Operative Techniques in Thoracic and Cardiovascular Surgery

# Treatment of Malignant Mesothelioma: Extrapleural Pneumonectomy with Intraoperative Chemotherapy

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Extrapleural pneumonectomy (EPP) is a radical en bloc resection of the lung, pleura, diaphragm, and pericardium. The inability to separate the fused pleural envelope from the central tendon of the diaphragm and the lateral portion of the pericardium also mandates resection of these structures to preserve the intact pleural envelope. EPP was originally developed to treat tuberculous empyema and now it has become the cornerstone of treatment for select patients undergoing multimodality therapy for malignant pleural mesothelioma (MPM).

MPM is an uncommon disease with only 3000 cases in the US each year.[1] Esophageal and lung cancer are, respectively, at least 4 and 50 times more common. Few surgeons will treat more than a handful of cases over their careers. The Brigham and Women's Hospital (BWH) and Dana Farber Cancer Institute (DFCI) in Boston, Massachusetts have gained a large amount of experience in the treatment of this malignancy.

Early application of EPP to the treatment of MPM was disappointing. Worn[2]reported an early series in 1974, but with median survival of only 19 months and 5-year survival of 10%. In 1976, Butchart and coworkers[3] reported a series with a perioperative mortality rate of 31%, median survival of 10 months, and 5-year survival of 3.5%.

Operative mortality after EPP at BWH declined with increasing experience, from an initial perioperative mortality of 6% after the first 18 patients in 1991[4] to 3.4% after 328 patients reported in 2004.[5] Despite advances in surgical technique, the unfortunate fact remains that nearly all patients eventually die of recurrent disease within 10 years, although more than 50% of patients with favorable prognostic variables live at least 5 years. Analysis of our late results reveals that most recurrences occur in either the abdomen or the ipsilateral hemithorax.[6]

The dose limitation of most adjuvant therapies is systemic toxicity to the patient. Intraoperative intracavitary heated cisplatin chemotherapeutic lavage (IOHC) has the advantage of permitting higher chemotherapy doses than are possible by systemic administration. Studies of IOHC in abdominal malignancies, including peritoneal mesothelioma, have been effective.[7,8] Ongoing phase I and II studies of IOHC in combination with EPP at our institution have shown encouraging results.

The conduct of EPP with IOHC can be reduced to the following 10 basic elements: (1) incision and exposure of the pleura via extended posterolateral thoracotomy; (2) extrapleural dissection to separate the tumor from the chest wall and mediastinum; (3) division of the lateral attachments of the diaphragm, (4) opening of the pericardium and division of the hilar vessels, (5) division of the posterior crus of the diaphragm and the posterior pericardium, (6) closure and division of the main bronchus with en bloc removal of the lung, pleura, pericardium, and diaphragm; (7) radical lymphadenectomy of the mediastinal nodes; (8) intracavitary lavage with heated cisplatin chemotherapy plus sodium thiosulfate or amifostine for renal protection; (9) diaphragmatic and pericardial reconstruction, and (10) closure.

All patients undergo standard intraoperative monitoring including arterial line, continuous oximetry, and central venous access. A thoracic epidural catheter is placed preoperatively. After induction of anesthesia and placement of a left-sided double-lumen endotracheal tube, the patient is positioned in a left lateral decubitus position in preparation for an extended right posterolateral thoracotomy.

## Operative Technique

### Left Extrapleural Pneumonectomy

For patients with disease of the contralateral hemithorax, left extrapleural pneumonectomy is required. This operation is technically similar to that on the right with a few important differences because of the more prominent presence of the aorta, esophageal hiatus, and long extrapericardial course of the pulmonary artery. First, when the pleura is dissected off the aorta, it is easy to inadvertently start dissecting behind the aorta. Beginning this part of the dissection on the arch can prevent this problem. Second, the left main pulmonary artery is divided extrapericardially while the pulmonary veins are divided intrapericardially. Finally, although the pericardial and diaphragmatic reconstructions are performed in a similar manner, 250 mL less air is withdrawn from the left cavity, since it is smaller.

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1522-2942/06/$-see front matter 
doi:10.1053/j.optechstcvs.2006.02.001

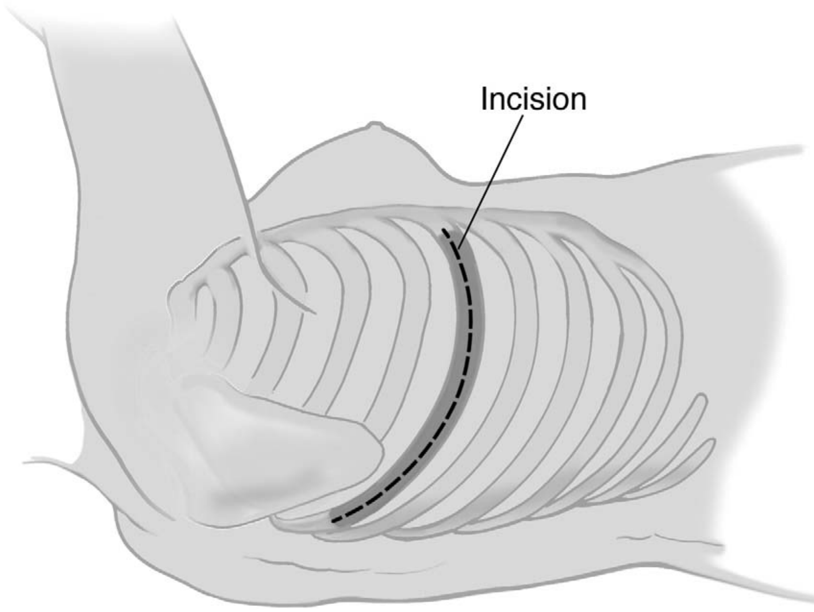


**Figure 1** Incision and exposure of the pleura via extended posterolateral thoracotomy. An extended right posterolateral thoracotomy incision is made along the bed of the sixth rib. The incision begins 2 cm from the costovertebral junction posteriorly and extends to the costochondral junction anteriorly. The latissimus and serratus muscles are divided and the sixth rib is removed. We include previous biopsy sites in the incision, if possible, or excise them separately with a minimum 1-cm margin to the level of the chest wall fascia.

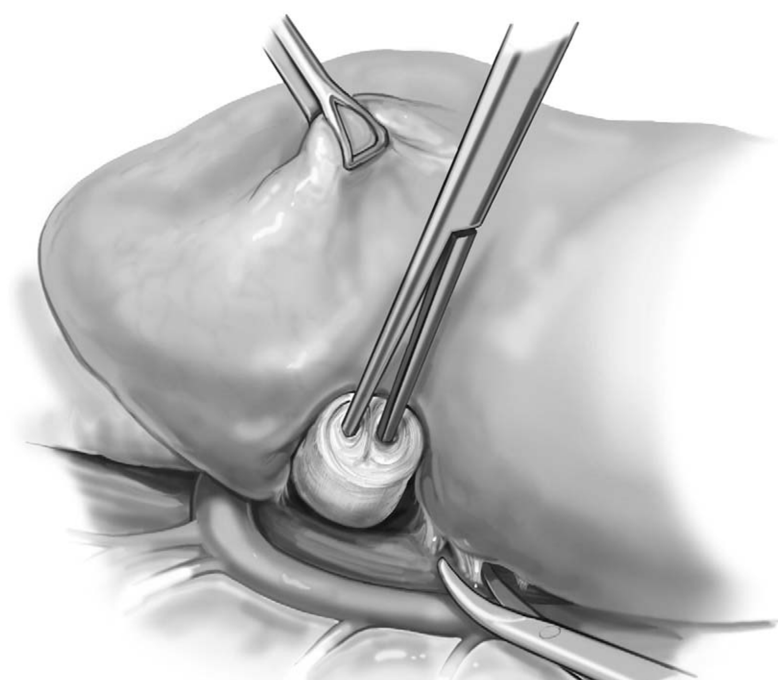

**Figure 2** Extrapleural dissection to separate the tumor from the chest wall and mediastinum. The extrapleural dissection is initiated along the bed of the excised rib and performed with a combination of blunt and sharp dissection as needed. It is not unusual to discover that a fracture plane between the parietal pleura and the chest wall is the easiest way to get started at the extreme anterior and posterior portion of the incision. Once the plane is started, finger fracture is used to extend the planes to the mediastinal reflections at the apex, anteriorly and posteriorly. The dissection is continued in an extrapleural plane until the right main stem and upper lobe bronchi are visualized. A nasogastric tube facilitates the identification of the esophagus. The esophagus is separated from the specimen using blunt and sharp scissors dissection. When the dissection approaches a vessel, sharp technique is preferred to avoid vascular injury. Blunt avulsive injury to the mammary vessels, azygos vein, subclavian vessels, and superior vena cava can occur since the tumor is often quite adherent to these vessels.

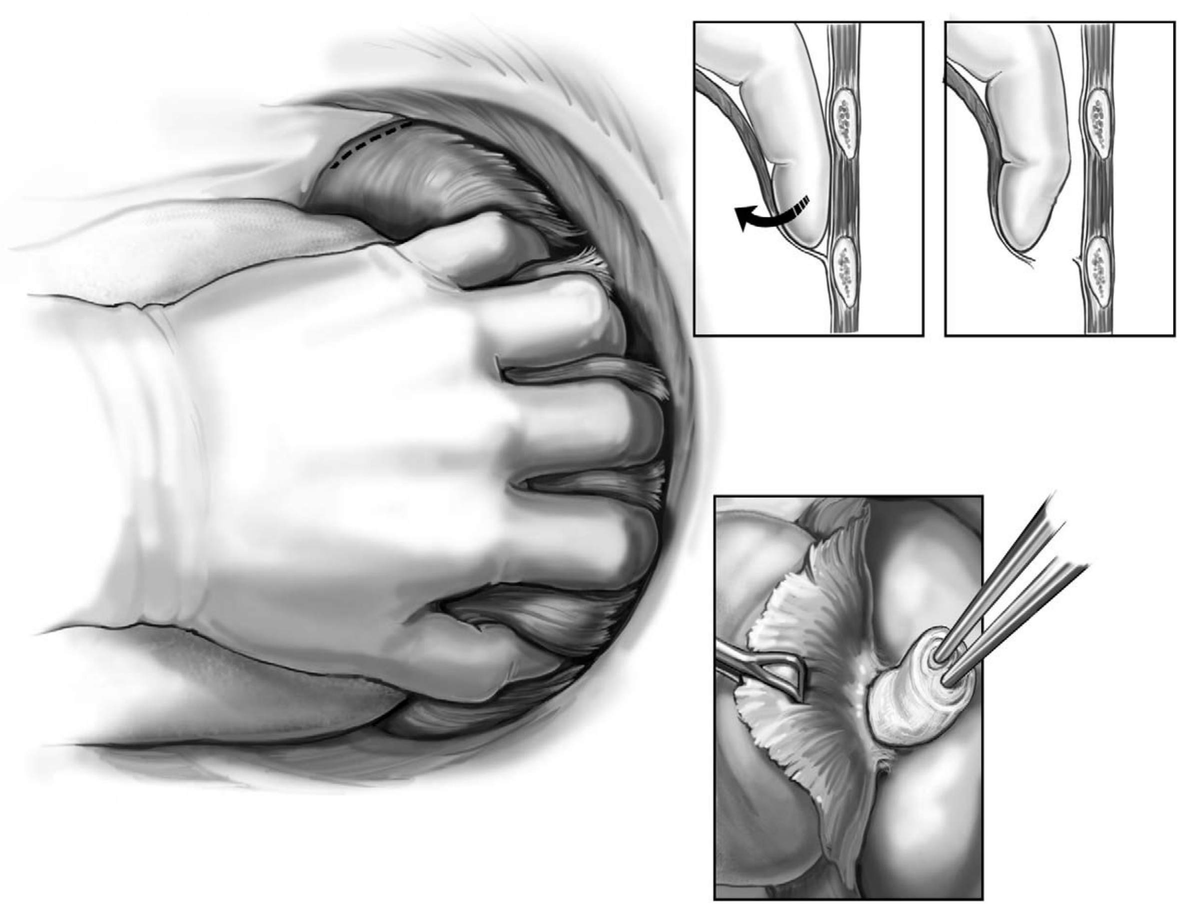

**Figure 3** Division of the lateral attachments of the diaphragm. The extrapleural dissection proceeds inferiorly and laterally into the sulcus between the pleura and diaphragm. The diaphragmatic resection begins at the anterior costochondral angle. The diaphragmatic attachments are avulsed and the peritoneum is dissected off the undersurface of the diaphragm. The avulsion of the lateral attachments of the diaphragm extends in a circumferential fashion laterally and posteriorly. The diaphragmatic muscle fibers are dissected off the peritoneum by placing Babcock clamps on the diaphragm to provide cephalad retraction with blunt caudal dissection on the peritoneum using a sponge stick. Openings within the peritoneum have little consequence if IOHC is being used, since the cannulae are placed in the pelvis.

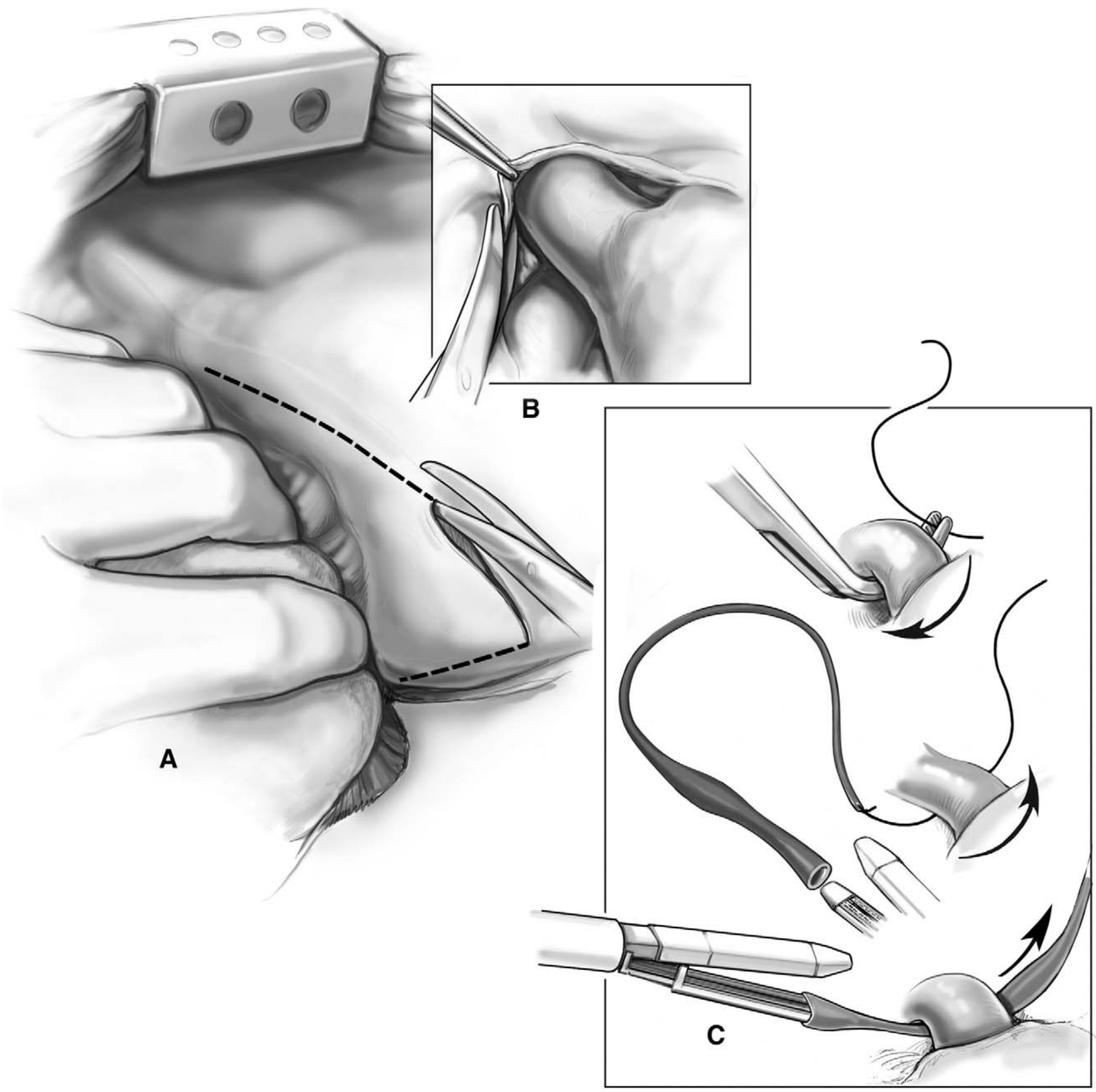


**Figure 4** Opening the pericardium and division of the hilar vessels. The pericardium is divided anteriorly in a cephalad direction, starting at the anterior diaphragmatic border. This permits assessment of the inside of the pericardium to make sure there is no direct invasion of the heart. The inferior pericardial cut is extended in a posterior fashion to view and protect the inferior vena cava. The pulmonary artery and veins are dissected and divided using the endovascular stapler guided with the red rubber catheter.

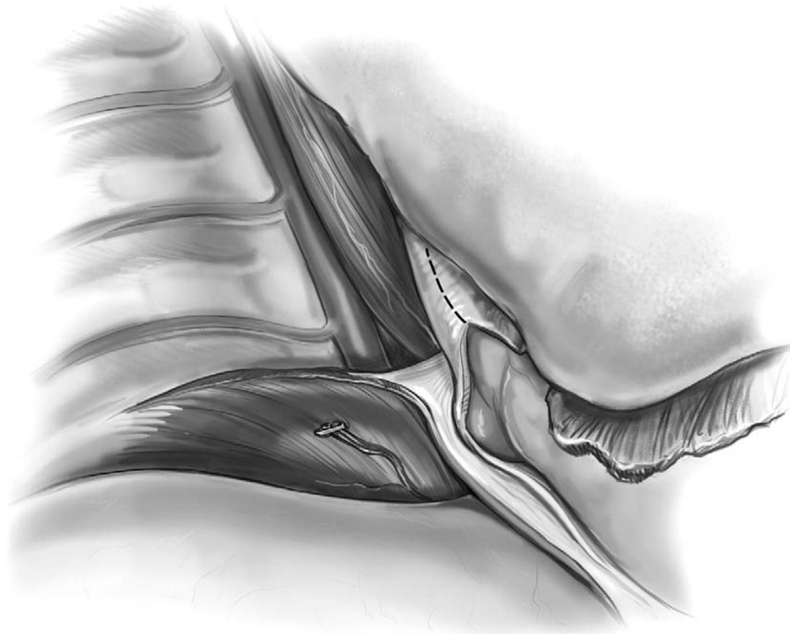

**Figure 5** Division of the posterior crus of the diaphragm and the posterior pericardium. Lateral to the inferior vena cava and the esophagus, the posterior diaphragmatic attachments are divided from the crural attachments to the transverse processes of the lumbar vertebrae. Care must be taken not to "buttonhole" the postero-inferior extent of the pleural envelope as it runs behind the crus. The phrenic vessels are clipped and divided on the undersurface of the crus. The specimen is retracted anteriorly and the pericardium is opened to the level of the bronchus.

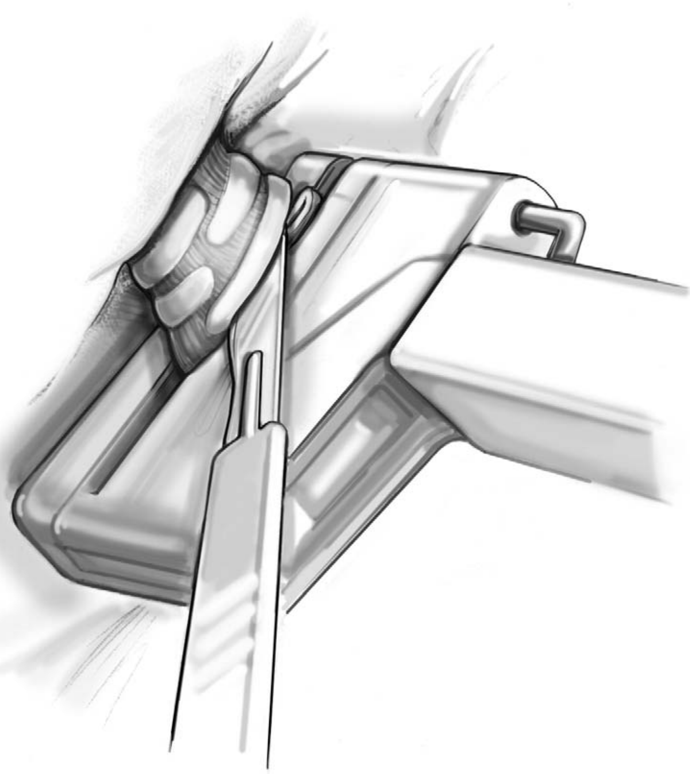

**Figure 6** Division of the main brohus and radical lymphadenectomy. After dividing the pulmonary veins, pulmonary artery, and bronchus, the specimen is removed. We use a stapler to reliably close the bronchus before it is divided. The subcarinal (station 7), tracheobronchial (station 4R), para-esophageal (station 8), inferior pulmonary ligament (station 9), and peridiaphragmatic nodes are found and removed. The entire hemithorax is inspected for hemostasis. Liberal use of the argon beam coagulator (Valleylab, Boulder, CO) on the chest wall facilitates hemostasis.

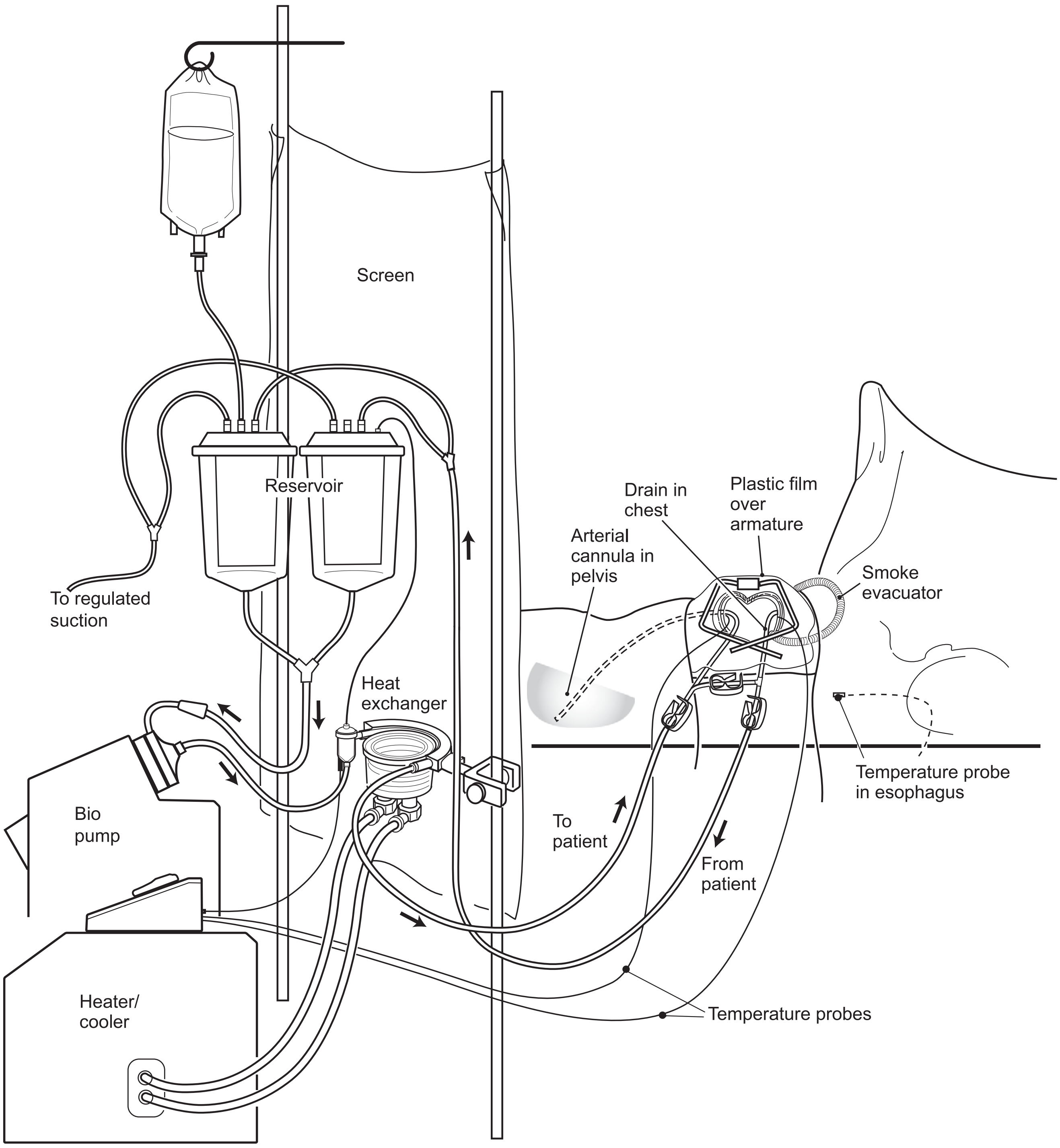


**Figure 7** Intracavitary lavage with heated cisplatin chemotherapy. At this point in the operation, the patient is considered to be macroscopically free of disease. The incision is partially closed at the anterior and posterior extremes. The Omni retractor is secured to the bed. The skin is secured to the Omni retractor to create a well. A smoke evacuator is placed beneath Ioband (3 mol/L, Los Angeles, CA) adhesive drapes to further augment the well. An inflow cannula attached to the arterial tubing of a standard pump tubing pack is placed in the pelvis while the outflow cannula is attached to the venous tubing and placed in the chest. The chemotherapy infusion is performed at a rate of 1 liter per minute at a constant temperature of 42°C for 60 minutes. Temperature sensors are placed on each cannula and in the patient's esophagus. The volume of perfusate is adjusted to keep the hemithorax full, thus maximizing surface area contact. Immediately after completion of the 1-hour cisplatin lavage, sodium thiosulfate infusion is administered via a bolus injection over 10 minutes, followed by continuous infusion for 6 hours.

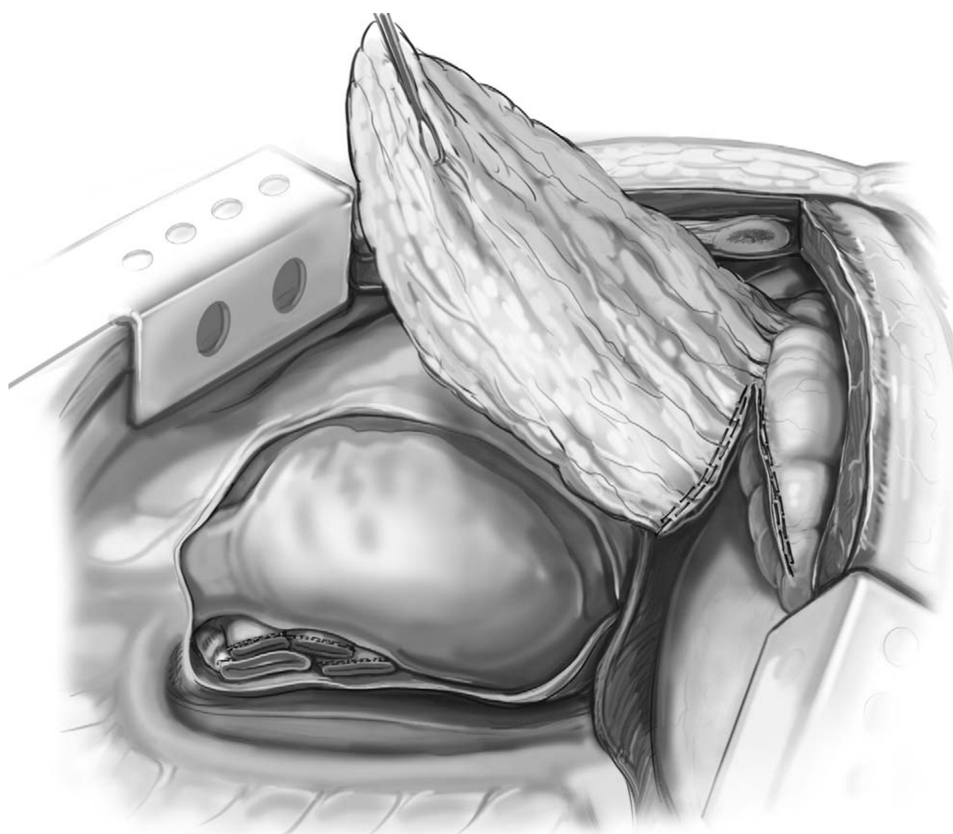

**Figure 8** Bronchial buttress. After the chemotherapy perfusion has been completed, an omental flap is prepared through the defect in the diaphragm. This flap is created using endo-GIA staplers to fashion a vascular pedicle flap to reach the bronchus. This is not sewn into place until the diaphragm and pericardium have been reconstructed.

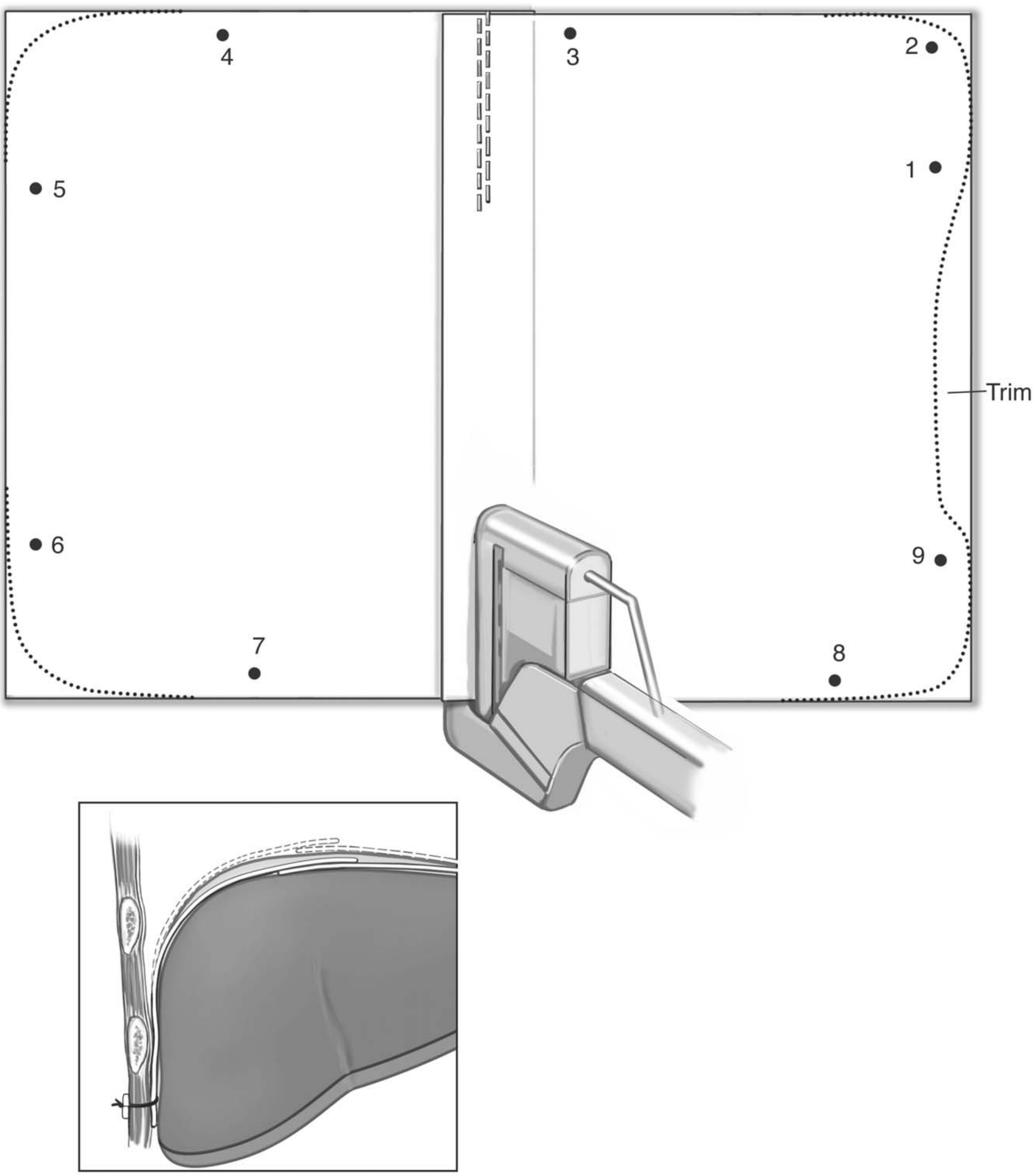


**Figure 9** Diaphragm reconstruction. Two 2-mm impermeable Gore-Tex patches (Gore-Tex Dual Mesh, W.L. Gore and Associates Inc., Flagstaff, AZ) are stapled to create a dynamic patch with reduced tension along the edges that is tailored to accommodate the mediastinal structures. Nine interrupted 0 Gore-Tex sutures are then placed along the lateral edge. The Gore-Tex sutures are first placed through the patch. Both ends of each suture are then brought through the intercostal space with an awl and tied to a 1-mm polypropylene button (Ethicon, Somerville, NJ) as a buttress.

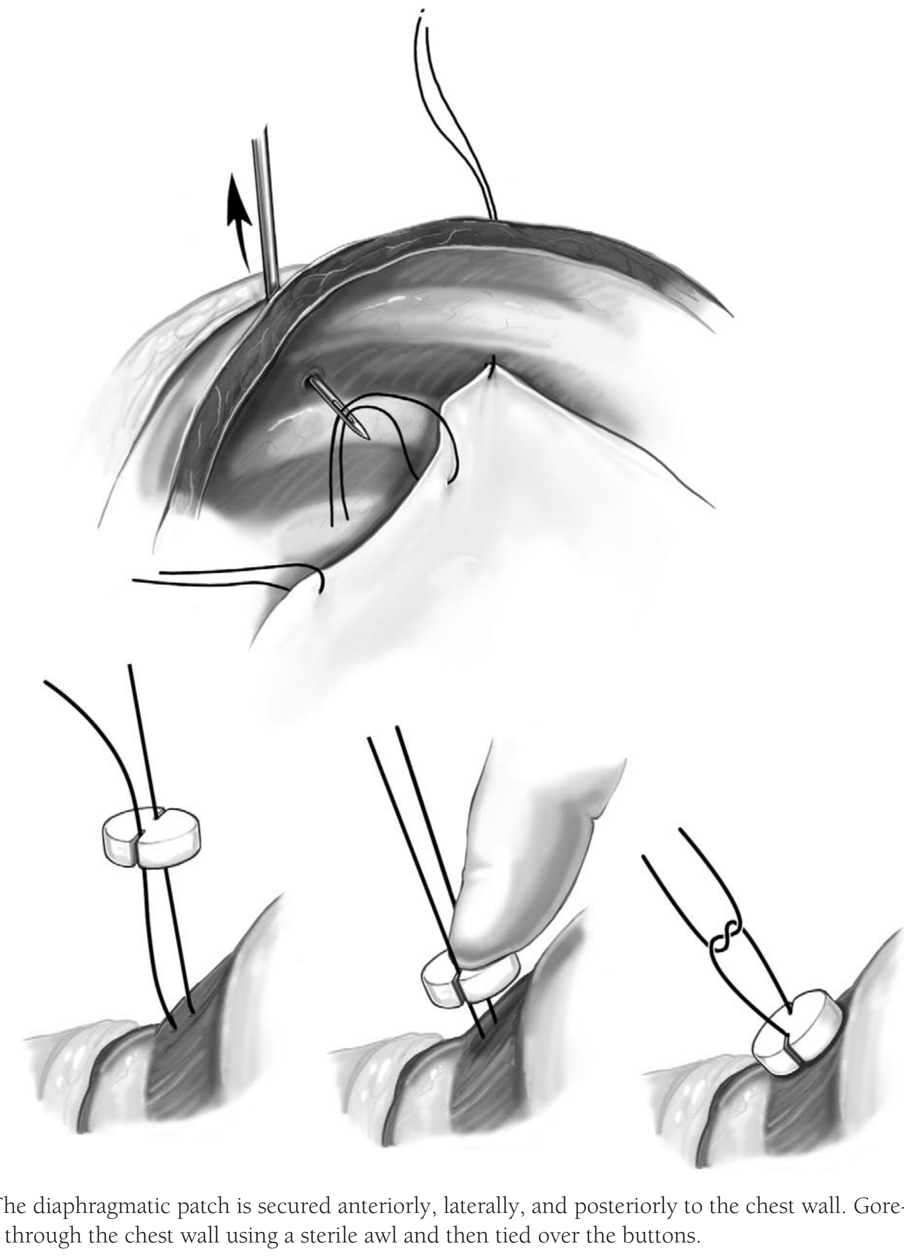

**Figure 10** The diaphragmatic patch is secured anteriorly, laterally, and posteriorly to the chest wall. Gore-Tex sutures are passed through the chest wall using a sterile awl and then tied over the buttons.

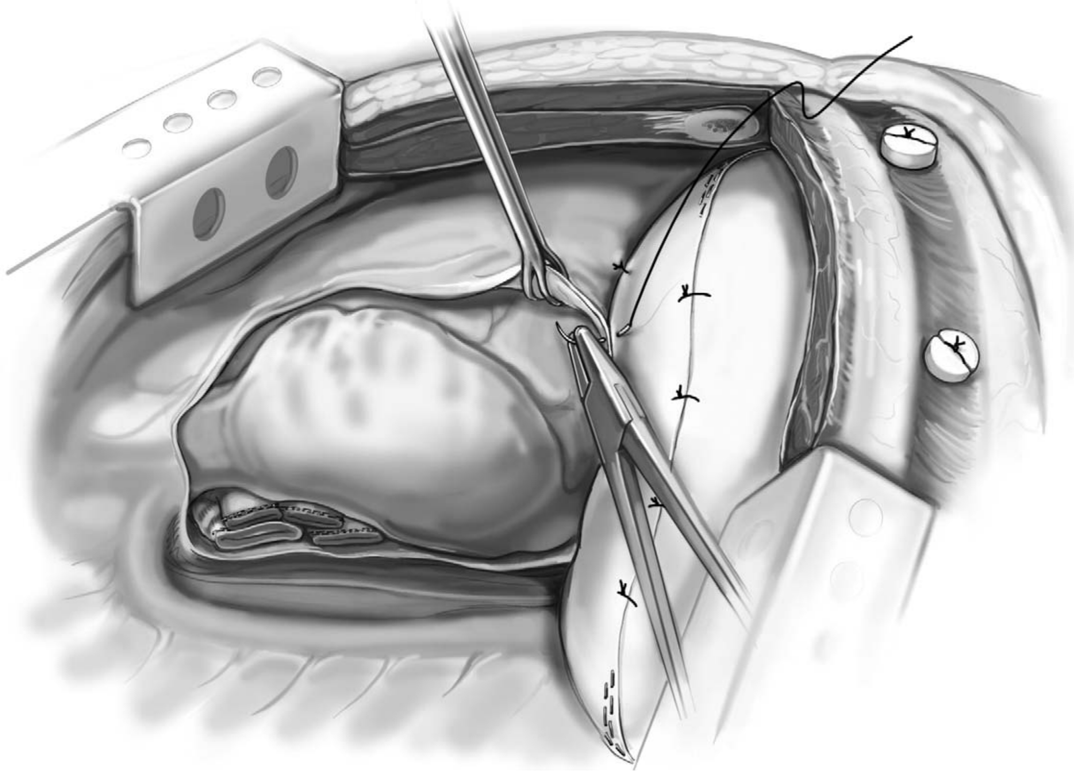

**Figure 11** The mediastinal edge of the Gore-Tex diaphragmatic patch is sutured to the inferior cut edge of the pericardium using 0 Gore-Tex sutures. Attention should be paid to avoid constriction of the inferior vena cava by the diaphragmatic patch. A wedge cutout of the patch may prevent compression of the inferior vena cava once the heart displaces into the pneumonectomy space after closure.

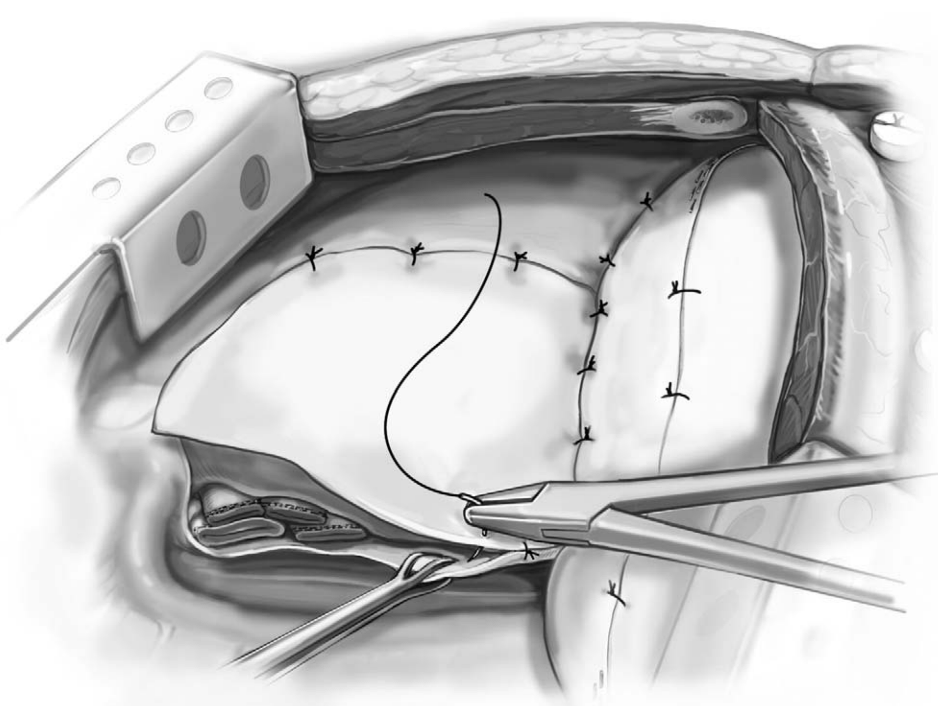

**Figure 12** The pericardium is always reconstructed with a prosthetic patch to prevent cardiac herniation. The pericardial patch is a 15 × 20 cm piece of 0.1-mm-thick synthetic membrane (Gore-Tex Pericardial Membrane, WL Gore and Associates, Inc.). The patch is secured to the superior, anterior, and posterior cut edges of the pericardium, while inferiorly it is sutured to the diaphragmatic patch with 0 Gore-Tex sutures.

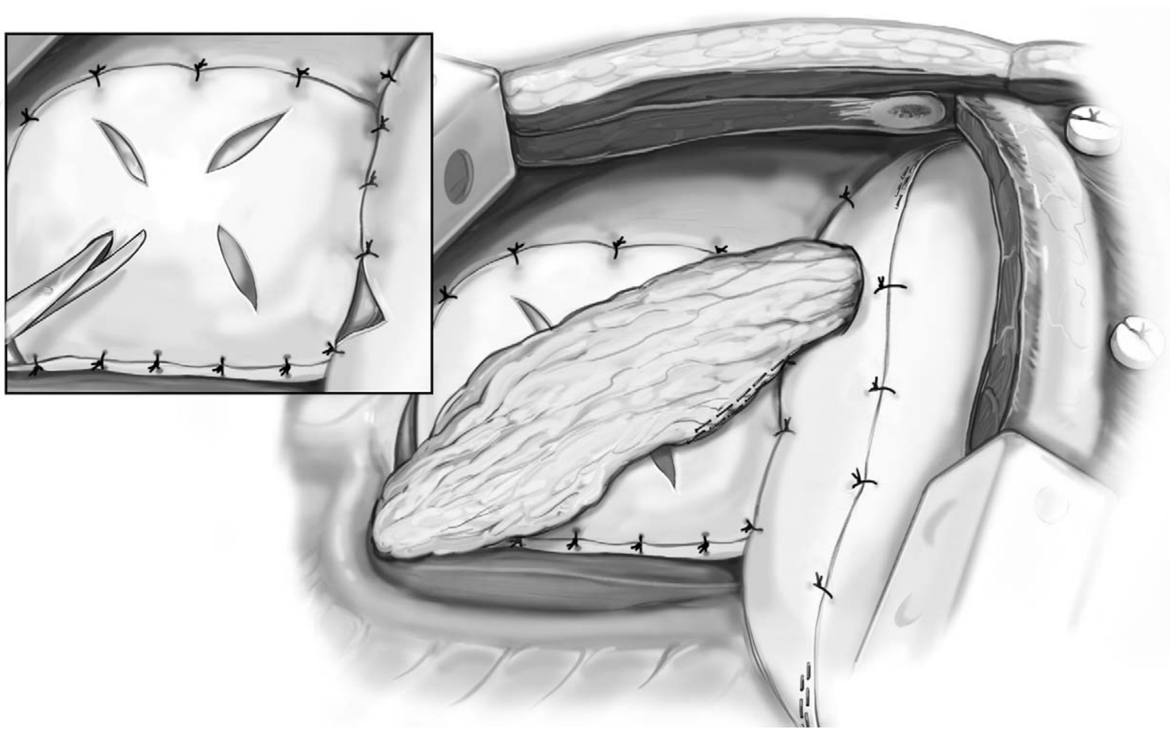

**Figure 13** The pericardial patch should be fenestrated to prevent cardiac tamponade caused by the buildup of serum beneath the patch. A patch that is made too tight will also produce tamponade physiology, since the heart will not be able to fill during diastole. The omental fat pad to buttress the bronchus is now placed. A small ellipse of the diaphragmatic patch is removed in the anterior and medial portion near the pericardium. The width of this slit should be sufficient to prevent compression of the vascular pedicle flap, but not so large as to allow visceral herniation of the abdominal contents. The omental flap is secured to the bronchus with interrupted vicryl suture.

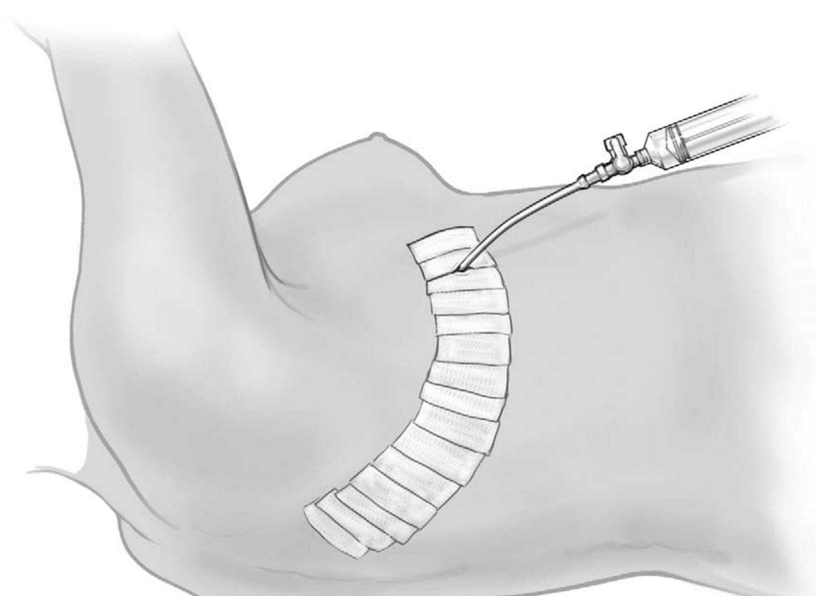

**Figure 14** Closure. The argon beam coagulator is again used to achieve hemostasis, after which the thoracotomy is closed in the usual fashion to ensure an airtight closure. A small (eg, No. 12 F) red rubber catheter is placed in the pneumonectomy space to permit mediastinal positioning, which is achieved by removing 1 liter of air for a male patient and 750 mL for a female patient. The patient is extubated in the operating room. On admission to the intensive care unit, a radiograph of the chest is obtained to check for midline position of the heart, nasogastric tube, and mediastinal structures. If these are not midline on the chest radiograph, the mediastinum can be balanced by introducing or removing air via the red rubber catheter.

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