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Patient Frailty is Associated with Increased Risk of Complications after Adrenalectomy

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INTRODUCTION

The frequency of adrenal tumors increases with patient age.[1] As the U.S. population continues to grow older, surgeons will more frequently be asked to evaluate elderly patients for adrenalectomy due to concern for adrenocortical cancer or to mitigate the effects of a hormonally-active tumor.[2] Frailty, a measure of physiologic reserve independent of age, is associated with an increased risk of postoperative morbidity and readmissions in patients undergoing a variety of elective surgeries,[3-5] but its association with complications following adrenalectomy has not been well established. The purpose of this study is to evaluate the association of patient frailty with complications following adrenalectomy.

METHODS

Using the American College of Surgeons National Surgical Quality Improvement Project database from 2005-2011, we identified patients who underwent laparoscopic or open adrenalectomy. Post-operative ICD-9 diagnosis codes were used to identify malignant versus benign pathology.

Outcomes of interest were length of stay (LOS) and any serious 30-day post-operative complication, which were previously described by Seib, et al.[3] Frailty was defined using the validated modified frailty index.[3] One point was given for each frailty variable and patients were categorized into four groups: 0, 1, 2, 3+ frailty variables.

Multivariable logistic regression was used to examine the impact of frailty on complications, adjusting for malignancy, sex, race, corticosteroid use for a chronic condition (within 30 days of

surgery), and smoking (current smoker within 1 year). Statistical significance was defined as $p<0.05$. Statistical analysis was performed using Stata version 14.2.

RESULTS

Of 4,043 patients, 3,091 (76.5%) underwent a laparoscopic adrenalectomy. Most patients had benign tumors (n=2,180, 53.9%), while 553 (13.7%) had malignant tumors and 1,310 (32.4%) had pathology that could not be classified. Median age was 53 years (range 16-90). 270 patients (6.7%) were > 75 years old. The majority (72.9%) of patients had a frailty score of 0 or 1, but 282 (7.0%) had a frailty score of 3+. The most common contributor to frailty was hypertension, present in 2,835 (70.1%) patients.

The 30-day complication rate was 8.0% (n=324). The most common complications were bleeding requiring transfusion (n=128, 3.2%), pneumonia (n=61, 1.5%), ventilator required >48 hours (n=57, 1.4%), and sepsis (n=57, 1.4%). Laparoscopic procedures were associated with fewer complications (4.3% vs. 20.0%, $p<0.001$) and shorter LOS (2.9 days [95% CI 2.7-3.1] vs. 7.7 days [95% CI 6.7-8.6], $p<0.001$). Patients with benign tumors also had fewer complications (6.2% vs. 16.1%, $p<0.001$) and shorter LOS (3.6 days [95% CI 3.2-4.1] vs. 5.9 days [95% CI 5.2-6.6], $p<0.001$). Higher frailty score was associated with increased complications and LOS regardless of type of operation or diagnosis (**Table 1**).

On multivariable logistic regression, risk of serious complications was associated with higher frailty score (frailty score 3+ vs. 0: odds ratio [OR] 7.21, 95% CI 4.06-12.79, $p<0.001$), open

operations (vs. laparoscopic: OR 4.81, 95% CI 3.50-6.61, p<0.001), and malignancy (OR 1.83, 95% CI 1.30-2.59, p=0.001) (**Table 2**).

DISCUSSION

We found that among patients undergoing adrenalectomy, higher patient frailty scores (as well as malignancy and open operations) are more predictive of complications than older age. This novel finding complements research by Murphy, et al., who did not find an association between age and complications, but did find worse outcomes associated with a higher Charlson comorbidity index. [6] These findings are in contrast to research by Kazaure, et al., who reported that increasing age was associated with higher risk of complications, but their analysis did not evaluate frailty.[1]

In this study, frailty was associated complications even following laparoscopic adrenalectomy, which has been shown to have shorter operative times, less blood loss, and decreased long-term morbidity than the open approach.[2] Therefore, our results suggest that patient frailty should be considered in patient selection for adrenal operations and should be addressed in informed consent discussions.

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Table 1. Outcomes and length of stay by frailty score; by type of procedure and diagnosis

		Total	Frailty Score				P-value
			0	1	2	3+	
By Type of Procedure	***Open Adrenalectomy***						
	At least one complication – n (%)	190 (20.0%)	34 (12.3%)	70 (18.1%)	54 (26.3%)	32 (38.1%)	<0.001*
	Length of stay – mean days (SD)	7.7 (14.3)	5.8 (5.5)	6.2 (5.8)	10.0 (26.7)	15.1 (15.5)	<0.001**
	Laparoscopic Adrenalectomy						
	At least one complication – n (%)	134 (4.3%)	15 (2.0%)	50 (3.3%)	38 (6.3%)	38 (15.7%)	<0.001*
	Length of stay – mean days (SD)	2.9 (5.1)	2.1 (2.2)	2.5 (3.7)	3.2 (4.8)	8.0 (13.6)	<0.001**
By Diagnosis ***	***Benign Tumors***						
	At least one complication – n (%)	135 (6.2)	13 (3.0)	54 (4.7)	42 (9.1)	26 (18.4)	<0.001*
	Length of stay – mean days (SD)	3.7 (9.7)	2.5 (2.3)	2.9 (4.3)	4.9 (18.0)	9.3 (14.0)	<0.001**
	Malignant Tumors						
	At least one complication – n (%)	89 (16.1)	18 (9.9)	29 (19.1)	22 (19.1)	20 (46.5)	<0.001*
	Length of stay – mean days (SD)	5.9 (8.2)	4.5 (4.9)	5.1 (5.9)	6.5 (7.9)	14.6 (18.9)	<0.001**

*Pearson chi-square test
**Bartlett's test for equal variances
***Functional tumors may be benign or malignant

Table 2. Univariate and multivariable logistic regressions predicting serious morbidity. (Bold indicates statistically significant with p<0.05.)

	Univariate		Multivariable – All patients	
	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value
Frailty				
0	Ref		Ref	
1	1.32 (0.94-1.86)	0.111	**1.71 (1.08-2.73)**	**0.023**
2	**2.53 (1.77-3.63)**	**<0.001**	**2.69 (1.62-4.47)**	**<0.001**
3+	**5.71 (3.82-8.53)**	**<0.001**	**7.21 (4.06-12.79)**	**<0.001**
Open (vs. Laparoscopic)	**5.50 (4.34-6.96)**	**<0.001**	**4.81 (3.50-6.61)**	**<0.001**
Malignant (vs. Benign)	**2.91 (2.18-3.87)**	**<0.001**	**1.84 (1.30-2.59)**	**0.001**
Age				
<50	Ref		Ref	
50-64	1.31 (0.99-1.73)	0.056	0.95 (0.65-1.39)	0.793
65-74	**1.68 (1.21-2.34)**	**0.002**	1.05 (0.66-1.66)	0.836
75+	**3.11 (2.13-4.55)**	**<0.001**	1.50 (0.86-2.62)	0.150
Race –				
White	Ref		Ref	
Black	1.35 (0.98-1.86)	0.069	1.27 (0.84-1.93)	0.262
Hispanic	1.37 (0.84-2.25)	0.210	1.72 (0.91-3.28)	0.097
Asian or Pacific Islander	0.60 (0.24-1.48)	0.267	0.76 (0.26-2.22)	0.620
Female	0.90 (0.71-1.13)	0.370	1.05 (0.77-1.44)	0.737
Steroid use within 30 days	**2.26 (1.32-3.84)**	**0.003**	0.98 (0.40-2.36)	0.956
Current smoker within 1 year	**1.32 (1.04-1.70)**	**0.025**	1.39 (0.99=1.95)	0.057