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Wilms Tumor-Follow-up Tailored Abdominal CT Examination

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Abstract
Purpose of Review Wilms tumor is the most common renal mass in infancy with peak incidence between 3 and 4 years old. Actual cure rates are around 90%. Current COG recommendations for imaging follow-up after treatment still include abdomino-pelvic CT for the first 18 months in a regimen that totals at least eight follow-up CTs before changing to US examinations. That represents a meaningful radiation exposure in patients who are more susceptible to stochastic effects, due to their low age.
Recent Findings Previous recent findings indicate that the pelvic segment can be safely excluded from routine follow-up CT examination, reducing radiation exposure and its risks, especially in regard of gonadal exposure with no loss of relevant oncologic information.
Summary There is currently no justification to sustain the recommendation of pelvic CT to follow up all Wilms tumor treated patients. In accordance with as low as reasonably achievable (ALARA) principle, this practice should not be routinely indicated.

Keywords Nephroblastoma · Wilms · Pelvic · CT · Radiation · Follow-up

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Introduction

Wilms tumor (WT) is the most prevalent renal mass in childhood, with peak incidence between 3 and 4 years old [1]. Contemporary survival for patients with WT is greater than 90% [2] and salvage rate for patients with relapsed disease is estimated at 50–60% [3]. Recommendations for imaging follow-up vary internationally. Regarding abdominal imaging follow-up, it may be performed using only abdominal ultrasound (US) up to 5 years after the end of therapy, as recommended by the Societé Internationale d'Oncologie Pediatrique (SIOP) and the UK Royal College of Radiologists [4], but it is still largely performed by serial abdomino-pelvic computed tomography (CT) during the first 2 or 3 years after the end of therapy, which may include 7–9 abdomino-pelvic CTs according to risk stratification, as the Children's Oncology Group (COG) recommendations [5].

Considering the good prognosis of WT, concerns are raised about the radiation exposure of repeated abdomino-pelvic CTs during diagnosis, treatment, and follow-up of this usually very young patient. Children are more sensitive to the stochastic effects of radiation and have more time to express these effects as they are expected to live longer [6]. Therefore, the overuse of CT should be curtailed, and limiting the size of the body region scanned is one way to minimize unnecessary dose [6]. The aim of this review is to question the value of including the pelvis on a routine follow-up abdomino-pelvic CT of Wilms tumor.

Our Previous Experience

It was based on our clinical experience that the CTs of the pelvic segment were not adding new relevant information nor changing clinical decisions that we did a review during

the year of 2009 of the medical records of 100 consecutive patients (between 2009 and 1997) with initial diagnosis of Wilms tumor at our institution (Pediatric Institute of Oncology, IOP/GRAACC/UNIFESP), which results were published as a residency conclusion monograph at our institution and as an oral presentation entitled "Image Gently Approach—Follow up of Wilms Tumor" on 2010 Society of Pediatric Radiology (SPR) meeting in Boston.

Patients who were mandatorily treated with adjuvant radiotherapy of total abdomen ($n = 14$), i.e., patients with disseminated peritoneal disease at diagnosis and those with ruptured tumor capsule pre-surgery or at surgery [7], were excluded from the analysis. At that time, we decided that abdominal radiotherapy would be an exclusion criterion due to futility to question diagnostic radiation. Another three cases were excluded, as follows: one case was misdiagnosed as WT and reclassified as a teratoid rhabdoid tumor after surgery; two others were excluded because they had pelvic malignancies at the time of diagnosis (one patient had a WT on an ectopic pelvic kidney and another one had a neurogenic second malignancy in the pelvis). Among all the 83 patients reviewed (Table 1), none presented relevant oncologic findings on routine pelvic CT follow-up, with a median follow-up period of 5 years and 3 months.

During the following years until mid of 2016, another 62 patients with low-risk WT were retrospectively reviewed for pelvic CT imaging findings (not published results). We consistently find no evidence of disease or of an eventual relevant secondary diagnosis that would change clinical management and stop including the pelvic CT segment for the follow-up imaging of these patients.

Recent Findings

Following our presentation at the SPR in 2010, the first paper addressing specifically the issue of the relevance of pelvic CT in this group of patients was published, by Kan et al. [8••], in 2011, with concordant results. Other papers with similar study questions were subsequently published, in 2013 [9•] and 2015 [10]. All of them endorsed the hypothesis that extending the CT evaluation to the pelvic segment would increase radiation exposure without adding relevant oncologic information and thus going against "as low as reasonably achievable" principle (Table 2).

Kan et al. [8••] reviewed 17 patients with WT and none of them was found to have pelvic metastasis during follow-up. The pelvic component of abdomino-pelvic CT examinations was relevant at initial diagnosis, picturing, for example, the 33% of patients that showed pelvic extension of the primary tumor and providing a whole idea of initial abdominal cavity involvement, but did not affect tumor staging at follow-up in any of the children.

Kaste et al. [9•] also questioned the value of routine pelvic surveillance imaging on the argument that lungs are the most common site of recurrence and are only seen in about 10% of patients. A secondary objective was to estimate the radiation dose savings when excluding the pelvic CT from the protocol. They found only three pelvic relapses among 110 patients, which occurred within 3 years from diagnosis. It is interesting to note that all of them were symptomatic at the time of recurrence and also had at least one risk factor previously described as to be associated with abdominal relapse, being older age at diagnosis (48 months at least) and higher stage (III). The authors conclude that omitting pelvic CT from routine off-therapy follow-up of Wilms tumor patients saves an average 30–45% effective dose without compromising disease detection.

Mirza et al. [10] studied 45 patients with Wilms tumor, with no significant difference in pelvic extension of disease at presentation. They report six metastatic cases noted on follow-up, one of them with pelvic metastasis.

Another study from 2015 [11] questioned the need of both abdomino-pelvic CT surveillance of WT, reviewed 64

Table 1 Demographics of our study population

Gender	Female	Male			
	59%	41%			
Laterality	Right	Left	Bilateral		
	46%	43%	6%		
Stages	I	II	III	IV	V
	12%	30%	38%	10%	6%
Size[a]	11.2 cm				
Age at diagnosis[a]	3 years 3 months (39 months)				

[a] Median values

Table 2 Manuscripts

Year	Author	Number of cases (Wilms tumor)	Pelvic disease at follow-up	% Pelvic +/total cases
2011	J Herman Kan et al.	17	0	0
2013	Sue C Kaste et al.	110	3	2,7
2015	Waseem Mirza et al.	45	1	2,2

patients, and found 9 (14%) relapses during the follow-up period: to the lungs, liver, and local recurrence, but none to the pelvis. They also cited that salvage rates were equally dismal in relapses detected clinically or by imaging and concluded that using US in preference to CT for abdominal surveillance of patients with WT, as SIOP recommends, would reduce radiation exposure and cost, without jeopardizing patient outcomes.

Discussion

Surveillance imaging varies widely among institutions, as do the recommendations among cooperative groups [12]. This important variation in recommendations for imaging both during and following therapy may hinder optimal clinical care for children with cancer [13].

CT accounts for 50% or more of the annual collective dose from medical imaging in developed countries but it seems that the number of CT requests is slightly declining in specialist pediatric centers, possibly related to an increase in the awareness of potential risks and more critical evaluation of requests [14]. Non-pediatric institutions are responsible for a significant portion of pediatric imaging in some countries [14], raising concerns about the considerable variability in the radiation dose of CT scanning and mainly, about the untailored CT examination for the pediatric patient—like performing multiphase CT studies, when portal-phase only would be preferred for the evaluation of WT, for instance [4]. Using adult protocols in children increases radiation exposure up to 6 times greater than the necessary to provide quality images [15].

Detecting a relapse earlier through aggressive radiological surveillance may not improve survival [13]. A review of 344 patients with unilateral WT has found that surveillance with CT/MRI scans was not associated with improved survival compared to surveillance with CXR/US [16]. Recurrence is seen in approximately 15% of favorable histology and 50% of anaplastic histology with most relapses occurring within 2 years of diagnosis [7]. Relapse occurs mostly in the lungs (60%), tumor bed and liver (30%), and rarely in the bone or brain.

Some authors suggest to abandon CT scanning for off-therapy surveillance imaging [1, 17], to replace it for magnetic resonance (MR) or to rely solely on clinical follow-up [17]. MR and CT have similar diagnostic performance and both can be used for imaging WT [18], with MR being superior in detecting contralateral lesion and recommended for nephroblastomatosis [4]. MR imaging, however, in this patient population, almost always requires sedation [18]. Although this is a relatively safe procedure on the operating room, the risks are increased when it is done on another physical environment—like the scanning room—or when the anesthetized patient has to be moved from one place to another [19]. Moreover, long-term risks of neurodevelopment impairment may be associated to general anesthesia in children younger than 2 or 3 years due to exposure to anesthetic agents during synaptogenesis [19]. Yet it is worth to mention that cost and unavailability of MR imaging are still an issue in limited resources environments [20].

One limitation of this review is that available results in literature regarding follow-up pelvic CT scanning in Wilms tumors are scarce and derived from exploratory research, based on observational retrospective studies and usually with a small sample size. Nevertheless, retrospective data represent an important source of information and we believe that this study question can be answered using data that have been already collected.

Conclusion

There is no actual consensus about routine abdominal imaging follow-up of WT after the end of treatment. Observational studies point to a lack of benefit and potential harm of including pelvic CT on the monitoring of patients, specially in early stages that do not disseminate to the pelvis. Pelvic CT should not be recommended to follow up off-therapy WT.

Compliance with Ethical Standards

Conflict of interest Renata de O. e S. Brenner, Rodrigo Regacini, and José Luiz de Oliveira Schiavon each declare no potential conflicts of interest. Henrique M. Lederman is a section editor for *Current Radiology Reports*.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • of importance and
- •• of major importance

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