Laparoscopic Surgery for Adrenocortical Carcinoma: Estimating the Risk of Margin-Positive Resection

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Background

- Adrenocortical carcinoma (ACC) is a rare but deadly cancer,
- About 600 diagnosis yearly in the United States and <50% 5-year survival.
- ACC has been previously managed with open resection, but recent guidelines from the American Association of Endocrine Surgeons has approved minimally invasive surgical (MIS) intervention.
- MIS is fraught with non-curative resection and locoregional recurrence
- Currently, risk factors for positive margins for patients receiving MIS resection are unknown.

Study Aim

- To Identify risk factors for margin positivity following MIS resection for ACC.
- To develop a nomogram suitable for pre-operative risk-stratification for patient counseling.

Methods

- **Study Design:** Retrospective cohort study of patients undergoing resection for ACC
- **Data Source:** National Cancer Database (NCDB), January 2010-December 2018
- **Exclusion Criteria:** Metastatic or non-invasive disease, incomplete records for facility type, days until surgery, tumor size, and laterality
- **Statistical Analyses:**
  - Uni- and multivariable logistic regression was used to identify risk factors for margin positivity
  - Model predictive quality was assessed using an 80/20 cross validation scheme with 10,000 iterations, with the test C-statistic (C-stat) being used as the indicator of prognostic utility
  - A nomogram was built from the final model
- **Predictors Considered:** Age, sex, race (white vs. non-white), Charlson-Deyo score (0-1 vs. 2+), facility type (academic vs. not), tumor stage (T1-2, T3, T4), tumor size, laterality, days until surgery
- All analyses were performed using R Studio (version 1.4.1717 R Studio; Boston, MA)

Principal Findings

- We identified 6904 patients with ACC in the NCDB database between 2010 to 2018. N was 1260 after applying the exclusion criteria. Only 38.6% (N=486) underwent MIS resection.
- Patients who underwent MIS resection were older, had higher Charlson-Deyo scores, had shorter intervals from diagnosis to surgery and were more likely to undergo surgery at non-academic centers.
- Patients who had Open Approach (OA) resection had advanced stage tumors, large tumor size and were more likely to have vascular invasion.
- MIS utilization increased significantly over time at non-academic centers (R=0.818, p=0.007)
- Among patients with resected ACC, non-academic center (OR 2.0, p<0.001), higher T stage (p<0.001), and clinically positive nodes (OR 4.3, p=0.011) were associated with positive margins (PM).
- For MIS subgroup, PM was associated with increasing age (OR 2.5-4.0, p = 0.01 to < 0.001), non-academic center (OR 1.8, p=0.006), cT3 (OR 4.7, p<0.001) or cT4 tumors (OR 14.6, p<0.001), and right-sided tumors (OR 2.0, p=0.006).

Table 1: Univariate and Multivariate Logistic Regression Models

Characteristics	Univariate OR	Univariate P	Multivariate OR	Multivariate P
Age				
<60	Ref	---	Ref	---
60-79	2.30	**<0.01**	2.49	**<0.01**
80+	2.92	**0.03**	4.00	**0.01**
Facility Type				
Non-Academic	Ref	---	Ref	---
Academic	0.61	**0.03**	0.56	**<0.01**
Tumor Stage				
T1-2	Ref	---	Ref	---
T3	4.08	**<0.01**	4.65	**<0.01**
T4	10.93	**<0.01**	14.64	**<0.01**
Unknown	2.43	**<0.01**	2.56	**<0.01**
Laterality				
Right	Ref	---	Ref	---
Left	0.57	**0.01**	0.50	**<0.01**

Fig 1: Yearly Proportion of ACC Tumors Resected via MIS stratified by facility type

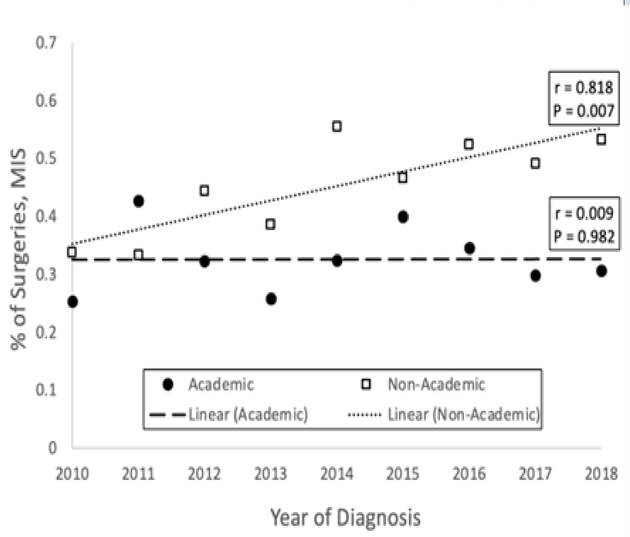
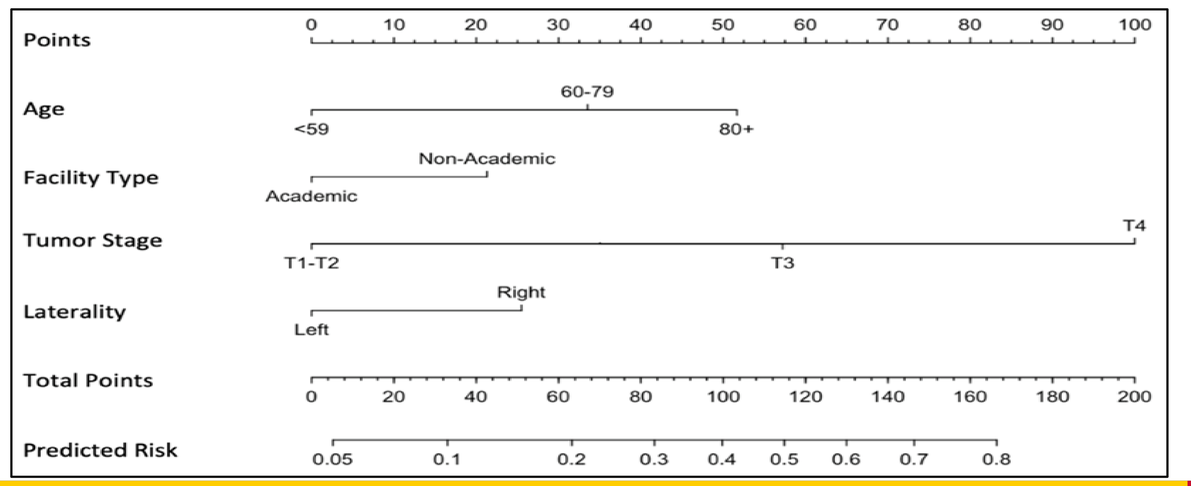


Fig 2. Nomogram. Training C-stat = 0.75 (95% CI: 0.69, 0.81), Test C-stat = 0.72 (0.60, 0.84)



Limitations

- Given the data available, establishing causality could be difficult.
- The NCDB lacks variables on granular tumor and some comorbidities, Thus, important variables which could improve our predictions were absent.

Example of Nomogram Use

A 65-year-old patient (33 pts) with a cT3 (57 pts), right-sided tumor (25 pts) at an academic center (0 pts) would have a 50% risk of margin-positive resection, while a 55-year-old patient (0 pt) with a cT2 (0 pts), left-sided tumor at the same center would have margin-positive risk of <5%.

Conclusion

- Use of MIS has increased over time, driven predominately by non-academic centers
- Four key preoperative variables can be used to accurately predict the risk of margin-positive, non-curative resection.
- By translating the logistic regression model into a nomogram, we also hope these results are more easily interpretable in a physician-patient counseling setting.

References

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Acknowledgement/Contact

Special thanks goes to Dr. Yinin Hu for his outstanding mentorship and all the co-authors in this project.

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