Minimally invasive surgery (MIS) for paediatric renal tumours: a narrative review of the technical aspects

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Background and Objective: Minimally invasive surgery (MIS) has assumed an important role in paediatric surgery and the indications continue to evolve as surgeon expertise and technology improve. Although there are no systematic reviews or clinical trials comparing MIS and open surgery for renal tumours in paediatric patients, there is an ever increasing amount of literature reporting experience with MIS in these cases. The objective of this article is to present a review of the literature evaluating the evolving role of MIS in the management of paediatric renal tumours and details regarding some of the technical aspects.

Methods: PubMed, Scopus and Cochrane databases were searched for articles published during the last ten years [2012–2022]. Search terms included minimally invasive surgery, laparoscopy, paediatric renal tumours, Wilms. We reviewed the literature searching for patient and tumour factors that are relevant in case selection for MIS. The literature was also searched to see if there were any differences in the adherence to oncological principles when performing MIS *vs.* open surgery.

Key Content and Findings: MIS can successfully be performed adhering to oncological principles and there is currently no outcome differences regarding tumour rupture or positive margins. Lymph node sampling remains problematic in both the open and MIS surgery groups, but indocyanine green fluorescent guidance during laparoscopic surgery may offer a further advantage to MIS when it comes to lymph node sampling. MIS has the advantages of decreased post-operative complications, less opioid requirements, improved cosmesis, shorter hospital stay and earlier administration of adjuvant chemotherapy.

Conclusions: With 246 cases of laparoscopic nephrectomies (and an additional 10 robotic procedures) reported in the literature between 2012 and 2022, it is clear that there is a role for MIS in the management of paediatric renal tumours.

Keywords: Minimally invasive surgery (MIS); laparoscopic nephrectomy; paediatric renal tumours; Wilms tumour

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Introduction

Minimally invasive surgery (MIS) has become a cornerstone of treatment in paediatric surgery. Advances in technology, availability of smaller instruments as well as increasing surgeon experience with this technique has led to a continuously expanding role for laparoscopic surgery, including the management of paediatric renal tumours.

The purpose of this article is to present a review of the literature evaluating the evolving role of MIS in the management of paediatric renal tumours and details regarding some of the technical aspects.

Clinical trials are lacking and there is a significant bias in the literature which can potentially be explained by the difference in approach between Children's Oncology Group (COG) and the International Society of Paediatric

Table 1 The search strategy summary

Items	Specification
Date of search	23/01/2022
Databases and other sources searched	PubMed, Scopus, Cochrane
Search terms used	Minimally invasive surgery, laparoscopy, kidney, renal tumours, masses, paediatric and children
Timeframe	2012–2022
Inclusion and exclusion criteria	Inclusion: full text articles and reviews in English. All renal tumours Exclusion: adult population, articles exclusively related to robotic surgery or nephron sparing surgery (NSS). All case reports with only 1 or 2 patients were excluded
Selection process	The articles identified were screened by the first author based on abstracts and relevant articles were selected. The selected articles were reviewed and their reference lists screened for further relevant literature outside the initial search time line

Oncology (SIOP). Although outcomes between the two groups are similar, COG favours upfront resection, whereas SIOP protocols utilise neoadjuvant chemotherapy in most cases. One of the key aspects when considering MIS in paediatric renal tumours is whether the patient has had neoadjuvant chemotherapy (tumour shrinkage and fibrosis of the capsule potentially reducing intra-operative tumour rupture).

Some interesting details regarding technical aspects such as how to improve lymphnode sampling with modification of the surgical technique and new technology such as indocyanide green is also highlighted.

Most authors currently practicing MIS for paediatric renal tumours are of the opinion that the utilisation of this technique will continue to expand and evolve as we gain more experience, especially in larger centres (1-3).

Background

Wilms tumours represent one of the most common malignancies of childhood (6%) and is by far the most common renal tumour (95%) encountered in the paediatric population (4). The management of Wilms tumour is one of the great success stories of modern medicine with an overall survival (OS) of more than 90% (5). This illustrates the power of collaboration, in improving patient outcomes. Craft and Pearson (6) are credited with the coining of the phrase 'cure at any cost to cure at least cost' referring to their article about the improvements in chemotherapy for childhood cancers in 1989 and this certainly holds true for the surgical interventions utilised today.

As a result, the focus of treatment has shifted to minimising the long-term effects of multi-modal therapy, including surgery, without compromising the oncological principles of clear resection margins, no intra-operative spill and adequate lymph node sampling. We present the following article in accordance with the Narrative Review reporting checklist (available at https://ls.amegroups.com/article/view/10.21037/ls-22-28/rc).

Methods

Scopus, PubMed and Cochrane databases were searched. The search was limited to the last ten years including articles from January 2012 to January 2022 (*Table 1*).

Keywords used including MeSH terms were minimally invasive surgery, laparoscopy, kidney, renal tumours, masses, paediatric and children.

Only full text articles in English corresponding to the relevant search terms were included. All renal tumours were included.

Exclusion criteria included articles referring to the adult population, articles exclusively related to robotic surgery or nephron sparing surgery (NSS). All case reports with only 1 or 2 patients were excluded.

The articles identified were screened based on abstracts and relevant articles were selected. The selected articles were reviewed and their reference lists screened for further relevant literature outside the initial search time line.

A total of 272 cases were identified. A breakdown of the cases is given in *Table 2*. *Table 3* details the results of papers describing MIS tumour nephrectomy.

Laparoscopic tumour nephrectomy (7,20)

The surgical approach is transperitoneal with a 12 mm port

Table 2 Breakdown of minimally invasive nephrectomy cases identified in the literature search

MIS technique	Number
Laparoscopic nephrectomies	246
Laparoscopic converted to open	16
Robotic nephrectomies	10
Total completed with MIS	256

MIS, minimally invasive surgery.

inserted in an infraumbilical position by Hasson technique.

Two or three other 5 mm ports are used with one in the epigastric area and one in the iliac area. The port in the iliac region should be within the proposed incision site for specimen retrieval. One further port is sited to facilitate retraction of the duodenum for right sided tumours, or the descending colon for left sided tumours.

Following reflection of the colon and exposure of Gerota's fascia, lymph node sampling is performed in the relevant draining nodal basins. On the left this includes the para-aortic area and on the right, the paracaval and interaortocaval areas. Following this step, nodes should be removed when they are seen during the dissection that follows.

Once adequate sampling has been performed, the hilar vessels are ligated with sutures. Ligasure electrocautery or Hem-o-lok clips, and then divided. Dissection of the tumour and remaining kidney is then performed in a tissue plane outside of Gerota's fascia. This is usually achieved with Ligasure or hook electrocautery.

Dissection can be facilitated by using transcutaneous retraction sutures and a 10 cm × 10 cm swab placed deep to the tumour. This latter iteration helps to elevate the kidney to provide access for dissection.

Once the specimen is free it should be placed within a retrieval bag. The iliac incision is then extended and the specimen removed.

After removal of the specimen the bowel should be replaced in its usual orientation and the wounds closed.

Points to note in respect of technical details:

- ❖ MIS nephrectomy should be performed by oncology surgeons with expert skills in MIS;
- ❖ Operative technique should be meticulous and there should be no possibility of intra-operative tumour rupture;
- ❖ Lymph node sampling can be difficult but is better performed prior to hilar dissection and renal mobilisation. Surgeons should aim for removal of the recommended number of nodes based on the treatment protocol being used;
- ❖ SIOP or COG protocolised guidelines for patient selection should be used to identify which tumours are suitable for MIS resection. In centres with a high volume of MIS tumour nephrectomies, these guidelines can be expanded but this should be done in discussion with national groups;
- ❖ Conversion to open surgery is a sensible decision making process in the context of MIS oncology surgery. It should not be viewed as a complication.

Discussion

Minimally invasive surgical techniques have expanded rapidly over the last 20 years and have been incorporated into various areas of paediatric surgery including the definitive treatment of paediatric renal tumours in carefully selected cases. We agree with Galazka *et al.*'s conclusion that 'Although existing data do not allow the recommendation of the use of MIS for all indications, this technique should currently be regarded as a standard of care in several areas of paediatric oncology' (21).

We acknowledge that one of the limitations of any narrative review is the likely publication bias towards positive results as authors and journals are often hesitant to publish results negative results.

However, surgeons should be encouraged to continue publishing their experience with MIS in a standardised way because it is only through this collaborative effort that we will be able gather enough evidence to offer patients the best treatment options.

Abdelhafeez *et al.* proposed reporting guidelines for MIS in paediatric renal tumours and this is perhaps a way forward to enable more effective comparison of the literature (22).

Critical questions regarding MIS in paediatric renal tumours include:

(I) What patient and tumour factors influence successful case selection?

(II) Can high fidelity oncological surgery be successfully carried out with MIS techniques? (negative margins, zero intra-operative tumour rupture and adequate lymph node sampling).

(III) How does MIS impact on OS, event free survival, and the incidence of recurrence?

Table 3 detailing results of publications on MIS in paediatric renal tumours

Article	Lap (N)	Robotic (N)	Publication year	Age	Tumour size/volume	Neoadjuvant	LOS (days)	Operative complications	Follow up	Survival
A single centre matched pair series comparing minimally invasive and open (Gavens) (7)	14	0	2020	37 [2–73] months	119 [34–759] mL	13/14	4 *vs.* 4	2 lymphatic leak and ICU admission for airway oedema	30 [6–44] months	Not recorded
Comparing oncologic outcomes after minimally invasive and open surgery for pediatric neuroblastoma and Wilms tumor (Ezekian) (8)	27	8	2018	<1 to over 5 yr	<5 to > 15 cm	Not recorded	5 *vs.* 6	Not recorded	Not recorded	3 yr OS, 88%
Comparison between laparoscopic and open radical nephrectomy for the treatment of primary renal tumors in children: single-center experience over a 5-year period (Romao) (9)	13	0	2014	4 yr (2 months to 17 yr)	6.95±1.88 cm (3.1–9 cm)	2/13	2.9 *vs.* 5.9	Incision hernia in each group (incisional hernia in MIS was at the Pfannenstiel incision); 1 in Open group post op small bowel obstruction	18 months	Not recorded
Laparoscopic nephrectomy in children with Wilms tumor. Considerations after 10 years of experience (Scuderi) (10)	7 (+2 converted)	0	2019	5.01 (1.59–9.15) yr	7.75 (1.3–3.5) cm	4/9	7 [5–8] *vs.* 7 [5–14]	Open group subacute bowel obstruction (no mention of surgery or not to resolve). One with pancreatitis. None in the MIS group	Not recorded	100% but no time frame on follow up for this figure
Feasibility of laparoscopic tumour nephrectomy in children (Harris) (11)	14 (+3 converted)	0	2018	2.5 [0–10] yr	163 [50–671] mL	14 (plus 3)	3 *vs.* 5	4 *vs.* 5 MIS injury to mesocolon colon ischemia; post op ileus; open diaphragm injury pneumonia urinary retention; one intra operative death in open group	98 [10–165] months	Not recorded
Laparoscopic Radical Nephrectomy of Wilms' Tumor and Renal Cancer in Children: Preliminary Experience from a Two-Center Study in China (Liu) (12)	7	0	2015	4.3 (1.5–10) yr	4.5–10 cm	3/7	8.5 [6–11] including first cycle of pre-op chemo	None	1.9±1.5 (0.3–2.9) yr	6/7 (one lost not follow up) at follow up
An analysis on the technical feasibility of laparoscopic excision of intra-abdominal tumors observing the principles of safe removal (Sharma) (13)	13	0	2020	34.7±14.9 months	1,068.1±366.8 cm^3	13	5.6±1.6 days (chemo started prior to discharge)	One port site recurrence	38.3±12.2 months (12–64 months)	100% at follow up
Laparoscopic approach for Wilms tumor (Cabezalí Barbancho) (14)	4	0	2014	3 yr and 7 months (23 months to 6 yr)	446.55 cm^3 (150.7 to 502.6 cm^3)	4/4	3 [2–4]	None	3 yr and 6 months	Not recorded
Laparoscopic nephrectomy for Wilms' tumor: Can we expand on the current SIOP criteria? (Burnard) (15)	18+ (2 converted)	0	2018	3.9 (0.6–15.1) yr	395 cm^3 (5–795 cm^3)	17/20	4 [2–9]	1 diathermy injury to colon. 1 Post op small bowel obstruction but the patient had a wedge resection on contralateral side via open surgery and obstruction was at the level of laparotomy scar) open group2 bleeding and 1 ureteric injury	1.6 (0.2–5.7) yr	100% at follow up
Laparoscopic total nephrectomy for Wilms tumor: Towards new standards of care (Flores) (16)	12+ (2 converted)	0	2018	20 days to 8 yr and 5 months	71.5 cc [7–169] cc	12 (+2)	2 (1.5–3.5)	None	32 months	100% at follow up
Laparoscopic treatment of renal cancer in children: A multicentric study and review of oncologic and surgical complications (Varlet) (17)	16 (+1 converted)	0	2014	26 months (5 months to 11 yr)	Up to 8 cm	16/17	3 [2–10]	1 ileal perforation repaired laparoscopically	42 [12–77] months	94% at follow up
Minimally invasive surgery for unilateral Wilms tumors: Multicenter retrospective analysis of 50 transperitoneal laparoscopic total nephrectomies (Bouty) (1)	44 (+6 converted)	0	2020	38 [6–181] months	673 [18–3,331] mL	44 (+6)	4 [2–8]	3 grade one Clavien-Dindo; AKI treated with diuretics; Flank oedema that settled with catheter placement. Pyrexia of unknown origin treated with antibiotics	34 [2–138] months	94% EFS at 3 yr
Patient selection and technical aspects for laparoscopic nephrectomy in Wilms tumor (Schmidt) (18)	9	0	2019	24 (12.0–57.5) months	74 [15–207] mL	9/9	Not recorded	None	48 [24–78] months	100%
Minimally invasive nephrectomy for Wilms tumors in children - data from SIOP 2001 (Warmann) (2)	24	0	2014	40.35 (14.3–65.4) months	73 (3.8–776) mL	24/24	Not recorded	1 splenic injury—laparoscopic splenectomy	47 [2–114] months	EFS 23/24, OS 100% at follow up
Videolaparoscopic radical nephrectomy after chemotherapy in the treatment of Wilms' tumor: Long-term results of a pioneer group (Duarte) (19)	24	2	2017	38.04±23.37 [10–93] months	Largest diameter was ≤10% of patients height	24	2.3 days	2 with prolonged ileus (not defined); one intra op transfusion due to pre-op anaemia. Umbilical hernia at port site that required surgical correction	6.65 yr	5 yr EFS 91.6%

yr, year; m, month; LOS, length of stay; OS, overall survival; MIS, minimally invasive surgery; AKI, acute kidney injury; EFS, event-free survival.

What patient and tumour factors influence successful case selection?

Criteria for MIS surgery in paediatric renal tumours is not clearly defined and continue to expand.

Collaborative and multi-modal treatment advances in childhood cancer have largely been accomplished through the guidance of steering committees such as COG, SIOP, German Paediatric Oncology Society (GPOH) and the Japanese Paediatric Liver Tumour Study Group (JPLT) The SIOP Renal Tumour Study Group RTSG 2016 Umbrella guidelines details the indications and contra indications for laparoscopic surgery in Wilms tumour (23).

Indications for MIS in the surgical treatment of Wilms tumour:

(I) Resection must adhere to oncological principles and include lymph node sampling.
(II) MIS is appropriate for small, central tumours with rim of "normal" renal tissue.
(III) Extraction of the specimen in a bag without morcellation through an adequate abdominal wall incision is mandatory, not only to control the risk of dissemination but also to ensure adequate histopathological staging.
(IV) If feasible, NSS should be preferred over MIS, even if an open approach is needed.

Contra-indications for MIS in the surgical treatment of Wilms tumour:

(I) Tumour infiltrating extra renal structures or extended beyond the ipsilateral border of spinal column.
(II) Thrombus in the renal vein or vena cava.
(III) Peripheral location if NSS is not deemed feasible.
(IV) Tumour without any response to chemotherapy (risk of tumour rupture).
(V) Little or no experience in laparoscopic nephrectomy.

Although level one evidence in the form of randomised control trials is lacking there are multicentre (1,17) and multinational (2) reports in the literature.

Several recent articles have questioned whether the current Umbrella guidelines can be expanded, specifically with regards to the extension of the tumour beyond the ipsilateral border of the spinal column, as numerous authors have reported successfully removing tumours that extended beyond the ipsilateral border of the spine, without compromising oncological principles or affecting outcome (3,7,15).

Caution should be exercised when considering cases that fall outside the current proposed criteria and surgeon experience and strict audit and follow-up is mandatory.

Interestingly, there is no specified tumour volumes or largest diameter in the guidelines. Literature shows that the median tumour volume (24) increased with increasing surgeon experience without a change in outcome, and 32% of the cases reported in Bouty *et al.*'s series extended beyond the lateral border of the spinal column (1).

There is also no standardised method for reporting this, making comparison of the literature very difficult. Maximum tumour dimension, contralateral kidney volume ratio and patient height have all been utilised.

Other factors to take into account include syndromes associated with a high risk of bilateral tumours where NSS would be a high priority, pre-operative rupture of the tumour, and whether pre-operative chemotherapy has been administered.

There are many variables that influences the feasibility of MIS including size of the patient, intra-abdominal space achieved by a pneumoperitoneum, degree of bowel dilatation, favourable position of the hilum for vascular control, position of the tumour and surgical experience. Case selection should take into account the size of the tumour but ultimately case selection will rely on a fine interplay between all of these patient, tumour and surgeon factors.

Can high fidelity oncological surgery be successfully carried out with MIS techniques? (negative margins, zero intra-operative tumour rupture and adequate lymph node sampling)

Because of the high success rate that has been achieved with the combined approach of chemotherapy (25), open surgery and radiotherapy in selected cases, there is an understandable concern about compromising these standards with MIS.

The incidence of positive margins reported in the literature is similar for open and MIS (2,3,9-11,17,19,21).

Tumour rupture is one of the feared complications of surgery as this upstages the patient and necessitates more intensive adjuvant treatment. Opponents of MIS have cited higher risk of tumour rupture with MIS. The difference in protocols between COG and SIOP potentially have implications for the acceptance and implementation of MIS. Some surgeons would consider the lack of pre-operative chemo as a relative contra-indication for MIS (7).

Risk of tumour rupture was not found to be increased during our review of the literature (2,7,8,17,19).

Tumour rupture can unfortunately occur during both types of surgeries and the rate of rupture with open surgery in the SIOP-9 protocol was 2.8% and in the NWTS-4 protocol where patients were treated with upfront open surgery the rupture rate was 11% (26).

Lymph node sampling is generally considered an important aspect of accurate staging especially in Wilms tumours, however the exact number of lymph nodes for adequate sampling, as well as the influence on recurrence and survival is debated. Shamberger *et al.*'s seminal article in 1999 suggests that risk of relapse is 6 times higher if no nodes were sampled (27). Kieran *et al.* reported no difference in 5-year survival relating to the number of lymph nodes sampled (28); but Zhuge *et al.*, similar to Shamberger *et al.*, found a significant decrease in 5-year survival when no nodes where sampled (29).

More than six nodes are often quoted as the number to be harvested, but in both surgical groups this seems to be problematic with up to 88% of patients undergoing open surgery having inadequate lymph node sampling in the SIOP WT 2001 subgroup and COG also reporting inadequate sampling in up to 10% of their open surgery group (7). Ezekian *et al.* reported that lymph nodes were sampled more frequently in open group but this did not reach statistical significance (8).

Some surgeons have also refined their technique of lymph node sampling, dissecting the lymph nodes first, prior to removing the specimen in an attempt to increase the lymph node yield and improve technical feasibility (11,18).

Godzinski *et al.* commented on an observation from analysis of the SIOP93-01 data which showed that lymph nodes were only positive in rare cases if the initial tumour volume was <318 mL, and Varlet noted that: "extensive lymph node sampling is probably not needed as no tumours had distal positive nodes when the hilar nodes were negative." (17,30).

Lymph node sampling remains an area of concern where ongoing research is taking place to refine the indications, number, extent and technique that will provide reliable and accurate information.

Another technique that may prove critical to improving MIS lymph node yield is the use of image guided surgery for example indocyanine green fluorescent technology (31).

How does MIS impact on OS, event free survival and the incidence of recurrence?

For any technique to be advisable as a substitute for replacing the quoted gold standard of open surgery there must be comparable oncological outcomes and an additional advantage.

The oncological outcomes can be judged by relapse rate and OS. Post operative complications is also an important factor.

The risk of local recurrence in Wilms tumours utilising MIS is reported as 3.8–5.9% (1,32). In trials looking at the recurrence rates utilising open surgery the SIOP-9 data had a relative risk (RR) of 2.7% and the NWTS-4 had a RR of 4.3% (26). These rates are comparable between the two surgical approaches (12,19).

The majority of recurrences are thought to occur within 8.5 months after surgery and mainly within the first two years (32).

OS between the two approaches has been comparable in most articles reported in the literature (1,2,8,16,17,19).

Post-surgical complications

Review of sequential National Wilms Tumor Studies (NWTS) revealed an overall incidence of surgical complications of 19.8% and 12.7% in NWTS-3 and NWTS-4, respectively. In NWTS-3 the most common complication was intestinal obstruction which occurred in almost 7% of patients. This was followed by extensive intraoperative haemorrhage (6%) defined as blood loss exceeding 50 mL/kg. Intraoperative injuries to other visceral organs (including intestine, liver, and spleen) and vascular structures occurred in about 2% of case. In NWTS-4 intestinal obstruction was a gain the most common complication (5.1%), followed by extensive haemorrhage (1.9%), wound infection (1.9%) and vascular injury (1.5%) (4).

The only report on bowel obstruction found was related to a case that had undergone an open wedge biopsy of the contralateral kidney prior to MIS. The level if obstruction was found at the laparotomy scar (15).

No other reports of bowel obstruction or intussusception after MIS could be found in the literature (26).

Only a single report of a port site recurrence was found, and this was successfully managed with excision of the port tract (13).

Further details regarding complications are available in the table and include splenic injury, bowel injury, and a lymphatic leak. The authors recommend that there should be a standardised why of reporting these complications to facilitate accurate comparison.

Complications can occur in both groups and are comparable in incidence but also unique in nature and related to the type of surgery. Other factors influence complications, such as histological subtype and tumour size and location as well a certain anatomical considerations and patient size.

We share the view of many authors that conversion to open should not be considered as a complication but rather a sound operative decision in the best interest of the patient.

Advantages of MIS include decreased post operative hospital stay, quicker resolution of post operative ileus, earlier mobilisation, less narcotic requirements, better cosmesis, decreased risk of wound infection and incisional hernias, earlier opportunity to give post op chemo due to more rapid recovery and better visualisation with magnification although there is loss of a degree of haptic feedback (11-13,33).

Disadvantages of MIS include that smaller body size of children leading to restricted working space. Visceral injury during port placement can happen during MIS. The surgeon may still need a fairly large incision to remove the tumour which may negate some of the benefit of MIS. The lack of surgeon experience and a steep learning curve are disadvantages that should certainly be taken into careful consideration (34). Anaesthetic difficulties including higher airway pressures and hypercarbia should be taken into account. Tumour spillage and incomplete resection as well as inadequate lymph node sampling is a risk during both open and MIS.

Conclusions

In carefully selected cases of paediatric renal tumours, MIS is the best surgical option.

Patient, tumour and surgeon factors need to be evaluated carefully in order to optimise successful case selection.

MIS has shown comparable oncological outcomes and an improved post operative course. Lymph node sampling remains problematic in both the open and MIS surgery groups, but indocyanine green fluorescent guidance during laparoscopic surgery may offer a further advantage to MIS when it comes to lymph node sampling.

We acknowledge that there is a bias towards MIS been applied to smaller more favourable tumours, but argue that these are exactly the type of tumours that are suitable for a newly evolving technique and as experience expands and outcomes remain favourable this bias will self-correct. Open and MIS surgery both have a role in the management of paediatric renal tumours and should not be viewed as competing entities but rather complimentary techniques that should be applied to the correct patient population for optimal benefit.

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