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Routine adrenalectomy for renal cancer: an antiquated practice

Gennady Bratslavsky² and W. Marston Linehan¹

¹Urologic Oncology Branch, National Cancer Institute, National Institutes of Health, 10 Center Drive, MSC 1-5940, Bethesda, MD 20892, USA (W. M. Linehan)

²Department of Urology, SUNY Upstate Medical University, 750 East Adams Street, Syracuse, NY 13210, USA (G. Bratslavsky)

Recent articles by Kutikov *et al.*¹ from the Fox Chase Cancer Center and Weight *et al.*² from the Mayo Clinic examine the role of a routine adrenalectomy for patients with renal cell carcinoma (RCC). Both articles provide compelling arguments against the routine removal of the adrenal gland and present strong data supporting their points. In particular, both articles discuss the following points: the effect of tumor size and location on the risk of adrenal involvement; the utility of preoperative imaging for identifying patients with adrenal involvement; whether routine removal of the adrenal during kidney surgery provides a survival benefit and compromises oncologic outcomes; and whether preservation of the adrenal gland might protect patients against the risk of adrenal insufficiency.

Evaluating the influence of tumor size and location on adrenal involvement, Kutikov and colleagues¹ examined the outcomes of patients with large (>7cm) tumors located within or outside the upper pole who underwent adrenalectomy. They found adrenal involvement to be present in only 4 (4.4%) of 91 patients: 3 of 46 patients with upper-pole tumors (6.5%) and 1 of 45 patients (2.2%) with non-upper-pole tumors ($P = 0.83$).¹

Similar to the study by Kutikov and colleagues,¹ Weight *et al.*² from the Mayo Clinic reported on a large cohort of 4,018 patients, and found ipsilateral adrenal involvement in only 88 patients (2.2%). Adrenal involvement was present in 42 (3.4%) of 1,229 patients with upper-pole tumors versus 46 (1.6%) of 2,789 patients with renal tumors in other locations.² Not surprisingly, by having a greater number of events patients than reported by Kutikov and colleagues,¹ Weight *et al.*² found a significant association between adrenal gland involvement and upper-pole tumors versus tumors in other locations ($P = 0.001$). In addition to tumor location, increasing tumor size (for each centimeter), increasing tumor stage, and nodal or distant metastases were predictive of ipsilateral adrenal metastases on multivariate analyses.² Nevertheless, the vast majority of adrenal glands were removed unnecessarily in both series.

In order to better distinguish patients who need adrenal removal from those who can be spared an unnecessary adrenalectomy, both studies evaluated the ability of preoperative imaging to identify adrenal metastases. In the study by Kutikov and colleagues,¹ all 4 patients with adrenal metastases were identified on preoperative imaging (sensitivity of

100%); although only these 4 out of a total of 12 patients with radiographic abnormalities were found to have adrenal involvement due to cancer (33%), all patients with normal adrenal gland appearance on preoperative imaging did not have adrenal involvement after surgical removal (negative predictive value of 100%). Similarly, in the Weight *et al.*² cohort, 32 of 33 patients with adrenal metastases (who had radiographic studies available for review) demonstrated suspicious findings of either non-visualized adrenal gland or nodular mass within the gland (sensitivity of 97%). While studies by Weight *et al.*² have not evaluated the negative predictive value of radiographic imaging, previous studies from other institutions have documented excellent performance of preoperative imaging for evaluation of adrenal gland involvement. For example, Tsui *et al.*³ identified 511 RCC patients treated with surgery, of whom 29 (5.7%) had adrenal involvement. 26 of these 29 patients had suspicious preoperative CT findings, making the sensitivity of imaging 90%. The negative predictive value was also consistently high at 99%.³ Such a great sensitivity and robust negative predictive value of preoperative imaging should allow the vast majority of patients to avoid an unnecessary adrenalectomy at the time of their surgery, and allow a surgeon to make their surgical planning decision preoperatively.

The concept of an unnecessary adrenalectomy during surgery for RCC in light of oncologic outcomes is further examined by both articles. Kutikov *et al.*¹ found no survival advantage in patients who underwent an adrenalectomy compared to patients who had their adrenal glands saved. These findings are similar to those of a study published 15 years earlier by Robey and Schellhammer,⁴ which compared the long-term outcomes of a small cohort of patients with RCC treated with nephrectomy and ipsilateral adrenalectomy and those with adrenal glands preserved. After 9 years of follow-up, they found no difference in survival between the two groups.

The group from the Mayo Clinic² has further demonstrated that routine adrenalectomy offers no oncologic benefit. On multivariate analysis, after adjusting for clinicopathologic characteristics, ipsilateral adrenalectomy was not associated with a decreased risk of death from RCC. More importantly, they demonstrated that a number of patients will develop contralateral or asynchronous adrenal metastases: interestingly, in patients who did not undergo adrenalectomy, the risk of developing asynchronous ipsilateral versus contralateral adrenal metastases was equivalent at 10 years. Such findings support even stronger argument against the removal and sacrifice of the “radiographically normal” adrenal gland.

Finally, the articles by Kutikov *et al.*¹ and Weight *et al.*² both appropriately discuss the risk of adrenal insufficiency associated with a routine adrenalectomy. Although they did not specifically evaluate endocrine parameters and the quality of life of patients who ended up with subnormal adrenal function or Addisonian crisis, previous studies have documented numerous detrimental effects on health and other issues associated with adrenal insufficiency.^{5,6} We have recently reviewed numerous risks that potentially threaten the adrenal glands, and advocated adrenal preservation via partial resection of affected adrenal gland in cases of primary adrenal tumors.⁷ While our study did not specifically evaluate adrenal preservation in patients with RCC, we determined that the notion of adrenal preservation is a growing concept, with numerous published series focusing on the importance of surgical preservation of the unaffected adrenal tissue.

In summary, there is a strong trend toward adrenal preservation. The evidence in the literature is increasingly supporting the adrenal preservation approach. The evidence-based practice should incorporate the most recent literature demonstrating no role for a routine adrenalectomy during RCC surgery. The availability and performance of modern cross-sectional imaging allows for highly sensitive identification of patients with adrenal gland involvement who might benefit from an adrenalectomy. In most cases, however, the adrenal gland should be left *in situ*, especially if it appears normal on preoperative imaging. Most importantly, a routine adrenalectomy does not provide oncologic or survival benefit, and might subject a substantial number of patients to the additional surgical risk and long-term sequela of adrenal insufficiency.

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STANDFIRST

For decades, complete removal of the kidney with all the contents of the Gerota's fascia (including the adrenal gland) has been a standard procedure for renal cell carcinoma (RCC). Two recent articles argue against routine adrenalectomy and encourage adrenal preservation for the vast majority of patients with RCC.