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Review Article

Current Surgical Role in The Management of Pediatric Renal Tumors

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Abstract **Pediatric renal tumors (PRT) belong to a group of cancers arising in early human life called the embryonal tumors. Wilms tumor is the predominant pathologic type, followed by rare entities including clear cell sarcoma of the kidney, malignant rhabdoid tumor of the kidney and pediatric renal cell carcinoma. Although there is some controversy regarding the optimal treatment sequence, surgery is usually the definitive treatment and radical nephrectomy remains the standard surgical option for unilateral tumors. Apart from tumor removal, data from lymph node sampling and recording of intraoperative spills are important for surgical staging. Bilateral PRT and complicated situations such as tumors in young infants, tumors with intravenous thrombus and concomitant intraabdominal metastases indicate upfront chemotherapy should be applied first followed by surgery. Nephron-sparing surgery in bilateral PRT is a surgically challenging situation requiring anatomical planning and meticulous care. In general, PRT has a good outcome unless there is metastasis, intraoperative rupture or unfavorable histopathological features at the diagnosis. The five-year overall survival in cases of non-metastatic Wilms tumor has reached 100% in large trial reports. However, outcomes in low-income countries remain poor because of late diagnosis and toxicity from treatment. Good surgical technique potentially reduces operative complications, especially spills. This review focuses on the current surgical role in the treatment of PRC.**

Keywords: **Wilms tumor, Renal tumor, Nephrectomy, Nephron-sparing surgery**

Introduction

Although pediatric renal cancer is an uncommon human malignancy comprising less than 1% of the whole pie of human cancers, it accounts for 6-9% of all childhood cancers[1,2]. The age-standardized incidence rates (ASR) of renal cancers in European countries and America have been reported as 8.8 and 8.29 new cases/million person-years, respectively[1-3]. In Thailand, a study from Thai Pediatric Oncology Group (TPOG) reported an increase in the pediatric renal cancer ASR from 2.5/million person-years during the decade 1990-2000 to 4.0/million person-years during 2001-2010[4]. Nephroblastoma or Wilms' tumor (WT) is the most common pathological diagnosis in this group, accounting for more than 90% of all cases[5]. The tumor's name was derived from Max Wilms, a German surgeon who published a monograph on 'Mixed tumors of the kidney' in 1899[6]. The other differential diagnoses include clear cell sarcoma of the kidney (CCSK), malignant rhabdoid tumor of the kidney (MRTK) and pediatric renal cell carcinoma (PRCC)[7]. While the majority of WT and CCSK tumors are diagnosed before

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5 years of age[8], MRTK and PRCC tumors are more occur in older children[9,10].

The most common presentation of WT is a palpable abdominal mass in an otherwise clinically well infant[5]. Hematuria is found in 30% of cases while other symptoms such as abdominal discomfort, fever, anemia and hypertension are occasionally found[11, 12]. About 10% of WT cases already have metastatic disease, usually hematogenous metastasis to the lungs and liver. Approximately 5-10% of WT cases have associated genetic syndromes, such as WAGR (WT, aniridia, genitourinary anomalies and mental retardation), Denys-Drask syndrome or Beckwith-Wiedemann syndrome[13]. These patients with syndromic predisposition have a higher chance of bilateral diseases and usually present at a younger age[14]. Ultrasound is the first line investigation in evaluating pediatric renal tumors, and is also the most reliable method for evaluating tumor thrombus within the renal vein and inferior vena cava[15,16]. Either computerized tomography (CT) or magnetic resonance imaging (MRI) is usually requested for more information regarding tumor extent, contralateral kidney evaluation and relationship of the primary tumor to surrounding structures. Moreover, CT and MRI give more information about nephrogenic rests, which is predispose towards renal parenchymal pathology. On contrast-enhanced CT, a so-called claw or bird beak sign is a characteristic radiological feature of WT (Figure 1)[15]. Currently, there are no known diagnostic serum markers for any pediatric renal cancers.

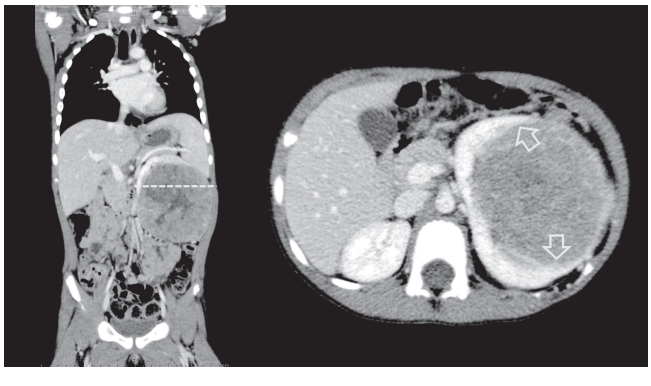


Figure 1 CT scan showing left-side Wilms tumor in a 4-year-old boy. Yellow arrows depict a bird beak signs which discriminate an intrarenal mass from renal parenchymal compression from an extrarenal lesion.

The current management of WT and other non-WT renal tumors is a multidisciplinary approach, comprising surgery, chemotherapy and external irradiation. The surgical role is either primary nephrectomy or delayed nephrectomy after upfront chemotherapy[16]. An open biopsy is rarely indicated unless upfront chemotherapy is planned and transcutaneous imaging-guided biopsy could not give a conclusive histological diagnosis[10]. The prognosis of WT is generally good, especially in the countries participating in large trials where 5-year survival has been reported at over 80%. Apart from stage and histological subtypes, the particular surgical technique used for a nephrectomy can influence longterm outcomes as relapse and residual disease are 2 main factors associated with poor outcome of WT[11]. CCSK and MRTK are more aggressive tumors and generally have an inferior prognosis compared to WT.

This review focuses on the standard of care in surgery of pediatric renal tumors, especially WT. Other related topics that are crucial in understanding surgical strategies such as tumor biology are also addressed.

Pathology and Biology of Pediatric Renal Cancer

The typical WT contains 3 histopathological elements: blastemals, stromal and epithelial tubules. Ninety percent of WTs are classified as favorable histology while 10% have anaplasia (unfavorable histology)[17,18]. The latter diagnosis is found mainly in older children which explains the poorer prognosis of WT in the older age group. Multifocal and extrarenal anaplasia is regarded as 'diffuse anaplasia' which has the worst prognosis among WTs. The classic histopathology of CCSK consists of a 'chicken wire' pattern of small blood vessels among nests of ovoid, epithelioid, or spindle cells[19] while MRTK consists of sheets of cells showing nuclear polymorphism and open cesicular nuclei, prominent nucleoli, and scattered hyaline eosinophilic cytoplasm[20]. The standard surgical staging of WT is shown in the Table 1.

WT belongs to a group of pediatric tumors arising in developing embryonal tissue which are called embryonal tumors. Germline mutations of WT1 on chromosome 11q13 result in defective metanephric mesenchymal differentiation and nephrogenic rests

Table 1 Staging system of pediatric renal tumors according to the International Society of Pediatric Oncology with some comments on comparison with the National Wilms Tumor Study (NWTS) staging

Stage I	A: Tumor is limited to kidney and is completely resected (resection margin clear)
	B: The tumor may be protruding into the pelvis and protruding into the ureter (but not infiltrating the walls)
	C: The vessels of the renal sinus are not involved (Comment: The NWTS allows renal sinus vessel involvement not more than 2 millimeters)
	D: Intrarenal vessel involvement may be present
Stage II	A: The tumor extends beyond the kidney or penetrates through the renal capsule and/or fibrous pseudocapsule into perirenal fat but is completely resected (resection margin clear)
	B: The tumor infiltrates the renal sinus and/or invades blood and lymphatic vessels outside the renal parenchyma but is completely resected
	C: The tumor infiltrates adjacent organs or vena cava but is completely resected
Stage III	A: Incomplete excision of the tumor, which extends beyond the resection margins
	B: Any abdominal lymph nodes involvement
	C: Tumor rupture before or intraoperatively
	D: The tumor penetrates through the peritoneal surface
	E: Tumor thrombi present at resection margins of vessels or ureter, transected or removed by surgeon
	F: The tumor has been surgically biopsied (wedge biopsy) prior to preoperative chemotherapy or surgery
	Comment: This category is similarly defined as 'Residual nonhematogenous sprading is present and confined to abdomen' by NWTS.
Stage IV	Hematogenous metastasis (lung, liver, bone, brain, etc.) or lymph node metastases outside the abdominopelvic region
Stage V	Bilateral renal tumor at diagnosis

which is a predisposing pathology of WT. Somatic mutations of CTNNB1 areconcomitantlydetectedin 50-75% of tumor samples with WT1 mutations[21,22]. Defective WT1 expression and CTNNB1 mutation leads to pathologic nuclear accumulation of beta-catenin protein, activation of Wnt signaling and tumorigenesis[23]. This WT1/CTNNB1 molecular subtype is associated with nephrogenic rests [21]. Other candidate genes for WT include WTX on chromosome Xq11.1[24], IGF2 on chromosome 11p15 and POU6F2 on chromosome 7p. Loss of heterozygosity at chromosome 1p and 16q is associated with poorer outcome and are used as indicators for more intensive therapy in some protocols.

The recent study of a molecular marker for CCSK has discovered in-frame internal tandem duplication of exon 15 of BCOR as the molecular signature of the tumor. Another mutually exclusive genetic pathology with BCOR duplication in CCSK is YWHAE-NUTM2 fusion[19]. Germline mutations of SMARCB1, a member of the SW1/SNF chromatin remodelling complex, are predisposing lesions of MRTK[20]. Reciprocal fusion of PRCC-TFE3 is a predominant genetic alteration in PRCC[25]. Some of these genetic markers have been studied in terms of therapeutic targets of small molecules or antibody therapy.

Multidisciplinary Care of Pediatric Renal Cancers

As with other pediatric solid tumors, care of patients with pediatric renal cancers requires a multidisciplinary approach. Currently, there are 2 main stream algorithms used in the management of WT, one from the International Society of Pediatric Oncology (SIOP) in Europe and the other from the National Wilms Tumor Study (NWTS) of the Children's Oncology Group (COG) in the US. While the SIOP promotes upfront chemotherapy before a nephrectomy (SIOP WT 2001) with an aim to reduce intraoperative spillage, the COG prefers a primary nephrectomy unless the tumor is considered unresectable. Major criticisms of the SIOP regimen involve the potential of inappropriate chemotherapy being given to non-Wilms tumor cases due to limited sampling of tissue from pre-treatment biopsy[26] and unreliable surgical staging when surgery is performed after the tumor has shrunk. According to the TPOG regimen for WT, chemotherapy can be given upfront or after a nephrectomy. In Songklanagarind Hospital, we have found that the risk of intraoperative rupture increases when the tumor size is larger than 10 centimeters[27]. Following that study, we chose to give pre-operative chemotherapy in WT cases with large tumor volume after an image-

guided biopsy. In order to avoid toxicity from high-dose chemotherapy and because there is a higher incidence of non-WT in the age group less than 6 months, immediate surgery after diagnosis is preferable.

The basic chemotherapeutic regimen for WT consists of vincristine and dactinomycin (regimen E, ThaiPOG-WT-1301). Patients with stage I-II and favorable histology receive 18 weeks of regimen E while those in stage I-II with focal anaplasia, stage I with diffuse anaplasia and stage III-IV receive 24 weeks of this basic combination plus doxorubicin (regimen D or TPOG-WT-1302). WT stages II-IV with diffuse anaplasia receive a combination of vincristine, doxorubicin, cyclophosphamide and etoposide (regimen I or TPOG-WT-1303). In patients with bilateral disease, carboplatin is also added to the protocol. Radiation therapy is given to stage III WT, either indicated by intraoperative spill or preoperative rupture or peritoneal seeding. Because the extent of radiation application depends on the area of tumor contamination, a careful record of operative findings is mandatory. Recent data from COG protocol AREN0532 suggests that patients in the 'very low risk' category of WT, referring to patients with stage I WT with favorable histology, tumor weight less than 550 grams and age at diagnosis less than 2 years, may receive a radical nephrectomy without adjuvant chemotherapy[28].

Surgical Management

There are 4 types of surgery for pediatric renal cancers: primary nephrectomy, delayed nephrectomy following neoadjuvant treatment, metastasectomy and emergency surgery in cases of life-threatening conditions such as rupture or hemorrhage. In an elective nephrectomy for a unilateral tumor, care should be taken to evaluate the contralateral kidney for synchronous disease and other pathologies such as nephrogenic rests. A coagulation study should be performed in all cases as acquired von Willebrand disease can be found in 8% of WTs and the condition may cause significant bleeding until the renal vessels are completely ligated[29,30]. Systemic hypertension can be a paraneoplastic manifestation caused by renin production or renovascular involvement of the tumor. Evaluation of the renal vein and vena cava for possible tumor thrombus by ultrasonography is essential as CT is less sensitive in this situation. Intraoperative ultrasound may add information regarding the intrarenal extent of a tumor and its thrombus[31].

In a non-complicated unilateral WT, the objectives of surgery are removal of the affected kidney together with the renal capsules, vessels and ureter of the ipsilateral side, and gathering information for surgical staging via lymph node sampling (Table 2). The preferred approach is transperitoneal and our preferred incision is a long midline incision. Even if

Table 2 Principles of nephrectomy for pediatric renal cancers

1. Standard radical nephrectomy (primary or after chemotherapy) in a unilateral tumor
   - Abdominal approach through a transverse curvilinear incision or a long midline incision
   - Thorough exploration, looking for peritoneal seeding, capsular leak and any thrombus within the renal vein, vena cava or ureter.
   - Right-side tumor may lie close to the liver surface, but rarely adheres or invades the parenchyma, while a left-side tumor may lie close to the pancreatic tail and spleen
   - Vascular control first, especially in a large tumors
   - Adequate mobilization of the ipsilateral colon, liver (right-side), spleen and pancreas (left-side) to the median help expose the tumor
   - Keep the dissection outside the renal capsule. Avoid tumor rupture
   - The ureter should be followed down to the ureterovesical junction
   - In cases of adherence, organ removal is rarely required
   - Lymph nodes sampling is mandatory for staging
   - Any leaks and spills MUST be clearly recorded
   - Drainage is optional
2. Nephron sparing surgery (indicated in bilateral diseases or a single renal unit)
   - Preoperative chemotherapy reduces surgical risk
   - Anatomical and functional planning before the procedure
   - Intraoperative ultrasound helps delineate the surgical margins
   - Warm ischemic time is only 30 minutes. Avoiding ischemia or reducing the temperature may help preserve the nephrons.
   - Adequate hemostasis
   - Drainage is mandatory

the tumor size is large, the "vascular control first" approach is possible and amenable to reducing intraoperative major hemorrhage, hence allowing "slow but safe" mobilization and low chance of intraoperative rupture. The midline vascular looping that has been widely used in renal trauma surgery can be applied well in this situation (Figure 2). After vascular control, the colon is mobilized from the anterior surface of the kidney A large left-sided tumor can adhere to the spleen, pancreatic tail and diaphragm. A right-sided mass may look inseparable from the posterior surface of the liver on CT scan, however direct invasion to the liver is uncommon. If the tumor adheres to the diaphragm, resection of a small portion may prevent tumor rupture[32]. However, resection of other adjacent organs should be avoided as the additional procedure may complicate the post-operative course. Mobilization of the kidney is performed outside the Gerota's fascia. After full renal mobilization, the ureter is followed down to the ureterovesical junction, then truncated and removed with the specimen. If the renal capsule is accidentally rupture during the operation, spillage should be controlled as quickly as possible and the extent of the contamination from the spill should be clearly noted as this will be necessary to plan the locoregional adjuvant radiotherapy. For complete staging, lymph nodes around the renal hilum and along the course of the renal vessel on the same side (peri-aortic on the left and pericaval on the right) should be sampled for histopathology. A recent analysis from the COG suggested that at least 7 lymph nodes should be sampled for optimal staging accuracy[33]. Care should be taken to close all mesocolic defects before closure of the abdomen. In general, a drain is not necessary unless there remains oozing from a raw surface. Post-operative care focuses on hemodynamic monitoring, adequate hydration, pain control and early enteral feeding resumption. Nephron-sparing surgery (partial nephrectomy) is not a current standard of care in unilateral WT because of an unacceptably high incidence of positive resection margins although survival outcomes might not be compromised. Unclear oncological benefits and technical difficulty makes nephron sparing surgery unpopular at the moment[34]. However, nephron sparing surgery is suggested in unilateral cases with genetic syndrome, nephrogenic rests or preoperative renal dysfunction[35]. A recent long-term split-renal function study after partial nephrectomy suggested that children have a relatively high capacity for compensatory growth of the operated-on kidney[36].

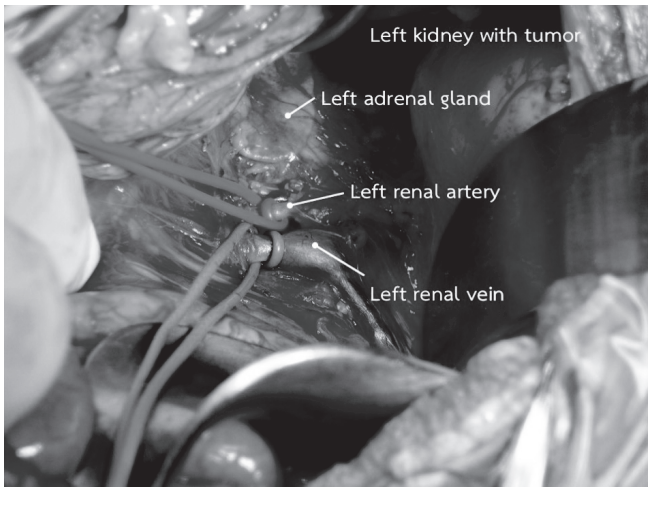


Figure 2 Intraoperative picture demonstrating the technique of midline vascular looping in a case of left-side Wilms tumor. Note that the vascular identification is performed through the mesocolon. With this ùcontrol firstû strategy, further mobilization can be done with less risk of inadvertent bleeding. Avoiding a blood-filled operative field allows the entire operation to be performed meticulously.

Minimally invasive surgery has been recently introduced to WT surgery in experienced centers[37, 38]. A study suggested that laparoscopic nephrectomy became more feasible after chemotherapy. However, laparoscopic sampling of lymph nodes, which is crucial for accurate staging, requires higher experience[38]. A novel technique known as zero-ischemia laparoscopic assisted partial nephrectomy has been shown to have the advantages of rapid recovery and better cosmesis. The zero-ischemia technic uses a laparoscopy to assist with lymph node sampling and renal mobilization within the abdomen. The kidney is then brought out through a small flank incision to perform a partial nephrectomy without total hilar cross clamping.

Complicated Situations in Nephrectomy

Certain situations in a nephrectomy for pediatric renal tumor are technically challenging. Examples of such situations include a tumor with thrombus extending into a renal vein or a ureter, bilateral WT or a unilateral tumor in a single renal unit, pre-operative rupture and hepatic metastasis. If possible, surgical

treatment of WT in these conditions should be preceded by neoadjuvant therapy.

1. Bilateral disease

Approximately 5% of WTs in large cohorts present with bilateral disease at the time of diagnosis. This group of WTs has a high chance to have some types of predisposing genetic syndrome including intrinsic renal pathology such as nephrogenic rests. The tumor masses and the associated pathologies leave the patient with bilateral WT at risk of renal insufficiency after surgical removal of the tumors. End-stage renal disease was reported in 10% of bilateral WTs, compared to 1% in unilateral tumors[39]. Nephron-sparing surgery after tumor down-sizing by chemotherapy is the current standard management in both the COG and SIOP protocols[40]. Tumor biopsy is not recommended unless an evaluation by imaging after 6 weeks of therapy does not show substantial response to chemotherapy.

Partial nephrectomies can be performed bilaterally during the same operation. Careful anatomical planning is necessary using an arterial phase CT scan, focusing on the renal vessels and kidney volume (Figure 3). In general, at least 50% of the renal volume on each side should be retained in order to avoid renal insufficiency in the postoperative period. A 99mTc-dimercapto-succinic acid (DMSA) scan may help in an assessing of split renal function per volume of non-tumorous parenchyma[36]. The preferred

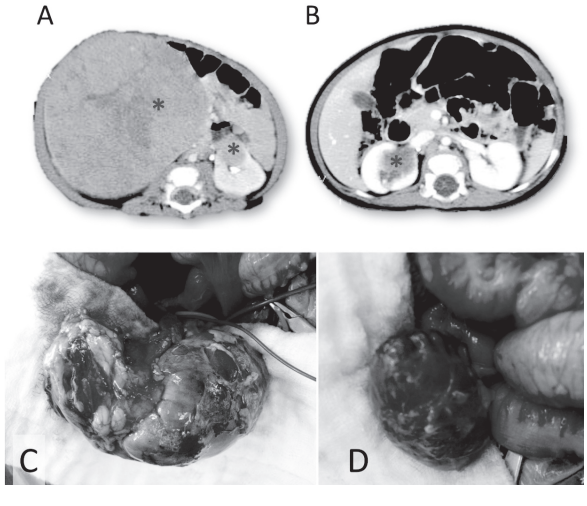


Figure 3 A case of bilateral Wilms tumor. A-B) CT scans demonstrating tumors (asterisks) and reduction of tumors after chemotherapy C) Operative findings of the remaining tumor on the right kidney D) The right kidney after nephrectomy.

incision in our institute is a long midline incision. In order to spare the better kidney in case of unexpected complications, the operation is usually begun on the side with higher anatomical risk. The colon is reflexed medially, allowing clear exposure of the renal vessels. The renal arteries and veins are separately controlled but total perfusion shutdown should be avoided as reperfusion injury may harm the functions of the residual parenchyma. Experimental clinical studies have shown that the warm ischemic time of a kidney is 30 minutes[41-43]. Cooling down the operative field using crushed ice may help increase renal tolerance to the ischemia. Modern surgical devices such as harmonic scalpel can facilitate parenchymal dissection by its advantages in vascular sealing ability and less collateral damage[44].

The open collecting system should be closed with fine absorbable sutures. A double J stent is routinely used to facilitate urine flow by some surgeons[6]. A soft drain, e.g. a Jackson-Pratt silicone catheter, is left in-place until a few days after urethral catheter removal and there is no excessive urine leak. Communicating with a pathologist to focus on the resection margin is advisable as adjuvant radiation therapy is indicated in cases with positive border[45].

2. WT in a single renal unit

The situation may occur in a patient with a horseshoe kidney or it can be a metachronous tumor arising in the only remaining kidney.

3. WT with extrarenal extension

Venous extension of WT was reported at 4% and 6% in NWTS-3 and NWTS-4, respectively, and this locally advanced tumor leads to a higher risk of surgical complications[46,47]. According to NWTS-4 data, 82% of venous extensions are confined to the vena cava while 18% had atrial extension. Although most patients have no specific symptoms, some may present with vena cava obstruction, cardiac failure or testicular varicocele. Upfront chemotherapy is the current standard for first treatment, even in those cases with venous obstruction, as a study showed that 70% of the cases had substantial response to this approach[48]. Before surgery, apart from a CT scan, evaluation of thrombus extension and possible venous obstruction can be performed using ultrasonography with or without a Doppler flow detector (Figure 4). When the thrombus extends

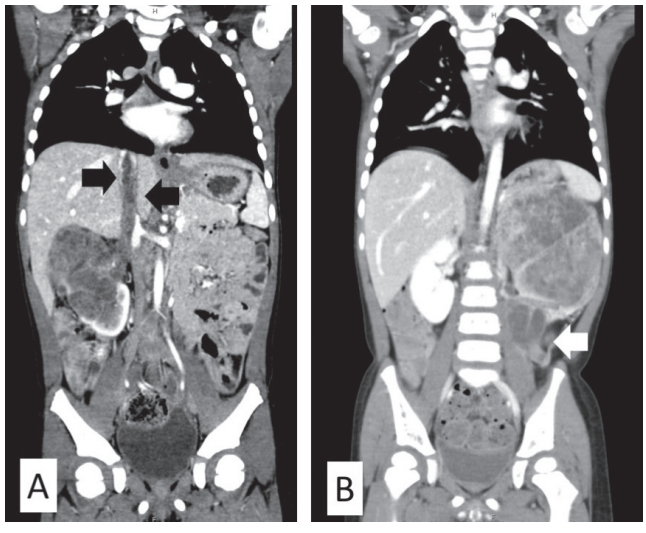


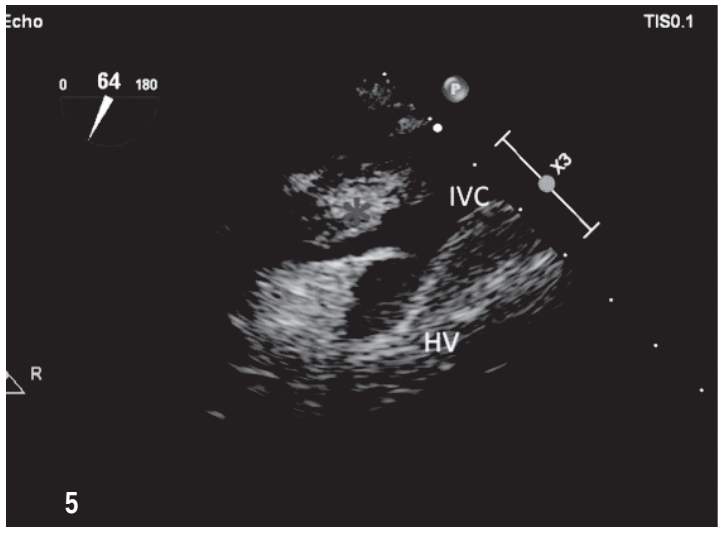
Figure 4 Wilms tumor with extrarenal extension A) Intracaval extension of the right-side Wilms tumor (black arrows) B) Left renal pelvic and ureteric extension of a left-side Wilms tumor (white arrow)

beyond the retrohepatic vena cava, stand-by cardiac surgeon consultation and cardiopulmonary bypass is recommended[49]. The main vascular access should be on the upper part of the body as impeded flow during vena cava control may result in preload reduction and hypotension.

After a radical nephrectomy, vascular control by snuggling with silicone slings is performed above and below the intended cavotomy site. If the tumor thrombus extends to the retrohepatic vena cava, right hepatic mobilization can facilitate vascular control. Additional retrohepatic or suprahepatic vena cava control reduces the risk of embolism during a thrombectomy. A longitudinal venotomy is made and removal of the thrombus can be performed using stone forceps extraction together with manual milking from above. Dissection of the thrombus from the intimal plane is necessary in some cases[49] if the thrombus has adhered to the venous wall. However, if the cranial end of the thrombus has adhered to the vein above the diaphragm, removal through a cardiotomy under circulatory arrest is recommended (Figure 5). In our experience, a transesophageal ecchocardiography is helpful in evaluating the level and completeness of a caval thrombectomy. Venous extension of other pediatric renal tumors other than WT can also occur and the current principles of treatment are similar. Ureteric extension requires careful mobilization of the ureter down to a point that is free from tumor thrombus. If vesical extension is doubtful, a pre-operative cystoscopy is suggested.

4. Renal tumor with synchronous hepatic metastasis

Synchronous hepatic metastasis at diagnosis was reported in 29 of 1365 WT patients (2.1%) by SIOP enrolment (1994-2004)[50] and 111 of 4,941 WT patients (2.2%) registered to NWTS-4 and NWTS-5[51].



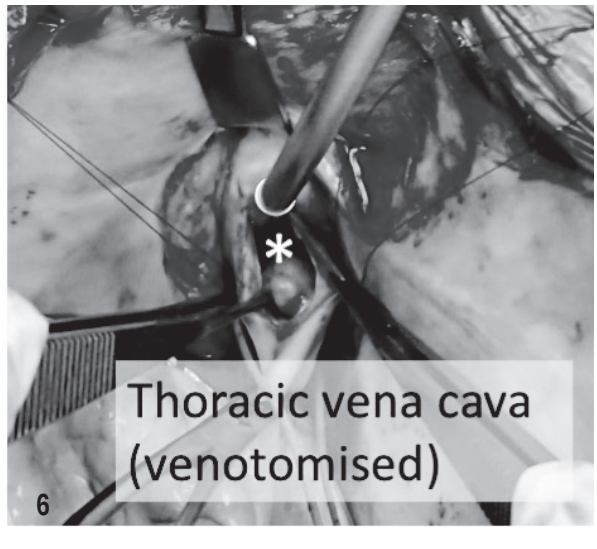


Figure 5 Operative findings in a case of venous thrombus extending to the thoracic vena cava. The thrombus was found floating within the vein and was removed under circulatory arrest.

Figure 6 Intraoperative transesophageal echocardiography showing a tumor thrombus (asterisks) floating within the inferior vena cava (IVC) above the hepatic vein (HV) and the operative findings in the same patient (courtesy of Dr.Jutarat Tanasansuttiporn, Department of Anesthesiology, Faculty of Medicine, Prince of Songkla University)

Approximately 65% of those with primary liver metastasis also had lung metastasis at diagnosis. Data from the NWTS showed better survival outcome in cases who underwent a primary liver resection compared to those who did not (5-year event free survival 86% and 68%, respectively) although the difference did not reach the statistical significance level[51]. However, it is generally advisable that if the nephrectomy is uncomplicated and the hepatic metastasis is considered resectable, the nephrectomy and hepatic resection should be performed together in one operation.

Sugical Management of Metastatic Renal Tumor

Although lung, liver, bone and brain are the predominant sites of metastasis in WT and bone metastasis often occurs in CCSK, uncommon metastatic sites have also been reported such as adrenal glands, vagina and duodenum[52-54]. Pulmonary metastasectomy has been proven to provide survival benefits when the patient has a solitary metastasis at the lung[55]. Surgery for WT metastasis to the liver has long been supported by a landmark retrospective review in 1978[56]. Although most supporting data are derived from small case series, analysis from SIOP data also emphasise the significance of complete resection of the metastatic foci[57].

Complications in Pediatric Renal Tumor Surgery

Surgical complications occur in approximately 12% of renal tumor surgeries. The most common surgical complication in WT surgery is intraoperative rupture which was reported at 15% in the NWTS study and 3% in the SIOP study[58-60]. In our series from Songklanagarind Hospital, the risk of operative rupture/leak increased when a primary nephrectomy was attempted in a case with tumor size larger than 10 centimeters[11] which was consistent with a report from NWTS[47] and also others[61,62]. To avoid this complication, we opt to give upfront chemotherapy in large pediatric renal tumor. Other complications include intestinal obstruction from adhesion, major vascular injury, excessive bleeding, and surgical site infection[47].

Sugery for Recurrent Disease

Locoregional relapse occurs in 10-15% of WT after primary nephrectomy and intraoperative spillage increases the risk of relapse. Apart from intraoperative leakage from the renal capsule, spillage includes unintentionally breaking into a vessel or a ureter that contains viable tumor cells. When recurrence occurs, longterm survival is significantly compromised. The first line treatment is an intensive chemotherapy regimen with a combination of ifosfamide, cyclophosphamide and etoposide[63]. After chemotherapy, removal of the residual tumor gives favorable outcomes in cases that the tumor is resectable[64].

Current Outcomes of Renal Tumor Management

Reported outcomes of WT from large trials have been generally excellent other than for patients in unfavorable subgroup. According to a recent post-hoc analysis using the UMBRELLA protocol by the SIOP renal tumor study group, localized WT had an estimated 5-year survival of more than 90% with survival in stage I reaching 100%[65-67]. In metastatic WT or bilateral diseases, 5-year survival have been reported at 70%[17]. Survival for those with bilateral WT was recently reported at 95% (AREN0534 protocol from COG)[68]. Survival rates decrease in patients with unfavorable histology or molecular markers, with large tumor volume or when there is intraoperative spillage[69]. In non-WT renal tumors, 5-year survival is around 80% in CCSK[70,71] and less than 25% in MRTK[72].

Conclusion

Although evolution in the treatment of pediatric renal tumors has come to the point that cure can be aimed at in the majority of cases, challenging circumstances still exist. In most complicated situations, pre-operative chemotherapy leads to reduction of tumor size and inactivation of metastatic foci, allowing tumor resection with less risk of renal insufficiency or inadvertent complications. Surgical resection plays a role not only in primary tumors but also in metastatic WT in the lungs or liver in case in which the primary tumor has been well controlled. WT and CCSK are curable cancers when diagnosed at an early stage with no unfavorable prognosticators.

Acnowledgement

Dave Patterson edited English language in the manuscript.

Ethical Issue and Conflict of Interest

The authors declare no conflict of interest.

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