed midline after a PLO. Several advantages of subcutaneous route placed at the left anterior chest include: decreased chance of skin flap necrosis along the sternum where skin is tightly adherent to sternum and skin is thin, higher compliance of the tunnel due to absence of sternal inflexibility posterior to the conduit and a direct route for oropharyngeal anastomosis at the left parasternal area simulating the esophageal location in posterior mediastinum [17]. The pharyngo-colostomy anastomosis was done through an end to end two layer suturing technique using 3-0 absorbable sutures.

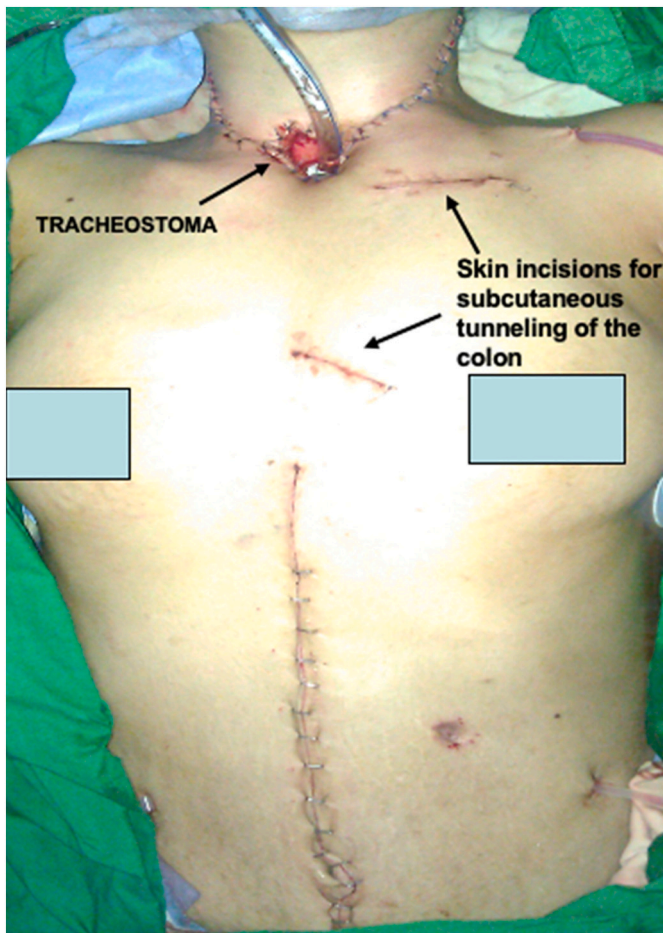


Fig. 5. Tracheostoma at lower neck and closed two skin incisions along left parasternal line.

In a recent systematic review and meta-analysis of conduit choice and outcome of colonic interposition after adult esophagectomy, twenty-seven observational studies involving 1849 patients undergoing colonic interposition for malignant ( $n = 697$ ) and benign ( $n = 1152$ ) pathology were analyzed [12]. It concluded that left colonic conduit placed retrosternally were the safest. However, these are post-esophagectomy with immediate reconstruction. Further analysis of included studies showed three studies that delved into colonic interposition after caustic injury. A study comprising 32 cases of subcutaneous colonic interposition for caustic injury had zero mortality and graft necrosis [18]. In another study, mortality in 117 patients undergoing colonic interposition by all three routes were compared. The mortality rate was 20.5% for antesternal (subcutaneous), 25% for retrosternal, and 50% for esophageal bed placement [19]. The high mortality rate reported in this series was because of intrathoracic leakage of anastomosis leading to mediastinitis and pyopneumothorax.

Another route that is less commonly done is the transpleural route. It is the only path that passes through a true space. In this technique the colon is pulled up to the thoracic cavity through the esophageal hiatus or anterior phrenotomy [18]. It is then positioned in between the lungs and the mediastinum and allowed to pass through either at the anterior or posterior pulmonary hilum. It is brought up to the neck out of the pleural space perforating the apical parietal pleura at the thoracic inlet behind the junction of clavicle and lateral portion of the manubrium. The technique is completed via cervical eso-coloplasty [20]. This route is usually avoided due to technical difficulty and poor outcome. It can easily lead to dilatation and redundancy of the colon graft. On the upside, it has the added protection of colon conduit by the rib cage and

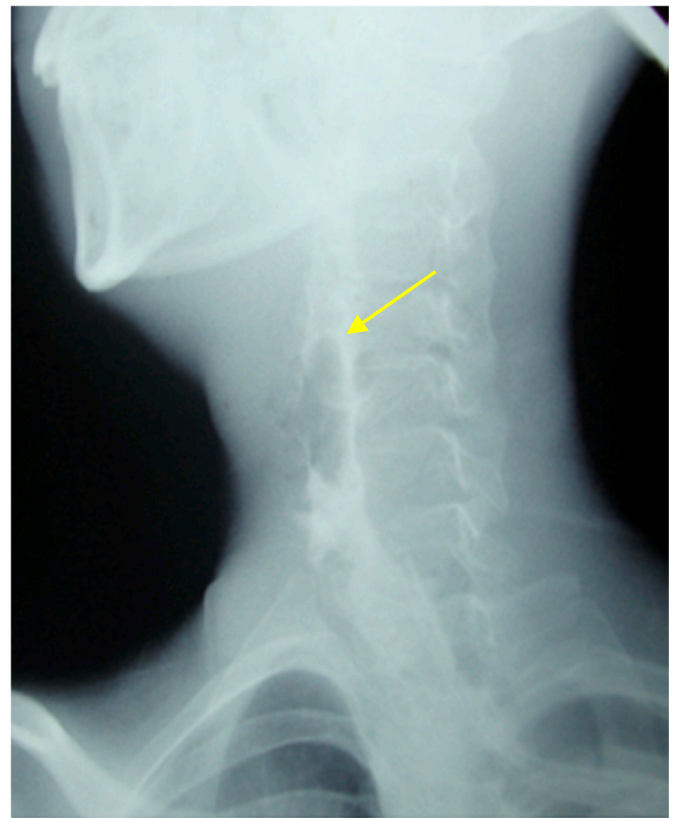


Fig. 6. Water soluble swallow done on the 6th postoperative day showing good flow of contrast (arrow) with no leak.

avoids thoracotomy.

Subcutaneous route is simpler than the other techniques, requires minimal dissection and has faster operative time. Thoracotomy is avoided and all its accompanying complications (i.e. pneumothorax, mediastinitis). If graft necrosis happen, it is picked up early and corresponding corrective surgery is easier due to accessibility. Overall, the advantages of subcutaneous technique done in this case include (1) avoidance of morbidities inherent with thoracic surgery, (2) more manageable complications such as anastomosis failure, leak, and conduit necrosis with less systemic toll, (3) easier revision of the anastomosis when warranted due to accessibility, (4) simpler technique compared to other tunneling routes and (5) suitable for more high risk patients.

The downfall that is usually reported using ante-sternal subcutaneous route is too tight tunnels which causes post-operative dysphagia [17]. The skin is firmly attached to the sternum and creation of adequate space for conduit can be difficult. Further dissection, can easily lead to ischemia and necrosis of overlying skin. Recent reports on the utility of tissue expanders to prepare tunnel helped to avoid this pitfall. Our case dealt with this problem by placing the tunnel at left parasternal anterior chest where skin is less tightly adherent to underlying chest wall. This allowed us to create the tunnel with less worry on skin flap necrosis and tunnel tightness.

Follow-up in post-reconstruction with unresected corrosive esophageal and gastric strictures involves (1) establishing the function of the constructed conduit and (2) surveillance for the increased risk of cancer of residual esophagus and stomach. Most studies report the long term outcome of their institution's experience on colonic reconstruction via standard questionnaire. It evaluates patient's swallowing function [21]. No routine additional tests (i.e. endoscopy or barium swallow) to monitor the function of the colon conduit were done. Ten years post-operatively, our patient remain to feed well per orem with no untoward

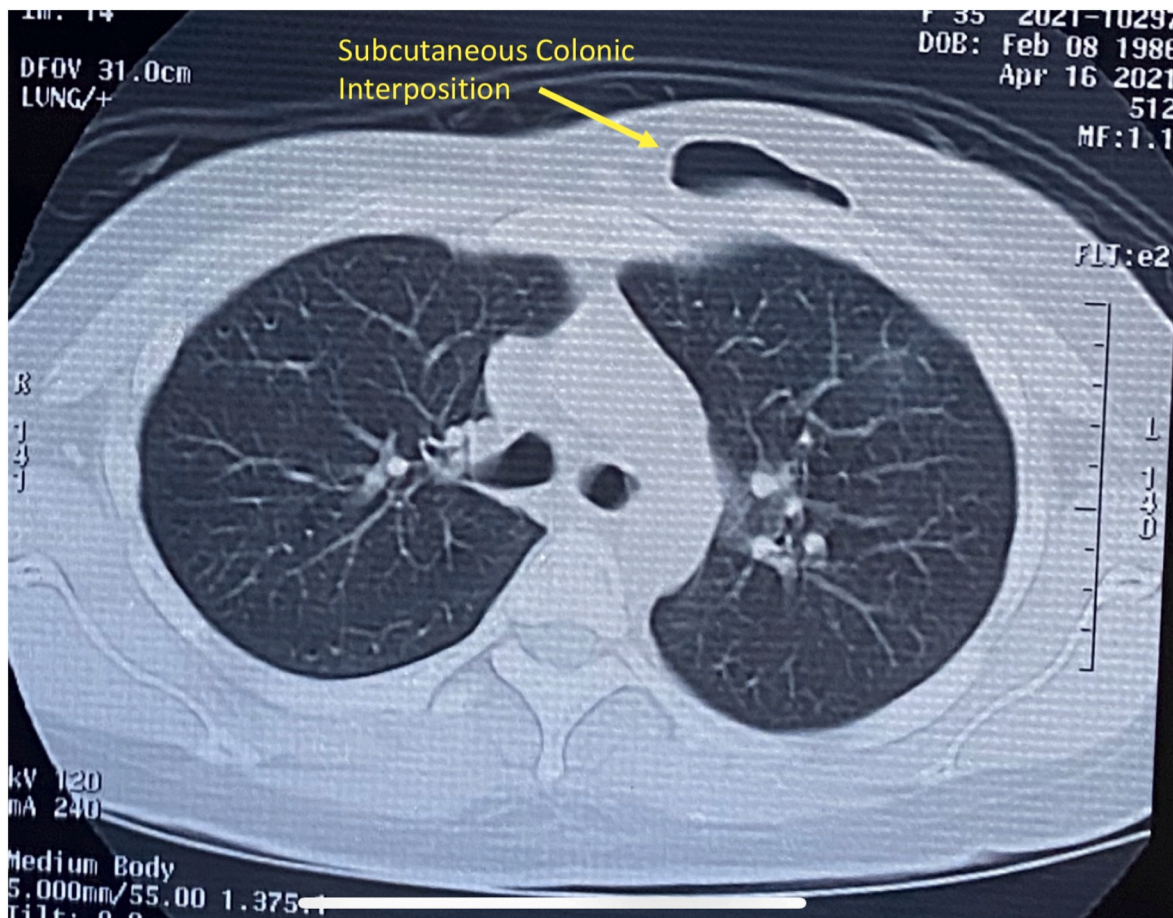


Fig. 7. Contrast enhanced Chest computed tomography (CECT) on patient's 10th year follow-up. Subcutaneous colonic interposition (arrow) showed normal gas pattern with no signs of obstruction. Absence of suspicious mass at residual esophagus and stomach.

associated symptoms, with normal BMI and has no suspicious pathology along the unresected strictured esophagus and stomach on imaging.

### 3. Conclusion

Key factors in managing caustic strictures include safety of strictured segment resection, choice of replacement organ for reconstruction and route of conduit. Colonic graft harvested must have sufficient length for tensionless anastomosis without redundancy and adequacy of vascular supply should be tested to ensure viability. Subcutaneous tunneling avoids anterior obstruction of tracheostoma in pharyngo-laryngectomy cases, offers more direct route for cervical anastomosis and left parasternal tunneling decreases the chance of skin flap necrosis along the tightly attached skin and sternum. Long term outcome of this procedure showed good alimentary function, weight gain and no observed complication.

### Provenance and peer review

Not commissioned, externally peer-reviewed.

### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

### Guarantor

Anthony R. Perez, MD, MHA.

### Ethical approval

Ethics approval obtained from University of the Philippines Ethics Review Board.

### Registration of research studies

Registered with the Research Grant Administration Office (RGAO) of UP Manila.

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### CRediT authorship contribution statement

Orlino C. Bisquera Jr. MD Study concept, writing the paper, final draft.

Anthony R. Perez, MD: Study concept, writing the paper, final draft.

Ma. Katrina B. Guillermo, MD: Data collection, review of literature, writing the paper.

Neresito T. Espiritu, MD: Data collection, review of literature, final draft.

Mary Ellen Chiong-Perez: writing the paper, final editing.

## Declaration of competing interest

There were no conflicts of interest.

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