# Preoperative Charlson Comorbidity Score Predicts Postoperative Outcomes Among Older Intracranial Meningioma Patients

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**Key words**
- Charlson score
- Elderly meningioma
- Preoperative risk assessment

**Abbreviations and Acronyms**
**ASA**: American Society of Anesthesiologists
**KPS**: Karnofsky Performance Status
**LOS**: Length of stay
**NIS**: Nationwide Inpatient Sample

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OBJECTIVE: **Preoperative determinants of surgical risk in elderly patients with meningioma are not fully defined. This study was undertaken to determine whether the Charlson comorbidity index could be used to accurately predict postoperative outcomes among older patients with meningiomas undergoing neurosurgical resection and thereby make a selection for surgery easier.**

METHODS: **We performed a multi-institutional retrospective cohort analysis via the Nationwide Inpatient Sample (1998-2005). Patients 65 years of age and older who underwent tumor resection of intracranial meningiomas were identified by International Classification of Diseases, 9th revision, coding. The primary independent variable in multivariate regression was the Charlson comorbidity score, and the primary outcome was inpatient death. Secondary outcomes included inpatient complications, length of stay, and total hospital charges.**

RESULTS: **We identified 5717 patients (66.6% female, and 81.8% white) with mean age of 73.6 years. Mean Charlson comorbidity score was 0.99. Inpatient mortality was 3.2%. Mean length of stay was 9.1 days, and mean total charges were $62,983. In multivariate analysis, the only factors consistently associated with worse outcome were increased Charlson comorbidity score and increased patient age (ie, >65 years of age). Only greater Charlson scores were additionally associated with greater odds of all major complications such as neurological, respiratory, and cardiac complications. Elective procedures were consistently associated with less inpatient death, length of stay, and total charges. All associations were statistically significant ($P < 0.05$).**

CONCLUSIONS: **The safe surgical resection of intracranial meningiomas among older patients is possible through the ninth decade of life. The Charlson comorbidity score has been shown to be a strong, consistent predictor of inpatient outcomes.**

## INTRODUCTION

Meningiomas account for nearly one-fourth of all primary brain tumors, with one-half of these lesions presenting in patients older than 65 years of age (11, 14, 16). There is an increasing incidence of these tumors, likely related to population demographics and the greater use of diagnostic imaging. Given the increasing numbers of patients in advanced age who will be diagnosed with meningioma in the coming decades, there is an increasing need to define reliable, preoperative predictors of safe neurosurgical intervention for these older patients (11, 18).

During the past 20 years, ambiguity has arisen regarding the decision of whether to resect meningiomas in older adults because of wide variability in reported mortality rates, which range from 1.8% to 45% (2-6, 15, 17, 19-21, 23, 25, 26). Some investigators have attempted to define preoperative indicators for safe neurosurgical intervention, with several demonstrating the predictive value of patient age, sex, tumor size, and general health indicators, such as American Society of Anesthesiologists (ASA) (6, 31) and Karnofsky Performance Status (KPS) (13, 15, 17) scores, whereas the authors of other series have negated the value of such measures (3-6, 8, 12-15, 17, 19, 21-23, 25-27, 29, 30, 32, 34).

In light of viable nonoperative management approaches, including conservative management or stereotactic radiosurgery, identification of reliable preoperative markers associated with successful tumor excision remains an important goal and allows for more informed operative decision-making and truly informed consent (7, 24). Through this multicenter, retrospective cohort study of the Nationwide Inpatient Sample, we demonstrate that the Charlson score is predictive of inpatient postoperative outcome among elderly patients with meningioma.

## MATERIALS AND METHODS

### Data Source

We obtained the National Inpatient Sample (NIS) in-hospital discharge database for the years 1998 through 2005. Compiled by the

**Table 1.** Comorbidities Included in the Charlson Comorbidity Score

| Weights | Clinical Conditions |
|---|---|
| 1 | Myocardial infarct, congestive heart failure, peripheral vascular disease, dementia, cerebrovascular disease, chronic lung disease, connective tissue disease, peptic ulcer disease, or chronic liver disease |
| 2 | Hemiplegia, moderate or severe kidney disease, uncomplicated diabetes, diabetes with complications, tumor, leukemia, lymphoma |
| 3 | Moderate or severe liver disease |
| 6 | Malignant tumor, metastasis, acquired immune deficiency syndrome |

Agency for Healthcare Research and Quality (Rockville, Maryland, USA), the NIS contains discharge information from a stratified random sample of 20% of all hospitals in 37 participating states (1). This publicly available, deidentified dataset was exempt for review by the Johns Hopkins Institutional Review Board.

### Inclusion and Exclusion Criteria

Inclusion criteria included patients 65 years of age and older with a meningioma (International Classification of Diseases, 9th revision diagnosis codes 225.2, 192.1, and 237.6 for meningiomas of benign, malignant, and uncertain behavior) who underwent a surgical resection, as identified by International Classification of Diseases, 9th revision procedural codes (01.51 and 01.59) for resection.

### Characteristics of Interest and Outcome Variables

The primary independent variable was the Charlson comorbidity score. The Charlson score is a well-validated, weighted patient comorbidity index that was recorded from the NIS database as a value between 0 and 15. It provides a score accounting for various comorbidities, including history of cancer, as well as cardiac, vascular, pulmonary, neurological, endocrine, renal, hepatic, gastrointestinal, and immune disorders (**Table 1**) (10). Other covariates included patient age, tumor grade, sex, race/ethnicity, and elective status of the procedure. Age was analyzed as a continuous variable for all patients 65 years of age or older. Tumor grade was analyzed in multivariate regressions as a binary covariate, either benign or malignant. Sex was a binary covariate, either male or female. Race/ethnicity was categorized as white, African American, Hispanic, Asian, or Native American. Elective procedure status was analyzed as a binary covariate.

The primary outcome was inpatient death. Secondary outcomes included total hospital charges (adjusted to 2008 inflation), total hospital length of stay (LOS), and postoperative complications, including neurological deficits, stroke, respiratory complications, and cardiac complications.

### Statistical Analysis

Univariate analysis included a descriptive account of the patient population, including mean and median values to describe continuous variables and proportions to describe categorical variables. Multivariate logistic and linear regression models were constructed to analyze binary and continuous outcomes, respectively. Multivariate analyses were adjusted for Charlson comorbidity score, patient age, tumor grade, sex, race/ethnicity, and elective status. $P$ values less than 0.05 were considered to be statistically significant. All data were analyzed by use of the software package STATA/MP 10 (College Station, Texas, USA).

## RESULTS

### Univariate Analysis

A total of 5717 patients were identified; among these, we found a slight female predominance (66.6%). Most patients (93.1%) had benign or low-grade (World Health Organization grade I), meningiomas. Mean age was 73.6 years (median, 73 years), and most patients were white (81.8%). Patients had a mean Charlson score of 0.99 (median, 0). Most (67.4%) patients underwent elective surgical procedures. Mean length of stay was 9.1 days (median, 6 days). Patients had mean total hospital charges of $62,983 (median, $44,669). Overall inpatient mortality was 3.2%. Postoperative complications include new neurological deficits (5.7%), stroke (5.3%), respiratory complications (4.8%), and cardiac complications (1.7%) (**Table 2**).

### Factors Associated with Inpatient Death

In multiple logistic regression models adjusted for patient age, tumor grade, sex, race/ethnicity, Charlson comorbidity score, and elective procedure status, only Charlson score, patient age, and elective status of the procedure were significantly associated with greater odds of death. Each one-point increase in Charlson score was associated with 18% increased odds of inpatient death (odds ratio [OR] 1.18, $P = 0.001$), and each 1-year increase in patient age beyond 65 years of age was associated with 9% greater likelihood of inpatient death (OR 1.09, $P < 0.001$). Elective procedure status (OR 0.51, $P < 0.001$) was the only factor associated with significantly decreased odds of inpatient death. Patient sex, tumor grade, and race/ethnicity were not associated with greater odds of inpatient death (**Table 3**).

### Factors Associated with Inpatient Complications

In multiple logistic regression models adjusted for patient age, tumor grade, sex, race/ethnicity, Charlson comorbidity score, and elective procedure status, the only factor consistently associated with greater odds of developing all major complications such as new neurological deficits, stroke, respiratory complications, and cardiac complications was Charlson comorbidity score. Each one-point increase in Charlson comorbidity score was associated with between a 20% and 35% greater odds of developing an inpatient complication ($P < 0.001$).

Although each 1-year increase in patient age greater than 65 years trended toward a significant relationship with all four complications, such trends between patient age and complications only reached statistical significance for new neurological deficits (OR 1.03, $P = 0.008$) and respiratory complications (OR 1.03, $P = 0.004$). Similarly, although the presence of higher grade meningioma (vs World Health Organization

**Table 2.** Demographics of 5717 Elderly Patients with Meningioma Undergoing Resection, 1998-2005

| Patient Demographics | n | % |
|---|---|---|
| Charlson index score | | |
| Mean (median) | 0.99 (0) | |
| Age, in years | | |
| Mean (median) | 73.6 (73) | |
| Tumor grade | | |
| Benign | 5306 | 93.1 |
| Malignant | 345 | 6.1 |
| Uncertain | 47 | 0.8 |
| Females | 3804 | 66.6 |
| Race/ethnicity | | |
| White | 3570 | 81.8 |
| African American | 341 | 7.8 |
| Hispanic | 234 | 5.4 |
| Asian | 126 | 2.9 |
| Native American | <10 | <0.5 |
| Other | 88 | 2.0 |
| Elective procedures | 3303 | 67.4 |
| Outcomes | | |
| Mortality | 183 | 3.2 |
| Length of stay, in days | | |
| Mean (median) | 9.1 (6) | |
| Total hospital charges | | |
| Mean (median) | $62,983 ($44,669) | |
| Postoperative complications | | |
| Neurological deficit | 326 | 5.7 |
| Stroke | 305 | 5.3 |
| Respiratory complications | 284 | 4.8 |
| Cardiac complications | 97 | 1.7 |

grade I meningioma) trended toward a significant relationship with all four complications, such trends only reached statistical significance for new neurological deficits (OR 3.33, $P = 0.006$) and stroke (OR 2.17, $P = 0.02$).

Patients undergoing nonelective/emergent procedures were significantly more likely than their elective counterparts to develop inpatient respiratory complications, such as pneumonia (OR 0.58, $P = 0.003$). Patient sex, tumor grade, and race/ethnicity were not consistently associated with the development of any major inpatient complications (**Table 4**).

### Factors Associated with Hospital LOS

In multiple linear regression models adjusted for patient age, tumor grade, sex, race/ethnicity, Charlson comorbidity score, and elective status, the following variables were associated with significantly longer inpatient LOS: each one-point increase in Charlson comorbidity score (0.51 increased days, $P < 0.001$), each 1-year increase in patient age older than 65 years (1.79 increased days, $P < 0.001$), and African-American race or Hispanic ethnicity (2.86 and 1.98 increased days, with $P < 0.001$ and $P = 0.005$, respectively) relative to white patients. Elective procedure status was associated with 4.95 days' shorter LOS ($P < 0.001$). Female sex, tumor grade, and Asian race were not associated with any significant change in total LOS (**Table 3**).

### Factors Associated with Total Hospital Charges

In multiple linear regression models adjusted for patient age, tumor grade, sex, race/ethnicity, Charlson comorbidity score, and elective status, each one-point increase in Charlson comorbidity score was associated with $1964 in total charges ($P = 0.002$). Significantly greater total hospital charges were also present among older patients ($8857 greater charges for each 1-year increase in age, $P = 0.02$) relative to 65-year-old counterparts, as well as African-American ($9,092 greater charges, $P = 0.04$) and Hispanic ($32,012 greater charges, $P < 0.001$) patients, relative to white patients. Patient undergoing elective procedures had $19,019 lower total hospital charges ($P < 0.001$). Female sex, tumor grade, and Asian race were not associated with any significant differences in total hospital charges (**Table 3**).

## DISCUSSION

The authors of numerous past series have attempted to define preoperative markers of safe neurosurgical intervention in older patients with meningiomas. Most have often focused upon patient age, sex, tumor size, and general health indicators, such as ASA and KPS scores, as possible predictive markers, often with conflicting results (3-6, 8, 12-15, 17, 19, 21-23, 25-27, 29, 30, 32, 34). Our study used a multicenter database to determine the value of a widely validated tool, commonly use in other surgical fields, the Charlson comorbidity score, in determining the relative odds of inpatient outcomes specifically among older patients after resection of meningioma patient population. After adjusting for other relevant factors, such as patient age, sex, tumor grade, race/ethnicity, and operative elective status, we were able to demonstrate for the first time that preoperative Charlson score is predictive of inpatient postoperative death, LOS, total hospital charges neurological, respiratory and cardiac complications, for these older patients.

**Table 3.** Odds of Increased Inpatient Death, LOS, and Total Hospital Charges in Separate Multivariate Regressions Among Elderly Meningioma Patients Undergoing Resection, 1998-2005*

| | Inpatient Death | | Increased LOS | | Total Hospital Charges | |
|---|---|---|---|---|---|---|
| **Patient Factors** | **OR (95% CI)** | ***P* Value** | **OR (95% CI)** | ***P* Value** | **OR (95% CI)** | ***P* Value** |
| Charlson score | 1.18 (1.07–1.29)* | 0.001* | 0.51 (0.33–0.68)* | <0.001* | $1,964 ($721–$3,207)* | 0.002* |
| Age | 1.09 (1.06–1.13)* | <0.001* | 1.79 (0.91–2.67)* | <0.001* | $8,857 ($1,267–$16,447)* | 0.02* |
| Tumor grade | | | | | | |
| Benign | 1.00 | – | – | – | – | – |
| Malignant | 1.52 (0.63–3.65) | 0.35 | 1.20 (−0.33 to 2.74) | 0.13 | $2,988 (−$7,385 to $13,361) | 0.57 |
| Females | 0.74 (0.51–1.06) | 0.10 | 0.27 (−0.24 to 0.77) | 0.30 | −$1,690 (−$4,778 to $1,397) | 0.28 |
| Race/ethnicity | | | | | | |
| White | 1.00 | – | – | – | – | – |
| African American | 1.20 (0.65–2.23) | 0.55 | 2.86 (1.34–4.37)* | <0.001* | $9,092 ($236–$17,947)* | 0.04* |
| Hispanic | 0.22 (0.03–1.77) | 0.33 | 1.98 (0.59–3.37)* | 0.005* | $32,012 ($16,145–$47,879)* | <0.001* |
| Asian | 1.57 (0.45–5.47) | 0.48 | 0.25 (−2.53 to 3.04) | 0.86 | −$2,577 (−$16,977 to $11,823) | 0.73 |
| Elective procedures | 0.51 (0.36–0.73) | <0.001 | −4.95 (−5.56 to −4.33) | <0.001 | −$19,019 (−$22,143 to −$15,895) | <0.001 |

CI, confidence interval; LOS, length of stay; OR, odds ratio.
*Statistically significant relationship.

### Charlson Score Is Predictive of All Major Inpatient Outcomes

Our study demonstrates that the Charlson comorbidity index is a useful predictor of inpatient postoperative death, complications, LOS, and total hospital charges within older patients with meningioma. Unfortunately, we could not dichotomize the impact of Charlson scores upon major outcomes at any particular threshold while maintaining statistical significance. Since first validated in 1994, the Charlson comorbidity index has been used as a preoperative predictor of complications and mortality in patients with varying forms of oncological disorders, with all major published reports shying away from dichotomizing this risk factor (9, 33). Rather, the Charlson score traditionally has been used as a continuous variable in practice to help guide patients through medical decision-making processes (28, 33, 35, 36).

**Table 4.** Odds of Various Inpatient Postoperative Complications by Patient Characteristic in Separate Multivariate Regressions

| | Complication | | | |
|---|---|---|---|---|
| **Independent Variable** | **Neurological Deficit** | **Stroke** | **Respiratory Complication** | **Cardiac Complication** |
| Charlson score | 1.30 (1.20–1.40) | 1.35 (1.26–1.45) | 1.20 (1.10–1.31) | 1.25 (1.13–1.41) |
| | *P* < 0.001* | *P* < 0.001* | *P* < 0.001* | *P* < 0.001* |
| Patient age | 1.03 (1.01–1.06) | 1.02 (0.99–1.05) | 1.03 (1.01–1.06) | 1.02 (0.98–1.07) |
| | *P* = 0.008* | *P* = 0.21 | *P* = 0.004* | *P* = 0.30 |
| High-grade tumor | 3.33 (1.41–7.87) | 2.17 (1.11–4.26) | 2.19 (0.93–5.12) | 2.45 (0.72–8.35) |
| | *P* = 0.006* | *P* = 0.02* | *P* = 0.07 | *P* = 0.15 |
| Elective procedure status | 1.08 (0.74–1.56) | 0.99 (0.70–1.41) | 0.58 (0.40–0.84) | 1.21 (0.70–2.10) |
| | *P* = 0.69 | *P* = 0.96 | *P* = 0.003* | *P* = 0.50 |

Values are expressed as odds ratio (confidence interval).
Only a greater Charlson score was associated with higher odds of all four major complications studied.
*Statistically significant.

Various investigators have attempted to assess the impact of patient comorbidities or general health indicators upon outcomes within this patient population (6, 13-15). However, none of them used the well-validated Charlson comorbidity score to predict postoperative outcome such as neurological deficit, stroke, respiratory and cardiac complications as well as mortality, LOS, and total hospital charges in this study population. Charlson comorbidity index has been proven in other surgical field as a predictive tool for various outcomes, and we have tested its accuracy in the neurosurgical field.

Relatively small series of between 34 and 250 patients have demonstrated the relationship between specific comorbidities, such as diabetes, hypertension, and obesity, with poor postoperative outcomes, although these analyses have been limited to unadjusted, univariate analyses and the study of only individual pre-existing health conditions, not more comprehensive comorbidity classification systems (12, 25).

Attempts have been made to use the ASA and KPS scales as models of general health and possible predictors of postoperative outcomes with mixed results. The series by Black et al. (6) of 57 ASA-class matched meningioma patients demonstrated no difference in postoperative outcomes between younger and older patients in univariate analysis. However, the series by Rogne et al. (29) demonstrated no significant association between ASA score and postoperative outcomes in 79 older patients with brain tumors, again in univariate analysis. However, the results of Rogne et al. have been contradicted by at least four separate reports describing 17 to 96 patients which demonstrate significant relationships between worse ASA or KPS scores and worse postoperative outcomes in univariate analysis of older meningioma patients (13, 15, 17, 26).

More robust multivariate analyses have also been used to demonstrate an association between general health and postoperative outcomes within this patient population. Sacko et al. (32) created a scale consisting of patient sex, KPS score, ASA score, location of tumor, and peritumoral edema known as the SKALE grading system. In multiple regression analyses of the component elements of SKALE, only tumor location was significantly associated with patient morbidity and mortality; patient KPS and ASA scores trended toward an association, but these trends did not achieve a level of statistical significance (32). Similarly, the Clinical-Radiological Grading System, developed by Caroli et al., which included elements such as tumor location, KPS score, and individual patient comorbidities, did not demonstrate an association between single comorbidities and patient outcomes in separate analyses (8). ASA and KPS score were predictive of outcomes in the multivariate analysis performed by Patil et al. (23), although this study comprised only 6% females and was specific to the VA population, potentially mitigating its generalizability to mostly female, generally older meningioma population. Curry et al. used Elixhauser index as a predictor for meningioma patients' mortality, however, their report studied a very different case mix of younger patients with meningioma, whereas our current study has focused exclusively on outcomes within the older patient subset (5, 14). This current study is the first thus far to demonstrate that a patient's general health or comorbidity score is predictive of not only inpatient mortality, but also of postoperative complications, LOS, and total hospital charges.

### Age Is Predictive of Most Major Inpatient Outcomes

Our findings demonstrate that each 1-year increase in patient age beyond 65 years of age is predictive of greater inpatient death, LOS, total charges, and some of inpatient complications. In previous studies in which investigators compared outcomes in older meningioma patients versus younger ones, greater patient age has been associated with other important outcomes, including intraoperative ability to achieve gross total resection and postoperative KPS (5, 12, 23, 27).

### Descriptive Patient and Outcomes Data

Our distribution of patient age, sex, tumor grade, race/ethnicity, and elective procedure status mirror results from other, similar studies (11, 14, 15, 32). The mortality rate of 4.4% in the current analysis of 5512 elderly meningioma patients 65 years of age and older is similar to the rates reported generally within the neurosurgical literature, ranging between 1.8% and 45% in case series of 17 to 250 patients (2-6, 13-15, 17, 19-21, 23, 25, 26). This disparity in inpatient mortality between different single institutions seems to further highlight the importance of using multi-institutional data to assess outcomes more broadly. Of the three large database studies conducted on this topic, our 4.4% inpatient mortality is much less than the 12.0% 30-day mortality reported by Patil et al., although this discrepancy may be attributable, in part, to different mortality end points (ie, inpatient vs 30-day mortality) or to underlying variations in patient populations captured within the NIS and the National Surgical Quality Improvement Program databases (23). Our reported 4.4% mortality is slightly greater than the 2.3% to 4.0% mortality rates reported by Curry et al. and Bateman et al., although these NIS-based analyses included patients of all ages, not just older patients, as were included within our study (5, 14).

Our total complication rate of 17.5% is similarly within the wide morbidity range of 2.7% to 52% that has been reported in the meningioma literature in studies ranging from small inpatient case series to larger, multicenter trials (5, 6, 15, 17, 19, 23, 27, 32). Our reported neurological deficit rate of 5.7% falls within the lower range of previous reports, including rates from 2.7% to 31% (4, 6, 12, 13, 25, 26, 29, 34). Similarly, our rates of stroke (5.3%), respiratory complications (4.8%), and cardiac complications (1.7%) either fall within or near previously reported ranges of 2.7% to 4% for stroke (12, 27, 32), 1.8% to 16.3% for respiratory complications (6, 8, 30), and 0.9% to 3.3% for cardiac complications (6, 8, 26).

Hospital LOS and total hospital charges have not been widely reported outcomes in older meningioma patients. The only widely cited study assessing patient LOS by Bateman et al. noted a mean LOS of 5.6 days in meningioma patients of all ages (5). The Bateman et al. study noted a trend toward longer LOS in older patients, however, mirroring our reported median LOS of 7 days specifically in older meningioma patients (5).

### Study Limitations

In addition to its retrospective design, the data elements within the NIS database are limited to single hospital stays with no outpatient follow-up data available. Moreover, the mortality rate is often underestimated in the NIS database because it relies on the patient's status at discharge instead of the accepted 30-days perioperative time period. Despite the large sample size of the NIS, we were unable to assess long-term outcomes, such as survival or complications that might have developed weeks and even years after resection. The NIS database was not primarily intended for clinical use, and important variables are missing. For example parameters that have shown to affect outcomes in other studies, including specific tumor size, location, peritumoral edema, and the number of repeat operations, were not available (14, 21, 34). The database also does not inherently carry other characteristics that have shown predictive value in several series, such as ASA or KPS scores (13, 15, 17, 26). The decision whether to operate was subjective, without similar criteria or protocol. As in other administrative databases that rely on administrative documents, the data may not always reported accurately. As reported by Woodworth et al.

(37), the overall sensitivity and specificity of administrative databases such as the NIS may often be sub-optimal, and may contain some inaccuracies. Furthermore, the decision to operate is determined by a variety of other factors that are not included in this database (eg, KPS, meningioma growth rate, and length of preoperative deficit), and therefore, it is difficult to reconcile our findings with these other factors.

Given that other studies have demonstrated the usefulness of such markers, incorporating these variables into future prospective studies may help to define a more precise decision-making algorithm for older meningioma patients considering operative treatment versus effective non-operative management, such as radiosurgery (7, 24).

Despite its limitations, we believe that our study provides unique and important information regarding operative risk in elderly patients with meningiomas. We found greater Charlson comorbidity scores to be a strong and consistent risk factor for postoperative death, greater LOS, greater total charges, and greater number of complications. It is true that in our analysis age and elective procedure were predictive of death, LOS, and hospital charges; however, when we look death, LOS, hospital charges, and all inpatient complications specifically, only the Charlson score was predictive of poor outcomes consistently. Our data support the recommendation of safe surgical resection of meningiomas within a select group of elderly patients up to the ninth decade of life. Incorporating both patient age and comorbidity score into preoperative decision making may help appropriately select elderly candidates for neurosurgical intervention.

## CONCLUSIONS

Our study provides unique and important information regarding the value of the Charlson comorbidity score in predicting inpatient postoperative death, as well as postoperative respiratory, neurological and cardiac complications, LOS, and hospital charges, among older patients with meningioma. Our data support the safe surgical resection of meningiomas within a select group of older patients with low Charlson scores up through the ninth decade of life. Incorporating the Charlson score into preoperative decision making may inform selection and decision-making for physicians and older patients with meningiomas and their families regarding neurosurgical intervention.

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