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Common iatrogenic pleural complications

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Abstract All invasive pleural procedures have the potential to cause harm. Complications from pleural procedures include empyema, intercostal artery laceration, hemothorax, and pneumothorax as well as other organ puncture. Many of these complications will be life threatening and will increase morbidity and hospital length of stay. An understanding of iatrogenic pleural disease helps clinicians to appreciate how these risks can be minimized and complications managed promptly and effectively. This review systematically evaluates the current evidence and guidelines regarding iatrogenic pleural complications and their management. Whilst impossible to eliminate procedural risk entirely, complications will be reduced to a minimum by ensuring adequate medical training, use of pleural ultrasound, and adherence to guidelines and standard operating procedures (SOPs).

Keywords Pleural effusion · Pneumothorax · Iatrogenic · Thoracentesis · Chest drain · Complication · Pleural disease · Thoracoscopy

Introduction

Invasive pleural procedures, including simple pleural fluid aspiration, thoracentesis, and chest drain insertions are commonly undertaken to aid the diagnosis and management of a variety of pleural diseases. Although in the vast majority of cases they occur safely, there are many reports of serious complications following these procedures [1]. These can be minimized by image guidance and adequate training [2, 3••, 4•].

The development of newer techniques, such as local anaesthetic thoracoscopy [5], and the insertion of indwelling pleural catheters has advanced the investigation and management of pleural disease. However, with the advent of these techniques, a thorough understanding of the procedural risks to patients is imperative to inform clinical decisions and provide guidance on how complications should be managed if they occur.

Given the close proximity of the pleura to structures in the neck and abdomen, pleural complications can also be caused by extra thoracic interventions, such as abdominal surgery and central venous catheter insertion. In addition, breach of the pleura during transthoracic lung biopsy may result in pleural complications and barotrauma secondary to mechanical ventilation is a well-known cause of iatrogenic pneumothoraces.

This review will evaluate the potential iatrogenic pleural complications and examine the current literature and guidelines on the subject.

Iatrogenic pneumothorax

Iatrogenic pneumothoraces are a common complication of a variety of interventions and the literature would suggest they occur more commonly than spontaneous pneumothoraces [6]. They can be induced by thoracic procedures, including transthoracic biopsies, transbronchial lung biopsy, thoracentesis, chest drain insertion or pacemaker insertion, or they can result from procedures involving the neck, such as central venous catheter insertion, or the abdomen, as well

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as barotrauma to the pleura from invasive ventilation [7, 8]. It can be associated with significant morbidity and mortality and may prolong the length of hospital stay, particularly if related to critical illness [9].

A number of potential mechanisms can contribute to the development of iatrogenic pneumothoraces. Puncture of the visceral pleura and lung during an invasive procedure can result in an air leak into the pleural cavity from the lung itself, or alternatively air can be entrained through the device being used for the procedure from the outside. Shearing forces on the pleural surface created during lung re-expansion in patients with pleural adhesions may result in a visceral pleural tear and subsequent pneumothorax developing.

In patients with underlying trapped lung, whereby a visceral pleural rind prevents lung re-expansion following the removal of pleural fluid, air can be sucked into the pleural cavity due to the more negative intrapleural pressure created by the less elastic visceral pleura [10••]. This results in an unavoidable pneumothorax, which is commonly termed pneumothorax “ex vacuo.” It is a fairly common finding and may occur in those with both pleural malignancy or benign pleuritis [11]. Insertion of a chest drain in this situation is unlikely to be beneficial as expansion of the underlying lung is restricted.

The incidence of iatrogenic pneumothorax varies depending upon the procedure performed and is particularly common following thoracentesis and central venous cannulation [7].

Pneumothoraces following thoracentesis are a relatively common finding and have been reported to occur in between 0% and 19.2% of patients [12•]. A recent meta-analysis found a number of potential risk factors, including an inexperienced operator performing the procedure, the use of a large bore needle, therapeutic thoracentesis as opposed to a diagnostic tap, witnessed aspiration of air during the procedure, multiple aspiration attempts, and concurrent mechanical ventilation [12•]. Large volume pleural aspirations may result in a higher risk of procedure-related pneumothorax, particularly if more than 1.8 L is aspirated in a single procedure [13]. A study by the Mayo Clinic, whereby improvements in training and the use of ultrasound guidance in pleural aspiration were instituted, found the iatrogenic pneumothorax rate was reduced from 8.6% to 1.1% with these interventions (P=0.0034) [4•].

Transthoracic lung biopsies may also result in the development of a pneumothorax. A recent large, population-based, cross-sectional analysis of 15,865 patients undergoing transthoracic needle lung biopsy for pulmonary nodules in four US states, found an overall pneumothorax risk of 15% (95% CI 14.0% to 16.0%), with 6.6% (95% CI 6.0% to 7.2%) of patients in the study requiring a chest tube to be inserted to treat a pneumothorax [14•]. A UK survey of 5444 percutaneous lung biopsies showed a pneumothorax risk of 20.5%, with 3.1% of patients in the survey requiring a drain insertion [15].

However, predicting which patients will develop a pneumothorax in this setting is difficult. The presence of COPD may be a risk factor [14•, 16, 17] as well as a smaller needle-pleural angle when taking the biopsy [18, 19]. Some studies suggest that the deeper the lesion being biopsied, the higher the risk of pneumothorax [17, 19], but this finding is not consistent across all studies [18, 20]. CT findings alone do not appear to be an accurate predictor [21].

Closed pleural biopsies also confer a risk of iatrogenic pneumothorax of between 0%–5% [22, 23]. Image guidance improves the diagnostic yield compared with blind pleural biopsy and may also be associated with fewer complications [24]. After the procedure, patients may be asked to lie on the side of the procedure to minimize the development of air leaks and pneumothorax, although this practice is only anecdotal and a small case control trial did not show it to be of benefit [10••, 25].

Radiofrequency ablation (RFA) of lung tumors is also associated with a significant risk of pneumothorax, as well as aseptic pleuritis [26]. A systematic review of the literature found the iatrogenic pneumothorax rate to be 4.5%–61.6% after RFA, but most cases were self-limiting [27]

Pneumothoraces on the intensive care unit are a common occurrence and can be related to barotrauma from positive pressure ventilation or be secondary to pleural puncture during invasive procedures (such as central line insertion or transbronchial biopsies). They occur in about 3% of patients admitted to the intensive care unit (ICU) and represent a potentially life-threatening event, particularly if associated with mechanical ventilation [9]. A prospective study of over 3000 patients from 11 French ICUs showed that those who developed a pneumothorax during the first 30 days of their admission were more than twice as likely to die as those who did not [9].

Shearing forces from positive pressure ventilation may result in the development of a bronchopleural fistula, which can quickly enlarge due to the continuous pressure from the ventilator and may result in a tension pneumothorax. Therefore, all patients with a pneumothorax in the context of mechanical ventilation require formal chest drainage to minimize the risk of a tension pneumothorax developing, and lung-protective ventilation strategies may also be helpful.

Given the dangers of pneumothoraces in the context of mechanical ventilation, there may be reluctance to drain effusions in this patient population. However, a recent meta-analysis evaluating the risks and benefits of draining pleural effusions in mechanically ventilated patients, showed that pleural fluid drainage improved oxygenation and may confer benefits with regard to respiratory dynamics in these patients. The pooled risk of pneumothorax was 3.4% (95% CI 1.7% to 6.5%) [28]. In order to minimize the risk of pneumothorax when inserting a chest tube in a patient on mechanical ventilation, the positive end-expiratory pressure (PEEP) should be turned off and the ventilator briefly disconnected as the drain is inserted [29].

Aside from iatrogenic pneumothoraces in the critical care setting, the management will depend on the size of the pneumothorax, the degree of patient's symptoms, and their comorbidities. The majority will resolve spontaneously by observation alone and in those who require an intervention, simple aspiration is usually sufficient [6]. A small proportion of patients may require chest tube drainage, and this is more likely in patients with underlying COPD [20].

However, patients who develop a pneumothorax in the context of mechanical ventilation do require a chest drain to be inserted to minimize the risk of a tension pneumothorax developing.

Subcutaneous emphysema

In severe cases of iatrogenic pneumothorax, whereby a large visceral pleural defect results in the creation of a bronchopleural fistula, air can be forced into the tissues of the chest wall, resulting in the development of subcutaneous emphysema. It may also occur if a chest drain becomes displaced and one or more of the drainage holes in the tube migrates into the subcutaneous tissues.

This initially results in localized thoracic swelling and crepitus on palpation, or may only be identified on chest radiography. Subsequently, the air may spread along fascial planes to become more generalized. In severe cases, the neck and face can become swollen, which may result in airway compromise [10••]. In a recent UK series of 824 chest drains inserted for a variety of indications, 3.4% of patients developed surgical emphysema as a complication [30•].

If a chest drain is already in situ, it should be carefully evaluated to ensure it is correctly positioned. If not, a drain should be inserted to treat the pneumothorax and in many cases this will prevent the surgical emphysema deteriorating. However, a small chest drain may be inadequate to keep up with a large air leak and hence a larger bore tube, or multiple chest tubes may be required. Use of thoracic suction may also be beneficial in such cases. Liaison with the thoracic surgeons regarding definitive surgical treatment of the bronchopleural fistula may become necessary.

Iatrogenic pleural infection

Invasive procedures create a tract whereby infection can enter the soft tissues and pleural cavity. Chest drain insertions carry a 2%–3% risk [31], but this is increased in the context of trauma [32]. Empirical antibiotics have been shown to be beneficial in reducing the incidence of pleural infection when a chest drain is inserted for trauma [33•, 34]; however, outside this context, there have been no clinical trials evaluating their use and they are not routinely given.

Making the diagnosis of iatrogenic pleural infection is the same as for other clinical contexts [35]. Fluid and blood should be sent for culture to help identify a causative organism and identify antibiotic resistance. Fluid drainage, antibiotics, and careful attention to nutrition are key components of management. Antibiotics should be broad spectrum and have good cover for hospital-acquired organisms, such as the gram negatives and methicillin-resistant *Staphylococcus aureus* (MRSA). If a chest drain becomes secondarily infected, it may be necessary to remove the infected drain and re-site a new one. Some patients may require surgical intervention if medical management fails.

Indwelling pleural catheters are increasingly used in the management of malignant pleural disease to allow intermittent pleural drainage in the community, but do confer an increased risk of pleural infection and localized chest wall cellulitis as they remain in situ for long periods of time [36]. Strict asepsis at the time of drain placement, along with careful patient education regarding drain care, may help to reduce the risk of infection.

Currently the rate of pleural infection in indwelling pleural catheters in the literature is 2%–12% [37–40]. In addition, as with any implanted device, colonization of the catheter may occur, particularly by coagulase-negative *Staphylococcus* [41], although the clinical relevance of this in causing subsequent infection is not clear.

Intrapleural hemorrhage

Due to the anatomy of the intercostal neurovascular bundle, pleural procedures confer a risk of intrapleural hemorrhage if these vessels are lacerated. The neurovascular bundle may be protected by the subcostal groove of the rib above; however, as the intercostal nerves and vessels travel more posteriorly, they become exposed, lying in the middle of the intercostal space, rather than being tucked under the rib. In addition, the intercostal collateral artery lies above the rib and is also vulnerable to damage [42]. Pleural procedures should therefore be performed in as lateral a position as possible and above a rib to try and prevent neurovascular damage [3••]. Some advocate using an area 30%–50% above the rib to also minimize the risk of damaging the intercostal collateral artery [42]. Figure 1 shows an intercostal artery laceration caused by a simple diagnostic pleural fluid aspiration using a posterior approach.

Rates of bleeding following pleural procedures are low however and range from 0%–2% in the literature but depend on the type of thoracic procedure performed [10••].

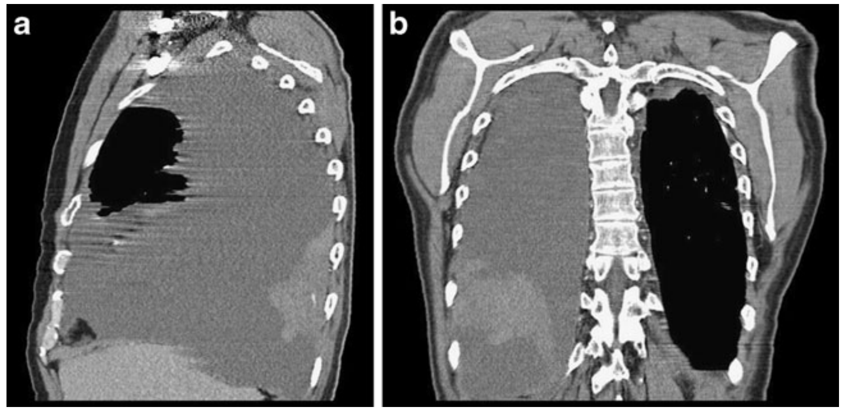

Fig. 1 A CT scan of a patient with a hemothorax caused by laceration of an intercostal artery during a diagnostic pleural aspiration performed with a posterior approach. Extravasation of CT contrast from the injured vessel into the pleural cavity can be seen

Any coagulopathy or platelet deficiency should be corrected prior to invasive pleural procedures in order to minimize the risk of intrapleural hemorrhage [3••].

Departments performing pleural interventions should have a Standard Operating Procedure (SOP) in place regarding the management of intrapleural hemorrhage. Resuscitation is paramount in the first instance and once the patient is stabilized, definitive treatment to stem the bleeding from the vessel is required. This can be done radiologically or surgically, depending on the patient's condition and local availability. An SOP template for the management of iatrogenic pleural hemorrhage can be found in Table 1, but would need to be adapted for use at individual centers where infrastructure may vary.

Drain malposition

Insertion of a chest drain may be indicated in a variety of clinical scenarios, including the management of symptomatic pleural effusion, pleural infection, and pneumothorax. Chest drains may be inserted using blunt dissection or a Seldinger technique, but insertion using a trochar is no longer recommended due to an increased risk of trauma to surrounding structures [3••]. The use of small-bore Seldinger drains has become very widespread [3••], and a recent study evaluating patients with pleural infection suggests that smaller drains are less painful than larger ones and are potentially as efficacious [43•]. However, as with all pleural procedures, the insertion of chest drains is not without potential complications (Table 2).

Malposition of drains can be associated with severe morbidity and mortality and was identified as a serious issue by the National Patient Safety Agency in 2008 [1]. They identified 12 deaths and 15 cases of serious harm to patients caused by chest drain insertion in the UK, which had been reported between January 2005 and March 2008 and several other cases of poor chest drain management [1]. This has led to the introduction of measures to improve the safety of these procedures with regard to improvement in training, guideline development, redesign of the equipment used, and regular audit of the activity [30•].

In 2008, a survey of UK acute hospital trusts regarding chest drain complications in the preceding 5 years was undertaken. A total of 67 responding trusts reported major complications, including lung or chest wall injury (47 cases), wrong side procedures (6 cases), lost guidewires (3 cases), and drain misplacement (31 cases). Eight deaths were reported as a result of these complications [44].

The British Thoracic Society undertook a national audit of chest drain practice in the UK, which included 824 drains inserted during the 2-month audit period. This also highlighted a number of potential complications, including pain after the procedure (18%), drains falling out prematurely (7.3%), drain malposition (2.4%), and drains becoming blocked (7.4%) [30•].

Placement of the drain into the lung parenchyma itself has been reported in up to 10% of drain insertions, although the incidence varies between studies given different insertion techniques and availability of radiological guidance [45, 46].

On occasion, the drain may inadvertently lie in a lung fissure, which may result in inefficient drain function. In one French study, evaluating the position of 122 chest drains using CT on a surgical ICU, intrafissural drain placement was found to be as high as 21% and occurred more commonly with right-sided drains due to the anatomy of the horizontal fissure when chest drains are inserted in the safe triangle [46]. However, the relevance of an intrafissural position is debated and drains should only be re-sited if they are not functioning correctly.

Rarely, drains can accidently perforate other structures, including the diaphragm, heart, stomach, mediastinum, thoracic duct, major vessels, and intra-abdominal organs, with occasionally catastrophic consequences [47]. Direct radiological guidance when inserting chest drains helps to delineate the anatomy of nearby structures and hence minimize the chances of this occurring.

Other rare complications of chest drain placement have been reported including inadvertent compression of vessels or nerves, resulting in pressure effects, including Horner's syndrome [48] and cardiogenic shock from compression of the right ventricle [49].

Table 1 A template standard operating procedure for the management of iatrogenic pleural hemorrhage

Standard operating procedure for the management of iatrogenic pleural hemorrhage
Evaluate need for immediate resuscitation:
Has the patient suffered, or do they appear close to cardiac arrest? Or, Are they suffering from severe hypotensive shock? Or, Is the bleeding very severe/torrential?
Yes:
1. Summon help from senior doctor, nursing staff, and/or cardiac arrest team as necessary
2. Initiate standard cardiopulmonary resuscitation if needed
3. Establish large bore venous access and initiate immediate large volume fluid replacement with plasma expander/blood
4. Urgently cross match 4 units of blood
5. Record blood pressure, heart rate, and oxygen saturations every 5 mins
6. Contact cardiothoracic surgeon and the intensive care team to arrange rapid transport to a suitable environment for emergency surgery
No:
1. Summon help of senior doctor and nursing staff
2. Apply direct external pressure to pleural puncture site if possible
3. Establish large bore venous access
4. Record blood pressure, heart rate, and oxygen saturations every 10 mins (or more often if required)
5. Initiate immediate large volume fluid replacement with plasma expander/blood if necessary
6. Urgently cross match 4 units of blood
7. If the patient becomes hemodynamically unstable or the bleeding becomes torrential, be ready to summon the cardiac arrest team and initiate standard cardiopulmonary resuscitation; if so, follow steps outlined above
8. Contact local respiratory consultant as a matter of urgency
9. Make personal contact with a senior interventional radiologist to begin planning for imaging and emergency intercostal artery embolization if needed
10. If embolization is not possible or unavailable, contact cardiothoracic surgical team to plan for surgery if required
11. Stop all anticoagulants, including heparin for DVT prophylaxis

In order to minimize drain malposition, pleural ultrasound is recommended to guide all pleural procedures for effusions [3••]. This allows direct visualization of the appearance and depth of the pleural fluid and may identify unforeseen features, such as loculations, a raised hemidiaphragm, or close proximity of other organs (for example the heart, liver, or spleen) which will alter the selection of a site for drain insertion. Similarly, on-table ultrasound should be used prior to local anaesthetic thoracoscopy to guide the selection of a suitable site for the port.

As a result of this, there has been a dramatic increase in the numbers of non-radiology trained physicians performing thoracic ultrasound to guide pleural procedures. With suitable training, this has been shown to be safe and effective [50]. National bodies such as the Royal College of Radiologists in the UK and the Australasian Society for Ultrasound in Medicine offer guidance and training syllabuses for performing thoracic ultrasound and it is important that clinicians undertaking ultrasound are suitably certified [51, 52]. However, despite the evidence for using ultrasound in this context, there is still a lack of availability. Only 52% of the chest drains included in the 2010 BTS audit were inserted using bedside ultrasound guidance [30•].

In some scenarios where the anatomy is difficult to delineate even with ultrasound, CT may be required to guide the drain insertion. On occasion, CT can also be useful when a drain has been inserted but is not functioning correctly to identify the anatomical location of the drain tract and guide subsequent management.

Malignant seeding

In the context of underlying pleural malignancy, in particular malignant pleural mesothelioma, invasive pleural procedures may cause seeding of tumor cells along the tract created during the intervention. This may result in the development of painful tumor deposits at the procedure site, known as procedure tract metastases (PTM), which can be difficult to treat once they develop. The larger the incision made in the chest wall, the higher the chance of tract metastases developing [53].

There is a significant time lag between the pleural intervention and the development of tract metastases. The timing varies greatly between studies, but a recent review of the literature found the mean time to development of PTM was 6.5 months (range 4.5–9 months) [54].

Table 2 Complications of chest drain insertion

First author	Date	Description	*n*	Complication (%)								
				CDM	IP	Bleeding	Skin infection	Pleural infection	Drain blockage	Drain displacement	SCE	Vaso vagal reaction
Bailey [32]	2000	Retrospective review of chest drains inserted for trauma	57	ND	ND	ND	10.5	1.7	1.7	3.5	ND	ND
Cafarotti [68]	2011	Retrospective review of 12F Seldinger chest drain insertions for all indications	1092	ND	ND	Hemo-thorax 0 Local bleeding 0.9	0.4	0	7.5	5.4	0.5	1.1
Chan [31]	1997	Retrospective case series of all drains inserted	352	1.1	15.1	ND	ND	1.1	ND	ND	ND	ND
Collop [69]	1997	Prospective series of all drains inserted (size 7–32 Fr)	126	1.5	0.8	ND	0.8	ND	2.3	1.5	ND	ND
Hooper [30•]	2011	UK national audit of all chest drain inserted over a 2-month period	824	2.4	2.7	1.3	0.8	0.73	7.4	7.3	3.4	2.1
Horsley [70]	2006	Prospective study of 12–20F Seldinger drains	52	0	4	Local bleeding 2	0	2	23	6	6	ND

CDM chest drain malposition; *IP* iatrogenic pneumothorax; *ND* not documented; *SCE* subcutaneous emphysema.

Prophylactic radiotherapy may be given to patients with mesothelioma who undergo invasive pleural procedures to try and prevent this occurring; however, its benefit is debated [55•]. Three randomized trials have been conducted to evaluate the role of prophylactic radiotherapy in mesothelioma; however, all were underpowered and the results were conflicting [56–58].

Tract metastases have also been reported in the context of indwelling pleural catheters, caused by both mesothelioma and adenocarcinoma [59]. Again the role for prophylactic radiotherapy in this context is not known.

Pleural complications from abdominal procedures

Procedures involving the abdomen can also result in diaphragmatic and pleural puncture and subsequent pleural complications. In our own center, a percutaneous drain insertion into a liver abscess resulted in pleural infection as the drain transected the diaphragm into the pleural cavity.

Retroperitoneal surgical procedures may expose the parietal pleura and thereby risk breaching the pleural surface. In a case series of 91 radical nephrectomies, 58 were complicated by a pleural injury and this was associated with a prolonged length of hospital stay, particularly in those who had a postoperative chest drain placed [60].

Diaphragmatic and pleural injury is also a complication of laparoscopic renal surgery, with an incidence of 0.6% in one large series [61]. Due to the use of pressurized intra-abdominal carbon dioxide during laparoscopy to improve visualization of the abdominal structures, diaphragmatic injury during the procedure may lead to a rapidly developing pneumothorax or pneumomediastinum with subsequent subcutaneous emphysema. Hence early recognition and repair is paramount.

A French study evaluating respiratory complications after 112 hepatectomies of living liver donors found the incidence of postoperative pleural effusion on CT at 7 days to be as high as 75% and was particularly high in those who had the right lobe of the liver removed. Empyema developed in three cases (2.7%) and pneumothorax in three cases (2.7%) [62].

Peritoneal dialysis is commonly used for renal replacement therapy in those with end-stage renal failure. Dialysate is infused into the peritoneal cavity via a tunnelled catheter and pleural effusions (particularly on the right) are a recognized complication due to the increased intra-abdominal pressure in the context of a diaphragmatic defect. The reported incidence is under 2% of patients having peritoneal dialysis [63] and if persistent may require the patient to use an alternative method for renal replacement therapy.

Pleural complications from other thoracic procedures

Due to the close proximity of the pleura to the other structures within the thorax, pleural complications may occur during thoracic procedures, including cardiothoracic and esophageal surgery.

Post-coronary artery bypass grafting (CABG) pleural effusion is a common complication and can occur early (< 30 days after the surgery) or late [64]. The prevalence is highest in the immediate post-operative period, but a significant effusion may still be present in around 10% of patients after 1 month [65]. Often in the case of early post-CABG pleural effusion, symptoms are minimal and most settle without treatment, but if they persist patients may require repeated therapeutic aspirations for symptomatic relief.

Iatrogenic esophageal leaks and perforations can result in the development of pleural effusions, mediastinitis, and pleural infection in the context of esophageal surgery. Minimally invasive esophagectomy may confer a lower risk of post-operative pleural effusion than open procedures, although the need for re-intervention may be higher [66].

Damage to other thoracic structures including the thoracic duct, resulting in a chylothorax and vessel puncture causing a hemothorax, are also potential complications of intrathoracic procedures [67].

Conclusions

Iatrogenic pleural complications can occur due to a variety of invasive procedures and are associated with significant morbidity and mortality. The increasing use of bedside thoracic ultrasound for pleural procedures, equipment incorporating safety features, and use of protocols and more extensive training, all help to minimize the risks. It is, however, important to recognize that complications cannot be entirely eliminated and standard procedures should be in place to optimize patient management if a complication does occur.

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- • Of importance
- •• Of major importance

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