Impact of Laparoscopic Adrenalectomy on Overall Survival in Patients with Nonmetastatic Adrenocortical Carcinoma

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BACKGROUND: Appropriate use of laparoscopic adrenalectomy (LA) for adrenocortical carcinoma (ACC) remains controversial because complete resection with negative margins is the best chance for potential cure. This study compared the oncologic outcomes and overall survival (OS) of LA and open adrenalectomy (OA) for ACC.

STUDY DESIGN: A retrospective analysis of the National Cancer Data Base (NCDB) between 2010 and 2014 identified 423 European Network for the Study of Adrenal Tumors (ENSAT) stage I to III ACC patients who had LA (n = 137) or OA (n = 286). Outcomes and OS were compared between the 2 groups.

RESULTS: Patients who underwent OA had more advanced stage disease (p = 0.0001), larger ($\geq$5 cm) tumors (p < 0.0001), and were younger (age less than 55 years, p = 0.05). Nodal assessment was rare in LA (n = 4) compared with OA (n = 88) (p < 0.0001). Margin positivity was affected only by surgical approach in patients with T3 tumors (LA 54.6% vs OA 21.7%; p = 0.0009). Neither surgical procedure nor any socio-demographic factor(s) affected OS for the entire cohort. Only positive margins (p = 0.007), positive nodes (p = 0.02), tumor extension (p = 0.01), and more advanced ENSAT stage (p = 0.004) increased mortality. When stratified by disease stage, LA decreased OS for patients with stage II disease (p = 0.04), and remained an independent risk factor for death on multivariate analysis (hazard ratio [HR] 1.86, 95% CI 1.02 to 3.38; p = 0.04). Only positive margins decreased OS in the entire cohort (HR 2.17, 95% CI 1.32 to 3.57; p = 0.002).

CONCLUSIONS: Use of LA may decrease OS in select patients with ACC. Because margin status remains the strongest predictor of mortality, caution should be used in selecting LA for patients with ACC. (J Am Coll Surg 2016;223:485−492. © 2016 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Adrenocortical carcinoma (ACC) is a rare endocrine malignancy that portends a poor prognosis secondary to its late stage at presentation and high recurrence rates.[1-5] Estimated 5-year survival is 82% for stage I disease, but drops dramatically for patients with advanced disease to 50% for stage III patients and only 13% for those with stage IV disease.[6] Often patients are diagnosed with large primary tumors that may invade adjacent tissues or organs, or demonstrate vascular involvement.[2,7] As such, complete operative resection with negative margins remains the only potential cure for patients with ACC.[4,8-11] In cases in which local invasion is already present, curative resection remains feasible, but overall survival (OS) in these patients is much lower.[12,13]

Laparoscopic adrenalectomy (LA) was initially described in 1992 and has become the gold standard for treatment of benign adrenal tumors.[14-17] In multiple retrospective studies, LA is associated with lower operative complication rates, shorter hospital stays, reduced 30-day morbidity, and lower overall costs.[18-22] However, the role of LA for treatment of patients with ACC remains controversial, particularly as it relates to its oncologic outcomes. Several studies cite an increased risk of tumor capsule violation, tumor fragmentation, port site or peritoneal carcinomatosis, as well as a reduced ability to achieve an R0 resection as reasons to avoid utilizing a laparoscopic approach.[2,3,23-26] However, other series have shown comparable results between the laparoscopic and open approaches, although the optimal tumor size and stage of patients selected for LA is still highly debatable.[7,27-31]

Given the rarity of ACC, most of the studies regarding laparoscopic vs open adrenalectomy have been single institution studies and are limited by small numbers.[2,3,7,23,24,27,29-31] In addition, many of the studies included only early stage patients or those with more favorable tumor characteristics such as smaller size and lack of tumor extension into adjacent fat or other nearby organs.[29-31] Given the conflicting data, it is impossible to make generalized conclusions as to the appropriateness of laparoscopic resection for malignant adrenal tumors. Therefore, this study compared the oncologic outcomes and OS of LA and OA in patients diagnosed with European Network for the Study of Adrenal Tumors (ENSAT) stage I to III ACC (nonmetastatic) in the National Cancer Data Base (NCDB) between 2010 and 2014.

METHODS
Patient population and data collection
The NCDB is a joint project of the American Cancer Society and the American College of Surgeons. It is a nationwide clinical oncology database of more than

1,500 Commission on Cancer (CoC)-accredited facilities, and it captures an estimated 70% of newly diagnosed cancers in the United States annually.[32] This study was determined by the Institutional Review Board to be exempt from oversight because of the de-identified nature of the data.

Table 1. Comparison of Demographic Characteristics Between Open Adrenalectomy and Laparoscopic Adrenalectomy Patients

Characteristic	OA group (n = 286)	LA group (n = 137)	p Value
Age, y, mean ± SD	53.3 ± 18.5	58.6 ± 15.0	0.002*
Age, y, n (%)			
<55	138 (48.3)	52 (38.0)	0.05*
≥55	148 (51.8)	85 (62.0)	
Sex, n (%)			
Female	170 (59.4)	89 (65.0)	0.28
Male	116 (40.6)	48 (35.0)	
Facility type, n (%)			
Academic	168 (58.7)	74 (54.0)	0.06
Community	106 (37.1)	62 (45.3)	
Other	12 (4.2)	1 (0.7)	
Facility location, n (%)			
West	27 (9.4)	13 (9.5)	0.03*
Midwest	68 (23.8)	29 (21.2)	
South	108 (37.8)	43 (31.4)	
Northeast	50 (17.5)	42 (30.7)	
Unknown	33 (11.5)	10 (7.3)	
Race, n (%)			
Asian/Pacific Islander	8 (2.8)	2 (1.5)	0.88
White non-Hispanic	233 (81.5)	113 (82.5)	
Black non-Hispanic	19 (6.6)	9 (6.6)	
Hispanic	13 (4.6)	8 (5.8)	
Other	13 (4.6)	5 (3.7)	
Insurance, n (%)			
Private	153 (53.5)	65 (47.5)	0.13
Public/government	103 (36.0)	61 (44.5)	
Uninsured	19 (6.6)	10 (7.3)	
Unknown	11 (3.9)	1 (0.7)	
Income, n (%)			
Comfortable	84 (29.4)	52 (38.0)	0.30
Moderate	158 (55.2)	64 (46.7)	
Low	43 (15.0)	20 (14.6)	
Unknown	1 (0.4)	1 (0.7)	
Education, n (%)			
High	55 (19.2)	16 (11.7)	0.17
Moderate	73 (25.5)	32 (23.4)	
Low	157 (54.9)	88 (64.2)	
Unknown	1 (0.4)	1 (0.7)	

*Significant.
LA, laparoscopic adrenalectomy; OA, open adrenalectomy.