Adrenalectomy for benign and malignant disease: utilization and outcomes by surgeon specialty and surgical approach from 2003-2013

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Introduction: *Data on the utilization of open, laparoscopic and robotic adrenalectomy on a national level is limited.*

Materials and methods: *Data on patients who underwent open, laparoscopic, or robotic adrenalectomy for benign or malignant disease in the US from 2003-2013 were extracted using ICD-9 codes from the Premier Hospital Database. Surgeon specialty, patient demographics, hospital characteristics, and complications were compared. Data were analyzed using univariate and multivariable logistic regression analyses.*

Results: *A total of 8,831 adrenalectomies were performed for benign and malignant tumors. There was no significant difference in rate of adrenalectomy with regards to comorbidities, insurance status, or hospital characteristics. Non-urologists performed adrenalectomy more often for both benign (57% versus 43%; p = 0.011) and malignant disease (66% versus 34%; p = 0.011). Across all indications, non-urologists performed open surgery most often followed by laparoscopic and robotic approaches (56.3% versus 37.4% versus 6.4%, respectively), compared to urologists (48.8% versus 38.4% versus 12.9%, respectively). Overall, urologists were more likely to use laparoscopic or robotic approaches (p = 0.001). There was no difference in complication rates or operative times between surgical specialties or by surgeon/hospital case volume. On multivariable regression analysis, the best predictor of major complication was a Charlson Comorbidity Index (CCI) ≥ 2 (OR 3.9, 95%CI 2.1-7.1; p = < 0.001). Compared to open surgery, laparoscopy had significantly reduced odds of major complication (OR 0.6, 95%CI 0.3-0.9; p = 0.03). Patients undergoing robotic procedures had the shortest length of stay.*

Conclusion: *In this retrospective study, adrenalectomy was more commonly performed by non-urologists via an open approach. Patients with CCI ≥ 2 were more likely to have postoperative complications while surgeon volume, hospital volume, and surgical approach did not influence complication rates.*

Key Words: adrenocortical carcinoma, adrenal mass, adrenalectomy, minimally invasive, robotic, laparoscopic, utilization

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Introduction

Adrenal masses have been reported on 0.8% to 5% of CT scans and up to 6% of autopsies.[1,2] While adrenal incidentalomas are relatively common, adrenal malignancy is rare. The incidence of adrenal cortical carcinoma is 2 per million and is responsible for 0.2% of all cancer deaths in the United States.[3] Traditionally,

adrenal neoplasms that are suspected to be malignant have been treated with open surgical resection.[4-6] However, with advances in the safety and efficacy of minimally invasive surgery (MIS), surgeons have adopted laparoscopic and robotic techniques for adrenalectomy. Since the first published account of laparoscopic adrenalectomy in 1992, laparoscopy has become the preferred approach for adrenal resection, even in patients previously considered poor candidates for laparoscopy.[7,8] The da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA, USA) was approved for robotic surgical procedures in 2000 and, like laparoscopic adrenalectomy, has been shown to offer benefits such as shorter operative time, less blood loss, faster recovery, and less postoperative pain when compared to open[7,9-11] and laparoscopic adrenalectomy.[12]

Data comparing national trends in adrenalectomy for benign and malignant indications are limited. Lee et al used the National Surgical Quality Improvement Program database and found significantly worse outcomes for open compared to laparoscopic adrenalectomy.[13] The current literature also lacks information on utilization of the different surgical approaches for the resection of benign versus malignant adrenal tumors, the specialties of the surgeons performing these operations, and the impact of surgeon/hospital operative volume on the risk of complications. The goal of this study was to assess the impact of surgeon specialty and surgical approach on utilization and outcomes of adrenal surgery for both benign and malignant neoplasms via open, laparoscopic, and robotic approach.

Materials and methods

Data source

This Institutional Review Board-approved study evaluated the nationally representative Premier Hospital Database (Premier, Inc., Charlotte, NC, USA) dataset, which captures an estimated 20% of inpatient hospital discharges in the United States. The database includes information regarding all hospital-based encounters, including inpatient and outpatient visits, a log of all billed items (including medications, laboratory and diagnostic tests), as well as primary and secondary diagnoses for each patient. There is a unique identifier for each patient thus permitting longitudinal analysis.

Study cohort and covariates

Using International Classification of Diseases, Ninth Revision (ICD-9) codes, we identified all patients who underwent adrenalectomy (07.2x, 07.3) for malignant (194.0, 194.9, 198.7, 237.2) or benign (255.x, 227) indications between 2003 and 2013. Patients undergoing a concurrent nephrectomy (55.4, 55.5x), with a renal mass (189.0, 189.8, 189.9, 198.0, 198.1, 223.0, 236.91, 593.9), or with a history of kidney cancer (V10.52) were excluded to ensure that patients in our cohort were undergoing adrenalectomy primarily rather than secondarily for concern of a renal malignancy.

We examined patient, hospital, and surgical characteristics as well as surgeon specialty. Patient characteristics included age (< 55, 55-64, 65-74, ≥ 75 years of age), gender, race (white, black, Hispanic, other/unknown), insurance status (Medicare, Medicaid, private, other/unknown), and Charlson Comorbidity Index (CCI; 0, 1, ≥ 2). Hospital characteristics included teaching status, hospital size (< 400, 400-600, or > 600 beds), location (urban or rural), and geographical region (Northeast, Midwest, West, or South). The cohort was also classified by surgical approach (open, laparoscopic or robotic), which was based mainly on data from charge description master as previously described[14] but also on ICD-9 codes (laparoscopy [54.21]; robotic surgery [17.4x, beginning in the final quarter of 2008]). We also dichotomized the cohort based on surgeon type (urologist or non-urologist), which was identified through billing data. The primary outcome measure was 90 day surgical complications based on the Clavien classification system using ICD-9 codes as previously described.[15] Complications were classified as minor (Clavien grades 1-2) and major (Clavien grade 3-5); mortality (Clavien grade 5) was identified through disposition codes.

Statistical analysis

Patient and hospital characteristics for subjects undergoing adrenalectomy for benign and malignant indications are summarized with descriptive statistics. Multivariable logistic regression models were constructed to determine predictors for 90 day surgical complications. We also conducted a secondary analysis for patients with malignant disease only to assess if there are any factors that contribute to overall complications in malignant disease. The Premier Hospital Database contains sampling weights validated based on the 1998 National Hospital Discharge Survey. Using these sampling weighting coupled with multilevel analyses accounting for hospital clustering, we were able to achieve a nationally representative estimation. All statistical tests were two-sided, and a p value of < 0.05 was considered statistically significance. All statistical analyses were performed with Stata 13 (StataCorp LP, College Station, TX, USA).

Results

Overall characteristics

From 2003 to 2013, 8,831 adrenalectomies in the United States for benign (4,049) and malignant disease (4,782) were identified, Table 1. The majority of patients undergoing adrenalectomy were more than 50 years old, male, and white (78.4%, 58.7%, and 74.8%, respectively). When stratified by comorbidities, patients with CCI of 0 comprised 54.9% of patients while patients with CCI 1 and ≥ 2 comprised 24.2% and 21%, respectively. With regard to hospital characteristics, the majority of adrenalectomies were performed in non-teaching (64.1%) and urban hospitals (96.6%). When comparing different surgical approaches, open was most common (49.9%), followed by laparoscopic (39.1%), and robotic (11.0%) adrenalectomy.

TABLE 1. **All adrenalectomies from 2003 to 2013, stratified by disease type**

	Benign n = 4049 (45.9%)	**Malignant n = 4782 (54.2%)**	**p value**
Patient characteristics			
Age (years, %)			0.001
< 50	26%	18%	
50 to 59	23.90%	21.80%	
60 to 69	29.20%	31.70%	
≥ 70	20.90%	28.60%	
Gender			< 0.001
Male	52.30%	64%	
Female	47.70%	35.90%	
Race			< 0.001
White	68.90%	79.80%	
Black	9.80%	4.50%	
Hispanic	2.90%	2.30%	
Other	18.40%	13.40%	
Charlson Comorbidity Index (%)			0.06
0	51.50%	57.80%	
1	27.40%	21.40%	
≥ 2	21.20%	20.80%	
Hospital characteristics			
Teaching hospital (%)			0.14
Yes	33%	38.30%	
No	67%	61.70%	
Region (%)			0.14
Midwest	24.60%	21.80%	
Northeast	23.70%	19.20%	
South	37.40%	37.70%	
West	14.30%	21.30%	
Surgical characteristics			
Type of surgeon			0.011
Non-urologist	56.90%	66.30%	
Urologist	43.10%	33.70%	
Approach			0.017
Open	45.40%	53.80%	
Laparoscopic	40.80%	37.70%	
Robotic	13.80%	8.60%	

Adrenalectomy by surgeon specialty

Non-urologists performed the majority of adrenalectomies for the entire cohort (62% versus 38%), as well as for both benign (57% versus 43%; p = 0.011) and malignant neoplasms (66.3% versus 34.7%; p = 0.011). In 2003, only 32% of adrenalectomies were performed by urologists. By 2013, this number increased to 44%. Among non-urologists, open surgery was most common, followed by laparoscopic and robotic approaches (56.3% versus 37.4% versus 6.4%, respectively). Urologists had a similar pattern of open, laparoscopic, and robotic use (48.8% versus 38.4% versus 12.9%, respectively). Urologists were more likely to use MIS techniques (laparoscopic or robotic) compared to non-urologists (17% versus 7% p = 0.001). The variables of age, race, gender, and hospital characteristics were not significantly different between urologists and non-urologists. In treating patients with adrenal malignancy, urologists were more likely to utilize MIS techniques compared to non-urologists (51.3% versus 43.8%). For this subset of cases, the median operating room time was 210 minutes for both urologists and non-urologists (p = 0.97). Robotic surgery was associated with the longest median length of surgery, followed by laparoscopic and open approaches (240 minutes versus 210 minutes versus 210 minutes, respectively; p = 0.03). Urology patients had a shorter median length of stay than non-urology patients (3 days versus 4 days; p = 0.001). Patients undergoing robotic procedures had a shorter length of stay than those who had laparoscopic or open surgeries (2 days versus 3 days versus 5 days, respectively; p = 0.01).

Adrenalectomy by surgical approach

Adrenalectomy performed by an open approach comprised about 50% of all adrenalectomies, followed by laparoscopic (39.1%) and robotic (10.9%) surgery. In 2003, 58.2% of adrenalectomies were done via open approach compared to 46.7% in 2013, Figure 1. By 2013, MIS accounted for a larger percentage of all adrenalectomies (53%) for both benign and malignant neoplasms (21.4% and 22.8%, respectively for laparoscopy; 40.6% and 24.4%, respectively for robotic), followed by open surgery (36.4% and 54.2%, respectively). With regard to patient characteristics, 30.3% of patients in the robotic group had a CCI ≥ 2 compared to 22.1% in the laparoscopic group and 18.1% in the open group (p = 0.016), Table 2. Furthermore, there was a significant difference among the approaches with regard to adrenalectomy for malignant indications, where 58.3% of open adrenalectomies had a concern for malignancy, compared to 52.1% for laparoscopic and 42.3% for robotic procedures. Finally, the rate of

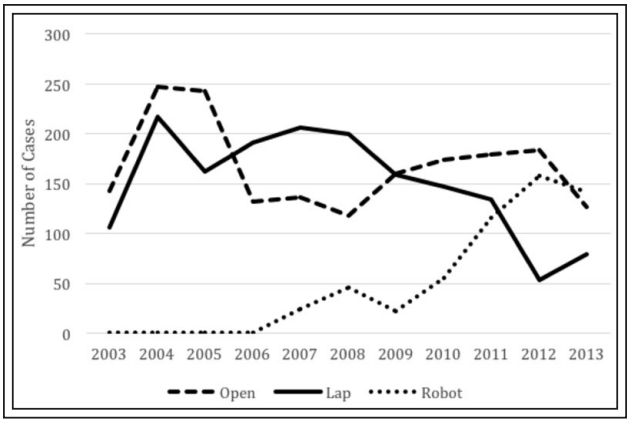

Figure 1. Trends in adrenalectomy by surgical approach. By 2011 robotic adrenalectomy is more prevalent that laparoscopic adrenalectomy.

major, minor, and no complications for the entire cohort of adrenalectomies performed for both benign and malignant disease was 9.4%, 20.6%, and 70%, respectively for open adrenal surgery; 6.1%, 17.3%, and 76.6%, respectively for laparoscopic surgery; 7.8%, 30.7%, and 61.5%, respectively for robotic surgery, Figure 2.

Adrenalectomy by disease type

For both benign and malignant neoplasms, the majority of the patients were greater than 50 years of age (74% and 83%), men (52% and 64%), and of white race (69% and 80%), Table 1. Among the groups there was no statistically significant difference with regard to comorbidities, hospital characteristics, or region. For benign disease, the majority of cases were

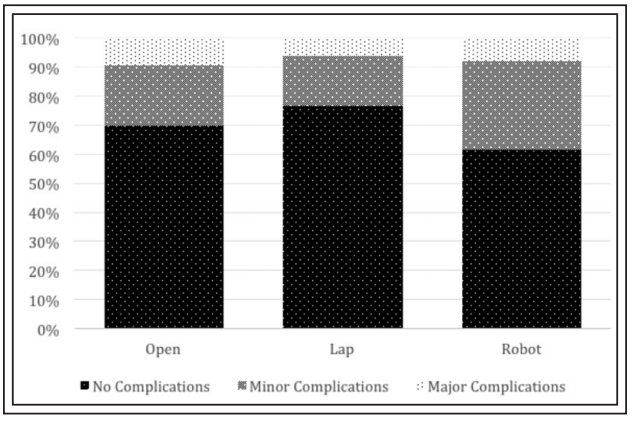

Figure 2. Complications by surgical approach for all adrenalectomy indications were not significantly different among the groups.

TABLE 2. **All adrenalectomies from 2003 to 2013, stratified by surgical approach**

	Open n = 4409 (49.9%)	Laparoscopic n = 3455 (39.1%)	Robotic n = 966 (10.9%)	p value
Patient characteristics				
Age (years, %)				0.45
< 50	23.70%	19%	21.80%	
50 to 59	22%	23.10%	25%	
60 to 69	28.20%	33.60%	30.50%	
≥ 70	26.10%	24.40%	22.80%	
Gender				0.45
Male	60.60%	56.60%	57%	
Female	39.40%	43.40%	43%	
Race				0.23
White	72.30%	76.50%	80.20%	
Black	6.20%	8.20%	5.70%	
Hispanic	3%	2.70%	0.80%	
Other	18.50%	12.70%	13.40%	
Charlson Comorbidity Index (%)				0.016
0	55.10%	55.60%	51.20%	
1	26.80%	22.40%	18.60%	
≥ 2	18.10%	22.10%	30.30%	
Insurance status (%)				0.007
Medicare	39.20%	43.30%	43.10%	
Medicaid	5.30%	3.50%	5.90%	
Private insurance	37%	41%	25.40%	
Other	18.50%	12.20%	25.70%	
Hospital characteristics				
Teaching hospital (%)				0.7
Yes	37.40%	33.40%	37.80%	
No	62.60%	66.60%	62.20%	
Surgical characteristics				
Concern for malignancy				0.02
Yes	58.30%	52.10%	42.30%	
No	41.70%	47.80%	57.70%	
Type of surgeon				0.001
Non-urologist	65.50%	63.40%	41.30%	
Urologist	34.50%	36.60%	58.70%	

performed with an open approach (45.4%) compared to laparoscopic (40.8%) and robotic procedures (13.8%). Similarly for malignant disease, the open approach comprised the majority of adrenalectomies (53.8%), followed by laparoscopic (37.7%) and robotic surgeries (8.6%) (p = 0.017).

Multivariable analysis

On multivariable regression analysis, the best predictor of 90 day major surgical complications across all indications was poor health status, designated by a CCI ≥ 2 (OR 3.9, 95% CI 2.1-7.1; p < 0.001), Table 3. Poor health was also predictive of major complications for adrenalectomy for malignant indications alone (OR 6.1, 95% CI 2.9-12.5; p < 0.001). For all adrenalectomies, surgeon specialty was not a predictor of complications (OR 0.7, 95% CI 0.4-1.1, p = 0.1), nor was it predictive of complications for the malignant cases alone (OR 0.1, 95% CI 0.4-1.4, p = 0.4). Major complications were also not associated with annual surgeon volume (OR 1.2, 95% CI 0.8-1.8, p = 0.4) or annual hospital volume (OR 0.97, 95% CI 0.8-1.1, p = 0.7).

TABLE 3. **Logistic regression model assessing odds of major complication with adrenalectomy in the United States, 2003 to 2013**

	Adjusted OR	95% CI	p value
Patient characteristics			
Age (years)			
< 50	Reference	Reference	
50 to 59	0.7	0.3 to 1.6	0.5
60 to 69	1	0.5 to 2.3	0.96
≥ 70	1.4	0.6 to 3.5	0.48
Gender			
Male	Reference	Reference	
Female	1.01	0.7 to 1.5	0.97
Race			
White	Reference	Reference	
Black	1	0.5 to 2.3	0.9
Hispanic	0.7	0.1 to 3.5	0.6
Other	0.5	0.2 to 1.2	0.1
Charlson Comorbidity Index			
0	Reference	Reference	
1	1.6	0.8 to 3.1	0.2
≥ 2	3.9	2.1 to 7.1	< 0.001
Hospital characteristics			
Teaching hospital			
Yes	Reference	Reference	
No	0.8	0.5 to 1.4	0.4
Surgical characteristics			
Type of surgeon			
Non-urologist	Reference	Reference	
Urologist	0.7	0.4 to 1.1	0.2
Suspected tumor type			
Malignant	Reference	Reference	
Benign	0.8	0.5 to 1.3	0.29
Approach			
Open	Reference	Reference	
Laparoscopic	0.6	0.4 to 0.9	0.02
Robotic	0.8	0.3 to 1.7	0.5

For malignant disease, there was no association with an increased risk of complications overall compared to benign etiology (OR 0.8, 95% CI 0.5-1.3, p = 0.29). Furthermore, there was no significant difference in overall, minor, or major complication rates when comparing non-urologists with urologists for malignant resections (OR 0.7, 95% CI 0.4-1.4, p = 0.4). Compared to open surgery, there was no increased risk of complications with laparoscopy (OR 0.6, 95% CI 0.3-1.3, p = 0.17) or robotic procedures (OR 0.8, 95% CI 0.3-2.4, p = 0.69). CCI ≥ 2 was again associated with increased risk of major complication (OR 6.1, 95% CI 2.9-12.5; p =< 0.001). Patients in a rural setting were less likely to have major complications (OR 0.1, 95% CI 0-0.61; p = 0.02). In univariate and multivariate logistic regression models for both the entire cohort as well as malignant indication alone, age, gender, race, insurance status, teaching status, geographic region, and hospital size were not predictors of complications.

Discussion

In this cross-sectional analysis there are a number of interesting findings. Recent trends show that since

2010 MIS techniques (laparoscopic or robotic surgery) comprise the majority of adrenalectomies for benign disease (57% MIS versus 43% open) as well as for malignant disease (62% MIS versus 38% open), which is interesting given that malignant disease has traditionally been removed via an open approach.[16] In addition, robotic adrenalectomy is more commonly performed for benign indications than open or laparoscopic approaches. Prior studies have shown that malignant disease is predictive of postoperative complications.[17] In this analysis, benign disease has slightly lower odds of major complication, but it did not reach significance (OR 0.8; 95% CI, 0.5-1.3; p = 0.3), possibly due to increased surgeon experience with MIS techniques providing a safe alternative to open adrenalectomy.

There is continuing debate over the use of MIS for the treatment of adrenocortical carcinoma. Adrenalectomy for adrenal cancer has traditionally been performed using an open approach. With recent advances in minimally invasive technology, laparoscopic and robotic approaches have also been used for adrenal malignancy. Laparoscopic adrenalectomy on adrenal cortical carcinoma can be a difficult procedure, as adrenal carcinomas tend to be larger than benign masses. Henry et al evaluated 150 consecutive laparoscopic adrenalectomies and found that no tumor smaller than 4 cm (n = 102) was malignant.[18] In contrast, 12.5% of tumors larger than 4 cm (n = 48) were malignant. Similarly, Prager et al noted that 21.2% of tumors larger than 6 cm were malignant versus 1.9% of lesions smaller than 6 cm.[19] Also, the possibility of invasion by malignant adrenal lesions into surrounding structures can prohibit successful laparoscopic/robotic surgery. Therefore, there has been concern that MIS for malignant adrenal tumors may result in failures to achieve complete resection and increase the risk of complications.[19] As we have shown, especially in the malignant adrenalectomy cohort, the rate of complication for MIS is not significantly different to that seen with open surgery (laparoscopic OR 0.6; 95% CI 0.3-1.3, p = 0.17; robotic OR 0.8; 95% CI, 0.3-2.4, p = 0.69).

Furthermore, MIS may offer some benefits in adrenal surgery. The results of this study indicate that patients who underwent minimally invasive adrenalectomy spent fewer days recovering in the hospital than those with open procedures. In a multicenter analysis, Shaligram et al compared open and laparoscopic adrenalectomies.[20] They found that patients who underwent laparoscopic surgery had significantly lower morbidity and intensive care unit admission rates in addition to a shorter length of stay than those with open procedures. The study also showed that laparoscopic surgery had significantly lower rates of major complication than open surgery for benign disease but did not find a significant difference between open and laparoscopic approaches for malignant disease. Brandao et al reported that robotic adrenalectomy can be performed as safely as a traditional laparoscopic procedure with regard to operative time and open conversion rate.[10] That study also found that robotic surgery demonstrated other advantages over laparoscopy, such as lower estimated blood loss, shorter hospital length of stay, and a slightly reduced postoperative complication rate. In contrast, Pineda-Solís noted no significant difference in length of stay and morbidity and a longer operative time for robotic adrenalectomy compared to traditional laparoscopy.[21]

Our results confirm the association of robotic procedures with a significantly longer operative time than both laparoscopic and open procedures. More research is required to determine clear differences in patient-reported outcomes between open, laparoscopic, and robotic adrenalectomies for both benign and malignant indications. While randomized data would be ideal, a prospective evaluation of open versus MIS approaches may be difficult to conduct given the rarity of adrenal malignancy.

The majority of adrenalectomy cases are still being performed by non-urologists. However, there has been a rapid increase in urologist-performed adrenalectomies, especially MIS adrenalectomies for benign disease. Interestingly, in a sample of 23,746 cases from 2003 to 2009, Monn et al found that urologists performed 60% of adrenalectomies.[22] Moreover, the current study indicates that urologists perform a higher percentage of robotic adrenal procedures than non-urologists. The data also indicates that urology patients have a shorter length of stay than non-urology patients. While it is possible that this shorter length of stay is attributable to the use of robotic surgery, we cannot definitively conclude this from the present study.

We found no significant difference in complication rates between urologists and non-urologists. A study by Park et al evaluating the effect of surgeon specialty and surgeon volume on complication rate using the Nationwide Inpatient Sample found that surgeon volume was ultimately the most important factor (OR 1.5, p = 0.02).[23] In our study we found that no association between the development of major complications and annual surgeon volume or hospital volume. However, the small number of cases performed by each surgeon and at each hospital makes it unlikely to find significant differences based on volume. Rather, a greater number of comorbidities (CCI ≥ 2) was predictive of major complications. Contrary to previously reported results, this study did not find age to be independently associated with a higher risk of major complications.[24]

This may reflect a possible selection bias of healthier, albeit older, patients who underwent major surgery.

Strengths of this study include the use of a nationally representative population-based cohort. In addition, this data captures robotic adrenalectomy utilization from its inception through dissemination in the surgical community. Furthermore, we are able to analyze all three surgical approaches from the same database, in the same era, and across surgeon specialty, which has not been previously reported. Our study does have some limitations. First, we used a retrospective database based on hospital claims data, which limits the amount of clinical information available. For example, although we were able to stratify our cohort by benign versus malignant indication based on ICD-9 codes, there is no specific surgical pathology data, which would be valuable to stratify treatments on the basis of adrenal mass size, histology, and tumor stage. Additional adjuvant and neoadjuvant therapies or complications occurring during a separate hospitalization are not available in this database, which may lead to bias and under-reporting of postoperative complications. Furthermore, this study suffers from a common limitation of research using administrative healthcare databases—the potential for coding errors and misclassification of patients.

Conclusion

Adrenalectomy for benign and malignant disease was more commonly performed by non-urologists via an open approach. Urologists were earlier adopters of laparoscopic and robotic surgery for adrenalectomy. Overall, patients with more comorbidities had a higher rate of postoperative complications, while surgical approach did not appear to influence complication rate. These findings indicate that MIS for adrenalectomy can be performed safely for both benign and malignant disease and may lead to shorter hospitalization without increasing complication rates. However, prospective studies are needed given the limitations of claims-based analyses. □

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