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Review Articles

Is adrenalectomy necessary during unilateral nephrectomy for Wilms Tumor? A report from the Children's Oncology Group☆,☆☆

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Abstract

Purpose: To determine whether performing adrenalectomy at the time of nephrectomy for unilateral Wilms tumor impacts clinical outcome.

Methods: We reviewed information on all patients enrolled on National Wilms Tumor Study-4 and -5. Data were abstracted on patient demographics, tumor characteristics, surgical and pathologic status of the adrenal gland, and patient outcomes. The primary endpoints were intraoperative spill and five-year event-free survival (EFS) in patients who did or did not undergo adrenalectomy.

Results: Of 3825 patients with complete evaluable data, the adrenal was left in situ in 2264 (57.9%) patients, and was removed completely in 1367 patients (36.7%) or partially in 194 patients (5.2%). Of the adrenal glands removed, 68 (4.4%) contained tumor. Adrenal involvement was more common in patients with stage 3 (9.8%) than stage 2 disease (1.9%; $p < 0.0001$). After controlling for stage and histopathology, five-year EFS was similar whether or not the adrenal gland was removed ($p = 0.48$), or involved with tumor ($p = 0.81$); however, intraoperative spill rates were higher in patients undergoing adrenalectomy (26.1% vs

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15.5%, $p < 0.0001$), likely due to larger tumor size or technical factors. No patient had clinical evidence of adrenal insufficiency or tumor recurrence in the adrenal gland during follow-up (median 9.9 years).
Conclusions: Sparing the adrenal gland during nephrectomy for unilateral Wilms tumor was not associated with a higher incidence of intraoperative spill and was associated with a similar oncologic outcome, on a per-stage basis, with cases where the adrenal was removed. Thus, adrenalectomy should not be considered mandatory during radical nephrectomy for Wilms tumor.
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The National Wilms Tumor Study Group (NWTSG) conducted a series of multi-institutional clinical trials, beginning in 1969, which have identified prognostic factors and optimized treatment regimens for patients with Wilms tumor [1]. Based on this experience, the current standard of care for patients with localized Wilms tumor in North America is upfront unilateral nephrectomy with lymph node sampling. Histopathologic subtype and pathologic stage of the tumor determine the need for, and duration and intensity of, adjuvant chemotherapy and radiation therapy [2,3].

While it is generally accepted that the primary surgical objective in patients with localized Wilms tumor is complete resection of the neoplasm without spill, extensive resection of adjacent viscera to achieve a complete resection is discouraged because of the sensitivity of Wilms tumor to adjuvant therapy. However, although a classic radical nephrectomy includes resection of the ipsilateral adrenal gland [4], there are currently no specific recommendations regarding adrenalectomy in patients with clinically localized Wilms tumor; the management of the adrenal gland has typically been left to the discretion of the operating surgeon. There is also a dearth of literature on the incidence of adrenal involvement in patients with Wilms tumor; two published series report adrenal involvement in fewer than 2% of patients [5,6]. In addition, no studies have specifically addressed differential spill and survival rates based on whether or not the adrenal gland was removed as part of a radical nephrectomy in patients with unilateral Wilms tumor. Although patients with adrenal involvement can still be classified as stage 2 if all disease is resected with negative margins [7], (and therefore receive only two-drug chemotherapy following nephrectomy), the need to perform adrenalectomy when the adrenal appears to be uninvolved with tumor is unclear and may be driven more by the desire to avoid tumor rupture.

Conversely, adrenal insufficiency has very rarely been described following unilateral adrenal resection for either primary adrenal disease or as part of radical nephrectomy [8-10] and has never been observed in the NWTS experience. Nevertheless, this condition can be life-threatening in its acute manifestation and, when chronic, mandates lifelong mineralocorticoid and glucocorticoid replacement, with the attendant side effects of these medications. Furthermore, metachronous contralateral tumors are seen in approximately 1% of patients with unilateral Wilms tumor [11], and patients in whom the ipsilateral adrenal gland was removed as a matter of course during resection of the primary tumor may have fewer options for management of the recurrent disease without inducing adrenal insufficiency. Given the need to balance oncologic control and the potentially deleterious side effects of adrenalectomy, we undertook this study to formally assess the impact of adrenalectomy on clinical outcomes. The goal of this study was to determine the prognostic impact of adrenalectomy in patients treated on NWTS-4 and -5; specifically, whether adrenalectomy was associated with variations in event-free survival (EFS) or intraoperative spill rates in patients with unilateral, localized Wilms tumor.

1. Methods

After obtaining Institutional Review Board approval, the records of 3913 patients were reviewed; all were enrolled in the NWTS-4 and -5 studies and had undergone unilateral nephrectomy for non-metastatic Wilms tumor. Enrollment for NWTS-4 and -5 was ongoing between August 1986 and May 2002. Since therapy for unilateral, nonmetastatic Wilms tumor was similar in NTWS-4 and -5, with the primary difference being duration of therapy for favorable histology disease, the results from these two studies were combined for analysis. Patients who received pre-nephrectomy chemotherapy or who underwent partial nephrectomy for bilateral (or unilateral) disease, as well as those with evidence of metastatic disease were excluded. Patients with a diagnosis of clear cell sarcoma of the kidney, rhabdoid tumor of the kidney, or renal cell carcinoma were also excluded.

Data collected included patient demographics, tumor histopathology, surgical status of the adrenal gland (e.g. removed, preserved, or partially removed), the presence or absence of tumor in the adrenal gland, margin status, tumor weight, presence and extent of intraoperative spill, and pathologic stage. All histopathologic data were abstracted from the central pathology report except when slides of resected adrenal tissue were not sent for central review; in these few patients, the institutional assessment of adrenal involvement was recorded.

Event-free survival (EFS) was defined as the time from study entry until the first occurrence of disease progression, relapse after response, or death as a first event from any cause. Follow-up for patients not experiencing an event was censored at the time of last follow-up. Kaplan–Meier curves were calculated to estimate five-year EFS for various patient subsets.

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