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The risk analysis index demonstrates superior discriminative ability in predicting extended length of stay in pituitary adenoma resection patients when compared to the 5-point modified frailty index

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ABSTRACT

Objective: To compare the predictive abilities of two frailty indices on post-operative morbidity and mortality in patients undergoing pituitary adenoma resection.

Methods: The National Surgical Quality Improvement Program (NSQIP) database was used to retrospectively collect data for patients undergoing pituitary adenoma resection between 2015-2019. To compare the predictive abilities of two of the most common frailty indices, the 5-point modified frailty index (mFI-5) and the risk analysis index (RAI), receiver operating curve analysis (ROC) and area under the curve (AUC)/Cstatistic were used.

Results: In our cohort of 1,454 patients, the RAI demonstrated superior discriminative ability to the mFI-5 in predicting extended length of stay (C-statistic 0.59, 95% CI 0.56-0.62 vs. C-statistic 0.51, 95% CI: 0.48-0.54, p = 0.0002). The RAI only descriptively appeared superior to mFI-5 in determining mortality (C-statistic 0.89, 95% CI 0.74-0.99 vs. Cstatistic 0.63, 95% CI 0.61-0.66, p=0.11), and NHD (C-statistic 0.68, 95% CI 0.60-0.76 vs. C-statistic 0.60, 95% CI: 0.57-0.62, p=0.15).

Conclusions: Pituitary adenomas account for one of the most common brain tumors in the general population, with resection being the preferred treatment for patients with most hormone producing tumors or those causing compressive symptoms. Although pituitary adenoma resection is generally safe, patients who experience post-operative complications frequently share similar pre-operative characteristics and comorbidities. Therefore, appropriate pre-operative risk stratification is imperative for adequate patient counseling and informed consent in these patients. Here we present the first known report showing the superior discriminatory ability of the RAI in predicting eLOS when compared to the mFI-5.

1. Introduction

Pituitary adenomas (PA) account for 18.1 % of all primary central nervous system tumors.[1] Surgical resection is the treatment of choice for many functional and larger non-functional PA's causing neurological symptoms and/or endocrinopathy.[2,3] Resection via modern minimally invasive techniques is considered safe with low rates of peri- and post-operative morbidity/mortality. However, most patients who experience postoperative complications share several characteristics, including increased age, body mass index (BMI), multiple medical comorbidities, and increased frailty.[4–7] Increased frailty status signifies decreased physiological reserve, increasing one's risk to adverse outcomes and impaired recovery after surgery.[8] Therefore, frailty has become the focus of many pre-operative risk stratification tools in attempt to further improve patient outcomes and minimize healthcare costs.[9]

Over the past decade, several frailty instruments have emerged, with the 5-point modified frailty index (mFI-5) most commonly utilized for

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neurosurgical outcomes research, including for PA resection studies.[9,10] However, recent surgical outcomes studies suggest the Risk Analysis Index (RAI) demonstrates robust and superior comparative discriminative utility to other existing frailty scales, including the mFI-5.[11–13] Compared to the mFI-5 which focuses on comorbidity burden alone, RAI more accurately measures physiological reserve by incorporating age and baseline functional status.[8,14] The RAI was developed to encompass the multi-dimensionality of frailty more accurately with 14 questions administered at the bedside which includes a patient's medical comorbidities, functional status, and ability to live independently.[8] Once calculated, a numerical score ranging from 0 (non-frail) to 81 (very-frail) is given and allows for proper pre-operative risk stratification, as higher scores correlate with worse surgical outcomes,[15] In contrast, the mFI-5 primarily focuses on medical comorbidities alone, including hypertension, diabetes mellitus, congestive heart failure chronic obstructive pulmonary disease, and functional status.

Numerous reports have shown the RAI outperforms the mfI-5 in outcome prediction, including in primarily elective surgical procedures,[15–17] PA patients are largely evaluated in the outpatient elective setting, where preoperative risk stratification can formally be assessed. Therefore, accurate preoperative risk stratification tools are needed to provide better surgical decision making in this patient population. Similarly, accurate assessments in this patient population may allow for the surgical optimization of these patients, thereby helping alleviate complications and unnecessary healthcare costs associated with PA resections.[4] In the present study, we examine the comparative predictive ability of the administrative-RAI (RAI-A) and the mFI-5 on post-operative mortality, extended length of hospital stay (eLOS), and non-home discharge (NHD) in patients undergoing PA resection.

2. Methods

2.1. Data source & patient selection

Data was collected through The American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database. We extracted data for patients undergoing PA resection between years 2015–2019. This study was performed under data user agreement (DUA) of the ACS with our institution and approved by our Institutional Review Board (Study ID 21–315). Due to the deidentified nature of the information in NSQIP database, patient consent was neither sought nor required. Patients undergoing PA resection were identified using Current Procedural Terminology (CPT) codes: 61,546 (Craniotomy for excision of pituitary tumor) and 61,548 (Hypophysectomy or excision of pituitary tumor, trans-nasal or transseptal approach, nonsteretoactic).

2.2. Modified frailty index-5 (mFI-5)

Initially, the modified frailty index was developed using eleven variables (mFI-11), however, NSQIP discontinued mandating six variables used within the mFI-11, resulting in the creation of the mFI-5. Variables used within the mFI-5 include hypertension, diabetes mellitus (DM), chronic heart failure (CHF), functional status, and chronic obstructive pulmonary disease (COPD), with their cumulative count representing a frailty score. Scores therefore range from 0 to 5, with a score of 0 representing "non-frail", 1 representing "pre-frail", 2 is considered "frail", and a score of ≥3 is considered "severely frail". Both the mFI-11 and mFI-5 have been shown to be independently predictive of adverse post-operative outcomes in various surgical subspecialties, including neurosurgical patients.[18–20]

2.3. Risk analysis index (RAI-A)

The RAI differ from the modified frailty indices in that they were specifically developed to encompass frailty. RAI was developed using data from the Veterans Affairs Surgical Quality Improvement Program along with a scoring model used in nursing home patients.[8,21] Frailty encompasses the multidimensional characteristics which determine a patient's overall physiological reserve and hence, their ability to withstand significant stressors, including surgical interventions. The risk analysis indices quantify these factors using a retrospective version (administrative RAI; RAI-A, RAI-rev) or prospective RAI (RAI-C) which can be measured at the bedside with the patient. Both indices have been validated and proven to be superior to other frailty indices.[14] The RAI includes various frailty parameters, including patient demographic variables such as age/sex, nutrition status, patient medical comorbidities, including hypertension, cancer, dyspnea, renal impairment, and a patients cognitive and functional performance. RAI scoring was stratified into four groups, RAI ≤10 is considered "non-frail", RAI 11–20 "pre-frail", RAI 21–30 "frail", and RAI ≥31 "severely frail".

2.4. Population characteristics & outcomes

Baseline demographic data extracted included age, sex, race, and body mass index (BMI). mFI-5 and RAI frailty distributions were recorded. Medical comorbidities were also recorded, these included hypertension, DM, COPD, CHF, smoker status, dyspnea, disseminated cancer, steroid use, weight loss, bleeding disorder, and functional status. Outcomes measured included mortality, eLOS (defined as LOS >75th percentile for the study cohort), and non-home discharge destination (NHD).

2.5. Statistical analysis

Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version-28 [International Business Machines (IBM) Corp. Armonk, NY]. Receiver operating curve analysis (ROC) and area under the curve (AUC)/C-statistic were used to assess the discriminatory power of each model and compared using DeLong test.[22] A p-value of <0.05 was considered statistically significant.

3. Results

A total of 1454 patients met our inclusion criteria, Table 1 depicts the clinical characteristics of the study population and the frailty scoring used for each index. The median age was 55-years, with the majority of patients being male (51.9 %, $n = 755$). The median BMI was 30.24 (IGR 26.59–34.85), with a median operative time of 139 min (IQR 98.75–198). The most common medical comorbidities were hypertension 43.7 % ($n = 635$), DM 19.7 % ($n = 287$), current smoker 11.8 % ($n = 172$), and preoperative steroid use 9.8 % ($n = 143$). In frailty scoring 15.4 % ($n = 224$) of patients were considered frail and 1.1 % ($n = 16$) were considered severely frail based on the mFI-5. Using RAI scoring, 2.8 % ($n = 41$) of patients were considered frail and 0.5 % ($n = 7$) were considered severely frail.

The mortality rate for our study population was 0.31 % ($n = 5$). 4.1 % ($n = 60$) of patients had NHD destinations and 30.4 % had eLOS (75 % percentile for our study cohort was 5 days). The RAI had superior discriminative ability to mFI-5 at predicting eLOS (C-statistic 0.59, 95 % CI 0.56–0.62 vs. C-statistic 0.51, 95 % CI: 0.48–0.54, $p = 0.0002$) (Fig. 1 & Supplemental Table 1). Due to the smaller sample size, RAI only descriptively appeared superior to mFI-5 in determining mortality (C-statistic 0.89, 95 % CI 0.74–0.99 vs. C-statistic 0.63, 95 % CI 0.61–0.66, $p = 0.11$), and NHD (C-statistic 0.68, 95 % CI 0.60–0.76 vs. C-statistic 0.60, 95 % CI: 0.57–0.62, $p = 0.15$).

4. Discussion

Patients with PA requiring surgical intervention often present in the outpatient, elective setting where preoperative risk assessment is critical for patient counseling and surgical decision making.

We present the first known report showing superior discriminative

Table 1
Baseline demographic and clinical characteristics including incidence of 30-day mortality, NHD, and eLOS of patients undergoing Pituitary Adenoma resection from NSQIP database 2015–2019.

Variable	Cohort (*n* = 1442)
Age (median + IQR)	55 (41–65) years
Male Patients (*n*, %)	755 (51.9 %)
BMI (median + IQR)	30.24 (26.59–34.85)
Operative time (median + IQR)	139 (98.75–198) minutes
Length of stay (median + IQR)	3 (2–5) days
Mortality	5 (0.3 %)
Non-Home Discharge	60 (4.1 %)
Frailty distribution based on mFI-5 score	
Robust (mFI-5 = 0)	738 (50.8 %)
Pre-frail (mFI-5 = 1)	476 (32.7 %)
Frail (mFI-5 = 2)	224 (15.4 %)
Severely frail (mFI-5 = 3 and above)	16 (1.1 %)
Frailty distribution based on RAI-A score*	
Robust (RAI-rev = 0–10)	1264 (187 %)
Prefrail (RAI-rev = 11–20)	84 (5.9 %)
Frail (RAI-rev = 21–30)	41 (2.8 %)
Severely Frail (RAI-rev = 31 and above)	7 (0.5 %)
Preop clinical status/comorbidities	
Functional Status	
Partially Dependent	19 (1.3 %)
Totally Dependent	10 (0.7 %)
Diabetes mellitus	287 (19.7 %)
COPD	26 (1.8 %)
CHF	3 (0.2 %)
Current smoker	172 (11.8 %)
Dyspnea	54 (3.7 %)
Hypertension	635 (43.7 %)
Disseminated cancer	28 (1.9 %)
Steroid use	143 (9.8 %)
Weight loss	15 (1 %)
Bleeding disorders	13 (0.9 %)

ability of RAI compared to mFI-5 in predicting eLOS following PA resection. Descriptively, RAI appeared superior to mFI-5 at predicting NHD and 30-day mortality, however, statistical comparison was limited by infrequency of outcome occurrence. The RAI's superior predictive abilities have been shown in various surgical subspecialties, including spine surgery, showing the RAI to be more predictive than other frailty measures (mFI-5) in predicting mortality, adverse outcomes, and serious complications.[11–13] These results are expected as the RAI is conceptually superior to mFI-5 as it was built with fidelity to the concept of phenotypic frailty.

The significant finding of the RAI predicting eLOS in this patient population is imperative, as eLOS is associated with higher risk of hospital acquired conditions, postoperative complications, healthcare resource utilization, and delayed recovery.[23] Prior studies have shown the average length of stay for PA resection to be between 1 and 4 days,[24] with one study citing 4 days as eLOS,[25] therefore the results of our study further exemplify the significance of using frailty scoring within this patient population, specifically the RAI. The results of our study align with previous reports which show frailty is a significant predictor of worse outcomes in patients undergoing pituitary surgery.[5,9,10,26] Various studies have examined the mFI-5 as a risk stratification tool within neurosurgery, concluding this index is useful in predicting post-operative complications and mortality[16,27–29] However, a recent study examining mortality rates and serious complications in noncardiac surgeries showed the RAI was better at predicting these outcomes when compared to the mFI-5, concluding the RAI more accurately reflects multidimensional frailty than the mFI-5.[12] Nevertheless, few studies have examined the predictive ability of RAI in neurosurgery patients. Agarwal et al,[30] recently examined the use of RAI in patients undergoing spine surgery, concluding RAI scoring was a significant predictor of post-operative morbidity and mortality.

In our cohort, the ROC-derived C-statistics for RAI appeared descriptively superior to mFI-5 in predicting mortality and NHD. Though mortality rates in our study were low, they align with previous reports showing rates being between 0.4 and 0.6 % for PA resection.[5,6] Importantly, for our study population, only 3.3 % of patients were considered frail or severely frail through RAI scoring, whereas, 16.5 % of patients were frail or severely frail through mFI-5 scoring, with RAI descriptively out predicting mortality, NHD, and eLOS in these populations. However, the analysis was limited by infrequency of outcome occurrence and thus the findings may be hindered by a type II error due to insufficient power. Future comparisons with larger sample sizes and prospective validation are imperative. Despite these limitations, our data demonstrate superior discriminative ability of RAI-A compared to the more well-established frailty scale in neurosurgery, i.e., mFI-5 and support the clinical utility of RAI in pre-operative risk assessment of patients undergoing PA resection, especially since the majority of these patients are evaluated in the elective outpatient setting.

5. Limitations

Limitations to the present study are attributable to the use of an administrative database and relatively smaller sample size. However, hospitals participating within the NSQIP database must adhere to rigorous guidelines and audits, therefore providing high quality data. Similarly, the RAI may have improved outcome prediction as it incorporates more variables than the mFI-5.

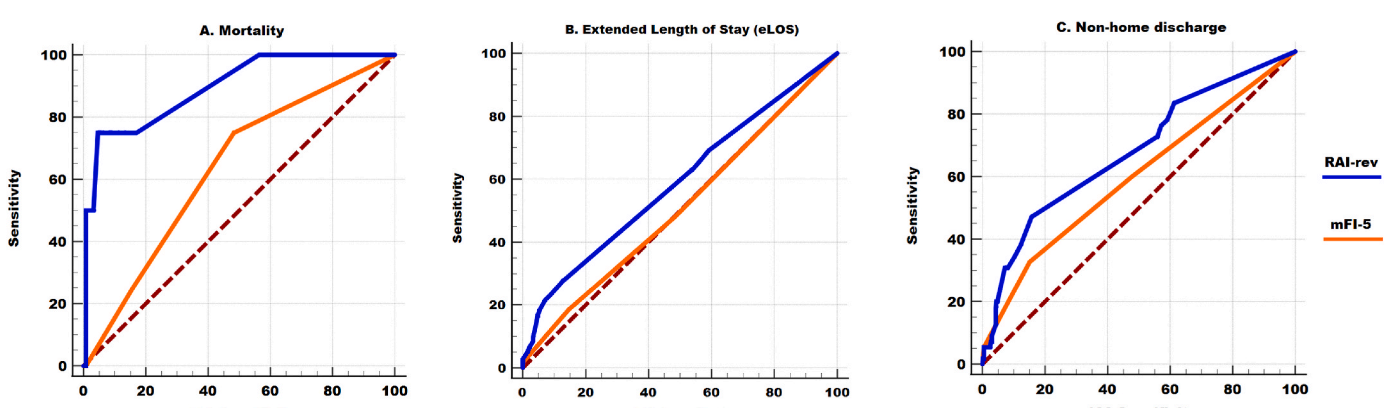

Figure 1. a-c ROC/AUC analysis for the relative predictive abilities of the RAI-A and mFI-5 on mortality, non-home discharge, and eLOS in Pituitary Adenoma resections patients from NSQIP database 2015-2019.
*Blue line represents RAI-rev (RAI-A), Orange represents the mFI-5

6. Conclusion

In this longitudinal cohort study, we show the RAI demonstrates superior discrimination when compared to the mFI-5 in predicting eLOS in patients undergoing pituitary adenoma resection surgery. The RAI encompasses the multidimensional facets of frailty and maintains fidelity to the frailty phenotype, which is largely unaccounted for with the mFI-5. Larger and prospective validation of these findings is necessary, however, the results of our study support suggest the RAI may be more useful in the preoperative risk stratification of PA resection patients, where preoperative risk is largely assessed in the outpatient elective setting.

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Ethical approval

The present study was performed under the data user agreement (DUA) of the ACS with the University of New Mexico (UNM) and was approved by the Institutional Review Board of UNM School of Medicine (Study ID 21–315).

Consent to participate

Given the de-identified nature of the information in NSQIP database, patient consent was neither sought nor required.

Consent for participation

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CRediT authorship contribution statement

Samantha Varela: Visualization, Methodology, Validation, Writing - review & editing, Formal analysis, Investigation, Data curation, Writing - original draft. **Rachel Thommen:** Resources, Data curation. **Kavelin Rumalla:** Writing - review & editing, Resources, Data curation. **Syed Faraz Kazim:** Data curation, Resources, Writing - review & editing. **William T. Couldwell:** Writing - review & editing. **Meic H. Schmidt:** Resources, Writing - review & editing. **Christian A. Bowers:** Formal analysis, Project administration, Validation, Conceptualization, Methodology, Visualization, Supervision, Investigation, Writing - review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.wnsx.2023.100259.

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Abbreviations

PA –: pituitary adenoma
BMI –: body mass index
mFI-5 –: 5-point modified frailty index
RAI: Risk analysis index
NHD –: non-home discharge
eLOS –: extended length of stay
NSQIP –: national quality improvement program
ACS –: American college of Surgeons
DUA –: data user agreement
CPT –: current procedural terminology
mFI-11 –: 11-point modified frailty index
DM –: diabetes mellitus
CHF –: congestive heart failure
COPD –: chronic obstructive lung disease
AUC –: area under the curve
CI –: confidence interval