Comparative Efficacy of Laparoscopic Versus Robotic Adrenalectomy for Adrenal Malignancy

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OBJECTIVE To evaluate whether the technical advantages of robotic-assisted surgery over standard laparoscopy, which are well established for complex renal surgery, lead to variable surgical outcomes between laparoscopic adrenalectomy (LA) and robotic adrenalectomy (RA).

METHODS Using the National Cancer Database, we identified patients who underwent LA or RA for nonmetastatic primary adrenal malignancy from 2010 to 2013. Primary outcomes were need for open conversion, surgical margin status, and performance of regional lymphadenectomy. Secondary outcomes were length of stay, readmission, and perioperative mortality. Baseline characteristics and outcomes were compared between approaches using the chi-square, Fisher's exact, and Mann-Whitney U tests.

RESULTS Two hundred thirty-eight (82%) LA and 51 (18%) RA cases were identified. The LA and RA groups did not show any significant differences in terms of patient age, gender, race, Charlson score, tumor laterality, size (median 4.2-9.0 cm), histology, grade, hospital type, and case volume. The rate of open conversion was 5.9% for RA versus 17.2% for LA ($P = .04$). There were no significant differences in rates of positive margins, lymphadenectomy, inpatient stay, readmission, or mortality.

CONCLUSION RA significantly decreases need for open conversion compared to LA. Although RA improves technical feasibility, the oncological adequacy of minimally invasive resection remains uncertain. UROLOGY 123: 146–150, 2019. © 2018 Elsevier Inc.

While majority of adrenal masses are benign, workup and management of adrenal tumors continues to be aggressive due to the possibility of adrenocortical cancer (ACC). For this reason, we adhere to surgical principles practiced in ACC when dealing with any adrenal masses.[1-4] ACC is a rare but aggressive malignancy with approximately 0.5-2 cases per million.[5] Local and distant recurrences are reported to be as high as 85% after resection with 5-year overall survival rate of 16%-47%. Five-year survival for unresected disease is a dismal 5%.[5] Therefore, complete resection with negative surgical margins is crucial to offer a chance at cure. Traditionally, open adrenalectomy (OA) has been favored over minimally invasive adrenalectomy (MIA) for treatment of adrenal malignancy due to the technical complexity of the surgery, which may require aggressive en bloc resection of surrounding organs and regional lymphadenectomy, and due to oncological concerns over the increased risks of incomplete resection and tumor spillage associated with MIA. However, these recommendations are rooted in weak evidence and do not account for the improved precision of robotic surgery, which has now been applied to MIA.[1,4,6-13] While MIA has long been an option for treating benign adrenal disease, recent reports have suggested that, in select cases, it also may be effective for the management of ACC.[14,15] In fact, in our prior study, we observed that surgical quality outcomes were comparable between MIA and OA for small, organ-confined ACC; however, we did not investigate whether these outcomes were influenced by the type of minimally invasive approaches used, ie, laparoscopic or robotic.[16] Given the improved dexterity, ergonomics, and optics afforded by robotics, we hypothesized that robotic adrenalectomy (RA) may offer better surgical outcomes compared to laparoscopic adrenalectomy (LA). Although the advantages of robotic versus laparoscopic surgery are well established for partial nephrectomy, another complex retroperitoneal surgery, and for adrenalectomy in benign disease, a comparative analysis of surgical outcomes between RA and LA for adrenal malignancy is lacking.[17,18]

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MATERIALS AND METHODS

Data Source and Study Population

The National Cancer Database (NCDB) is a hospital-based clinical oncology database sponsored by the American Cancer Society and the Commission on Cancer of the American College of Surgeons that captures 70% of incident cancer diagnoses in the United States. Institutional review board approval was obtained prior to study initiation.

Using the endocrine cancer dataset, we identified 289 adult patients diagnosed with nonmetastatic (M0/x) primary malignancy of the adrenal gland between 2010 and 2013 who underwent MIA. Surgical approach (laparoscopic or robotic) was only recorded in the NCDB after 2009.

Study Variables

The study variables included patient age, gender, race, Charlson-Deyo comorbidity index, tumor laterality, tumor size, histology, grade, pathologic and clinical N stage, hospital type, and hospital volume were included. Race was reclassified as non-Hispanic white and other. Charlson-Deyo comorbidity index was reclassified as ≤ 1 and >1. Grade was reclassified as low (G1-2), high (G3-4), and unclassified. Hospital type was reclassified as academic/research and other based on Commission on Cancer designations. Hospital volume (low or high) was assigned based on the annual minimally invasive surgical volume for adrenal malignancy (<5 or ≥ 5), respectively, with high-volume centers at or above the 89th percentile.

Study Outcomes

The primary outcomes were open conversion, incomplete resection, positive margins, and performance of a locoregional lymph node dissection. Incomplete resection was defined as surgical debulking, based on 2013 Facility Oncology Registry Data Standards site-specific surgery codes, or tumor grossly present at the surgical margin. Positive margins were defined as nongrossly (microscopically) positive surgical margins (PSM). LND was defined as a lymph node yield ≥ 4, as previously defined.[16] Secondary outcomes were inpatient length of stay, 30-day readmission, and perioperative (30- and 90-day) mortality.

Statistical Analyses

Continuous variables were expressed as median (interquartile range). Comparisons between the laparoscopic and robotic groups were performed using the chi-square and Wilcoxon-Mann-Whitney tests. The associations between approach and the outcomes were assessed by the chi-square, Fisher exact, and Wilcoxon-Mann-Whitney tests. Survival analysis was performed using the Kaplan-Meier method and the log-rank test. Statistical tests were run using SAS University Edition (SAS Institute Inc., Cary, NC). All tests were two-sided, and statistical significance was set at $P < .05$.

RESULTS

Of the 289 patients included in the study, 238 (82.4%) underwent LA and 51 (17.6%) underwent RA. For the overall cohort, median tumor size was 6.5 (4.4-9.0) cm, and 57% of tumors were cT1 stage. Adrenal pathology included adrenocortical carcinoma (62.3%), malignant pheochromocytoma (24.0%), and other malignant histologic types (13.8%). Tumors predominantly involved the left adrenal gland (52%). The LA and RA groups were comparable without significant differences in their baseline characteristics (Table 1).

The rate of open conversion was 17.2% for LA versus 5.9% for RA ($P = .04$). The rate of regional lymphadenectomy was slightly lower for LA (0.8% vs 3.9%), but this difference was not significant ($P = .14$). For LA and RA, respectively, rates of incomplete resection (0.84% vs 2.0%, $P = .44$) and PSM (16.4% vs 15.7%, $P = .90$) were not significantly different (Table 2). In terms of secondary outcomes, length of stay, readmission, and mortality did not differ significantly between LA and RA (Fig. 1).

COMMENT

Adrenal masses are worked up and managed aggressively due to concern for ACC. As a result, principles of wide en bloc resection are utilized in management of ACC to offer the best chance at cure. Guidelines by European Society of Endocrine Surgeons and European Network for the Study of Adrenal Tumors published in 2017 endorse for OA for masses demonstrating local invasion or concerning for ACC.[19] Bearing these recommendations in mind, we examined the difference in outcomes between open and MIA in a previous study. We found that MIA may have comparable outcomes for small, organ-confined adrenal masses.[16] Previously, we did not differentiate between laparoscopic versus robotic approaches. In the present study, we compared LA and RA with the hypothesis that the robotic technique may improve surgical outcomes.

In accordance with clinical practice guidelines, which reserve the use of MIA for small masses, the majority of tumors treated with MIA were less than 10 cm.[20] The rate of conversion to open surgery was significantly lower in the RA group. Although the reasons for open conversion are not reported in the NCDB, the lower rate of conversion with the robot may be explained by improved dexterity, ergonomics, and optics afforded by the robotic platform.[17] Conversely, surgeons may have a lower threshold to convert to open in LA, due to ease of conversion, especially in a hand-assisted case. Studies comparing the intraoperative and perioperative outcomes of robotic partial nephrectomy compared to laparoscopic partial nephrectomy have demonstrated the utility of robotics in large, complex masses, including central and hilar lesions. While this finding may not apply to all renal or adrenal cases, it does validate the utility of robotic surgery in executing complex retroperitoneal surgeries without the need for open conversion.[20]

In terms of the other outcomes, there was no significant difference in the rates of PSM, incomplete resection, or lymph node dissection. One reason for the surprisingly high PSM for both LA and RA (16.4% and 15.7%, respectively) may be that MIA is the preferred approach for small masses that are often considered to be benign preoperatively. Therefore, aggressive en bloc resections for oncologic control may not have been performed in all

Table 1. Patient, tumor, and provider characteristics for malignant adrenal cases treated between 2010 and 2013 by approach

Variables	Laparoscopic (n = 238)		Robotic (n = 51)		*P* Value
Median age, yr (IQR)	60	(48-68)	61	(52-69)	.31
Female, n (%)	136	(57.1)	29	(56.9)	.97
White, n (%)	186	(78.2)	44	(86.3)	.19
CCI > 1, n (%)	79	(33.2)	16	(31.4)	.80
Left-sided tumor, n (%)	120	(50.4)	31	(60.8)	.18
Median tumor size, cm (IQR)	6.6	(4.5-9.0)	6.0	(4.2-9.0)	.98
Tumor size					.85
<10 cm	194	(81.5)	41	(80.4)	
≥10 cm	44	(18.5)	10	(19.6)	
Histology					.39
ACC, n (%)	144	(60.5)	36	(70.6)	
MP, n (%)	59	(24.8)	10	(19.6)	
Other, n (%)	35	(14.7)	5	(9.8)	
Grade					.38
Low, n (%)	16	(6.7)	2	(3.9)	
High, n (%)	27	(11.3)	9	(17.7)	
Unclassified, n (%)	195	(81.9)	40	(78.4)	
pT stage					.98
1, n (%)	137	(57.6)	29	(56.9)	
2, n (%)	33	(13.9)	8	(15.7)	
3, n (%)	55	(23.1)	11	(21.6)	
4, n (%)	13	(5.5)	3	(5.9)	
cN stage					.08
0, n (%)	237	(99.6)	49	(96.1)	
1, n (%)	1	(0.4)	2	(3.9)	
Academic center, n (%)	105	(44.1)	24	(47.1)	.70
High-volume center, n (%)	29	(12.2)	4	(7.8)	.38
Median follow-up, mo (IQR)	23.8	(12.2-36.1)	25.3	(14.6-33.6)	.95

ACC, adrenocortical carcinoma; CCI, Charlson-Deyo comorbidity index; cN, clinical N; IQR, interquartile range; MP, malignant pheochromocytoma; pT, pathologic.

cases. Lastly, while the frequency of lymph node dissection between LA and RA did not reach statistical significance ($P = .14$), this may be due to a selection bias, small sample size, or the relative infancy of robotic adrenal surgery during the study period. Although there was no difference in the length of stay, readmission rates, or mortality rates between the two approaches, MIA by either approach is associated with a low 90-day mortality rate (LA = 2.9%; RA 2.6%).

Table 2. Outcomes by approach

	Laparoscopic		Robotic		*P* Value
Primary					
Open conversion, n (%)	41	(17.2)	3	(5.9)	.04
Incomplete resection, n (%)	2	(0.84)	1	(2.0)	.44
Positive margins, n (%)	39	(16.4)	8	(15.7)	.90
Lymph node dissection, n (%)	2	(0.8)	2	(3.9)	.14
Secondary					
Median LOS, d (IQR)	3	(2-5)	3	(2-5)	.51
30-day readmission, n (%)	5	(2.1)	2	(3.9)	.36
30-day mortality[†], n (%)	2	(1.1)	0	(0.0)	1.00
90-day mortality[‡], n (%)	5	(2.9)	1	(2.6)	1.00

[†] N = 216 after excluding patients lost to follow-up.
[‡] N = 212 after excluding patients lost to follow-up.

Our study is the single largest study comparing surgical outcomes between RA and LA. Nonetheless, the overall number of cases was small given the infrequency of ACC and the infancy of this approach during the study period. As might be expected, there were more LA cases compared to RA cases due to the evolving use of robotic surgery. The pattern of increasing RA is observed mainly in the United States, and due to the limitation of this database, we are unable to comment on the practice trends globally. Since 2013, the adoption of retroperitoneal adrenal surgery has increased.[17] Given the volume-outcome relationship in surgery, we suspect that RA outcomes may be better in current practice and may differ from the results in this study. Nonetheless, we endorse for adrenalectomies to be performed at high volume centers to optimize outcomes. Finally, due to the retrospective nature of this study, there is risk for selection bias. The lack of data on the reasons for open conversion is another limitation of this study.

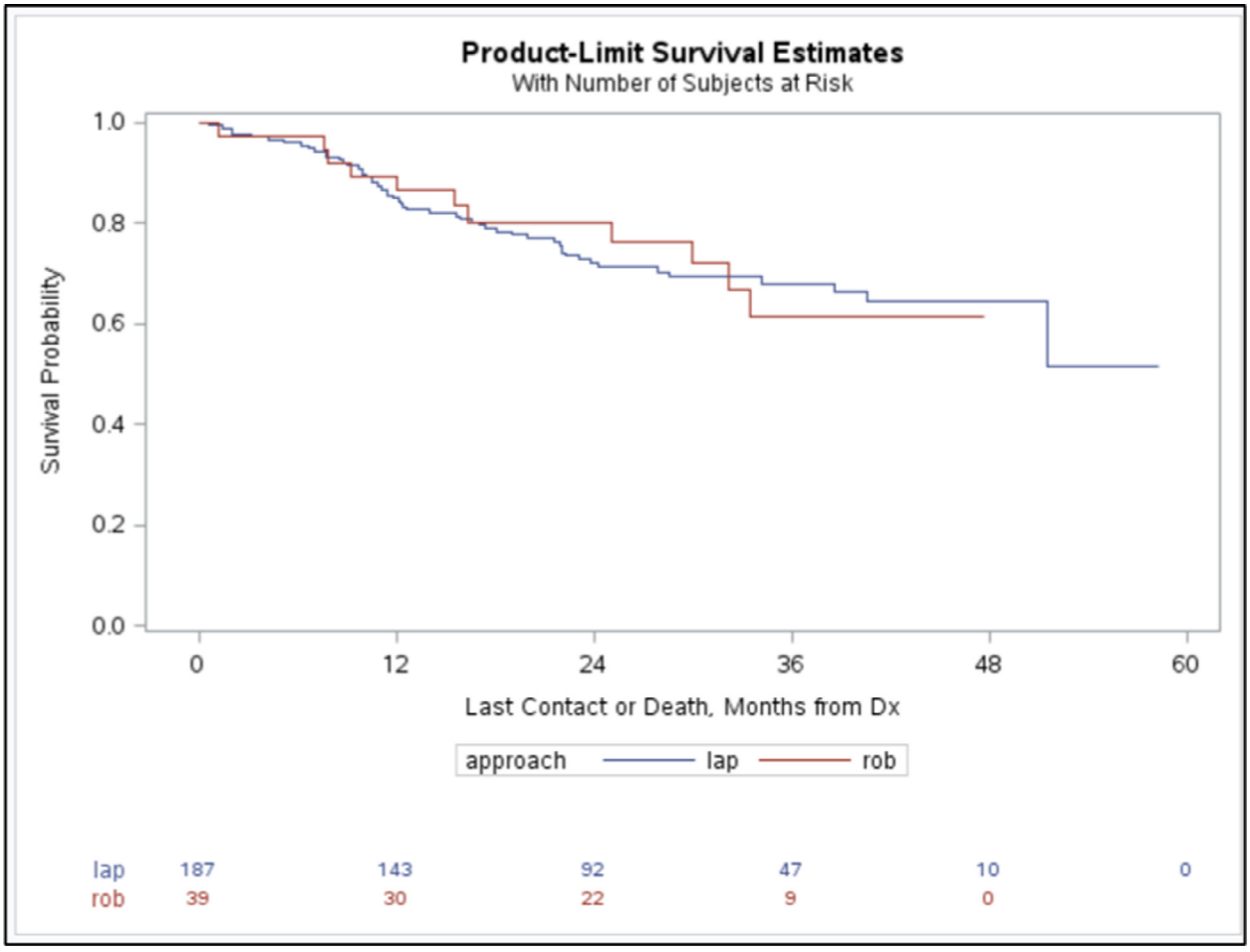

Figure 1. Kaplan-Meyer curves showing survival in laparoscopic group compared to the robotic group ($P = .99$). Color version available online.

CONCLUSION

For small adrenal masses that appear noninvasive, the robotic platform improves the feasibility of adrenalectomy compared to the standard laparoscopic approach. RA and LA did not differ in terms of other technical or survival outcomes.

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