Minimally Invasive Surgery in the Diagnosis and Treatment of Childhood Cancer

36

George W. Holcomb III and Benno Ure

One of the earliest reports about the use of minimally invasive surgery (MIS) in children described thoracoscopy for evaluation and biopsy of intrathoracic conditions [1]. In that 1979 report, 57 children underwent 65 thoracoscopic procedures. Fifteen of the operations were performed for the diagnosis of an intrathoracic tumor. Three years later, Rodgers and Ryckman described over 150 thoracoscopic operations for evaluation of intrathoracic pathology [2]. Twenty-five of these were undertaken for the potential diagnosis or staging of cancer in patients from 8 months to 18 years of age. Twelve were performed for parenchymal tumors, 11 for mediastinal masses, and two for pleural disease. Interestingly, there were very few publications over the next 10 years describing the use of laparoscopy or thoracoscopy for the treatment of benign or malignant disease in children. With the advent of the MIS revolution in the late 1980s and early 1990s, a number of adult surgeons began to describe their experience using thoracoscopy for lung and esophageal cancers [3–8]. In addition, a number of papers described the utility of laparoscopy in adults for pancreatic, ovarian, gastric and colon cancers [9–17].

The use of MIS in children for benign disease was slow to evolve as was its utilization for malignancies. Over the past 10 years, experience with MIS in children with cancer has grown to the point that this modality can now be considered an acceptable approach for many tumors. In the abdomen, laparoscopy is used primarily for biopsy of new lesions or for second look purposes (Fig. 36.1). In addition, it is being increasingly used for resection of Wilms tumors or other renal lesions which have previously been treated with chemotherapy and have decreased significantly in size [18–20]. This is especially true in Europe where chemotherapy is often given prior to attempted tumor resection. Another optimal candidate is a small baby with a suspected neuroblastoma which is well localized. Although rarely performed, an abdominal staging procedure for Hodgkin's Disease is also a good indication for laparoscopy in children with cancer.

The use of thoracoscopy matured much faster than laparoscopy for malignant disease, primarily due to the fact that biopsy of mediastinal masses or wedge resections of pulmonary lesions are straightforward procedures in children. Also, resection of posterior mediastinal masses can be accomplished thoracoscopically. This chapter will describe the use of laparoscopy and thoracoscopy for children with cancer, the impact of MIS on tumor cell behavior, and will review the recent literature describing these minimally invasive approaches in children with cancer.

Laparoscopy in Pediatric Oncology

The spectrum of malignancies in children for which a laparoscopic biopsy might be useful includes the whole range of pediatric abdominal and retroperitoneal tumors such as neuroblastoma, nephroblastoma, hepatoblastoma, rhabdomyosarcoma, teratoma, lymphoma and several others [21–25]. The feasibility is reported to be excellent with a conversion rate of less than 5 % in some series and a diagnostic accuracy of laparoscopic biopsies for various malignant conditions of up to 100 % [22, 26, 27].

A number of reports have confirmed that laparoscopy is a valid approach for resection of solid malignancies in selected children. However, the feasibility of laparoscopic tumor resection is limited in most reports that include a wide spectrum of tumors. Warmann et al. [22] had to convert in 5 out of 9 resections and Metzelder et al. [25] reported a conversion rate of 42 % with 24 attempted laparoscopic resections of various solid tumors. On the other hand, a 2007 report from Hong Kong described 38 patients over 10 years undergoing laparoscopy for tumor resection [28]. The mean age at operation was 7.5 years (1 day to 15 years). The operation

G.W. Holcomb III, MD, MBA (✉)
Department of Surgery, Children's Mercy Hospitals and Clinics, Kansas City, MO, USA
e-mail: gholcomb@cmh.edu

B. Ure, MD
Pediatric Surgery, Hannover Medical School, Hannover, Germany

R. Carachi, J.L. Grosfeld (eds.), *The Surgery of Childhood Tumors*, DOI 10.1007/978-3-662-48590-3_36

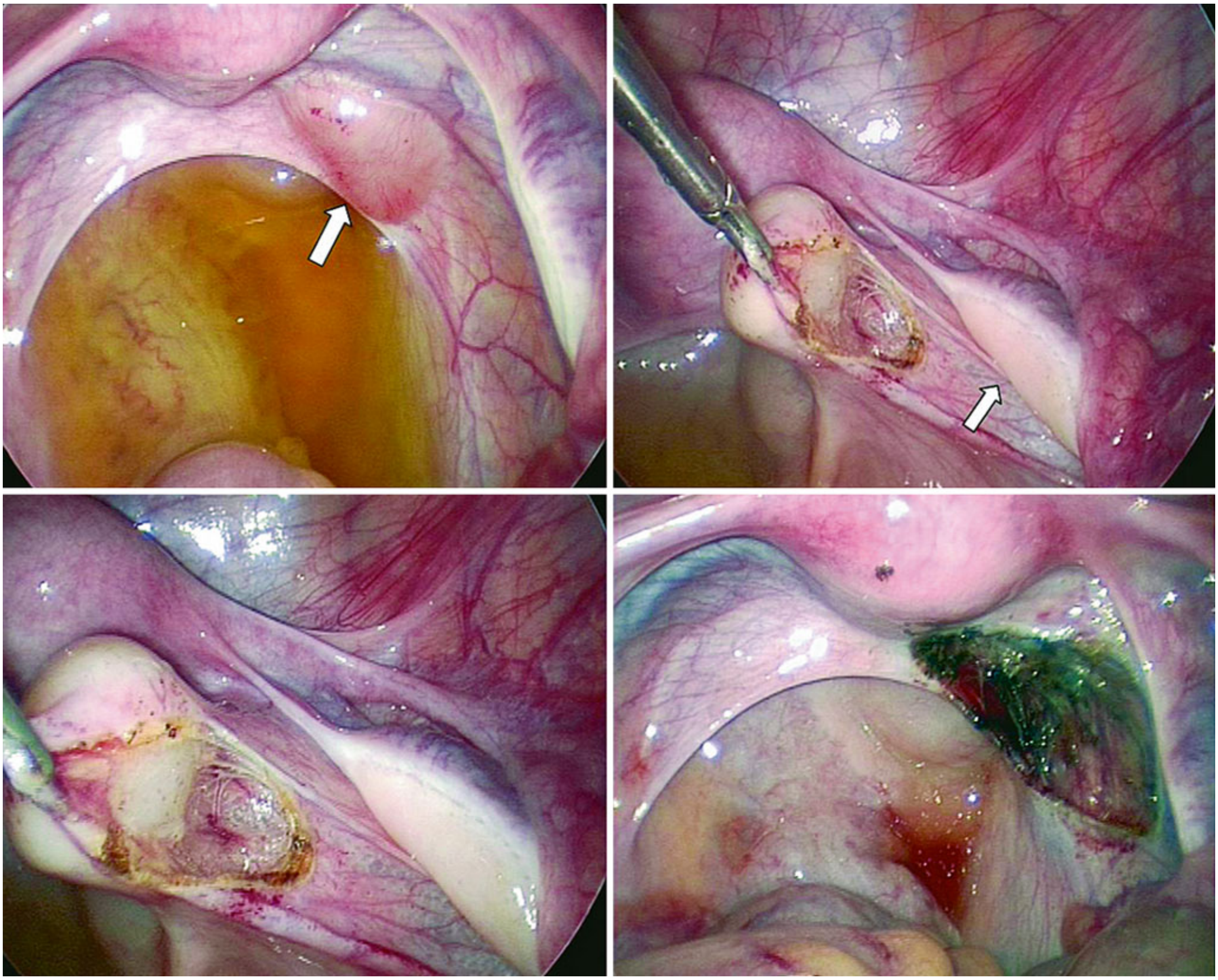

Fig. 36.1 Second-look laparoscopy can be useful after adjuvant therapy in certain circumstances. In this teenage patient who previously had undergone laparotomy and resection of a large germ cell tumor, second-look laparoscopy was performed to determine whether evidence of residual disease existed. *Upper left* , Residual disease is seen along the right pelvic side wall (*white arrow*). *Upper right*, this mass is being resected from the pelvic side wall. Note the normal right ovary (*white arrow*). *Lower left* , further dissection of the mass is achieved. *Lower right*, the mass has been completely excised with hemostasis controlled by cautery. (Reprinted with permission from Pediatric Surgery, 4th edn, Ashcraft , Holcomb, Murphy, eds, Elsevier, 2005, p 676.)

was able to be performed successfully in 30 of the 38 patients. Eight patients required conversion because of limited intraperitoneal space in seven and bleeding in one. Seven of these patients had malignant tumors, and there was no recurrence with an average follow-up of 3.1 years. Similarly, St. Peter et al. reported a low conversion of 10 % for laparoscopic adrenalectomy in 140 children [29].

The patient is usually positioned supine on the operating table, although it may be helpful to place a roll underneath the left or right flank depending on the nature of the laparoscopic operation. For adrenal operations, it is often easier to perform the procedure with the patient positioned in a true lateral position. An orogastric tube should be inserted, and the bladder should be emptied following induction of anesthesia. The bladder can be emptied with a Credé maneuver or a urinary catheter can be introduced if a long procedure is anticipated. For an upper midline abdominal lesion, it is often helpful to place the patient in lithotomy, and the surgeon will stand between the patient's legs, much like for a laparoscopic fundoplication. For a right or left upper abdominal procedure, the patient positioning and location of the personnel should be similar to a laparoscopic cholecystectomy or a splenectomy, respectively.

If the target lesion is in the pelvis, a single monitor is usually needed and positioned at the foot of the bed. The surgeon and assistant stand opposite each other. In general, if the lesion is a left lower abdominal or left pelvic mass, the surgeon should stand on the patient's right side and vice versa for a right lower abdominal or pelvic mass. For a pelvic lesion, it is important to evacuate the bladder completely so a temporary urinary catheter may be advisable. If a nephrectomy is planned, the patient should be positioned in a 45° or a 90° lateral position, depending on the surgeon's preference.

It is important to use an endoscopic retrieval bag to extract specimens to prevent port site recurrences. No port-site recurrences were observed in any of the larger series of children undergoing laparoscopic resection of neuroblastoma [23, 24, 29]. However, Chui and Lee [30] recently described peritoneal dissemination of a Wilms tumor 3 months after laparoscopic resection and Metzelder and Ure [31] reported on a child with port-site metastasis after biopsy of a Burkitt's lymphoma.

In summary, the laparoscopic approach can be recommended in children with suspected abdominal or retroperitoneal malignancy requiring biopsy. With meticulous selection of patients, the feasibility of laparoscopic resection in children with neuroblastoma and several other types of malignant tumors is excellent. The known short-term benefits of MIS such as less pain and fast recover are obvious, but data on long-term results in larger series of children are needed to establish general recommendations.

Impact of Laparoscopy on Tumor Cell Behavior

The benefits of MIS have been attributed to several underlying mechanisms, including a specific effect on the immune system. Experimental studies have confirmed that MIS interferes with the function of various cell populations which play a key role in the host defense, such as monocytes-macrophages, polymorphnuclear leucocytes and lymphocytes [32, 33]. These specific immunological effects have been attributed to less injury associated with the minimally invasive approach and to metabolic properties of the gas used for the pneumoperitoneum.

Most studies investigating MIS and its effect on tumor biology have focused on laparoscopy. Experimental studies confirm that laparoscopy versus laparotomy and the use of CO_2 versus air for pneumoperitoneum have similar effects, such as a lower migration of polymorphnuclear cells to the abdominal cavity, and lower abdominal macrophage cytokine release [34]. The use of CO_2 during laparoscopy compared to mini-laparotomy with a similar length of abdominal incision was associated with lower circulatory cytokine release, prevented hepatic macrophages from expansion, and preserved normal intraabdominal cell distribution [35]. Effects of CO_2 used for pneumoperitoneum have also been identified in distant organs. The pulmonary macrophage reactive oxygene species release is reduced after pneumoperitoneum with CO_2 compared to air [34]. Besides its effect on macrophage functions, the chemotaxis and migration of polymorphnuclear cells is also blocked by CO_2 [36]. The underlying mechanism of these immune effects is a low pH [37, 38], which is at CO_2 exposed areas of the abdominal cavity during laparoscopy [38]. These effects may even have an impact on survival after sepsis. In a rodent model, CO_2 pneumoperitoneum versus exposure to helium or air significantly reduced the 7 day mortality [39].

Currently, controversy exists about the role of CO_2 in patients with malignant disease. It has been postulated that the alteration of host defense mechanisms may interfere with the clearing of tumor cells spread during the operation. In addition, a direct impact on the behavior of tumor cells has been suggested. The in-vivo behavior of neuroblastoma cells after pneumoperitoneum was investigated by Iwanaka et al. [40] There was no significant difference in survival, tumor growth, or distant metastasis in mice with CO_2 pneumoperitoneum versus laparotomy when the tumor remained untouched. Also, port site recurrences were found to be similar whether biopsies were performed during CO_2 or gasless pneumoperitoneum. On the contrary, Schmidt et al. investigated several pediatric tumor cell lines in-vitro [41]. The proliferation rate of neuroblastoma, hepatoblastoma, hepatocellular carcinoma, and lymphoma cells was significantly reduced for up to 4 days after exposure to CO_2 when compared to air or helium.

CO_2 also causes alterations to the peritoneal surface. Exposure to CO_2 alters the electronmicroscopic structure of mesothelial cell layers and enhances neuroblastoma cell migration through this layer [36]. C-myc and HMCB1 expression of neuroblastoma cells are increased after CO_2 incubation in-vitro [42]. In the mouse model, the incidence of liver metastasis is significantly increased 28 days after CO_2 pneumoperitoneum when compared to laparotomy [43].

It is important to appreciate that these findings might not reflect the clinical environment as children usually receive chemotherapy after the operation. However, as clinical reports on long-term outcomes are scarce and no randomized or controlled clinical trials comparing MIS with conventional surgery have been conducted, definitive recommendations for the use of MIS in children with solid tumors cannot be made. It will be necessary to wait for longer term results.

Thoracoscopy in Pediatric Oncology

The important principles for performing a thoracoscopic operation in a patient with cancer have not changed over the past 15 years. The location of the mass to be biopsied or excised will determine whether or not preoperative localization is needed. Most surface lesions can be visualized at thoracoscopy, and do not need localization. However, if the lesion is small, there should be consideration for preoperative localization as sometimes it can be difficult to visualize a

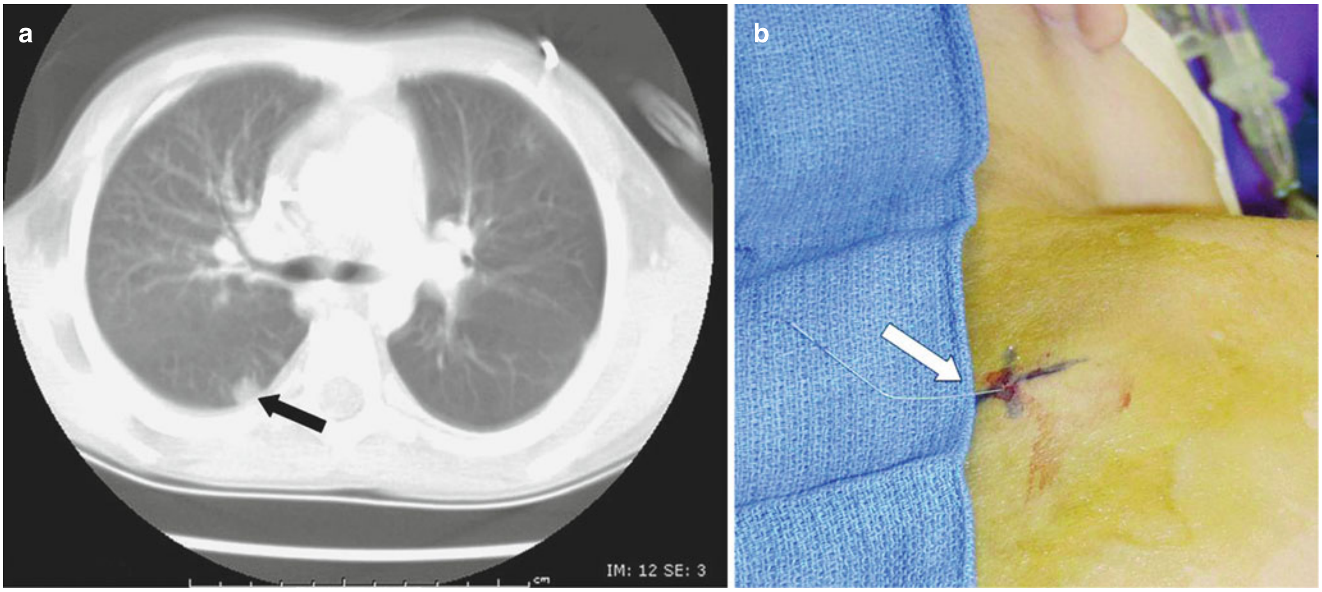

Fig. 36.2 (**a**, **b**) Preoperative localization is important for thoracoscopic operations when compared to the open operation because of the lack of tactile sensation with one's hands. Preoperatively, the patient was noted to have a posterior lung nodule (*black arrow*) (**a**). This lesion was localized preoperatively and the wire is seen exiting the patient' skin (*white arrow*) (**b**)

small lesion on the surface of the lung when the lung is collapsed. Preoperative localization is important for the thoracoscopic procedure as compared with the open operation because of the loss of tactile sensation resulting in the inability to palate the lesion with one's hands. If the lesion is deeper in the parenchyma, preoperative localization should be strongly considered. A number of techniques are possible, including percutaneous placement of a wire into the lesion using CT guidance (Fig. 36.2) [44]. Also, the application of methylene blue or a drop of the patient's own blood may be instilled in the area to be resected in case the wire is dislodged [45, 46]. The use of methylene blue has been banned by many institutions so a blood patch from the patient may be better. It is important not to collapse the lung too quickly following bronchial blockade and insufflation as the wire may become dislodged from the lesion as the lung is pulled away from the chest wall. Localization of parenchymal nodules has also been described using thoracoscopic ultrasound [47].

Another important preoperative consideration is whether or not to use a double lumen endotracheal tube. The smallest double lumen tube is 26 French. Thus, the smallest patient in whom this tube can be utilized is usually 6–8 years of age. Therefore, if a thoracoscopic operation is planned for a younger patient and collapse of the ipsilateral lung is important, other modalities should be considered to effect collapse of the ipsilateral lung. If the patient is undergoing a left thoracoscopic operation, a relatively easy technique is to place an uncuffed endotracheal tube into the right main stem bronchus, which usually allows minimal ventilation into the left lung. If a right thoracoscopy is needed, it is sometimes possible to position an uncuffed endotracheal tube down the left main stem bronchus, although this is not as easy as on the right side. A bronchial blocker can also be introduced down the right main stem bronchus with the endotracheal tube positioned in the trachea to collapse the right lung.

Positive pressure insufflation is a useful technique to create working space in the thoracic cavity. Most surgeons who perform thoracoscopic procedures frequently now use valve cannulas and positive pressure insufflation to effect lung collapse. An insufflation pressure of 6–8 torr usually will result in good parenchymal collapse in most patients. Also, positive pressure helps augment the initial lung collapse if endobronchial blockade is being employed.

An important consideration for a thoracoscopic operation is patient positioning. By positioning the patient on the operating room table in different positions, the surgeon can take advantage of gravity to improve visualization. For an anterior mediastinal lesion, the patient should be placed about 30° supine with a roll under the ipsilateral side. Following lung collapse, the lung should fall more posteriorly and improve visualization of the anterior mediastinum. Conversely, for a posterior mediastinal lesion, the patient should be positioned approximately 30° prone, which allows the lung to fall anterior and improve exposure to the posterior mediastinum (Fig. 36.3). For a parenchymal nodule, the patient can be placed more or less in a 90° decubitus position, although the patient can be tilted anteriorly or posteriorly if the lesion is more posterior or anterior. For a lesion on the diaphragm which requires evaluation for possible biopsy or excision, the patient should be positioned more in a reverse

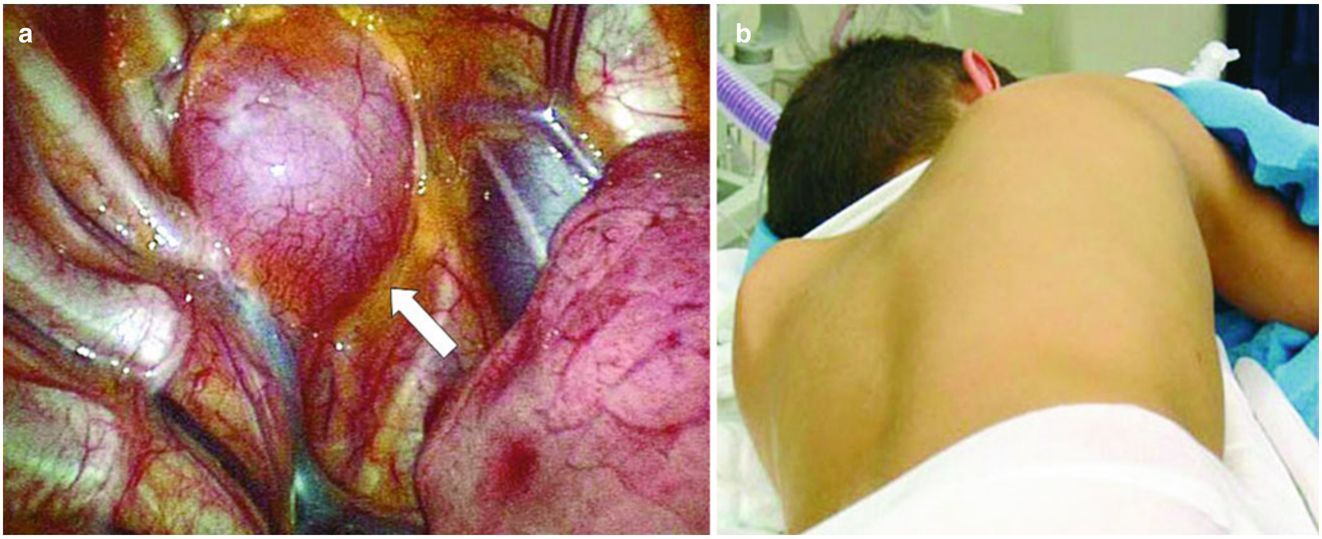

Fig. 36.3 (**a**, **b**) Patient positioning is an important preoperative consideration for a thoracoscopic (or laparoscopic) operation. This teenager had a posterior mediastinal mass (*white arrow*) which turned out to be a ganglioneuroma (**a**). For access to this posterior mediastinal lesion, the patient was placed in a 30° prone position to allow the lung to fall away from the posterior mediastinum (**b**)

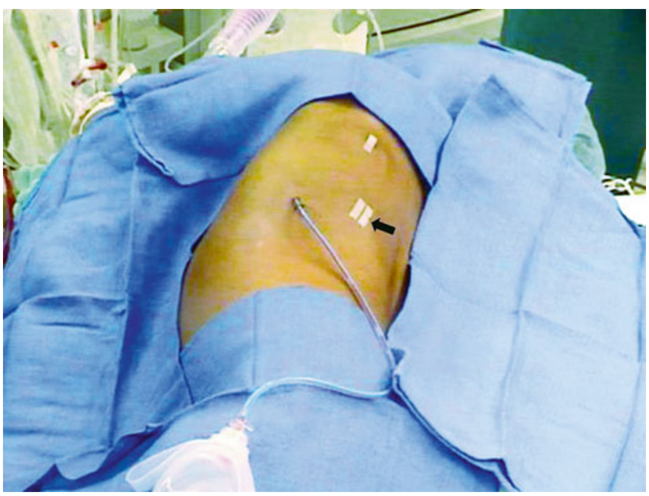

Fig. 36.4 The port positions for a young child undergoing thoracoscopic wedge excision of a metastatic lesion are seen. The largest incision (*arrow*) was positioned as far away from the lesion as possible so that the stapler could be opened within the chest cavity. A small silastic drain was exteriorized through a stab incision

Trendelenburg position to allow the lung to fall away from the diaphragm. Conversely, for a lesion in the apex of the thoracic cavity, the table can be placed more in a head-up position to promote the lung falling more caudal and away from the target area. Positioning of monitors and operating room personnel is the same regardless of whether the operation is for benign or malignant disease.

Another issue in children is whether or not an endoscopic stapler can be utilized for parenchymal resections. For anterior and posterior mediastinal lesions, it is unlikely that a stapler will be needed as there is no need to divide the lung parenchyma. However, for parenchymal disease, a stapler can make the operation safer and more efficacious. On the other hand, the current staplers are made primarily for adult patients, and it is important to modify their use in infants and small children. Therefore, the site for introduction of the stapler should be placed as far away from the lesion as possible in order to be able to introduce the stapler and open the cartridge (Fig. 36.4). It is important to remember that 4–5 cm of the stapler must be in the thoracic cavity before the stapler can be opened. Sometimes, it is necessary to remove the port so that the cartridge can be introduced into the thoracic cavity and opened. The angulated staplers are generally easier to manipulate, ligate, and divide the lung parenchyma (Fig. 36.5). If an additional instrument is needed for retraction, a "stab incision technique" often allows introduction of a 3 or 5 mm instrument without using a cannula. The advantage of using the stab incision technique is that there is greater mobility with an instrument placed directly through the thoracic interspace rather than working through a cannula as angulation and movement of the cannula is often limited by the ribs and size of the interspace. There is rarely a problem with leak of CO_2 through the stab incision if an adequate insufflation flow is used.

Port site metastases remain a concern in these patients, but there are very few literature reports describing this problem. There has been a report of a port site metastases in a child undergoing a thoracoscopic operation for osteogenic sarcoma [48]. However, despite the fact that this problem does not occur as often as initially feared, it is important to place all specimens into an endoscopic retrieval bag for exteriorization (Fig. 36.6). Morcellation

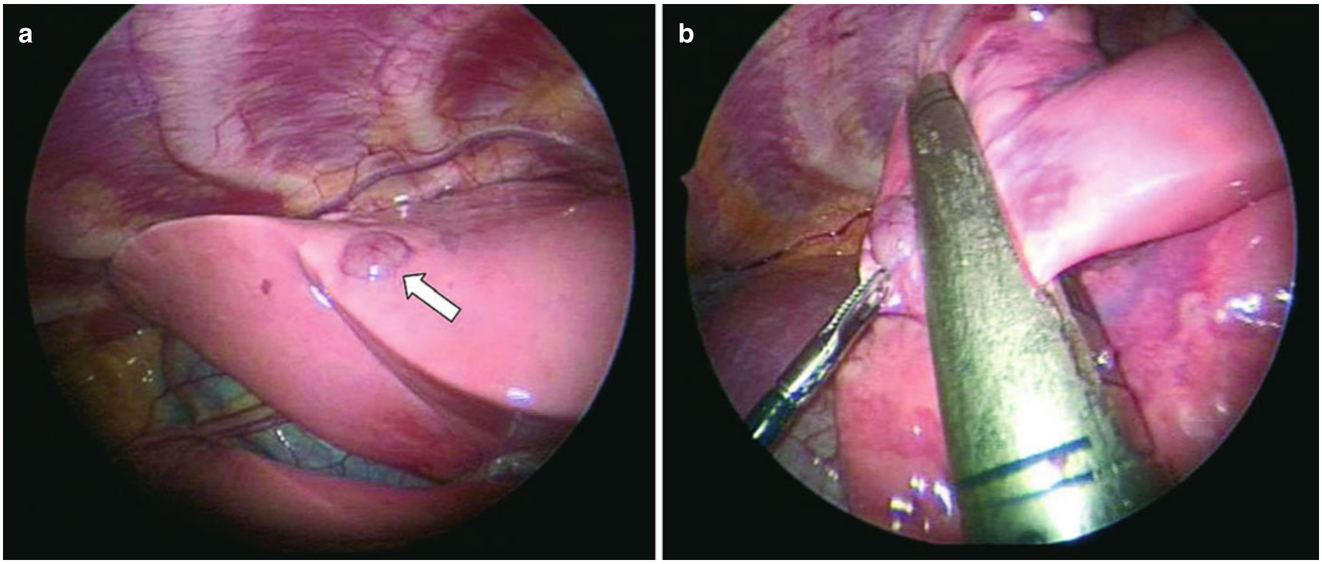

Fig. 36.5 (**a**, **b**) Staplers are the easiest and safest means to extract a pulmonary parenchymal lesion. In this patient with a suspected metastatic Wilms' tumor, the lesion (*arrow*) is seen on the edge of the right upper lobe (**a**). The stapler has been placed across the parenchyma and the lesion has been incorporated in the wedge resection (**b**)

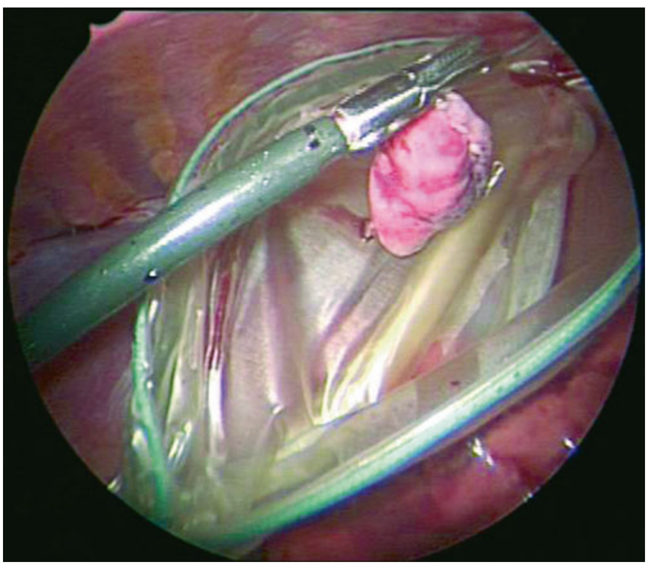

Fig. 36.6 Cancer specimens should be placed into an endoscopic retrieval bag prior to removal from the patient

of cancer specimens is not advisable. Endoscopic retrieval bags are now available in 10 and 15 mm sizes. The 10 mm bag is usually sufficient. It is very important not to extract a specimen that is too large through a small port site as the bag may tear and result in spillage of the specimen which could lead to implantation on the parietal surface of the thoracic cavity or port site recurrences. Therefore, the skin and soft tissue at the site of extraction should be enlarged so the bag and specimen can be exteriorized without tearing the bag.

Literature Review

A 2010 Cochrane review could not come to any definitive conclusion about the efficacy of MIS for patients with cancer because there were no randomized controlled trials or case control trials comparing the open approach versus the minimally invasive approach [49]. Thus, the current literature on this subject comes primarily from retrospective case series and cohort studies.

The first large series describing the use of laparoscopy and thoracoscopy in children with cancer was published in 1995 and described 85 children from 15 CCG (now Children's Oncology Group) institutions who underwent 88 minimally invasive procedures [21]. Twenty-five patients had a laparoscopic operation and 60 patients underwent a total of 63 thoracoscopic procedures. In 2002, Rothenberg and his colleagues described 52 patients undergoing 63 thoracoscopic operations over a 7 year period [50]. Eight patients required conversion to the open approach.

In 2004, the group from St. Jude's Hospital reported 101 patients undergoing 113 minimally invasive operations [23]. Sixty-four patients underwent a laparoscopic operation and 49 had a thoracoscopic procedure. In this series, seven abdominal tumors were excised. In the patients who underwent a thoracoscopic procedure, most of them required wedge resection of a lung nodule. In 14 patients (29 %), the operation had to be converted to an open thoracotomy because of the inability to localize the suspected lesion. None of these patients requiring conversion had undergone attempted preoperative localization.

In a 2007 review, the diagnostic and ablative roles of MIS in children with cancer were evaluated in a consecutive series of 276 patients with cancer [25]. This prospective study included all patients who underwent abdominal and thoracic operations for cancer over a 5 year period. Three hundred and one operations were performed at this single institution and a minimally invasive approach was attempted in 90 of these patients (30 %), and was successful in 69 (77 %) patients. Twenty-one MIS operations for cancer (23 %) were converted to an open procedure. Regarding the abdominal operation, 41 operations for biopsy or staging were attempted laparoscopically and all but six were successfully performed. Twenty-four laparoscopic resections were attempted, and the authors were successful in 14 (58 %). In the chest, thoracoscopy for biopsy was attempted in 14 thoracic operations, and was successful in all but one (93 %). The thoracoscopic approach was attempted in 11 patients for tumor resection, and was successful in seven. Conversions from the MIS approach to the open operation occurred mainly due to limited visibility. Three bleeding complications occurred with one patient requiring a blood transfusion. There were no port site recurrences after a median follow-up of 39 months.

Most reports of laparoscopic tumor resection deal with neuroblastoma. Iwanka and colleagues have described laparoscopic biopsy for neuroblastoma in 25 children and laparoscopic excision in nine patients with localized disease [51]. De Lagausie et al. resected 9 adrenal neuroblastomas and converted one case due to adhesions [52]. Similar success was reported in other small series [53–55]. In their multicenter study, Leclair et al. analyzed 45 children [56]. The conversion rate was 9 %, and the survival rate in children with localized neuroblastoma was 96 % with a median follow-up of 28 months. There was no control group and no information on selection criteria for the laparoscopic approach.

Several authors from Japan have described laparoscopic resection of neuroblastoma identified by mass screening [57, 58]. The feasibility has been excellent with localized disease and well encapsulated tumors with a size of less than 5 cm in diameter. However, the appropriate indication for laparoscopic resection of neuroblastomas identified by mass screening remains a matter of debate. Two Japanese groups have suggested resecting tumors which do not regress for several months or increase in size to more than 5 cm [59, 60]. Other authors have resected smaller neuroblastomas less than 4 cm [61]. Tanaka and co-authors confirmed that over 70 % of 53 patients who fulfilled specific criteria could be observed without surgery and no unfavorable biologic factors were noted in excised tumors [62].

A report from South Korea described 10 children who underwent laparoscopic surgical resection for malignant solid tumors between 2005 and 2010 [63]. Six patients underwent laparoscopic adrenalectomy for neuroblastoma (5) or adrenal cortical carcinoma (1). Two patients underwent laparoscopic partial hepatectomy for hepatoblastoma, one patient underwent laparoscopic salpingo-oophorectomy for yolk sac tumor, and one underwent laparoscopic tumor excision of the rhabdomyosarcoma in the pelvis. Complete resection was achieved in all cases. The tumors ranged from 2.5 to 5.3 cm in maximum diameter. There were no conversions and no postoperative complications or recurrences during the 17.3 month median follow-up.

Several small series of children undergoing laparoscopic nephrectomy for unilateral Wilms tumor have been described. Varlet et al. operated on three children without tumor rupture and event-free survival after 18 months [18]. Duarte et al. reported on 15 cases without information on long-term results [64].

Technical aspects of laparoscopic surgery in children with suspected malignancy include using low pressure pneumoperitoneum to preserve the integrity of the peritoneal cell layers, and minimizing the spread of tumor cells by using retrieval bags. Iwanaka [40] showed experimentally that local or intravenous chemotherapeutic agents, such as cyclophosphamide, reduced the incidence of port-site metastasis from neuroblastoma. The authors therefore recommended chemotherapy as soon as possible after laparoscopic biopsies in children with chemotherapy-sensitive tumors. However, clinical evidence of the advantages of this approach is lacking.

The feasibility of laparoscopic resection for other tumors can only be derived from case reports. Pancreatic tumors including insulinoma [65, 66], pseudopapillary tumors [67], hepatoblastoma [68] renal clear-cell sarcoma [18], and numerous other rare conditions have been successfully resected via laparoscopy. These initial data are encouraging, but long-term follow-up is not yet available.

Although many authors prefer the transabdominal approach for optimal laparoscopic tumor exposition, the transperitoneal route has been also recommended in children with retroperitoneal tumors [69, 70]. On the other hand, Steyaert et al. [71] successfully used a retroperitoneoscopic approach in 10 and Theilen et al. in 16 cases [72]. In this last series, 16 patients with a median age of 16.4 years underwent retroperitoneoscopy between 2004 and 2010 for oncologic disease. Nine patients underwent lymph node sampling, six patients underwent diagnostic biopsy and one patient required resection of a metastatic nodule. Three patients underwent conversion to the open operation. Pampaloni et al. has suggested a transabdominal laparoscopic surgery for right-sided lesions and prefers the retroperitoneoscopic approach for left-sided tumors [73].

Retroperitoneal lymph node dissection (RPLND) is recommended in children 10 years or older with paratesticular rhabdomyosarcoma. Primary tumors greater than 5 cm in size are an additional risk factor for disease recurrence in the retroperitoneum. Recently, three patients with a mean age of 13.6 years underwent laparoscopic modified RPLND after radical orchiectomy [74]. Their primary testicular masses measured a mean 7.5 cm. The laparoscopic RPLND was performed a mean of 8.6 days after the radical orchiectomy.

A relatively recent report from the Children's Oncology Group Hodgkin's Lymphoma study reviewed 185 patients with Hodgkin's lymphoma with 169 having complete data [75]. Ten of these patients underwent MIS biopsy. An open biopsy was performed in 148 patients, computed tomography-guided core biopsy was performed in five patients, and fine needle aspirations were performed in four patients. There were no staging laparotomies or laparoscopies performed. The diagnostic accuracy was 98.5 % for the open biopsy, 80 % for the core biopsy, 60 % for the thoracoscopic-laparoscopic biopsy and 25 % for the fine needle aspiration.

A number of surgeons have described their experience with thoracoscopy for neurogenic tumors. The group from Great Ormond Street recently described 43 children undergoing thoracoscopic excision of a mediastinal neurogenic tumor [76]. Twenty of these were neuroblastomas, 13 were ganglioneuroblastomas and 10 were ganglioneuromas. Most (86 %) patients were symptomatic with cough, dyspnea, wheezing, spinal compression, dancing eye syndrome and Horner syndrome. Thirty-eight patients underwent an open operation and five underwent a thoracoscopic procedure. Those undergoing thoracoscopy had smaller tumors.

In one institution, a total of 149 cases of neuroblastoma were identified over 17 years [77]. Thirty-seven patients had a tumor located in the thorax. Open thoracotomy was used in 26 cases while the thoracoscopic approach was possible in 11. The authors felt the thoracoscopic approach was effective for this tumor and offered shorter hospitalization and decreased blood loss when compared to open thoracotomy. However, the patients were not matched so that these conclusions may not be valid.

In a multicenter French review of 139 thoracoscopies for either resection or biopsy of pulmonary lesions found the thoracoscopic approach to be safe and effective for the evaluation and resection of solid mediastinal tumors as well as for biopsy and/or resection of metastatic lesions, especially for nephroblastoma [78].

There is no doubt that the minimally invasive approach is beneficial for selected patients with malignancy. It appears especially helpful in patients requiring biopsy or staging. It does not appear to be advantageous for resection of large solid tumors. However, localized tumors which have decreased in size from preoperative chemotherapy are good candidates for the MIS approach. Resection of metastatic nodules in the chest will likely remain the primary utility of thoracoscopy for malignant disease. Patients with neurogenic tumors in the chest are also good candidates, provided that a complete resection can be performed.

Whether the operation is being performed laparoscopically or thoracoscopically, it is important to remember the principles of oncology regarding spillage and port site recurrences. Fortunately, port site recurrences do not appear to be a significant problem for children undergoing the MIS approach for their malignancy.

References

1. Rodgers BM, Moazam F, Talbert JL. Thoracoscopy in children. Ann Surg. 1979;189:176–80.
2. Ryckman FC, Rodgers BM. Thoracoscopy for intrathoracic neoplasia in children. J Pediatr Surg. 1982;17:521–4.
3. Sisler GE. Malignant tumors of the lung: role of video assisted thoracic surgery. Chest Surg Clin N Am. 1993;3:307–17.
4. Kirby TJ, Rice TW. Thoracoscopic lobectomy. Ann Thorac Surg. 1993;56:784–6.
5. Naruke T, Asamura H, Kondo H, et al. Thoracoscopy for staging of lung cancer. Ann Thorac Surg. 1993;56:661–3.
6. Shennib HA, Landreneau R, Mulder DS, et al. Video-assisted thoracoscopic wedge resection of the T1 lung cancer in high-risk patients. Ann Surg. 1993;218:555–60.
7. Krasna MJ, McLaughlin JS. Thoracoscopic lymph node staging for esophageal cancer. Ann Thorac Surg. 1993;56:671–4.
8. Dowling RD, Ferson PF, Landreneau RJ. Thoracoscopic resection of pulmonary metastases. Chest. 1992;102:1450–4.
9. Warshaw AL, Gu ZY, Wittenberg J, et al. Preoperative staging and assessment of resectability of pancreatic cancer. Arch Surg. 1990;125:230–3.
10. Cuschieri A. Laparoscopy for pancreatic cancer: does it benefit the patient? Eur J Surg Oncol. 1988;14:41–4.
11. Fockens P, Huibretse K. Staging of pancreatic and ampullary cancer by endoscopy. Endoscopy. 1993;25:52–7.
12. Spinelli P, DiFelice G. Laparoscopy in abdominal malignancies. Prob Gen Surg. 1991;8:329–47.
13. Watt I, Stewart I, Anderson D, et al. Laparoscopy, ultrasound and computer tomography in cancer of the esophagus and gastric cardia: a prospective comparison for detecting intra–abdominal metastases. Br J Surg. 1989;76:1036–9.
14. Colin-Jones DG, Rosch T, Dittler HJ. Staging of gastric cancer by endoscopy. Endoscopy. 1989;25:34–8.
15. Phillips EH, Franklin M, Carroll BJ, et al. Laparoscopic colectomy. Ann Surg. 1992;216:703–7.
16. Bleday R, Babineau T, Forse RA. Laparoscopic surgery for colon and rectal cancer. Semin Surg Oncol. 1993;9:59–64.
17. Buschbaum HJ, Lifshitz S. Staging and surgical evaluation of ovarian cancer. Semin Oncol. 1984;11:227–37.
18. Varlet F, Stephan JL, Guye E, et al. Laparoscopic radical nephrectomy for unilateral renal cancer in children. Surg Laparosc Endosc Percutan Tech. 2009;19:148–52.
19. Duarte RJ, Dénes FT, Cristofani LM, et al. Laparoscopic nephrectomy for Wilms' tumor after chemotherapy. BJU Int. 2006;98:155–9.
20. Rauth TP, Slone J, Crane G, et al. Laparoscopic nephron-sparing resection of synchronous Wilms' tumors in a case of hyperplastic perilobar nephroblastomatosis. J Pediatr Surg. 2011;46:983–8.
21. Holcomb 3rd GW, Tomita SS, Haase GM, et al. Minimally invasive surgery in children with cancer. Cancer. 1995;76:121–8.
22. Warmann S, Fuchs J, Jesch NK, et al. A prospective study of minimally invasive techniques in pediatric surgical oncology: preliminary report. Med Pediatr Oncol. 2003;40:155–7.
23. Spurbeck WW, Davidoff AM, Lobe TE, et al. Minimally invasive surgery in pediatric cancer patients. Ann Surg Oncol. 2004;11:340–3.

24. Iwanaka T, Arai M, Kawashima H, et al. Endosurgical procedures for pediatric solid tumors. Pediatr Surg Int. 2004;20:39–42.
25. Metzelder ML, Kuebler JF, Shimotakahara A, et al. Role of diagnostic and ablative minimally invasive surgery for pediatric malignancies. Cancer. 2007;109:2343–8.
26. Waldhausen JH, Tapper D, Sawin RS. Minimally invasive surgery and clinical decision-making for pediatric malignancy. Surg Endosc. 2000;14:250–3.
27. Sandoval C, Strom K, Stringel G. Laparoscopy in the management of pediatric intra-abdominal tumors. JSLS. 2004;8:115–8.
28. Chan KW, Lee KH, Tam YH, et al. Minimal invasive surgery in pediatric solid tumors. J Laparoendosc Adv Surg Tech A. 2007;17: 817–20.
29. St. Peter SD, Valusek PA, Hill S, et al. Laparoscopic adrenalectomy in children: a multicenter experience. J Laparoendosc Adv Surg Tech A. 2011;21:647–9.
30. Chui CH, Lee AC. Peritoneal metastases after laparoscopic nephron-sparing surgery for localized Wilms' tumor. J Pediatr Surg. 2011;46:e19–21.
31. Metzelder M, Ure B. Port-site metastasis after laparoscopic biopsy of a posttransplant Burkitt lymphoma in a child. Eur J Pediatr Surg. 2009;19:126–7.
32. Neuhaus SJ, Watson DI. Pneumoperitoneum and peritoneal surface changes: a review. Surg Endosc. 2004;18:1316–22.
33. Ure BM, Suempelmann R, Metzelder MM, et al. Physiological responses to endoscopic surgery in children. Semin Pediatr Surg. 2007;16:217–23.
34. Ure BM, Niewold TA, Bax NMA, et al. Peritoneal, systemic, and distant organ immune responses are reduced by a laparoscopic approach and carbon dioxide vs. air. Surg Endosc. 2002;16:836–42.
35. Jesch NK, Vieten G, Tschernig T, et al. Mini-laparotomy and full laparotomy, but not laparoscopy, alter hepatic macrophage populations in a rat model. Surg Endosc. 2005;19:804–10.
36. Yu Y, Kuebler J, Groos S, et al. Carbon dioxide modifies the morphology and function of mesothelial cells and facilitates transepithelial neuroblastoma cell migration. Pediatr Surg Int. 2010;26:29–36.
37. Kos M, Kuebler JF, Jesch NK, et al. Carbon dioxide differentially affects the cytokine release of macrophage subpopulations exclusively via alteration of extracellular pH. Surg Endosc. 2006;20:570–6.
38. Kuebler JF, Vieten G, Shimotakahara A, et al. Acidification during carbon dioxide pneumoperitoneum is restricted to the gas-exposed peritoneal surface: effects of pressure, gas flow, and additional intraperitoneal fluids. J Laparoendosc Adv Surg Tech A. 2006;16:654–8.
39. Metzelder M, Kuebler JF, Shimotakahara A, et al. CO2 pneumoperitoneum increases survival in mice with polymicrobial peritonitis. Eur J Pediatr Surg. 2008;18:171–6.
40. Iwanaka T, Arya G, Ziegler MM. Mechanism and prevention of port-site tumor recurrence after laparoscopy in a murine model. J Pediatr Surg. 1998;33:457–61.
41. Schmidt AI, Reismann M, Kübler JF, et al. Exposure to carbon dioxide and helium alters in vitro proliferation of pediatric tumor cells. Pediatr Surg Int. 2006;22:72–7.
42. Reismann M, Wehrmann F, Schukfeh N, et al. Carbon dioxide, hypoxia and low pH lead to overexpression of c-myc and HMGB-1 oncogenes in neuroblastoma cells. Eur J Pediatr Surg. 2009;19:224–7.
43. Metzelder M, Kuebler J, Shimotakahara A, et al. CO(2) pneumoperitoneum increases systemic but not local tumor spread after intraperitoneal murine neuroblastoma spillage in mice. Surg Endosc. 2008;22:2648–53.
44. Waldhausen JHT, Shaw DWW, Hall DG, et al. Needle localization for thoracoscopic resection of small pulmonary nodules in children. J Pediatr Surg. 1997;32:1624–5.
45. Martin AE, Chen JY, Muratore CS, et al. Dual localization technique for thoracoscopic resection of lung lesions in children. J Laparoendosc Adv Surg Tech A. 2009;19:S161–4.
46. Pursnani SK, Rausen AR, Contractor S, et al. Combined use of preoperative methylene blue dye and microcoil localization facilitates thoracoscopic wedge resection of indeterminate pulmonary nodules in children. J Laparoendosc Adv Surg Tech A. 2006;16:184187.
47. Gow KW, Saad DF, Koontz C, et al. Minimally invasive thoracoscopic ultrasound for localization of pulmonary nodules in children. J Pediatr Surg. 2008;43:2315–22.
48. Sartoreli KH, Patrick D, Meagher DP. Port-site recurrence after thoracoscopic resection of pulmonary metastasis owing to osteogenic sarcoma. J Pediatr Surg. 1996;31:1443–4.
49. de Lijster MS, Bergevoet RM, van Dalen EC, et al. Minimally invasive surgery versus open surgery for the treatment of solid abdominal and thoracic neoplasms in children. Cochrane Database Sys Rev. 2010;(17):CD008403.
50. Smith TJ, Rothenberg SS, Brooks M, et al. Thoracoscopic surgery in childhood cancer. J Pediatr Hematol Oncol. 2002;24:429–35.
51. Iwanka T, Kawashima H, Uchida H. The laparoscopic approach of neuroblastoma. Semin Pediatr Surg. 2007;16:259–65.
52. de Lagausie P, Berrebi D, Michon J, et al. Laparoscopic adrenal surgery for neuroblastomas in children. J Urol. 2003;170:932–5.
53. Nerli RB, Reddy MN, Guntaka A, et al. Laparoscopic adrenalectomy for adrenal masses in children. J Pediatr Urol. 2011;7:182–6.
54. Sukumar S, Jadhav S, Nair B, et al. Laparoscopic adrenal surgery in children: lessons from a single centre experience. J Minim Access Surg. 2011;7:141–4.
55. deBarros F, Romão RL, de Pinho-Apezzato ML, et al. Laparoscopic adrenalectomy in children for neuroblastoma: report of case series. Surg Laparosc Endosc Percutan Tech. 2012;22:79–81.
56. Leclair MD, de Lagausie P, Becmeur F, et al. Laparoscopic resection of abdominal neuroblastoma. Ann Surg Oncol. 2008;15: 117–24.
57. Yamamoto H, Yoshida M, Sera Y. Laparoscopic surgery for neuroblastoma identified by mass screening. J Pediatr Surg. 1996;31:385–8.
58. Nakajima K, Fukuzawa M, Fukui Y, et al. Laparoscopic resection of mass-screened adrenal neuroblastoma in an 8-month-old infant. Surg Laparosc Endosc. 1997;7:498–500.
59. Tajiri T, Souzaki R, Kinoshita Y, et al. Risks and benefits of ending mass screening for neuroblastoma at 6 months of age in Japan. J Pediatr Surg. 2009;44:2253–7.
60. Komuro H, Makino S, Tahara K. Laparoscopic resection of an adrenal neuroblastoma detected by mass screening that grew in size during the observation period. Surg Endosc. 2000;14:297.
61. Kouch K, Yoshida H, Matsunaga T, et al. Extirpation of mass-screened adrenal neuroblastomas by retroperitoneoscopy. Surg Endosc. 2003;17:1769–72.
62. Tanaka M, Kigasawa H, Kato K, et al. A prospective study of a long-term follow-up of an observation program for neuroblastoma detected by mass screening. Pediatr Blood Cancer. 2010;54:573–8.
63. Kim T, Kim DY, Cho MJ, et al. Use of laparoscopic surgical resection for pediatric malignant solid tumors: a case series. Surg Endosc. 2011;25:1484–8.
64. Duarte RJ, Denes FT, Cristofani LM, et al. Laparoscopic nephrectomy for Wilms' tumor. Expert Rev Anticancer Ther. 2009;9:753–61.
65. Lo CY, Tam PK. Laparoscopic pancreatic resection of an insulinoma in a child. Asian J Surg. 2003;26:43–5.
66. Carricaburu E, Enezian G, Bonnard A, et al. Laparoscopic distal pancreatectomy for Frantz's tumor in a child. Surg Endosc. 2003;17:2028–31.
67. Tsai FJ, Lee JY, Chang YT. Laparoscopic resection of a giant solid pseudopapillary neoplasm of uncinate process of the pancreas in a child. J Laparoendosc Adv Surg Tech A. 2011;21:979–82.
68. Kim T, Kim DY, Cho MJ, et al. Surgery for hepatoblastoma: from laparoscopicresectiontolivertransplantation.Hepatogastroenterology. 2011;58:896–9.

69. Skarsgard ED, Albanese CT. The safety and efficacy of laparoscopic adrenalectomy in children. Arch Surg. 2005;140:905–8.
70. Castilho LN, Castillo OA, Denes FT, et al. Laparoscopic adrenal surgery in children. J Urol. 2002;168:221–4.
71. Steyaert H, Juricic M, Hendrice C, et al. Retroperitoneoscopic approach to the adrenal glands and retroperitoneal tumours in children: where do we stand? Eur J Pediatr Surg. 2003;13:112–5.
72. Theilen TM, Paran TS, Rutigliano D, et al. Experience with retroperitoneoscopy in pediatric surgical oncology. Surg Endosc. 2011;25:2748–55.
73. Pampaloni EL, Valeri A, Mattei R, et al. Initial experience with laparoscopic adrenal surgery in children: is endoscopic surgery recommended and safe for the treatment of adrenocortical neoplasms? Pediatr Med Chir. 2004;26:450–9.
74. Tomaszewski JJ, Sweeney DD, Kavoussi LR, et al. Laparoscopic retroperitoneal lymph node dissection for high-risk pediatric patients with paratesticular rhabdomyosarcoma. J Endourol. 2010;24:31–4.
75. Ehrlich PF, Friedman DL, Schwartz CL. Monitoring diagnostic accuracy and complications. A report from the Children's Oncology Group Hodgkin lymphoma study. Children Oncology Group Hodgkin Lymphoma study section. J Pediatr Surg. 2007;42:788–91.
76. Fraga JC, Aydogdu B, Aufieri R, et al. Surgical treatment for pediatric mediastinal neurogenic tumors. Ann Thorac Surg. 2010;90:413–8.
77. Malek MM, Mollen KP, Kane TD, et al. Thoracic neuroblastoma: a retrospective review of our institutional experience with comparison of the thoracoscopic and open approaches to resection. J Pediatr Surg. 2010;45:1622–6.
78. Guye E, Lardy H, Piolat C, et al. Thoracoscopy and solid tumors in children: a multicenter study. J Laparoendosc Adv Surg Tech A. 2007;17:825–9.