Visiting Professor, Armando Lorenzo, MD, MSc, FRCS, FAAP

February 4th from 6pm-8pm

Location: Dr. Duncan Wilcox home
4223 S. Bellaire Circle
Englewood Co, 80113
*Click here for Map*

Dinner catered by Stellar Catering
Sautéed Vegetables tossed with a Curry Coconut Sauce and Grilled Julienne Chicken Breast…
Long Grain and Wild Rice
Field Green Salad with Roma Tomatoes and Choice of Dressing Homemade Whole Wheat Rolls and Butter Desserts of Homemade Bar Cookies, Puff Shells with Custard

Journal Club Articles:
*Click on each name of article to open the Journal Club Article*


2. Current referral patterns and means to improve accuracy in diagnosis of undescended testis.

3. Inappropriate Use of Ultrasound in Management of the Pediatric Cryptorchidism.

Comparison between laparoscopic and open radical nephrectomy for the treatment of primary renal tumors in children: Single-center experience over a 5-year period


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Objectives: To compare the outcomes of laparoscopic nephrectomy (LN) with open radical nephrectomy (ORN) in the management of consecutive pediatric neoplasms.

Patients and methods: Retrospective cohort study of consecutive children treated for primary renal tumors between 2006 and 2011, segregated based on surgical modality (LN/ORN). Pre-, intra- and postoperative data and outcomes were collected.

Results: Demographics from the 45 patients (13 LN, 32 ORN) were similar, and tumors in the LN group were smaller [6.59 ± 1.8 cm vs. 10.99 ± 2.99 cm ORN (p < 0.05)]. Six patients had preoperative chemotherapy (two LN, four ORN). No tumor ruptures occurred with either technique. Wilms tumor (seven LN, 24 ORN) was the most common diagnosis, followed by renal cell carcinoma (four LN, four ORN). Procedure length was similar between groups (282 ± 79 LN, 263 ± 81 min ORN). Mean length of stay was significantly shorter for LN (2.9 vs. 5.9 days; p = 0.002). Postoperative narcotic requirements and use of nasogastric tube were higher in
Introduction

The last decade has seen a sharp increase in the number of minimally invasive surgery (MIS) options being performed for a growing range of conditions. MIS has been successfully introduced in adult practice, often favored over open procedures, and is currently one of the preferred methods for treating renal malignancies in many centers around the world [1,2]. In principle, MIS has the potential of becoming the modality of choice for virtually any procedure, provided the results are comparable to those obtained with open counterparts, and benefits in terms of surgical morbidity and recovery are clear. Having progressively done so, and although initially faced with expected criticism, laparoscopic radical nephrectomy can now be considered one of the most significant recent advances in the field of urology [3].

This successful paradigm shift has been carefully introduced into the pediatric arena, a transition that has mostly centered on benign pathologies (which are proportionally more common in children). Interestingly, despite being well established in the treatment of renal tumors in adults, the application of minimally invasive options to pediatric tumors has clearly lagged behind. Indeed, MIS modalities are yet to gain wide acceptance in the treatment of renal neoplasms in this age group. Many surgeons remained skeptical about laparoscopic nephrectomy (LN) for pediatric malignant neoplasms owing to important differences in terms of size at presentation, oncological implications of rupture during manipulation, and difficulties proving superiority over the already very successful standard of care—open radical nephrectomy (ORN)—when treating the most common pediatric malignancy, Wilms’ tumor (WT).

Reports from as early as the 1930s show a survival rate of 32% of children with WT treated with surgery alone [4]. The National Wilms’ Tumor Study Group has eloquently described the critical role of surgery as a cornerstone in the management of WT by establishing fundamental surgical principles to be followed [5], namely the surgeon requires familiarity with childhood cancer; the surgical approach used must allow exposure to facilitate removal without surgical rupture; and the surgeon must provide critical intraoperative staging through visualization of the peritoneum and submission of lymph nodes. An approach including immediate surgery regardless of tumor size remains the standard North American approach to WT within modern clinical trials. Nevertheless, remarkable improvements in imaging, together with surgical innovations, challenge the status quo to consider alternative surgical approaches that minimize the impact of the surgical procedure while maintaining the established surgical principles and current outstanding oncological results.

At our institution (The Hospital for Sick Children and University of Toronto), we enjoy a very close collaboration between pediatric oncologists, surgeons, and urologists, with the common mindset of carefully embracing different evolving technologies that can translate into potential benefit for our patients. Based on the approach set by the vast adult oncology experience, over the last decade LNs have been selectively offered and conducted. Herein, we provide a comparative analysis of surgical and oncological outcomes for consecutively treated children with either LN or ORN over a 5-year period. The primary outcome of interest was recurrence rate, as our primary goal was to determine whether LN offers a safe alternative to the gold standard method (ORN) in terms of cancer treatment. We also tried to ascertain if surgical morbidity and recovery would be superior with LN based on pain management, duration of nasogastric drainage, and length of hospital stay.

Materials and methods

After obtaining approval by the research ethics board, a retrospective chart review of all patients undergoing nephrectomy at a tertiary pediatric referral center between 2006 and 2011 was conducted (The Hospital for Sick Children and University of Toronto). Only patients with a confirmed histological diagnosis of a primary renal neoplasm were included in the analysis. Variables collected included preoperative information (age at surgery, mode of presentation, tumor size, administration of neo-adjuvant chemotherapy); intraoperative details (modality of surgery (LN vs. ORN), length of the procedure, occurrence of tumor spillage, number of lymph node sampled); and postoperative data (duration of nasogastric drainage, narcotic requirements, length of hospital stay, short- and long-term surgical complications, tumor histology/staging, length of follow-up, and recurrence episodes).

For the purpose of comparative analysis, patients were segregated into two groups, categorized by the employed surgical modality (LN or ORN), and therefore following a retrospective cohort study design. Indications for laparoscopy were selective, based on tumor size, surgeon’s impression of the feasibility of the procedure based on preoperative imaging studies, and the child’s age (Fig. 1), as well as family agreement. The latter was obtained through informed consent following full disclosure of risks (in particular, intraoperative rupture and consequent...
spillage), potential benefits, and paucity of pediatric data for laparoscopic resection. ORN was conducted following the surgical steps delineated by the Children’s Oncology Group (COG) protocols [6].

In cases performed laparoscopically, 3–4 trocar peritoneal access was employed (with liberal addition of a fourth trocar for liver or spleen retraction), with the intact specimen retrieved in a retrieval bag system through a Pfannenstiel-type incision as summarized in the short video (Supplementary Video S1). The steps followed closely mimic those described for laparoscopic radical nephrectomy in adults, as well as the principles presented in the limited number of pediatric reports [7–9].

Supplementary video related to this article can be found at http://dx.doi.org/10.1016/j.jpurol.2013.11.002.

Continuous variables were compared using a parametric or non-parametric test based on data distribution. Ordinal variables were compared with the Wilcoxon rank-sum test. For categorical variables, chi-square and Fisher’s exact test were employed. A p-value <0.05 was considered statistically significant. All tests were conducted with commercially available software [SPSS 18.0 (IBM, Chicago, IL, USA) and SAS 9.3 (SAS Institute, Cary, NC, USA)].

Results

During the study period, 45 patients met the inclusion criteria (13 and 32 consecutive children underwent laparoscopic or open radical nephrectomy for a primary renal neoplasm, respectively). Preoperative data are shown in Table 1. In general, there was no significant difference in age between the groups (p = 0.11), and ORN patients had larger tumors than their LN counterparts (p < 0.001). Mode of presentation also differed; hematuria was more common in the LN group (5/13; 38%) followed by incidental finding (3/13; 23%), whereas in the ORN group, palpable mass (17/32; 53%) was the most common finding. Overall, 6/45 patients had preoperative chemotherapy (four ORN and two LN), and indications are detailed in Table 1.

Intraoperatively, procedure duration was similar (282 ± 79 min LN vs. 263 ± 81 min ORN; p = 0.5), and there were no intraoperative ruptures in either group. Lymph node sampling could be adequately performed with the LN technique (median 2, range 1–14 lymph nodes obtained), although ORN yielded a larger number of nodes (median 5, range 2–29; p = 0.008).

The adrenal gland was spared in 10/32 (31%) ON and 9/13 (69%) LN (p = 0.04) patients.

### Table 1: Preoperative data: age, tumor size, laterality, and indications for preoperative chemotherapy.

<table>
<thead>
<tr>
<th></th>
<th>Open – 32 patients</th>
<th>Lap – 13 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age – median (range)</td>
<td>3.5 years (2 months–15 years)</td>
<td>4 years (2 months–17 years)</td>
</tr>
<tr>
<td>Side</td>
<td>L 21</td>
<td>L 7</td>
</tr>
<tr>
<td></td>
<td>R 11</td>
<td>R 6</td>
</tr>
<tr>
<td>Preop chemo</td>
<td>4/32</td>
<td>2/13</td>
</tr>
<tr>
<td></td>
<td>3 Wilms – 2 unresectable, 1 venous thrombus beyond hepatic veins</td>
<td>2 Wilms</td>
</tr>
<tr>
<td></td>
<td>1 RCC – extensive disease</td>
<td>1 venous thrombus beyond hepatic veins</td>
</tr>
<tr>
<td>Size – mean ± std. deviation (range)</td>
<td>10.99 ± 2.99 cm (4.2–18.5 cm)</td>
<td>6.59 ± 1.88 cm (3.1–9 cm)</td>
</tr>
</tbody>
</table>
Postoperative pain management strategies and duration are summarized in Table 2. In brief, ORN patients had longer duration of narcotic requirement despite liberal use of regional anesthesia (i.e., epidural blocks). A nasogastric tube was left in place in 18/32 (56%) ORN patients for a mean of 1.6 days, while no patients in the LN group left the operating room with, or subsequently required, nasogastric tube placement. Length of stay was significantly shorter in the LN group (2.9 vs. 5.9 days; \( p = 0.002 \)). Histological diagnoses are shown in Fig. 2; as expected, WT (7/13 LN; 24/32 ORN) was the most common diagnosis in both groups, and there was no statistical difference between the two modalities in terms of WT staging (\( p = 0.94 \)). Tumors accounting for the "other" columns were (one of each) mesoblastic nephroma and perivascular epithelioid cell tumor in the LN group, and rhabdoid, clear cell sarcoma, undifferentiated sarcoma, and cystic nephroma in the ORN group.

After a median follow-up of 18 months (1–35 months) LN and 33 months (1–60 months) ORN, one (7.7%) and four (12.5%) recurrences have taken place, respectively (\( p = 1.0 \)). The recurrence in the LN group was localized to the renal/adrenal gland bed in a patient who presented initially with significant neoplastic extension into the collecting system up to the lower third of the ureter. Although there was no evidence of tumor rupture at the time of surgery and upon review of the surgical video, a rupture within the retrieval bag was questioned for this patient, which resulted in a recommendation by the central review (COG Renal Tumor Committee) to upstage him to stage III. In the ORN group, 3/4 recurrences were metastatic. In terms of long-term surgical complications, one patient in each group developed an incisional hernia (in the patient who underwent a LN the hernia was at the site of the Pfannenstiel incision). In addition, one ORN patient had an episode of postoperative small bowel obstruction.

A sub-analysis was performed taking into consideration only ORN patients with tumors <10 cm (\( n = 11 \)), thus rendering the groups more comparable in terms of the difficulty of the surgical procedure. In terms of the primary outcome of interest, recurrence rates were still similar (1/13 LN, 1/11 ORN; \( p = 1.0 \)). Although the LN procedure had a longer duration in this scenario (281 ± 82 vs. 214 ± 35 min; \( p = 0.01 \)), length of hospital stay and duration of nasogastric drainage were still significantly shorter [2.92 ± 1.38 vs. 4.5 ± 1.69 days (\( p = 0.02 \)); 0 vs. 2.7 days (\( p < 0.001 \))]. Duration of postoperative narcotics did not reach statistical significance; nonetheless, almost all patients in the ORN group received an epidural block.

### Discussion

Our results suggest that LN may be an appealing alternative to open surgery in selected cases of primary renal tumors in the pediatric population. Based on the selection pattern in our series, the best cases for MIS appear to be small, incidentally detected lesions not amenable to nephron-sparing surgery and tumors that experience significant size reduction after preoperative chemotherapy. As is usually the case with MIS, patients undergoing LN seemed to have a more favorable recovery profile after surgery, which can be inferred based on the shorter hospital stay. These children were also less likely to receive epidural analgesia or gastrointestinal decompression with a nasogastric tube. Although admittedly limited, our results also suggest equivalent oncological outcomes and support efforts to continue exploring minimally invasive options for the treatment of renal neoplasms in children.

Following the pattern seen in adult surgery, the use of MIS in pediatric surgery for benign conditions has progressively grown, becoming widespread and favored in many centers around the world. Reports on LN for conditions such as poorly functioning or non-functioning kidneys associated with reflux, urinary tract infections, or dysplasia have been available for over a decade [10,11]. For these conditions, others have previously described some of the benefits detected in this series. For example, in a comparative study, Hamilton et al. [12] showed that LN for benign conditions led to shorter hospital stay, albeit with a longer operative time. Nevertheless, when it comes to pediatric malignant conditions, the role of MIS becomes less clear. In a recent systematic review aimed at comparing overall survival, event-free survival, port-site metastases, and surgical morbidity between open and minimally invasive pediatric surgical oncology procedures, de Lijster et al. [13] were unable to provide any evidence-based recommendations, as no randomized or controlled clinical trials were

### Table 2 Postoperative pain management data.

<table>
<thead>
<tr>
<th>Pain control modality</th>
<th>Open – 32 patients</th>
<th>Lap – 13 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidural catheter</td>
<td>24/32</td>
<td>Morphine infusion – 6/13</td>
</tr>
<tr>
<td>Morphine infusion</td>
<td>2/32</td>
<td>PRN narcotics – 5/13</td>
</tr>
<tr>
<td>PRN narcotics</td>
<td>6/32</td>
<td></td>
</tr>
</tbody>
</table>

| Mean duration of narcotics (days) | 3.26 | 2.15 (p = 0.04) |

Figure 2  Histological diagnosis divided by surgical modality.
Note. RCC = renal cell carcinoma.
identified. Several small case series have been published attesting to the feasibility of the laparoscopic approach in children for conditions such as neuroblastoma [14], pancreatic tumors [15], and even hepatoblastoma [16]. However, small sample sizes and lack of control groups make it difficult to generate reliable conclusions in terms of the safety profile of these procedures and their potential to offer similar oncological outcomes to open surgery.

In adult oncological surgery, well-designed studies and an impressive body of literature have addressed the role of MIS. Unsurprisingly, LN is now considered by many the treatment of choice for localized renal cell carcinoma (stage T1 or T2) that is not amenable to nephron-sparing surgery [17]. In stark contrast, the most common pediatric renal malignancy, WT, is well known for presenting with large palpable masses, making laparoscopic procedures less appealing and unlikely to provide great benefit in the absence of size reduction with neo-adjuvant chemotherapy. Other areas of great concern are the feasibility of performing an adequate lymph node sampling for accurate staging [18] with LN and the possibility of tumor upstaging by intraoperative rupture, which results in the need for additional therapy (particularly radiation). That probably explains why, following the first report of LN for WT in 2004 by Duarte et al. [8], not many surgeons have been interested in or comfortable attempting it. The initial report consisted of two patients undergoing the procedure after preoperative chemotherapy. The same authors later updated their series and reported on 15 patients followed for as long as 61 months with no adverse oncological outcomes [19], concluding that LN following preoperative chemotherapy was demonstrated to be feasible and safe. Following an initial period of performing LN only on biopsy-proven favorable histology WT, they later abandoned the practice of preoperative biopsy, concluding that all the steps followed in open surgery could be reproduced, with the added advantage of a shorter hospital stay and improved cosmesis. Although not of primary concern when treating pediatric cancer, it is certainly appealing to resort to the option with the most favorable aesthetics (Fig. 3) provided that oncological results are equivalent. Varlet et al. [9] also reported on five patients who had LN for WT after preoperative chemotherapy with no adverse oncological results. As previously mentioned, these studies suffer from many limitations, including the lack of a control group for comparison.

The role of MIS in the treatment of pediatric renal malignancies has to be discussed in the context of current treatment protocols and the differences in management between them [20]. In North America, patients are routinely treated with upfront surgical resection, followed by postoperative chemotherapy and sometimes radiation therapy based on risk stratification that includes surgical staging, pathology, and tumor biology information (COG). Conversely, in most of Europe and other parts of the world, preoperative chemotherapy is administered to all patients, followed by surgical resection [as recommended by the International Society of Pediatric Oncology (SIOP)]. Therefore, tumors are usually smaller at the time of surgery. Furthermore, chemotherapy often leads to the development of a “fibrous capsule”, allowing more comfortable handling of the mass and making tumor rupture less likely to occur. This appears to be of greater importance in children who present with large renal masses. In a study of the risk factors for intraoperative spillage, Barber et al. [21] suggested that patients with large tumors (>1000 cc) who didn’t receive neoadjuvant chemotherapy were at higher risk of rupture than the ones who did; this difference was not evident for smaller tumors. The pediatric oncology literature acknowledges that both protocols have merits and result in acceptable outcomes. Nevertheless, based on stage migration and size reduction, it appears that preoperative chemotherapy could offer a potential advantage for families interested in pursuing laparoscopic resection. Not surprisingly, the largest series to date have followed this approach [8,19,22]. Interestingly, in our series (composed predominantly, but not exclusively, of WT cases), only two patients received preoperative chemotherapy, and the average tumor size at the time of surgery was 6.5 cm.

Figure 3 Postoperative pictures of open and laparoscopic nephrectomy. Note small Pfannenstiel incision for tumor removal below the belt line in a patient undergoing laparoscopic nephrectomy.
Likewise, in the only North American reports of upfront LN for renal malignancies available in the literature, two patients with 8-cm lesions underwent pre-chemotherapy LN without complications [23]. Hence, LN may be a consideration in the setting of both the SIOP and COG protocols, that is, for resection after preoperative chemotherapy or upfront surgery up to a certain dimension, particularly if patients are carefully selected. Duarte et al. [19] reported that a tumor dimension/height ratio >10% precluded a laparoscopic approach in their series. This is likely to remain a very controversial topic until more experience is gained [24]. Although we are unable to provide definitive guidance, our data support the value this approach may have and serves as additional information to support the potential value of exploring the merits of MIS in this setting.

Important limitations of our methodology have to be highlighted. First, our approach to LN in the setting of renal tumors has, admittedly, been biased by patient selection. Although we report on consecutive patients, there was no attempt whatsoever to randomize patients to one procedure or the other; therefore, patients undergoing LN were probably less challenging from a surgical prospective than the ORN ones. Nevertheless, despite the difference in tumor size, the groups were similar in terms of staging. Second, the other source of bias introduced by the surgeon is that postoperative management is affected by the surgical modality, as this study is obviously not blinded (i.e., usually there is a drive to discharge patients who undergo MIS earlier and be more restrictive in terms of nasogastric drainage and narcotic usage). Still, length of stay and nasogastric drainage were markedly better in the LN group even when patients with larger tumors (>10 cm) were excluded from the analysis, suggesting that the benefits of MIS in this setting mirror what has been demonstrated by other open versus laparoscopic series [7,12]. Finally, the length of follow-up is not long enough to guarantee that the oncological outcomes will be the same as the ones obtained with open surgery, and long-term monitoring is mandatory.

Despite these limitations we propose there is value in the presented data. Our report adds to the existing literature by providing a control group and further reiterating the feasibility of LN for selected cases of pediatric primary renal neoplasms. We also present a careful multidisciplinary introduction of MIS for this purpose. The discussion about potential catastrophic complications by indiscriminate and uncontrolled attempts at different surgical approaches should be kept in mind, as underscored by the case report by Chui et al. [25], where a 2-year-old girl presented with peritoneal metastases after a laparoscopic partial nephrectomy for WT. Although a formal randomized clinical trial is unlikely to be feasible in this setting, given the variability in clinical presentation, responsible reporting and multicentric collaboration will help define the exact role of MIS in the treatment of pediatric solid abdominal malignancies. Based on our data, we recommend careful consideration of laparoscopic radical nephrectomy for upfront surgery in pediatric renal tumors <10 cm or after preoperative chemotherapy when significant response is observed; also, surgical principles applied to open surgery must be followed strictly, namely effort for complete resection without tumor rupture and generous lymph node sampling.

Conclusion

LN is an attractive alternative to open surgery in selected cases of pediatric renal tumors, particularly smaller lesions detected early or following chemotherapy. Procedure length and incidence of intraoperative rupture were not increased; postoperative recovery was quicker and hospital stay shorter for LN. Longer follow-up is mandatory to confirm similar oncological outcomes to conventional open surgery.

Conflict of interest

None.

Funding

None.

References


Current Referral Patterns and Means to Improve Accuracy in Diagnosis of Undescended Testis

WHAT’S KNOWN ON THIS SUBJECT: Primary care providers (PCPs) identify patients with undescended testis (UDT) and refer them to surgical specialists. Referral beyond the recommended times for orchiopexy has been reported, and PCPs’ accuracy in identifying and distinguishing UDTs from retractile testes has been questioned.

WHAT THIS STUDY ADDS: We describe 3 observations that are strongly correlated with UDT, that is, birth history of UDT, prematurity, and visible scrotal asymmetry. UDT diagnoses are best made by 8 months of age, to reduce confusion with testicular retraction and to facilitate timely orchiopexy.

abstract

OBJECTIVES: The goals were to determine current referral patterns for boys suspected of having undescended testes (UDT) and to identify factors to assist primary care providers in distinguishing retractile testes from UDTs on the basis of history, physical examination, or imaging findings.

METHODS: By using a standardized history assessment, visual inspection of the scrotum for symmetry, physical examination, and review of previously obtained imaging findings, we performed a prospective observational study with consecutive patients referred to a pediatric urologist for evaluation of UDT.

RESULTS: Of 118 boys, 51 (43%) had descended testes, 60 (51%) had UDTs, and 7 (6%) had initially indeterminate findings. Boys with UDT were referred at a median age of 43.3 months. Patients referred at <1 year or >10 years of age were significantly more likely to have UDT than were those referred at 1 to 10 years of age. History of UDT at birth, prematurity, and scrotal asymmetry strongly increased the risk of UDT. Genital ultrasonography had been performed for 25% of patients, incorrectly indicating UDT for 48%.

CONCLUSIONS: Most boys were referred well beyond the recommended age of <12 months for orchiopexy. Only one-half of the patients had UDT, with most errors in diagnosis being made for boys 1 to 10 years of age, which suggests difficulty distinguishing UDT from retractile testes. Positive birth history findings, prematurity, and scrotal asymmetry predicted UDT and can be used by primary care physicians in their assessment before referral. Genital ultrasonography did not distinguish UDTs from retractile testes. Pediatrics 2011;127:e382–e388

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KEY WORDS undescended testis, orchiopexy, retractile testis

ABBREVIATIONS CI—confidence interval
PCP—primary care provider
OR—odds ratio
UDT—undescended testis

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Testicular descent from the abdomen to the scrotum normally occurs at ~28 weeks of gestation, with incomplete descent reported for ~3% of term neonates,1–3 which makes undescended testis (UDT) the most common birth defect among boys. Most UDTs migrate into the lower scrotum within the first 3 months of life, presumably as a consequence of a postnatal testosterone surge, with <1% remaining undescended by 1 year of age.1,2

The low likelihood of spontaneous descent after 1 year of age and the observation that germ cell counts decrease in UDTs after 1 year resulted in a recommendation that orchiopexy be performed by 12 months.4,5 UDT diagnoses usually are made by primary care providers (PCPs), with referral to pediatric surgeons or urologists for surgery. Previous reports on referral patterns emphasized the patient age at presentation for orchiopexy,6–9 with all noting that most patients were referred beyond the recommended age for therapy.

Similarly, we noted patients with diagnoses at birth who were referred at >1 year of age when UDT persisted; in addition, we observed other boys with normal examination results who were referred for evaluation of possible UDT despite a history of normal descent. To document findings, we performed a prospective study with a standardized parent questionnaire and physical examination by a single pediatric urologist (Dr Snodgrass) for consecutive boys referred for evaluation of UDT. There were 2 study objectives, that is, (1) to document current referral patterns for UDT and (2) to identify factors to assist PCPs in distinguishing retractile testes from UDT on the basis of history, physical examination, or imaging findings.

METHODS

Consecutive patients referred for evaluation of UDT in January through April 2009 first underwent standardized history-taking with a questionnaire (Appendix). Queries for parents addressed a history of prematurity (<37 weeks of gestation), whether the diagnosis of UDT had been discussed with them before hospital discharge, and whether the PCP who made the referral had been the provider since the initial outpatient newborn evaluation or was a new provider. Visual inspection of the scrotum then was made with the patient supine, to determine whether at least 2 hemiscrota appeared symmetric or 1 side was hypoplastic (Fig 1). Finally, physical examination was performed by a single pediatric urologist (Dr Snodgrass). BMI was calculated on the basis of height and weight at presentation. Genital ultrasound scans obtained before referral by the PCP were reviewed. Data were recorded prospectively in a database and were reviewed with institutional review board approval for this report.

Examinations were performed with all patients supine. A nurse assisted in maintaining a slightly frog-legged position for infants and young boys, whereas older patients were instructed to assume this position and to avoid contraction of the abdominal musculature during inspection and palpation. Testes were considered normally descended if they resided in the middle to lower scrotum without palpable tension on the spermatic cord. Testes that were found in the upper scrotum or lower inguinal canal adjacent to the base of the penis, could be manipulated into the middle to lower scrotum without spermatic cord tension, and then remained there when released were considered retractile. Testes that could not be delivered into the middle to lower scrotum or could be manipulated there only with persistent spermatic cord tension that immediately returned the testis cephalad upon release were considered undescended. Findings of testes that could be palpated in the middle to lower scrotum and did not immediately return to a higher position when released but had tension on the spermatic cord were considered indeterminate. Patients with such findings underwent additional examinations to distinguish retractile testes from UDTs.

Because retractile testes may present variable examination findings, sometimes residing within the middle to lower scrotum and sometimes being noted in the upper scrotum or lower groin, but are considered a normal variant not requiring surgery, no distinction was made between descended testes and retractile testes in data analyses. Therefore, in this report, testes were defined as descended, undescended, or indeterminate. Patients with histories of ipsilateral inguinal or scrotal surgery were excluded, as were those with multiple-malformation syndromes.

We summarized continuous variables as means and SDs and categorical variables as frequencies and proportions. The variables (risk factors) were compared between subjects with UDTs and those with descended testes by us-
ing Student’s t test, Fischer’s exact test, or $\chi^2$ tests. Logistic regression models with binary outcomes (undescended versus descended) were constructed to assess the association between testis position and predetermined risk factors, including birth history, age at diagnosis, scrotal asymmetry, BMI, history of prematurity, and practitioner (new provider versus established provider). Univariate logistic regression models determined the relationship of individual factors to testis position, whereas multivariate logistic regression analyses assessed the joint effect of these factors. A stepwise variable selection procedure was used to construct the final multivariate model. Statistical significance was declared for $P$ values of $<.05$. All analyses were conducted by using SAS 9.2 (SAS Institute, Cary, NC).

**RESULTS**

A total of 121 consecutive patients were referred for evaluation of UDT, of whom 3 were excluded from additional analyses; 2 had descended testes with hydroceles and 1 had been adopted, with an unknown birth history. Of the remaining 118 boys, 51 (43%) had descended testes, 60 (51%) had UDTs, and 7 (6%) had initially indeterminate findings. Subsequent examinations diagnosed UDT in 4 cases, for a total of 64 patients with UDTs, 51 patients with descended testes, and 3 cases that remained indeterminate, with future reevaluation scheduled. UDT was unilateral in 57 cases and bilateral in 7 cases, and testes were not palpable in 21 cases (bilateral in 3 cases). The median age at referral for all boys with UDT was 43.3 months.

The various demographic and clinical factors assessed at referral for subjects with and without UDT are summarized in Table 1. Discussions of a UDT diagnosis after hospital newborn examination were reported for 34 patients, of whom 32 (94%) had UDT. Only 21 of those patients (62%) were referred at $<12$ months of age (median age: 21.4 months [range: 4–111 months]). The parents of the remaining 32 patients with UDT did not recall the diagnosis being discussed before hospital discharge; this group included 11 of 21 patients with nonpalpable testes and 2 of 3 patients with bilaterally nonpalpable testes.

Of 35 patients referred before 12 months of age, 27 (77%) had UDT, as did 6 (85%) of 7 boys referred during puberty, at $>10$ years of age. In contrast, only 31 (42%) of 73 patients referred between 1 and 10 years of age had UDT ($P = .003$) (Table 2). Regardless of age at referral or other risk factors, a history of prematurity was associated with higher risk of UDT, which was found for 11 (73%) of 15 boys born at $<37$ weeks of gestation.

Visual inspection of the scrotum before palpation revealed asymmetry for 46 patients, of whom 45 had UDT. Asymmetry was noted for 44 of 57 patients with unilateral UDT, 1 of 7 patients with bilateral UDTs, and 1 patient with descended testes.

Genital ultrasonography was performed before referral for 30 patients (25%) and indicated UDT for 29 patients, of whom 14 had descended testes on physical examination. For 9 patients, testing was performed between birth and 1 year of age. Of those patients, 4 were evaluated between birth and 6 months, with findings confirming suspected UDT in each case. Among 5 boys 7 to 11 months of age, ultrasonography in 3 cases indicated bilateral inguinal testes that were demonstrated to be descended in subsequent physical examinations. Another 20 patients were between 1 and 10 years of age at the time of genital ultrasonography, 4 with nonpalpable testes. Of the remaining 16, 12 were reported to have bilateral inguinal testes but had normal physical examination results. Ultrasonography was performed for 1 pubertal boy with UDT.

These 121 patients were referred by a total of 92 PCPs, of whom 49 were the established providers since the initial outpatient newborn examinations and

### TABLE 1 Demographic and Clinical Features of Patients With UDT, Compared With Patients With Normal Examination Results

<table>
<thead>
<tr>
<th></th>
<th>UDT (N = 64)</th>
<th>Normal Results (N = 51)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>UDT discussed with caregivers at birth, n (%)</td>
<td>32 (50)</td>
<td>2 (3)</td>
<td>$&lt;.0001$</td>
</tr>
<tr>
<td>Gestational age of $&lt;37$ wk, n (%)</td>
<td>11 (17)</td>
<td>4 (7)</td>
<td>.149</td>
</tr>
<tr>
<td>Scrotal asymmetry on physical examination before palpation, n (%)</td>
<td>45 (70)</td>
<td>1 (1)</td>
<td>$&lt;.0001$</td>
</tr>
<tr>
<td>BMI, mean $\pm$ SD, kg/m$^2$</td>
<td>18.3 $\pm$ 2.6</td>
<td>19.0 $\pm$ 4.0</td>
<td>.271</td>
</tr>
<tr>
<td>Referred by new PCP, n (%)</td>
<td>18 (28)</td>
<td>25 (49)</td>
<td>.003</td>
</tr>
<tr>
<td>Nonscrotal position demonstrated through testicular ultrasonography, n (%)</td>
<td>15 (23)</td>
<td>14 (27)</td>
<td>.587</td>
</tr>
</tbody>
</table>

Findings were determined by an experienced pediatric urologist and were evaluated with Student’s t test, Fisher’s exact test, or $\chi^2$ test as appropriate. Three patients with multiple indeterminate physical examination results were excluded from this analysis.

### TABLE 2 Risk Factors for UDT According to Age Group

<table>
<thead>
<tr>
<th></th>
<th>0–12 mo</th>
<th>13 mo to 10 y</th>
<th>$&gt;10$ y</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>35</td>
<td>73</td>
<td>7</td>
</tr>
<tr>
<td>With UDT, n (%)</td>
<td>27 (77)</td>
<td>31 (42)</td>
<td>6 (85)</td>
</tr>
<tr>
<td>UDT diagnosed at birth, n (%)</td>
<td>21 (60)</td>
<td>13 (17)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Scrotal asymmetry, n (%)</td>
<td>24 (68)</td>
<td>7 (25)</td>
<td>4 (57)</td>
</tr>
</tbody>
</table>

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43 were new providers. New PCPs were more likely to refer patients for UDT who were found to have descended testes than were established providers (Table 1).

Multivariate logistic regression analyses identified a history of UDT at birth (odds ratio [OR]: 21.4 [95% confidence interval [CI]: 3.8–120.8]), scrotal asymmetry (OR: 121.3 [95% CI: 14.3 to >999]), and gestational age of <37 weeks (OR: 6.8 [95% CI: 1.5–32.3]) as important factors that increased the odds of a UDT diagnosis, achieving a C statistic of 0.925, which indicates a high discriminative power to distinguish high-risk patients from low-risk patients (Table 3). Although simple logistic regression analyses did not identify it as an independent risk factor, history of prematurity was associated with a higher risk of UDT with controlling for the other risk factors, such as age at referral and scrotal asymmetry. Of 15 boys born at <37 weeks of gestation, 11 (73%) had UDT.

**DISCUSSION**

Although the diagnosis of UDT ultimately is established through physical examination by a surgical specialist, the initial responsibility for assessing testicular position resides with PCPs, including providers in both newborn nurseries and outpatient clinics. The small numbers of affected boys (3% of term newborns and <1% of infants 12 months of age) mean that individual PCPs do not encounter the condition frequently. Evaluation is complicated by the potential for changes in testicular position over time, that is, descent of most newborn UDTs during the first 6 months of life and retraction of descended testes above the scrotum through cremaster muscle contractions between ~12 months of age and the onset of puberty. We identified 3 readily assessed factors that increased significantly the odds that a patient would be diagnosed as having UDT on physical examination by an experienced pediatric urologist, namely, a history of UDT mentioned to the caregivers at birth, prematurity, and visible scrotal asymmetry.

The odds of having UDT were >20 times higher for boys whose parents recalled being told of the UDT at birth. Among 34 patients for whom the diagnosis of UDT was discussed with caregivers at the time of the hospital newborn examination, 32 (94%) had UDT, compared with only 2 of 51 patients with normally descended testes. Similarly, 73% of boys born prematurely had UDT, and 77% of boys with unilateral UDT (which constituted the majority) exhibited ipsilateral underdevelopment of the scrotum on visual inspection.

Although it is subject to recall bias, the observation that approximately one-half of the patients with UDT did not have the diagnosis discussed with parents at birth raises concerns regarding the accuracy of newborn examinations, as highlighted by the 2 cases with bilateral nonpalpable testes in which evaluation for intersexuality should have been performed. It is possible that the newborn physical examination identified UDT in some of the remaining cases but this finding and its clinical significance, including the need for surgery in the event the testicles did not descend spontaneously by 6 months of age, were not communicated effectively to the family.

Of patients with a reported diagnosis of UDT at birth, 38% were referred for surgery after 12 months of age. The mean age at referral for all boys with UDT in this series was 43.3 months, well beyond the currently recommended 12 months for orchiopexy. Other authors noted a tendency for similar late referrals, at 42.6 months and 50.4 months, and, although review of a New York statewide database showed decreases in the age at orchiopexy from 1984 to 2002, the authors noted that, in the last cohort (1999–2002), 62% of surgically treated patients were >2 years of age. However, multiple authors noted a tendency for similar late referrals, at 42.6 months and 50.4 months, and, although review of a New York statewide database showed decreases in the age at orchiopexy from 1984 to 2002, the authors noted that, in the last cohort (1999–2002), 62% of surgically treated patients were >2 years of age. However, multiple factors influence the timing of specialist referral in the United States, including not only the age at diagnosis of the UDT by the PCP but also the parents’ ability to schedule and to attend the appointment. There were no differences in wait times to see the specialist in this single-surgeon series, and insurance status did not affect wait times from the date of referral to the date of appointment for our patients. However, we could not control for possible effects of insurance status on time to presentation to the PCP.

Most errors in diagnosis occurred for boys between 1 and 10 years of age. PCPs’ difficulty in distinguishing descended testes from retractile testes is suggested by the observation that, with subtraction of the 12 patients in this age group with positive birth history findings and UDTs, only 19 (26%) of 73 boys had UDT. Among boys 1 to 10 years of age who lacked any of the 3 risk factors (not told of UDT at birth, symmetric-appearing scrotum, and term gestation), only 5 (6%) of 73 had UDT. Our data indicate that term boys 1 to 10 years of age with negative birth history findings and scrotal symmetry

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>UDT discussed with caregivers at birth</td>
<td>21.4 (3.8–120.8)</td>
<td>.0005</td>
</tr>
<tr>
<td>Scrotal asymmetry on examination</td>
<td>121.3 (14.3 to &gt;999.9)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Prematurity (&lt;37 wk of gestation)</td>
<td>6.8 (1.4–32.3)</td>
<td>.0148</td>
</tr>
</tbody>
</table>

Multivariate logistic regression analyses were performed by using stepwise selection of the variables in Table 1. The variables indicated were found to be statistically significant predictors of UDT.
might complicate examinations, but scended. We thought that obesity testes also were considered de-
terms of testes residing in the middle to lower scro-
tum, with subsequent palpation along the inner thigh or scrotum stimulating a cremasteric reflex that retracts the testis to the upper scrotum/lower inguinal canal. Patients with symmetric scrota were much more likely to have retractile testes than UDTs, whereas most patients with asymmetry had UDTs. However, limitations of visual inspection include its subjective nature and the potential for false-negative findings with bilateral UDTs, which represent the minority of cases.

We did not distinguish between descended and retractile testes in this report. Most of the patients we describe as having descended testes were observed to have both testes lying in the middle to lower portion of a symmetric scrotum. In some but not all cases, retractile activity of a scrotal testis was noted before palpation, but we assumed that others might have demonstrated similar retraction during examination by the PCP before referral. Some patients had scrotal symmetry, with testes residing in the lower groin, which were manipulated readily into the scrotum without tension on the spermatic cord; these retractile testes also were considered descended. We thought that obesity might complicate examinations, but mean BMI values were similar for patients with and without UDTs (Table 1). Of the 15 patients >2 years of age with BMI-for-age values of >95th percentile, 5 had UDTs and 10 had normally descended testes (data not shown).

Genital ultrasonography was performed before referral for 20 patients (27%) between 1 and 10 years of age, including 4 with nonpalpable testes. Of the remaining 16 boys, ultrasonography indicated bilateral inguinal testes for 12, all of whom exhibited descended testes in physical examinations. Genital sonography does not distinguish accurately retractile testes from UDTs, presumably because of cremaster muscle contraction during the examination.

Some patients with negative birth history findings and previous normal examination results might have been referred for evaluation of possible “ascending testes.” This term refers to testes that are thought to be descended normally and then ascend to an abnormal location. Proposed causes include inadequate spermatic vessel growth, tethering by a fibrous remnant of the processus vaginalis, and an inadequate postnatal testosterone surge to stabilize the testis within the scrotum. A recent, prospective, longitudinal study of newborn boys examined by a team of trained research nurses reported a prevalence of UDT among 784 boys of 5.9% at birth, which decreased to 2.4% by 3 months of age as a result of postnatal descent but then increased to 6.7% at 12 months of age as a result of testicular ascent. The authors concluded that testicular ascent accounts for UDTs presenting in older infants and children.

Although 74% of our patients with negative birth history findings who were referred between 1 and 10 years of age did not have UDT, we cannot state whether those with UDT had the condition from birth or acquired it subsequently. However, the diagnosis of ascending testis assumes accurate birth examination results to confirm that normal descent occurred originally. The accuracy of newborn and infant genital examinations has been questioned, and our observation that 11 of 21 patients with nonpalpable testes did not recall the diagnosis being mentioned at birth supports that concern. An alternative explanation is that ascending testes are either retractile testes or UDTs that were not detected previously. It is apparent that newborn and subsequent examinations during the first year of life for boys should be performed carefully, to document that the testes reside without tension in the middle to lower scrotum.

Although examination by an experienced provider is considered the standard method for diagnosing UDT, our study was limited to a single surgeon at a single institution. Orchio-pexy rates greater than the anticipated incidence of UDT after 12 months of age have been reported, which suggests that the results of physical examinations even by experienced pediatric surgical and urologic specialists are not always accurate and may result in patients with retractile testes undergoing orchiopexy. We considered initial evaluation results indeterminate for 6% of referred patients, but it is possible that some cases we diagnosed as UDT were only testicular retraction and some considered normal represented UDT. However, of 18 patients 1 to 10 years of age with negative birth history findings whom we diagnosed as having UDT, 8 had a nonpalpable testis, and a patent processus vaginalis, which commonly occurs with UDTs and would not be expected with retractile testes, was found for 5 during orchiopexy. Furthermore, no patient with a diagnosis of UDT was found to have a descended testis after induction of general anesthesia for orchio-
pcy, when cremaster muscle contraction should be reduced. Agarwal et al\textsuperscript{15} reported that retractile testes sometimes are later found to be undescended, especially when there is tension on the spermatic cord (ie, cases we characterized as indeterminate). The 3 patients whose evaluations remained unclear continue with follow-up examinations scheduled as recommended.

Applying evidence-based findings regarding means to change physician practices, Brown et al\textsuperscript{14} considered physician education alone ineffective to prompt earlier referral. They instituted a regional system that combined a letter from the newborn nursery informing PCPs of UDT, parent leaflets when the birth examination yielded positive findings for UDT, and a policy that referrals to surgical specialists should be made by 8 months of age in all cases in which there was doubt by PCPs regarding normal testicular position. Reductions in both age at referral and number of orchiopexies performed were noted after these 3 measures were instituted.

We agree with Brown et al\textsuperscript{14} that a universal policy among PCPs that referrals should be made by 8 months for all patients with a question of abnormal testicular position would increase the number of orchiopexies performed during the recommended time period. For cases in which a question arises after 8 months, our observations that term boys 1 to 10 years of age with negative birth history findings and visibly symmetric scrotum rarely have UDT should reduce unneeded referrals for retractile testes and should clarify the role, if any, of secondary testicular ascent.

CONCLUSIONS

In this study, only one-half of the patients referred by PCPs for evaluation of UDT had UDT, and their median age significantly exceeded recommendations that orchiopexy be performed before 12 months of age. Boys <1 year or >10 years of age were more likely to have UDTs than were those between 1 and 10 years of age, which suggests confusion in distinguishing UDTs from retractile testes. A history of UDT diagnosed at birth, prematurity, and the finding of scrotal asymmetry increased the odds for UDT by 21.4-, 6.8-, and 121.3-fold, respectively. Boys without these risk factors should undergo repeat examinations for retractile testes before referral to a surgical specialist. Genital ultrasonography does not distinguish UDTs from retractile testes.

ACKNOWLEDGMENTS

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REFERENCES

APPENDIX  Standardized History Questionnaire for Patients Referred for Evaluation of UDT

Was your child born full term or premature?
Did the doctors at the hospital where your child was born mention a problem with his testicle?
If not, when was the first time a doctor said the testicle was not in the normal position?
Was the doctor who first mentioned a testicle was not in the correct place a new PCP or has he had the
same PCP his whole life after discharge from the hospital?
Have any x-ray tests been performed to evaluate the testicles?
Current Referral Patterns and Means to Improve Accuracy in Diagnosis of Undescended Testis
Warren Snodgrass, Nicol Bush, Michael Holzer and Song Zhang
Pediatrics 2011;127:e382; originally published online January 24, 2011;
DOI: 10.1542/peds.2010-1719

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DOI: 10.1542/peds.2010-1719

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/127/2/e382.full.html
Inappropriate Use of Ultrasound in Management of Pediatric Cryptorchidism

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BACKGROUND AND OBJECTIVES: There is a limited role for ultrasound in the management of an undescended testicle (UDT). We hypothesized that ultrasound remains overused by referring physicians. Our goal was to characterize the trends, patterns, and impact of ultrasound use for UDT and to reaffirm its limited diagnostic value for this indication.

METHODS: The records of boys aged 0 to 18 years with UDT in Ontario, Canada, between 2000 and 2011 were reviewed by using health administrative data housed at the Institute for Clinical and Evaluative Sciences (ICES). A second review of boys referred to our institution with UDT between 2007 and 2011 was conducted to complement the health administrative data. Trends in frequency, distribution, and costs of ultrasound use were assessed. Time delays between diagnosis and definitive management were compared between the ultrasound and non-ultrasound groups. Using our institutional data, we analyzed demographic patterns of ultrasound use and compared its diagnostic accuracy by using surgical findings as the gold standard.

RESULTS: Ultrasound was used in 33.5% of provincial referrals and 50% of institutional referrals. Children who underwent ultrasound experienced an approximate 3-month delay in definitive surgical management. Ultrasound correctly predicted physical examination findings in only 54% of patients. Physicians in community practice, and those with fewer years in practice, were more likely to order ultrasound.

CONCLUSIONS: Ultrasound has limited value for the management of UDT but remains widely overused, with an increasing trend over time. This practice has negative implications for access to care and cost-containment. Widespread educational efforts should be undertaken, targeting current and future referring physicians.

WHAT’S KNOWN ON THIS SUBJECT: The value of ultrasound imaging for the diagnosis, prognosis, and surgical planning of cryptorchidism is limited at best.

WHAT THIS STUDY ADDS: Ultrasound remains grossly overused by referring physicians throughout Ontario, Canada, which resulted in a 3-month delay to definitive surgery and unnecessary expenditures.
Cryptorchidism (or undescended testicle [UDT]) represents one of the most common congenital genitourinary anomalies in boys, affecting ~3% of term infants and 30% of premature infants. Most gonads descend to their expected location during the first 3 months of life, a process believed to be mediated by the physiologic testosterone surge in the neonatal period, such that only ~1% of boys still have cryptorchidism by 6 to 12 months of age. In these cases, contemporary management involves accurate diagnosis according to physical examination and timely surgical management, as highlighted in the recent American Urological Association guidelines on the evaluation and treatment of children with cryptorchidism. The goals of surgical exploration include identification of the gonad, obliteration of the often-associated patent processus vaginalis, and relocation of the testis into its normal anatomic location to facilitate screening for malignant degeneration (by self-examination) and maximize future spermatogenesis. Although there is little controversy regarding the benefits of orchidopexy, extensive literature discusses the ideal timing for the procedure. In general, consensus favors earlier orchidopexy (ie, between 6 and 12 months of age) to achieve these goals.

The value of ultrasound imaging for the diagnosis, prognosis, and surgical planning of UDT is limited, which is underscored in the American Urological Association guidelines. Indeed, a growing body of literature supports the low sensitivity and specificity of this imaging technique. Performing a potentially unnecessary ultrasound not only results in avoidable health care expenditures but could also occupy equipment and technician time, thereby delaying testing for patients who truly require a timely diagnostic ultrasound. Furthermore, false-negative and false-positive ultrasound results for UDT can misguide surgical decision-making and counseling, and may generate unnecessary parental anxiety. Despite the technique’s reportedly poor diagnostic performance, cost, and disadvantages, recent survey data suggest that obtaining an ultrasound before referral to a specialist is common among surveyed medical practitioners. Objective data that describe and unify the usage, costs, benefits, and potential consequences of ultrasound for UDT are lacking. We hypothesized that ultrasound remains significantly overused in this context. The present study analyzed the use and expense of this imaging technique within a “universal access to health care” setting, resulting in the largest analysis to date on the subject. We determined how the practice may adversely affect access to timely definitive surgical care. In addition (included as Supplemental Information), we re-examined the diagnostic accuracy of ultrasound for UDT and evaluated the demographic characteristics of referring practitioners to help focus future educational efforts.

**METHODS**

This study was approved by the Research Ethics Board at The Hospital for Sick Children, Toronto, Ontario, Canada. A 2-pronged approach was used for data collection. We obtained access to a provincial population-based health administrative (HA) database, which includes data on all hospital and ambulatory services in our universal access, single-payer health care system in Ontario. To complement the inherent weaknesses of HA data, a chart review was conducted of patients referred to our institution, which is the largest pediatric tertiary referral center in the nation. Findings from this review were validated by examining data from McMaster Children’s Hospital. These 2 institutions serve as one of the largest pediatric urology referral centers in Canada and North America, with a combined catchment of ~7.2 million people.

**Population-Based Analyses**

Records of boys aged 0 to 18 years diagnosed with UDT in Ontario between 2000 and 2011 were linked by using unique, anonymized, encrypted identifiers across HA databases housed at the Institute for Clinical and Evaluative Sciences (ICES). ICES is a publicly funded nonprofit research organization that evaluates health care services and delivery in Ontario. The data sets used in this study (Canadian Institute for Health Information–Discharge Abstract Database, Canadian Institute for Health Information–Same Day Surgery, Canadian Institute for Health Information–National Ambulatory Care Reporting System, Ontario Health Insurance Plan, and the Registered Persons Database) contain information on all publicly insured hospital and physician services, and they are described in Supplemental Appendix 1. Diagnoses originating from inpatient or emergency department visits were identified by using International Classification of Diseases, Ninth Revision, codes and ambulatory diagnoses according to the Ontario Health Insurance Plan code (Supplemental Appendix 2). Patients were stratified into groups based on whether an ultrasound (abdominal, pelvic, and/or scrotal) was performed within 1 year before specialist referral for assessment of cryptorchidism. If the ultrasound diagnostic code was missing, the patient was still included provided that the index diagnosis was “cryptorchidism,” there was a subsequent referral to a defined specialist, and an orchidopexy was performed. Specialists who perform orchidopexy were defined as urologists (adult/pediatric) and general surgeons (adult/pediatric). Patients who were referred to
specialists were segregated into those who underwent orchidopexy for UDT and those who did not, based on the combined findings of diagnostic and procedure codes for UDT and related surgeries, respectively. Patients who underwent orchidopexy for unrelated conditions (eg, testicular torsion) were excluded. To ensure an adequate follow-up window, patients whose index diagnosis was <1 year from the study end date were also excluded. Trends in frequency of performing ultrasound for UDT over the decade were assessed. Expenditures were calculated based on the sum of physician and technical fees for ultrasound reimbursement according to provincial fees (Ontario Schedule of Benefits), adjusted to the year the ultrasound was performed. Of note, charges, fees, and final reimbursements for specific services do not differ within a calendar year because they are centrally regulated by the single-payer provincial health plan. For patients with complete records from diagnosis and referral to surgery, times between index diagnosis by referring physician and specialist visit (Dx-Sp), index diagnosis by referring physician and surgery (Dx-Sx), and specialist examination to surgery (Sp-Sx) were compared between the ultrasound and non-ultrasound groups.

Tertiary Referral Center Analyses
Consecutive referrals for evaluation of UDT between June 1, 2007, and December 31, 2011, were evaluated; boys aged 0 to 18 years were included, and those with previous ipsilateral inguinal/scrotal surgery were excluded. Patients were stratified on the basis of whether an ultrasound was obtained by the referring practitioner before specialist assessment. Trends in the frequency of ultrasound use were compared. Costs incurred were estimated based on the type of ultrasound performed and contemporary reimbursement fees. Data were contrasted with information available from a neighboring academic pediatric institution.

Because detailed content of all reports and referrals was accessible, the relative timing of each ultrasound with respect to the referral date was accurately calculated. Patients were thus divided into 3 groups for comparison: (1) index diagnosis and referral occurred on the same day with no ultrasound ordered; (2) index diagnosis and referral occurred on the same day, and ultrasound occurred while patient awaits specialist appointment; and (3) the ultrasound was ordered at index diagnosis and completed before referral to specialist. As described in the population-based analysis, time delays were compared. If available, dated copies of ultrasound requisitions were obtained to further quantify the time between index diagnosis and ultrasound in the last group.

Detailed methods regarding referring practitioner data, ultrasound diagnostic accuracy, and statistical analyses are included in the Supplemental Methods.

RESULTS
Population-Based Analyses
Diagnosis and Ultrasound Use
During the study period, 101,278 boys were diagnosed with inguinal/scrotal pathologies including UDT and closely related conditions (defined in Supplemental Appendix 2). Of these, 16,160 (16.0%) had 1 ultrasound before definitive assessment, and 2450 (2.4%) had >1 ultrasound. Of all boys in the cohort, 46,234 (45.7%) were ultimately assessed by a specialist within 1 year of diagnosis. Of the children who were assessed by a specialist, 7466 (16.1%) underwent surgical exploration for a suspected diagnosis of UDT, and of these, 2483 (33.3%) had at least 1 previous ultrasound. The remaining 38,768 (83.9%) patients were assessed by a specialist but did not undergo surgical exploration, indicating an alternative diagnosis (eg, retractile testes). Of the 18,610 patients who underwent ultrasound in the entire cohort, 16,014 (86%) did not undergo surgery within 1 year of the ultrasound examination, again indicating the presence of an alternative, nonsurgical diagnosis.

Ultrasound Trend Over Time
Of the 7466 boys who underwent surgical exploration for UDT, there was a 31.4% increase in ultrasound use by referring practitioners over the decade ($P < .0001 for trend), as shown in Fig 1. Patients with an index diagnosis in 2010 were excluded to ensure adequate follow-up.

Ultrasound Costs
When accounting for changes in the reimbursement schedule over the studied decade, of Can$1.8 million spent on ultrasounds for the study population, approximately $270,000 were devoted to children who underwent surgical exploration for UDT. Approximate contemporary provincial reimbursement for the technical and physician fees of an abdominal, pelvic, or scrotal ultrasound was $80 per test.

Time Delays
Complete data points (including dates of index diagnosis, ultrasound [if obtained], specialist referral, specialist visit, and surgery [if conducted]) were available in 1999 (27%) of 7466 patients. The remaining patients were excluded because: (1) ≥1 of the listed dates were missing; or (2) the time between the first and last data points exceeded a reasonable time period, arbitrarily chosen as 84 months. Patients who underwent ultrasound before specialist referral had statistically significantly longer Dx-Sp and Dx-Sx times than patients who did not have ultrasound, by a median of 3 and 2 months, respectively ($P < .001). Sp-Sx times did not differ between groups, indicating that the
surgical delay was not related to specialists’ delays in performing surgery but rather in time to be assessed. Details are summarized in Table 1.

**Tertiary Center Analysis**

**Patient Demographic Characteristics and Ultrasound Use**

During the study period, 1310 consecutive patients presented for evaluation, and 119 were excluded due to previous ipsilateral inguino-scrotal surgery. Of the remaining 1191 patients, 598 (50%) had at least 1 ultrasound, arranged by the referring practitioner, before specialist assessment. Table 2 summarizes the patients’ demographic characteristics.

**Diagnosis and Ultrasound Use**

Of the 1191 patients included, 58 patients were ultimately not evaluated because of missed/canceled appointments or other unknown reasons. Of the remaining 1133 patients who were evaluated by a pediatric urologist, testicles were in a normal location or retractile in 449 (39.6%) patients; palpable UDT were noted in 471 (42.6%), nonpalpable UDT in 207 (18.3%), and atrophic (“nubbin”) testes in 6 (0.5%). Ultrasound was obtained in 41% (182 of 449) of normal/retractile testes, 53.7% (253 of 471) of palpable UDT, 62% (128 of 207) of nonpalpable UDT, and 100% (6 of 6) of nubbin testes. Patients with nonpalpable testes were more likely to have an ultrasound than patients with palpable testes ($P = .0002$).

**Ultrasound Trend Over Time**

There was a 15.6% increase in the proportion of patients with UDT who were referred with an ultrasound. This finding represents an increase from ~46.7% (42 of 90) of patients referred with ultrasound in 2007, to 54% (169 of 313) in 2011 (Fig 2).

**Ultrasound Costs**

Using the 2012 Ontario Schedule of Benefits, the technical and physician fees for an abdominal or pelvic ultrasound are $81.95 each and $77.05 for a scrotal ultrasound. Based on the dictated ultrasound reports, abdomen/pelvis/scrotum examinations were performed in 46 patients, abdomen/pelvis examinations in 8 patients, and pelvis/scrotum examinations in 544 patients. Serial pelvic/scrotal ultrasound examinations were performed for 18 patients. Based on these calculations, the estimated cost of ultrasound for UDT over the study period was Can$101 713.

**Access to Care and Treatment Delays**

Compared with patients with no ultrasounds, patients with ultrasounds before referral waited a median 110 days longer to see a specialist (Dx-Sp) and overall 104 days longer for surgery (Dx-Sx). There was no difference in median Sp-Sx between the ultrasound and non-ultrasound groups, as in our population-based review. Details are summarized in Table 3. In 104 patients for whom ultrasound request dates were also available, median time from ultrasound request (index diagnosis) to referral was 76 days. Detailed results regarding referring physician data, ultrasound diagnostic accuracy, and external validation are provided in the Supplemental Results.

**DISCUSSION**

Despite its limited value in the evaluation of UDT, ultrasound remains widely used. Our study reports this practice in 33.5% of provincial referrals and 50% of institutional referrals. Moreover, trends indicate that ultrasound use has increased over time. This overuse represents a substantial added cost in an already strained single-payer, universal access system. Perhaps more importantly, it delays timely corrective surgery by ~3 months, which may adversely affect outcomes. These findings have widespread implications for resource utilization and access to care, even outside of the Canadian context.
The inaccuracy of ultrasound for cryptorchidism has been established previously.2,4,13 Our results confirm the unreliability of the test, but additionally, we highlight diagnostic pitfalls that can result in mismanagement, challenging parent counseling scenarios, and avoidable medico-legal concerns. For example, some “normal” or retractile testes on ultrasound were identified as intra-abdominal during surgery. With a falsely reassuring ultrasound, the referring physician may avoid or delay a necessary referral. Ultrasound also misdiagnosed absent testes as inguinal. Preoperative parental expectations in this case can result in awkward and difficult postoperative counseling scenarios, and even unnecessary added surgery or imaging. Numerous other potential clinical pitfalls exist, which, when combined with the cost and time-delay findings, make the drawbacks of ultrasound apparent. As highlighted in current guidelines, a thorough physical examination by an experienced examiner is the best preoperative assessment in most cases.3,12,18

Unfortunately, our data show that overreliance on ultrasound is increasing despite a growing body of evidence recommending against it. A literature review revealed that several smaller studies and editorials, in addition to those by Talian, Copp, and Elder, have been published discussing the limited utility of ultrasound.2,4,13,19–24 There is a clear disparity between published evidence and the practice we have uncovered. Why the discrepancy, and how can we rectify the problem? As noted by Elder,25 this evidence has been largely published in the urology literature, rather than journals circulated among referring physicians and tertiary care subspecialists. Similarly, physicians with fewer years in practice may rely more heavily on diagnostic imaging overall. Due to faster, more accurate, and more widely available technologies, the use of radiologic tests has increased.26 In pediatric populations, there is a push toward minimizing ionizing radiation, thus favoring investigations such as MRI and ultrasound.27 For many conditions, earlier imaging has resulted in increased diagnostic yield and earlier presentation.28 Ultrasound for UDT should remain a clear exception to this trend. Focusing educational efforts at the medical school and internship levels may be the most effective long-term approach for achieving a durable change in practice.

We further defined the problem by identifying high-yield groups: those in community practice and less experienced physicians. Perhaps physicians in nonacademic practice have less access to specialists, routine university rounds, or multidisciplinary continuing education activities. Technologies such as videoconferencing and e-newsletters can potentially improve the dialogue between community physicians and tertiary care subspecialists. Similarly, physicians with fewer years in practice may rely more heavily on diagnostic imaging overall. Due to faster, more accurate, and more widely available technologies, the use of radiologic tests has increased.26

An additional unexpected finding of our study was that only ~50% of children were referred before 2 years of age. This significant delay counters current guidelines and could negatively affect testicular function.5,29 This finding held true regardless of whether an ultrasound was ordered. In addition, it is unlikely that this delay resulted from limited specialist access in Canada; a similar finding has been recently published from a group based in the United States.30

### TABLE 2

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (N = 1191)</th>
<th>Ultrasound (n = 598)</th>
<th>No Ultrasound (n = 593)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age at referral, mo (IQR)</td>
<td>23.5 (10–64)</td>
<td>19.3 (9–63)</td>
<td>23.3 (10–65)</td>
<td>.34</td>
</tr>
<tr>
<td>No. (%) of patients &lt;1 year of age at referral</td>
<td>361 (30.3)</td>
<td>196 (32.7)</td>
<td>165 (27.8)</td>
<td>.15</td>
</tr>
<tr>
<td>No. (%) of patients &lt;2 years of age at referral</td>
<td>631 (53)</td>
<td>328 (54.9)</td>
<td>303 (51.1)</td>
<td>.18</td>
</tr>
</tbody>
</table>

IQR, interquartile range.
States. Wider dissemination of updated practice guidelines is clearly needed. When coupled with our other relevant findings, they may result in a more compelling case for change.

Cost-effective assessment of cryptorchidism should limit the use of ultrasound to select scenarios, a decision that can be safely deferred to the specialist. Even when considering the relatively low cost of ultrasound in our health care setting, the additive economic impact may be substantial. In addition, there are other hidden costs to society, including unmeasured figures such as loss of productive time and parent absenteeism. Lastly, in a strained system, obtaining an unnecessary ultrasound can lead to secondary delay for other patients truly in need of timely ultrasound assessment.

Although large population-based data sets are a powerful research tool, they introduce several limitations. One weakness of these retrospectively coded HA data are the possibility of missing or inaccurate codes. To address this bias, we eliminated patients from the time-delay analysis with missing or incongruent codes in their timeline. Although this method offers a cleaner data set, the study power is diminished. Another limitation results from the complete anonymity outside of the coded system, whereby researchers cannot access imaging report details, specific test indications, or surgical reports. Consequently, some assumptions must be made within the code-searching algorithm. The algorithms can be selective and complex, but we cannot ensure that no inappropriate inclusions or exclusions exist. Thus, to supplement these population-based analyses, we conducted tertiary care reviews, which still represent a sizable population, to help complete the picture by accessing to more detailed clinical information. There is a notable discrepancy in the ultrasound rates between the HA and local data. This outcome could represent an underestimate by the HA data due to misclassification, or an overestimate by the local data due to referral bias, because those referred to our high acuity tertiary center would more likely need surgery. Reality may lie in between, which reinforces the value of complimentary data sets. The conclusion that ultrasound is tremendously overused holds true regardless, which is also validated by data from the neighboring McMaster University. Despite these limitations, we paint a valuable picture of current practices by using these combined approaches and highlight worrisome trends. As we optimize evidence-based management of this common condition, there is a clear need to increase value and make productive, decisive strides toward improving management by effective use of finite health care resources.

**TABLE 3  Median Time (IQR) Between Specialist Evaluation and Surgery Stratified According to Whether and When an Ultrasound Was Performed (N = 1191)**

<table>
<thead>
<tr>
<th>Median Time Interval in Days</th>
<th>Ultrasound Before Referral (n = 477)</th>
<th>Ultrasound After Referral (n = 121)</th>
<th>No Ultrasound (n = 583)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dx-Sp</td>
<td>221</td>
<td>153</td>
<td>111</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Dx-Sx</td>
<td>323</td>
<td>246</td>
<td>219</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Sp-Sx</td>
<td>93</td>
<td>103</td>
<td>85</td>
<td>.64</td>
</tr>
</tbody>
</table>

IQR, interquartile range.

**CONCLUSIONS**

Ultrasound has limited value for diagnosing, treatment planning, and prognosticating UDT. Although ultrasound may appear to be a harmless investigation, we found that it can delay access to timely corrective surgery and can mislead referring physicians and specialists alike. This weighty misallocation of resources could be channeled to children in need; it is also an area of potential cost savings at a time when health care budgets are under scrutiny. Furthermore, children are being referred late, regardless of whether ultrasound is used, which is another area with significant room for improvement.

Although widespread educational efforts should be undertaken, the targeting of current and future referring physicians is crucial. A multifaceted approach will likely have the biggest impact. Potential ideas include dissemination of guidelines in the pediatric and radiologic literature, interdisciplinary e-rounds, mandatory continuing medical education credits, telemedicine journal clubs, online “ask-the-expert” sessions, and targeted efforts in medical school. With the variety of communication and social media technologies available today, there is no better time to initiate a lasting change in practice.

**ACKNOWLEDGMENTS**

The HA data sets used in this study were linked by using unique encoded identifiers and analyzed at ICES.

**ABBREVIATIONS**

Dx-Sp: time between index diagnosis by referring physician and specialist visit
Dx-Sx: time between index diagnosis by referring physician and surgery
HA: health administrative
ICES: Institute for Clinical and Evaluative Sciences
Sp-Sx: time between specialist examination and surgery
UDT: undescended testicle
REFERENCES


THE PERKOS OF FREQUENT DINING: My wife and I recently had dinner with one of her brothers and his wife at an upscale restaurant in Brookline, MA that my brother-in-law likes very much. We had just returned from an overseas trip and wanted to thank him for taking us to the airport and picking us up upon our return. Unfortunately, our flight was delayed, so we were running late for our dinner reservations. My brother-in-law called the restaurant to let them know we would be late. He then asked the receptionist what table we had been assigned. After getting the answer (a number) he told us that the table was his least favorite, as it was immediately adjacent to the swinging doors entering the kitchen. I was a bit surprised that he knew the tables so well. He and his wife rarely cook and eat out frequently so his response made me contemplate the relationship between restaurants and frequent diners.

As reported in The Wall Street Journal (Life: May 12, 2015), restaurants keep close tabs on frequent diners – called VIPs, as corporate accounts from repeat customers can make up a substantial portion of revenue. A frequent diner is one who eats at a restaurant two to three times in two weeks. Restaurants use all sorts of methods to better understand their frequent diners including Google searches, a web site that pulls photos from Facebook and LinkedIn profiles, meticulous notes from discrete conversations with the diner, and ordering history. The favorite foods, beloved special sauces, favored seating arrangements, and table preferences are carefully noted so that all are ready upon arrival of the frequent diner. The top VIP diners may be showered with birthday presents, secret food deliveries, and free champagne. All this is done so that the frequent diners feel comfortable and do not have to look like they are asking for something special in front of clients.

As for me, I found the food at the restaurant good, and the doors did not bother me. I guess my brother-in-law – who mostly just dines with his wife – was not a VIP in the eyes of the restaurant, but he certainly is to me.

Noted by WVR, MD
### Inappropriate Use of Ultrasound in Management of Pediatric Cryptorchidism

Niki Kanaroglou, Teresa To, Jingqin Zhu, Luis H.P. Braga, Elias Wehbi, Mohammed Hajiba, Darius J. Bägli, Joao Pippi Salle, Martin A. Koyle and Armando J. Lorenzo

*Pediatrics* 2015;136;479; originally published online August 10, 2015;
DOI: 10.1542/peds.2015-0222

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/content/136/3/479.full.html
Minimally invasive nephrectomy for Wilms tumors in children – data from SIOP 2001

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Tumor resection

A B S T R A C T

Purpose: To analyse the surgical and oncological outcome of minimally invasive surgery (MIS) for tumor nephrectomy in Wilms tumor (WT) patients.
Methods: WT patients from the SIOP 2001 trial, undergoing MIS for tumor nephrectomy were analyzed with regard to demographic characterization, surgical specifications, complications, and outcome.
Results: There were 24 children matching the inclusion criteria. Median age at operation was 40.35 months (14.3–65.4). All patients received preoperative chemotherapy. Median tumor volume was 177.5 ml at diagnosis (46.5–958) and 73.0 ml at surgery (3.8–776). There was one surgical complication (spleenic injury), no intraoperative tumor rupture occurred. Abdominal stage was I in 14, II in 7, and III in 3 patients. Adequate lymph node sampling was performed in only 2 patients. One local relapse occurred. Event-free survival was 23/24, overall survival was 24/24, median follow up was 47 months (2–114).
Conclusions: We present the largest series so far of minimally invasive nephrectomies for nephroblastoma based on a multinational trial. Treatment results were comparable to those of open surgery; however, experience of operating surgeons was generally high. Discipline of lymph node sampling was inadequate. Based on this analysis a prospective study on MIS in nephroblastoma is planned by the SIOP Renal Tumor Study Group.

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Surgery plays a key role as local treatment for nephroblastoma. The guidelines for resection of Wilms tumors (WT) have been well established and have by now been thoroughly analyzed [1–4]. From the surgical point of view, complete tumor resection is one of the main prognostic factors in the treatment of WT [3,4]. For many years, open nephrectomy was the common surgical approach in unilateral cases. However, alternative surgical concepts have been introduced during recent years and are meanwhile used to a relevant extent. Minimally invasive surgical (MIS) procedures are regularly used in pediatric surgery for standard as well as complex operations [5,6]. This approach is especially relevant in pediatric urologic operations of the upper urinary tract [7,8]. MIS also plays a certain role in pediatric surgical oncology although the exact relevance in most entities has not yet been determined [9–11]. The use of MIS in patients suffering from WT has been reported in singular cases [12–14], however, a systematic analysis has not been undertaken so far and by now there are no evidence based data available. This is of importance since the minimally invasive approach seems to be increasingly used. Current treatment protocols do not contain surgical guidelines or recommendations concerning indications and contraindications for MIS in WT. In this study we systematically assessed for the first time the role of MIS in the treatment of Wilms tumors based on a multicenter prospective data registration. The outcome parameters were technical/surgical aspects (including tumor rupture, lymph node sampling, and complications), as well as oncological measures (event-free survival and overall survival).

1. Materials and methods

1.1. Patients

Patients with newly diagnosed nephroblastoma were registered in the multicenter trial SIOP 2001 by participating institutions. We
retrospectively analyzed all children suffering from unilateral WT who underwent laparoscopic tumor resection between June 2001 and July 2013. Data were obtained from the central SIOP 2001 data base in Amsterdam/The Netherlands. Patients’ characteristics, surgical data as well as clinical and oncological outcome measures were assessed. The multi-institutional study was approved by the Institutional Review Board of the Ärztekammer des Saarlandes, Germany (No. 136/01).

1.2. Treatment

All patients registered within the above cited time frame were to be treated following the SIOP 2001 protocol guidelines. According to this protocol, patients older than 6 months should receive neoadjuvant chemotherapy depending on the tumor stratification: Actinomycin D/Vincristin (AV) over 4 weeks in localized cases, Actinomycin D/Vincristin/Doxorubicin (AVD) over 6 weeks in metastasized cases. The recommended doses were: Actinomycin D 45 μg/kg once every 2nd week, Vincristin 1.5 mg/m² once every 4 weeks, Doxorubicin 50 mg/m² every 4 weeks. Doses should be reduced to 2/3 in cases of body weight below 12 kg (and further to 1/2 if poorly tolerated). Tumor response to initial chemotherapy was defined comparing volume at diagnosis and volume at surgery. Primary tumor response was assigned as complete response (CR: complete disappearance of the tumor), partial response (PR: volume regression more than 50%), stable disease (SD: volume regression between 0 and 50%), and progressive disease (PD: volume increase under chemotherapy).

Neoadjuvant chemotherapy was to be followed by resection of the primary tumor as local treatment [3,15]. According to the protocol, laparoscopy was not banned as approach for tumor nephrectomy. The postoperative treatment strategy (chemotherapy ± radiotherapy and treatment of possible metastases) depended on the postoperative staging and the histological risk stratification [16,17].

2. Results

2.1. Population demographics (Table 1)

The total number of registered patients within SIOP 2001 during the study period of this analysis was 4763, 4220 of the patients had nephroblastoma. Overall there were 24 children undergoing MIS for Wilms Tumor resection during the study period, 16 female and 8 male patients. Of all patients, 11 were enrolled from the Children’s Cancer and Leukaemia Group (CCLG) in the UK, 7 from the Society of Pediatric Oncology and Hematology (GPOH) in Germany, 5 from the French Society against cancers in children and adolescents (SFCE) in France, and 1 from the Brazilian Wilms Tumor Study Group (GCBTTW) in Brazil. Median age of patients at diagnosis was 39.35 months (range 11.9–63.9). Tumor localization was on the right side in 14 patients and on the left side in 10 patients. The median tumor volume at diagnosis was 177.5 ml (range 46.5–958). Localized tumors were present in 22 children, metastatic tumors in 2 (lung metastases in 1 patient and abdominal metastases in 1 patient, Table 1).

### Table 1

<table>
<thead>
<tr>
<th>Pat. No.</th>
<th>Gender</th>
<th>Age at diagnosis [M]</th>
<th>Side</th>
<th>Neoadjuvant chemotherapy</th>
<th>Tumor volume [ml]</th>
<th>Initially</th>
<th>At surgery</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>51.6</td>
<td>L</td>
<td>AV</td>
<td>251.7</td>
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<td>F</td>
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<td>F</td>
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<td>R</td>
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<td>300.0</td>
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</tbody>
</table>
2.2. Chemotherapy/radiotherapy

Before operation, all children received neoadjuvant chemotherapy (19× AV, 4× AVD, no data for 1 patient). The median tumor volume regressed under chemotherapy from initially 177.5 ml (range 46.5–883) to 73.0 ml (3.8–776, Table 1). Taken together there was partial response to chemotherapy in 18 tumors, stable disease in 2 tumors, and progressive disease in 2 tumors (no data for 1 patient). All children except one received postoperative chemotherapy (12× AV, 9× AVD, 2× other regimens). Postoperative local radiotherapy was applied in 2 children (Table 2).

2.3. Surgical and pathological data (Tables 1–2)

All patients underwent transperitoneal laparoscopic tumor nephrectomy (Fig. 1). The median age of patients at surgery was 40.35 months (range 14.3–65.4). Before surgery the median tumor volume on imaging was 73 ml (3.8–776). There was one preoperative tumor rupture (patient #15). Among the operating surgeons, there were 17 with pediatric surgery as subspecialty (no data for 7 cases). During the 2 previous years the number of nephrectomies for WT performed within the listed institutions was more than 10 in 7, 6–10 in 8, and 1–5 in 2 instances (no data in 7). The number of tumor nephrectomies for WT performed by the listed operating surgeon during the previous 2 years was more than 10 in 5 cases, 6–10 in 8 cases, and 1–5 in 4 cases (no data in 7 cases).

Complete tumor nephrectomy was performed in all children. There was one intraoperative complication (splenic injury, surgically managed by splenectomy). No conversion to open surgery had to be carried out. The median value of largest tumor diameter was 5.0 cm (2.8–12), median weight of resected specimen was 134 g (47–730).

According to the operating surgeon the tumor capsule was grossly intact in 17 specimens, operating surgeons were uncertain in 3 cases, and they regarded the capsule as not being intact in 2 cases (no data for 2 cases). Tumors were removed from the abdominal cavity using a Pfannenstiel incision in 6 cases or using an anterior transverse abdominal incision in 1 case (no data given for 17 patients).

Pathologically, there were positive margins in the 2 cases, in which the operating surgeon also had regarded the capsule as not being intact. Additionally, there were pathologically positive margins in one case, in which the surgeon had regarded the capsule as intact. Local tumor stage according to SIOP was I in 14, II in 7, and III in 3 instances. Reasons for stage III were positive margins in all three cases, in one of them there were also positive lymph nodes and in another one there was preoperative tumor rupture additionally.

Histological workup according to SIOP classification revealed intermediate risk histology in 20 (13× regressive, 4× mixed, 3× stromal subtype), and high-risk histology in 3 tumors (all blastemal subtype). There were no data for 1 case).

2.4. Lymph nodes

Lymph nodes (LN) were sampled in 15 of the 24 patients. Numbers of sampled nodes differed between 0 and 11. Positive LN were observed in 5 patients (Table 3).

2.5. Oncological outcome

One local relapse occurred in one patient (patient No. 12). In this patient initial treatment consisted of 4 weeks AV histological subtype was blastemal. The tumor had shown partial response under neoadjuvant chemotherapy, local stage was I, there were 3 lymph nodes sampled (all negative). Postoperative treatment consisted of AVD; no local irradiation was applied. The relapse occurred 8.5 months after surgery. After a median follow-up of 47 months (2–114) all patients were in complete remission, resulting so far in an event-free survival of 23/24 and an overall survival of 24/24 (Table 3).

3. Discussion

Minimally invasive techniques are well established in pediatric surgery. Urology represents one major field within this field. Laparoscopic procedures have become the standard approach for several operations on the upper urinary tract. This especially includes pyeloplasties and nephrectomies for benign pathologies [9,18,19]. In adults, MIS is regularly used for the surgical treatment of renal malignancies [20]. In children, Wilms tumors (WT) are more and more often resected laparoscopically, however, only infrequent analyses have been published by now, mostly reporting on small patients’ cohorts [12–14,21,22]. Very recently, Varlet et al. published the first multi center study on 17 children undergoing laparoscopic nephrectomy for renal malignancies. This study included 15 children with WT [23].

Guidelines and recommendations for minimally invasive techniques and criteria for their use have commonly not been included in the multicenter treatment protocols so far. On its meeting in Rome in 2012, the surgical panel of the SIOP Renal Tumor Study Group (RTSG) found it important to retrospectively analyze respective data of the most recent study (SIOP 2001) in order to define recommendations and guidelines for MIS in nephroblastoma to be included in the upcoming new treatment protocol. Based on these guidelines a prospective data acquisition and evaluation is then to be undertaken within the next trial.

The present study retrospectively analyzed data, which were obtained from various countries worldwide. Several limiting aspects of the analyses have to be considered.

The patient number is small and general conclusions are thus difficult to draw. Furthermore, follow-up in some patients is short with respect to an oncological analysis. Nevertheless, we are presenting the largest cohort of respective patients with important implications. The main purpose of this study was not to present a complete evaluation but rather to build up a basis for the further prospective analysis of MIS for nephroblastoma as stated above.
By the time the study, from which the analyzed data were collected, was set up, MIS did not play a great role in pediatric oncology and urology. Many technical improvements, surgical advances, and innovations of MIS in children have only been introduced during recent years through which MIS for nephroblastoma became more and more feasible. As a consequence, the number of laparoscopic WT operations was altogether low in the present study. Although feasibility is not the main aim of surgery in oncological patients, it seems very likely that the rate of laparoscopic nephrectomies for WT will further increase.

Another limitation of the present study results from the data collection. Many relevant details of surgical procedures were not recorded because MIS did not play a relevant role at the time when the collection modalities of surgical data were established. For example, there was no information about why surgeons chose the laparoscopic approach or why they didn't. Details of the operative technique were regularly lacking including trocar number and positioning, insufflation parameters, modality of specimen removal, and others. Furthermore, it is not known whether the removed kidneys were extracted in a bag without breakage (to allow an adequate pathologic evaluation), because this information was not considered in the surgical form. This information will be included in the next study. The same holds true for the extent of surgical incision to allow excision of the bag. With these experiences in mind, the surgical data acquisition will be adapted and improved for the next trial.

Despite the cited limitations there were numerous relevant aspects drawn from the analyzed data. There is an ongoing debate about indications and the general role of MIS in nephroblastoma. The SIOP 2001 protocol commonly recommends neoadjuvant chemotherapy in unilateral Wilms tumors except in patients younger than 6 months or older than 16 years. All children in this study received chemotherapy before surgery. Arguments pro and contra chemotherapy before operation have been thoroughly discussed between different Study Groups. Following the SIOP protocol, the rate of intraoperative ruptures with spillage of tumor cells is lower after neoadjuvant chemotherapy compared to primary surgery due to tumor shrinking and encapsulation [3]. This certainly holds true in MIS and therefore the authors emphasize the recommendations of preoperative chemotherapy before laparoscopic WT resection. There is a relevant difference of approaching nephroblastoma between different study trials. This mainly concerns the use of upfront surgery in North America (COG) without neoadjuvant chemotherapy in tumors that seem resectable. However, because of the stated risks of intraoperative tumor rupture and subsequent spillage, MIS should only be considered in Wilms tumors after initial chemotherapy.

Although, large tumors are an important issue because large tumors have a negative impact on Overall- and Event Free-Survival in Wilms Tumor protocol [31], NSS should be performed. If NSS is not possible because of unresectable tumor tissue, chemotherapy must be continued until the tumor is resectable. If NSS is not possible because the tumor is too close to a major blood vessel or the kidney is not considered resectable, an en-bloc nephrectomy without preoperative chemotherapy is recommended. The surgical approach can be chosen based on the results of the SIOP protocol.

Lymph node (LN) sampling was documented by surgeon in patient No. 23; however, biopsies did not contain LN material; Postop Chemotherapy: AV-1 = Actinomycin-D + Vincristin, AVD = Actinomycin-D + Vincristin + Doxorubicin, VCCD = VP-16 + Cyclophosphamid + Carboplatin + Doxorubicin; Outcome: NED = No evidence of disease.

Table 3

<table>
<thead>
<tr>
<th>Pat. No.</th>
<th>LN sampled</th>
<th>LN positive</th>
<th>Postoperative chemotherapy</th>
<th>Postoperative Radiotherapy</th>
<th>Relapse</th>
<th>Outcome</th>
<th>Follow-up [M]</th>
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<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>2</td>
<td>AVD</td>
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<td>-</td>
<td>NED</td>
<td>114</td>
</tr>
<tr>
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<tr>
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<td>-</td>
<td>-</td>
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WT patients (stage III, favorable histology) [32]. These aspects are especially important with regard to MIS. The adequate number of LN to be sampled (more than 6) has been determined previously [16,17], indicating an inadequate LN sampling in the present study. Because of the above stated limits of data collection in the analyzed study, the reasons for this were not recorded. Deficits of the discipline of LN sampling in WT surgery have been previously reported analyzing the open surgical approach [3]. These deficits seem even more severe in MIS. Because of the small total number of patients, a statistical negative impact of the inadequate sampling could not be calculated. Nevertheless, the laparoscopic approach for WT nephrectomy can only be accepted provided that the common oncological guidelines are strictly respected. Technical aspects of the operative approach must never be reason for compromises concerning the correct way of performing WT surgery. A thorough analysis of the role of MIS in WT surgery is mandatory, especially since there are already reports on the combined laparoscopic approach for WT nephrectomy can only be accepted provided that the common oncological guidelines are strictly respected, especially with regard to LN sampling. The future prospective evaluation of MIS for WT will bring further insight into the role of MIS in surgery for nephroblastoma.

Acknowledgement

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References


† Deceased.
Driving directions From CHCO to 4223 S Bellaire Cir, Englewood, CO 80113

1. From AMC Campus, Proceed East on E. Colfax Ave.
2. Turn right to merge onto I-225 South, proceed 8.7 miles
3. Take Exit 2A toward Tamarac St / DTC Blvd.
4. Merge onto I-225 Frontage Rd.
5. Turn Right at S. Tamarac St.
6. Take a slight left at E. Quincy Ave., proceed 0.9 miles
7. Turn right at Happy Canyon Rd., proceed 436 ft.
8. Turn left at E. Quincy Ave., proceed 1.3 miles
9. Turn Right at S. Bellaire Cir.
10. Destination will be on the left (4223 S. Bellaire Circle)