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Predictors of Inpatient Death and Complications among Postoperative Elderly Patients with Metastatic Brain Tumors

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ABSTRACT

Objective. Risks of brain surgery in elderly patients with brain metastases are not well defined. This study was designed to quantify the postoperative risk for these patients after brain surgery for metastatic disease to the brain.

Methods. We performed a retrospective analysis of the Nationwide Inpatient Sample (1998–2005). Patients aged 65 years or older who underwent tumor resection of brain metastases were identified by ICD-9 coding. Primary outcome was inpatient death. Other outcomes included systemic postoperative complications, length of stay (LOS), and total charges.

Results. A total of 4,907 patients (53.6% men) were identified. Mean age was 72.1 years. Mean Charlson comorbidity score was 7.8. Inpatient mortality was 4%. The most common adverse events were pulmonary complications (3.4%). Mean length of stay was 9.2 days. Mean total charges were \$57,596.39.

In multivariate analysis, patients up to age 80 years had no significantly greater odds of inpatient death, relative to their 65- to 69-year-old counterparts. Each 1-point increase in Charlson score was associated with 12% increased odds of death, 0.52 days increased LOS, and \$1,710.61 higher hospital charges. Postoperative pulmonary complications, stroke, or thromboembolic events increased LOS and total

charges by up to 9.6 days and \$57,664.42, respectively. These associations were statistically significant (P < 0.05). **Conclusions.** Surgical resection of brain metastases among the elderly up to the ninth decade of life is feasible. Age older than 80 years and higher Charlson comorbidity scores were found to be important prognostic factors for inpatient outcome. Incorporating these factors into preoperative decision making may help to select appropriately those elderly candidates for neurosurgical intervention.

Cancer is the second leading cause of death in the United States. Brain metastases represent the most common neurological manifestation of cancer, occurring in 10–30% of cancer patients. The incidence of brain metastases has been increasing during the past three decades. This may be the result of improved survival of cancer patients, an earlier detection of brain lesions by improved imaging modalities, and the aging of the populations in the United States and other developed countries.

During the 20th century, life expectancy in most developed countries increased by approximately 30 years and continues to increase almost linearly. Coupled with the fact that the incidence of cancer increases with age, an increasingly large proportion of the population is now being evaluated for the treatment of brain metastases. Traditionally, aged 65 years has been widely used as a cutoff for defining elderly. However, many individuals categorized as elderly continue to be physiologically similar to their younger counterparts. The impact of surgery on inpatient complications and outcomes in this older subset of patients has yet to be fully explored.

Brain metastases are associated with poor prognoses, and the optimal therapy is still evolving.^{8,9} Current therapeutic modalities include surgery, stereotactic radiosurgery (SRS), whole brain radiation therapy (WBRT), and chemotherapy.²

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522 R. Grossman et al.

Several prospective, randomized studies have established the value of surgical resection for the treatment of brain metastases combined with radiation therapy, by relieving mass effect and improving survival, which has now become an accepted therapeutic option for surgically accessible solitary brain metastases. ^{10–12} However, surgery also appears to play a role in patients who present with several metastases. It seems that carefully selected patients can benefit from surgery when combined with other modalities, such as stereotactic radiosurgery. Hence, the role and indication of surgery for patients with brain metastases are increasing.

Given the poorly understood contribution of surgical procedures to morbidity and mortality within an aging cancer population, the decision to recommend operative care to elderly patients often remains a difficult one. 13 Although there are large series in the general surgery literature that detail morbidity and mortality among the elderly, including cardiothoracic, vascular, pancreatic, and colorectal procedures, only a handful of studies have analyzed the postoperative outcomes for removal of brain metastases, and none have actively focused on elderly patient outcomes. 14-27 This study was undertaken to help define the inpatient mortality and postoperative complications trends in older patients undergoing surgical resection to remove brain metastases using a national, multi-institutional inpatient database. Through this unique analysis of 4,907 patients, for the first time we are able to quantify in this patient population the inpatient operative risk of patients older than age 65 years who undergo an operation for the removal of brain metastases, providing new risk stratification data to inform operative decision-making.

MATERIALS AND METHODS

Patient Population

We obtained the National Inpatient Sample (NIS) inhospital discharge database for the years 1998–2005, compiled by the Agency for Healthcare Research and Quality (Rockville, MD, USA). The NIS contains discharge information from a stratified random sample of 20% of all nonfederal hospitals in 37 participating U.S. states. More than 1,000 hospitals are sampled by the NIS, with more than seven million patient discharge records per year available. This publicly available, de-identified dataset was exempt for review by the Johns Hopkins Institutional Review Board.

Inclusion and Exclusion Criteria

Inclusion criteria included patients aged 65 years or older with one or more brain metastases who underwent a resection, as identified by ICD-9 diagnosis code (198.3) and ICD-9 procedural code (01.59), respectively.

Characteristics of Interest

Independent patient level variables included patient age, sex, race, Charlson comorbidity score, and type of insurance or primary payer. Age was analyzed as both continuous and categorical variables. Sex was a binary covariate, either male or female. Race was categorized as white, African-American, Hispanic, Asian, Native American, or other. The Charlson score is a well-validated, weighted patient comorbidity index. The Charlson index provides a score accounting for 22 comorbidities, including history of cancer, as well as cardiac, vascular, pulmonary, neurologic, endocrine, renal, hepatic, gastrointestinal, and immune disorders. Type of insurance or primary payer was divided into four categories: Medicare, Medicaid, private insurance, or self-paid.

Outcome Variables

Systemic postoperative complications were identified using the following ICD-9 diagnosis codes: pulmonary complications including acute respiratory distress syndrome (518.81–518.85 and 997.3), stroke (253.5, 998.11, 997.02), thromboembolic complications, including deep venous thrombosis and pulmonary embolism (415, 387, 415.11–415.19, 451.0–451.9, and 453.0–453.9), and cardiac complications (410 and 997.1). The primary outcome was inpatient death. Secondary outcomes included total hospital charges and total hospital length of stay (LOS).

Statistical Analysis

Multivariate logistic and linear regression models were constructed to analyze binary and continuous outcomes, respectively. Multivariate analyses were adjusted for age, sex, race, Charlson comorbidity score, and type of insurance or primary payer. *P* values <0.05 were considered to be statistically significant. All data were analyzed using the software package STATA/MP 10 (College Station, TX, USA).

RESULTS

Univariate Analysis

A total of 4,907 patients were identified with slight male predominance (53.6%). Mean (median) age was 72.1 (71) years; and most patients were white (87.1%). Patients had a mean (median) Charlson score of 7.8 (8). The most common systemic postoperative complications were pulmonary

TABLE 1 Demographics of 4,907 elderly patients with brain metastases undergoing resection, 1998–2005

Patient demographics	n	%
Males	2,629	53.6
Age (years)		
Mean (median)	72.1 (71)	
Age group (years)		
65–69	1,901	38.7
70–74	1,531	31.2
75–79	951	19.4
80+	524	10.7
Race		
White	3,295	87.1
African-American	227	6.0
Hispanic	131	3.5
Asian	60	1.6
Native American	5	0.1
Other	64	1.7
Charlson index score		
Mean (median)	7.8 (8)	
Primary payer		
Medicare	4,269	87.0
Medicaid	53	1.1
Private insurance	522	10.6
Self-pay	26	0.5
Complications		
Pulmonary	165	3.4
Thromboembolic	129	2.6
Stroke	91	1.9
Cardiac	50	1.0
Outcomes		
Mortality	196	4.0
Length of stay (days)		
Mean (median)	9.2 (7)	
Total hospital charges		
Mean (median)	\$57,596.39 (\$43,175.46)	

complications (3.4%), thromboembolic complications (2.6%), stroke (1.8%), and cardiac complications (1%). Mean (median) length of stay was 9.2 (7) days. Patients had mean (median) total hospital charges of \$57,596.39 (\$43,175.46). Overall inpatient mortality was 4% (Table 1).

Multivariate Analyses

Factors Associated with Inpatient Death In multiple logistic regression models adjusted for age, sex, race, Charlson score, and complications, odds of death increased significantly among patients older than aged 80 years (odds ratio (OR), 1.86; P = 0.049) relative to 65-69 years (Fig. 1). Furthermore, each 1-point increase in Charlson

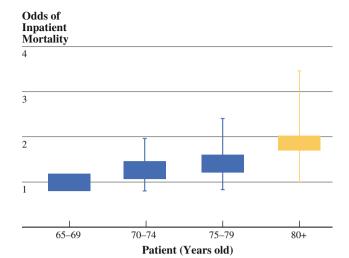


FIG. 1 Adjusted odds of inpatient death among elderly patients with brain metastases undergoing neurosurgical resection. The odds of postoperative mortality were 1.27, 1.42, and 1.86 among patients aged 70–74 years, 75–79 years, and 80+ years, respectively, compared with 65–69-year-old counterparts. The adjusted postoperative mortality odd was significantly higher in patients aged 80 years or older, relative to their 65–69-year-old counterparts

comorbidity score was associated with a 12% increased odds of death (OR, 1.12; P=0.047). Among systemic postoperative complications that occurred during the hospitalization, those patients who developed postoperative pulmonary complications, such as acute respiratory distress syndrome (OR, 7.74; P<0.001), stroke (OR, 7.89; P<0.001), cardiac complications (OR, 4.22, P=0.009), or thromboembolic complications (OR, 2.22; P=0.050) had 7.44 times, 7.89 times, 4.22 times, and 2.22 times increased odds of inpatient mortality, respectively (Table 2).

Factors Associated with Inpatient Complications In multiple logistic regression models adjusted for age, sex, race, and Charlson score, increasing Charlson comorbidity score was associated with significantly higher odds of stroke and pulmonary complication. Each 1-point increase in Charlson score was associated with 16% increased odds of developing stroke (OR, 1.16; P = 0.049), and 29% higher odds of developing pulmonary complications (OR, 1.29; P < 0.001). African-American and Asians had 2.38 times and 3.66 times increased odds of postoperative thromboembolic complications (OR, 2.38, P = 0.005; and OR, 3.66, P = 0.008, respectively).

Factors Associated with Hospital Length of Stay In multiple linear regression models adjusted for age, sex, race, and Charlson score, the following independent variables were associated with significantly longer inpatient LOS: patients aged \geq 75 years (up to 1.82 days increased LOS, P < 0.001), each 1-point increase in Charlson comorbidity

524 R. Grossman et al.

TABLE 2 Odds of inpatient death in multivariate logistic regression among elderly patients with brain metastases undergoing resection, 1998–2005

Patient factors	OR (95% CI)	P value
Age (years)		
65-69	1.00	-
70–74	1.27 (0.82-1.96)	0.28
75–79	1.42 (0.84–2.41)	0.19
80+	1.86 (1.00-3.46)	0.049
Females	0.71 (0.48-1.05)	0.086
Race		
White	1.00	_
African-American	1.50 (0.82-2.73)	0.19
Hispanic	0.66 (0.23-1.88)	0.44
Asian	0.79(0.12-5.21)	0.80
Other	0.33 (0.41-2.74)	0.31
Charlson score	1.12 (1.00–1.26)	0.047
Primary payer		
Medicare	1.00	
Private insurance	1.11 (0.58–2.11)	0.75
Self-pay	1.17 (0.26-5.31)	0.84
Complications		
Pulmonary	7.74 (4.63–12.94)	< 0.001
Thromboembolic	2.22 (0.99-4.95)	0.05
Stroke	7.89 (3.88–18.08)	< 0.001
Cardiac	4.22 (1.44–12.36)	0.009

Data shown in bold-italics = statistically significant relationship

score (0.52 increased days, P < 0.001), African-American or Hispanic race (2.48 and 1.77 increased days, with P = 0.002 and P = 0.016, respectively) relative to whites, postoperative stroke (increased 9.62 days, P < 0.001), thromboembolic complications (increased 9.34 days, P < 0.001), and pulmonary complications (increased 7.80 days, P < 0.001; Table 3).

Factors Associated with Total Hospital Charges In multiple linear regression models adjusted for age, sex, race, and Charlson score, significantly higher total hospital charges were present among patients aged ≥ 80 years (\$7,865.77 higher charges, P=0.01), those with higher Charlson scores (\$1,710.61 higher charges, P=0.003), as well as Hispanics (\$32,613.42 higher charges, P<0.001) relative to whites. Among complications, those with stroke (\$57,664.42 higher, P=0.001), pulmonary complications (\$54,974.63 higher, P<0.001), or thromboembolic complications (\$49,683.04 higher, P<0.001) had higher charges relative to those without complications (Table 4).

Insurance type was not significantly associated with death, postoperative complications, hospital LOS, or total hospital charges.

TABLE 3 Increased length of stay in multivariate linear regression among 4,907 elderly patients with brain metastases undergoing resection, 1998–2005

Patient factors	Increased days (95% CI)	P value
Age (years)		
65–69	_	_
70–74	0.56 (-0.004, 1.13)	0.052
<i>75–79</i>	0.67 (0.03, 1.31)	0.04
80+	1.82 (1.00, 3.46)	< 0.001
Females	$0.31 \; (-0.16, 0.79)$	0.19
Race		
White	_	_
African-American	2.48 (0.92, 4.04)	0.002
Hispanic	1.77 (0.33, 3.21)	0.016
Asian	-0.46 (-2.87, 1.94)	0.71
Other	-0.64 (-2.16, 0.88)	0.41
Charlson score	0.52 (0.35, 0.69)	< 0.001
Primary payer		
Medicare	_	_
Medicaid	$0.43 \ (-2.08, -2.92)$	0.73
Private insurance	0.77 (-0.25, 1.80)	0.14
Self-pay	1.43 (-1.44, 4.30)	0.33
Complications		
Pulmonary	7.80 (5.18, 10.42)	< 0.001
Thromboembolic	9.34 (6.17,12.50)	< 0.001
Stroke	9.62 (4.63, 14.62)	< 0.001
Cardiac	1.23 (-1.55, 4.02)	0.38

Data shown in bold-italics = statistically significant relationship

DISCUSSION

The population of patients with brain tumors has been aging dramatically in recent decades.⁵ More than 25% of the patients with brain metastases are older than age 65 years.^{29–31} This finding is supported by the clinical observation that the frequency of brain metastases increases with age.³² Although a precise definition of elderly has not been determined, aged 65 years is the most accepted cutoff and is used in the Recursive Partitioning Analysis (RPA) classification.³³

The safety and efficacy of surgical removal of brain metastases for elderly patients has not been fully characterized, potentially complicating the surgical decision-making process for such patients and their providers. We report outcomes of 4,907 elderly patients with brain metastases who underwent resection from 1998–2005 from a nationally representative sample of U.S. hospitals.

Charlson Comorbidity Score

Charlson comorbidity score was found to be an important and consistent predictor of outcome. Higher Charlson

TABLE 4 Increased total hospital charges in multivariate linear regression among 4,907 elderly patients with brain metastases undergoing resection, 1998–2005

Patient factors	Increased Charges (95% CI)	P value
Age (years)		
65–69	_	_
70–74	\$1,665.25 (-\$1,520.69; \$4,651.19)	0.31
75–79	\$2,397.31 (-\$1,844.9; \$6,639.51)	0.27
80+	\$7,865.77 (\$1,881.30; \$13,850.24)	0.01
Females	-\$634.91 (-\$3,255.1; \$1,985.27)	0.63
Race		
White	_	_
African-American	\$6,001.97 (\$2,355.37; \$14,359.3)	0.16
Hispanic	\$32,613.42 (\$14,980.35; \$50,246.48)	< 0.001
Asian	-\$12,285.02 (-\$24,862.39; \$292.35)	0.056
Other	\$928.09 (-\$11,961.54; \$13,817.73)	0.88
Charlson score	\$1,710.61 (\$592.64; \$2,828.56)	0.003
Primary payer		
Medicare	_	_
Medicaid	\$5,915.42 (-\$20,545.59; \$8,714.75)	0.43
Private insurance	\$5,665.35 (-\$550.18; \$11,880.89)	0.074
Self-pay	\$8,366 (-\$3,360.32; \$20,093.24)	0.16
Complications		
Pulmonary	\$54,974.63 (\$38,319.51; \$71,629.75)	< 0.001
Thromboembolic	\$49,683.04 (\$31,904.53; \$67,461.55)	< 0.001
Stroke	\$57,664.42 (\$25,144.48; \$90,184.36)	0.001
Cardiac	\$13,344.08 (-\$3,141.93; \$29,830.1)	0.11

Data shown in bold-italics = statistically significant relationship

comorbidity score was associated with higher risk of mortality (Table 2), increase LOS (Table 3), total hospital charges (Table 4), as well as postoperative stroke, and pulmonary complications. The same trend was reported by Patil et al., in a study using the NIS database.³⁴ Complication rate and outcome among patients with spinal metastases was positively correlated to the number of preoperative patient comorbidities.³⁴ Although it may be intuitive that a larger number of preoperative comorbidities would lead to worse outcomes, this was the first time that such a relationship was quantified within this patient population using the NIS. Pietila et al. analyzed the postoperative outcome of 44 patients older than aged 80 years who underwent surgery for removal of brain metastases, glioma, meningioma, or pituitary adenoma. Preoperative cerebrovascular conditioning and the existence of multiple preoperative concomitant diseases were important determining factors for the occurrence of postoperative complications.³⁵

The relatively high mean (median) Charlson score of 7.8 (8) indicates that the elderly patient population in our study has a relatively high number of comorbidities.³⁶

Inpatient Age

Age was a consistent predictor for an outcome in our study. The adjusted odds of inpatient death significantly increased in patients older than aged 80 years, compared with 65- to 69-year-old counterparts (Fig. 1). We also found that age was a predictor for increasing LOS and total hospital charges. The adjusted odds of increased LOS and total hospital charges significantly increased in patients older than aged 75 and 80 years respectively compared with 65- to 69-year-old counterparts (Tables 3 and 4).

Surgery in elderly patients has been associated with elevated surgical risk in several reports.^{25,35} However, for the first time, base on multi-institutional data, we define an age cutoff for worse outcome following neurosurgical resection of brain metastases.

Several single-institution studies have reviewed the outcome of elderly patients who undergo resection of brain metastases. ^{24–26,37} Barker et al. in a NIS-based study found that age was an important predictor of death among patients of all ages who underwent craniotomy for resection of brain metastases. However, this study did not specifically report the relative odds of death among the elderly. ¹⁸ Pietila et al. concluded that the postoperative mortality of elderly patients was higher than in the general population. However, their study was not powered enough to define an age cutoff beyond which mortality significantly increased within the elderly population, nor did they specify odds of inpatient death. ³⁵

Postoperative Systemic Complications

Among systemic postoperative complications, stroke, pulmonary, and thromboembolic complications were correlated with higher odds of mortality, increase LOS, and total hospital charges. Interestingly, age was not found to be a risk factor for postoperative systemic complications. Our report is in agreement with what was described by Patil et al., who reported that the effect of postoperative complications on mortality, LOS, and hospital charges was correlated to the number of postoperative complications. One postoperative complication lead to a 7-day increase in the mean LOS, quadrupled the mortality rate, and increased dramatically the hospital charges. ³⁴

The total postoperative complications rate in our study among patients older than aged 65 years was 8.9%. This value is compatible with other single-institution studies, whose values varied from 8–32%. ^{20,21,23,24,26,27,38} This wide range of complications is associated with the widely varying number of complications studied in these different reports. For example, in the current study we focused on systemic complications, which may explain the relatively low overall complication rate. The most common

R. Grossman et al.

postoperative adverse event studied in our report was pulmonary complication, with a rate of 3.4%. This value is higher than the rates reported by several other single-institution series, and yet, all other studies were composed of younger patient populations. ^{23,24,26,27} For example, a 1.8% rate of pulmonary complication was reported by Tan et al. among adult-aged patients who underwent image-guided craniotomies by a single surgeon for the treatment of brain metastases. ³⁹ The median age of the patients in this study was only 58 years, compared with our median age of 71 years. ³⁹

A total of 1.9% of patients in the current analysis had postoperative stroke. Srivastava et al. reported a risk of 1.17% intracranial hemorrhage (ICH) among 776 adult patients with non-small cell lung carcinoma (NSCLC) with brain metastases. 40 This value is slightly lower than in our study. However, Srivastava et al. included only NSCLC origin brain metastases, whereas our series includes metastases from many different primary sites and histologies. Furthermore, almost all patients from Srivastava's series were treated with adjuvant radiation therapy, which is known to decrease angiogenesis, normalize abnormal tumor blood vessels, and thus decrease the risk of ICH; we were unable to quantify with high fidelity the proportion of our patients who underwent adjuvant therapy. Other adverse events, such as thromboembolic complications and cardiac complications, were readily comparable with the results of other series. 21,23,24,26,27,41

Race

In our study, Hispanics and African-Americans were associated with increased LOS, but only Hispanics had higher total hospital charges compared with whites (Tables 3 and 4). Race, however, was not associated with increased inpatients mortality when compared with whites. Our study demonstrated that African-Americans and Asians had higher risk of developing postoperative thromboembolic complications compared with whites. It has been published that African-Americans not only have the highest incidence of both idiopathic and secondary venous thromboembolism (VTE) rates, but also have a higher risk for pulmonary emboli (PE) compared with all other racial groups. 42 The incidence of asymptomatic VTE was reported to be high among Asian patients who undergo major orthopedic surgical procedures and who did not receive proper thromboprophylaxis.⁴³

Less Hispanics, African-Americans, Asians, and Native Americans were included in our study (3.5%, 6%, 1.6%, and 0.1%, respectively) than one would expect from general population-based estimates.⁵ Based on the Census Bureau's statistics for the year 2005 in the United States, Hispanic, African-American, Asian, and Native American

populations make up 14%, 13%, 4%, and 1% of the population, respectively. This discrepancy in racial or ethnic identification has been reported in several other NIS-based studies and may represent an inherent limitation to the dataset. Additionally, Liu et al. Feported in the general surgical literature that African-Americans, Hispanics, and Asians experienced poorer access to certain healthcare institutions for surgical procedures. The American Cancer Society reported that minority populations are more likely to be diagnosed with advanced-stage disease than are whites. Thus, if a patient is diagnosed at a stage in which he or she already has multiple brain metastases, surgical treatment may not be the treatment of choice. This may explain in part the disparity in minority representation in our study.

Descriptive Data

The mortality rate of 4% in the current analysis among elderly patients older than aged 65 years is comparable to the mortality rate seen in the neurosurgical literature, ranging from 0% to 18.2%, based mainly on single-institution studies. 11,12,18,20,22,24–27,37,41 In two prospective, randomized trials assessing the value of surgical removal of single brain metastases among all ages, the mortality rates were 4% and 9%. 11,12 Unfortunately, the limited clinical depth of the NIS database made it impossible in the current study to quantify the number of brain metastases and to correlate it with outcome. Rabadán et al. reported, in a series of 236 craniotomies for resection of gliomas and brain metastases, a mortality rate of 4% among patients older than aged 60 years.²⁴ Stark et al. reported, in a series of 177 patients who underwent surgical removal of up to three brain metastases a mortality rate of 18.2% among patients older than aged 70 years. 26 This disparity of inpatient mortality between different single institution studies seems to further highlight the importance of utilizing national level data to assess more broadly the outcomes of surgical removal of brain metastases.

Our distribution of patient age, sex, and insurance or payer types is similar to trends seen in previous studies focusing on patients with brain metastases. 17,18,20,21,37 As we would expect for an elderly population, most coverage is from Medicare, followed by private insurance. Sex and insurance/provider type were not significantly associated with inpatient mortality. This has been previously confirmed by several studies in the neurosurgical literature among patients with brain metastases. 12,24,28

In the current analysis, mean (median) LOS was 9.2 (7) days, which is in line with several others brain metastases reports. ^{23,25,47} This LOS is similar to the results of Paek et al. ²³—1 day longer than the 6 days median LOS reported by Mehta et al. ⁴⁷ and 2 days longer than the report

by Sawaya et al.²⁵ None of the above-mentioned series, however, focused on the elderly population. In a recent multicenter, prospective study of elderly patients who underwent meningioma resection, LOS was even greater than in our reported outcomes, totaling 15.2 ± 18.4 days.³¹

Study Limitations

The NIS provides a powerful tool to study trends and outcome among various patient populations. However, there are inherent limitations with any administrative database that relies on administrative documents and may not always be reported accurately. In addition to its retrospective nature, the data elements within the NIS database are limited to single hospital stays with no outpatient follow-up data available. Moreover, the reported mortality rate in the NIS database is probably underestimated because it is limited to the status at discharge, not the 30-day mortality as accepted by the literature.

Thus, despite the large sample size of the NIS, we were unable to assess long-term outcomes, such as survival or complications that developed several years after procedures. Furthermore, information regarding outpatient follow-up care or complementary treatment, such as WBRT, was not available. The database also does not inherently carry characteristics, such as Karnofsky Performance Score (KPS) or RPA, the location, size, or number of brain metastases, the staging of systemic malignancy, or information on previous oncologic treatments, such as SRS, WBRT, previous craniotomies, or chemotherapy. Such information may help to more fully decide which optional treatment modalities would be best for each patient. Woodworth et al. argued in their study of cerebrovascular patients that administrative databases, such as the NIS, may have certain inaccuracies, such as low sensitivity with regard to endovascular treatment modalities.⁴⁸ Interestingly, however, Eichler et al. concluded in their report, based specifically on a population with brain metastases, that relevant health care data elements based on ICD-9 diagnostic coding was both valid and accurate. 42 We approached use of the NIS with care in choosing ICD-9 codes with great specificity to the research question at hand, fully aware of the database's strengths and weaknesses.

Despite its limitations, we believe that our study provides unique and important information regarding operative risk in elderly patients with brain metastases. We defined a new threshold beyond which patients are at higher risk of post-operative inpatient mortality, greater LOS, higher total charges, and a higher number of postoperative complications. Neurosurgical removal of brain metastases among selected elderly patients is feasible. Patients with postoperative pulmonary, cardiac thromboembolic complications, or stroke had higher risk of postoperative mortality. Moreover,

we found that age and greater Charlson comorbidity scores were a strong and consistent risk factor for postoperative death, greater LOS, higher total charges, and higher number of complications. Surgical resection of brain metastases within a select group of elderly patients up to the ninth decade of life is feasible. Incorporating both patient age and comorbidity score into preoperative decision making may help to select appropriately the elderly candidates for neurosurgical intervention.

CONCLUSIONS

The current study suggests that neurosurgical removal of brain metastases among selected elderly patients is feasible. Age older than 80 years and higher Charlson comorbidity scores were found to be important prognostic factors for inpatient death, greater LOS, higher total hospital charge, and higher number of postoperative complications, such as stroke, as well as pulmonary, cardiac, and thromboembolic complications.

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REFERENCES

- Cancer facts and figures. Statistics for 2005 http://www.cancer. org/downloads/STT/CAFF2005f4PWSecured.pdf.
- Norden AD, Wen PY, Kesari S. Brain metastases. Curr Opin Neurol. 2005;18(6):654–61.
- 3. Kanner AA, Bokstein F, Blumenthal DT, Ram Z. Surgical therapies in brain metastasis. *Semin Oncol.* 2007;34(3):197–205.
- Kaal EC, Niel CG, Vecht CJ. Therapeutic management of brain metastasis. *Lancet Neurol.* 2005;4(5):289–98.
- Anderson GF, Hussey PS. Population aging: a comparison among industrialized countries. *Health Aff (Millwood)*. 2000;19(3): 191–203.
- Christensen K, Doblhammer G, Rau R, Vaupel JW. Ageing populations: the challenges ahead. *Lancet*. 2009;374(9696): 1196–208.
- Carnes BA, Olshansky SJ. Heterogeneity and its biodemographic implications for longevity and mortality. *Exp Gerontol*. 2001; 36(3):419–30.
- 8. Kalkanis SN, Linskey ME. Evidence-based clinical practice parameter guidelines for the treatment of patients with metastatic brain tumors: introduction. *J Neurooncol*. 2010;96(1):7–10.
- Robinson PD, Kalkanis SN, Linskey ME, Santaguida PL. Methodology used to develop the AANS/CNS management of brain metastases evidence-based clinical practice parameter guidelines. *J Neurooncol.* 2010;96(1):11–6.
- Noordijk EM, Vecht CJ, Haaxma-Reiche H, et al. The choice of treatment of single brain metastasis should be based on extracranial tumor activity and age. *Int J Radiat Oncol Biol Phys.* 1994;29(4):711–7.

- Patchell RA, Tibbs PA, Walsh JW, et al. A randomized trial of surgery in the treatment of single metastases to the brain. N Engl J Med. 1990;322(8):494–500.
- Vecht CJ, Haaxma-Reiche H, Noordijk EM, et al. Treatment of single brain metastasis: radiotherapy alone or combined with neurosurgery? Ann Neurol. 1993;33(6):583–90.
- Eiseman B. Surgical decision making and elderly patients. Bull Am Coll Surg. 1996;81(2):8–11, 65.
- Fukuse T, Satoda N, Hijiya K, Fujinaga T. Importance of a comprehensive geriatric assessment in prediction of complications following thoracic surgery in elderly patients. *Chest.* 2005; 127(3):886–91.
- Usman AA, Tang GL, Eskandari MK. Metaanalysis of procedural stroke and death among octogenarians: carotid stenting versus carotid endarterectomy. J Am Coll Surg. 2009;208(6):1124–31.
- Makary MA, Winter JM, Cameron JL, et al. Pancreaticoduodenectomy in the very elderly. *J Gastrointest Surg.* 2006;10(3): 347–56.
- Rabeneck L, Davila JA, Thompson M, El-Serag HB. Outcomes in elderly patients following surgery for colorectal cancer in the Veterans Affairs Health Care System. *Aliment Pharmacol Ther*. 2004;20(10):1115–24.
- Barker FG II. Craniotomy for the resection of metastatic brain tumors in the U.S., 1988–2000: decreasing mortality and the effect of provider caseload. *Cancer*. 2004;100(5):999–1007.
- Bindal RK, Sawaya R, Leavens ME, Hess KR, Taylor SH. Reoperation for recurrent metastatic brain tumors. *J Neurosurg*. 1995;83(4):600–4.
- Bindal RK, Sawaya R, Leavens ME, Lee JJ. Surgical treatment of multiple brain metastases. J Neurosurg. 1993;79(2):210–6.
- Brell M, Ibanez J, Caral L, Ferrer E. Factors influencing surgical complications of intra-axial brain tumours. *Acta Neurochir* (Wien). 2000;142(7):739–50.
- 22. Lang FF, Sawaya R. Surgical treatment of metastatic brain tumors. *Semin Surg Oncol.* 1998;14(1):53–63.
- 23. Paek SH, Audu PB, Sperling MR, Cho J, Andrews DW. Reevaluation of surgery for the treatment of brain metastases: review of 208 patients with single or multiple brain metastases treated at one institution with modern neurosurgical techniques. *Neurosurgery*. 2005;56(5):1021–34; discussion 1021–34.
- 24. Rabadan AT, Hernandez D, Eleta M, et al. Factors related to surgical complications and their impact on the functional status in 236 open surgeries for malignant tumors in a Latino-American hospital. Surg Neurol. 2007;68(4):412–20; discussion 420.
- Sawaya R, Hammoud M, Schoppa D, et al. Neurosurgical outcomes in a modern series of 400 craniotomies for treatment of parenchymal tumors. *Neurosurgery*. 1998;42(5):1044–55; discussion 1055–56.
- Stark AM, Tscheslog H, Buhl R, Held-Feindt J, Mehdorn HM. Surgical treatment for brain metastases: prognostic factors and survival in 177 patients. *Neurosurg Rev.* 2005;28(2):115–9.
- Tan TC, Mc LBP. Image-guided craniotomy for cerebral metastases: techniques and outcomes. *Neurosurgery*. 2003;53(1): 82–9; discussion 89–90.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40(5): 373–83.
- Frazier JL, Batra S, Kapor S, et al. Stereotactic radiosurgery in the management of brain metastases: an institutional retrospective analysis of survival. *Int J Radiat Oncol Biol Phys.* 2010;76(5):1486–92.
- 30. Lutterbach J, Bartelt S, Momm F, Becker G, Frommhold H, Ostertag C. Is older age associated with a worse prognosis due to

- different patterns of care? A long-term study of 1346 patients with glioblastomas or brain metastases. *Cancer*. 2005;103(6): 1234–44.
- 31. Patil CG, Veeravagu A, Lad S, Boakye M. Craniotomy for resection of meningioma in the elderly: a multicenter, prospective analysis from the National Surgical Quality Improvement Program. *J Neurol Neurosurg Psychiatry*. 2010;81(5):502–5.
- 32. Ampil F, Caldito G, Milligan S, Mills G, Nanda A. The elderly with synchronous non-small cell lung cancer and solitary brain metastasis: does palliative thoracic radiotherapy have a useful role? *Lung Cancer*. 2007;57(1):60–5.
- Gaspar L, Scott C, Rotman M, et al. Recursive partitioning analysis (RPA) of prognostic factors in three Radiation Therapy Oncology Group (RTOG) brain metastases trials. *Int J Radiat* Oncol Biol Phys. 1997;37(4):745–51.
- Patil CG, Lad SP, Santarelli J, Boakye M. National inpatient complications and outcomes after surgery for spinal metastasis from 1993–2002. *Cancer*. 2007;110(3):625–30.
- Pietila TA, Stendel R, Hassler WE, Heimberger C, Ramsbacher J, Brock M. Brain tumor surgery in geriatric patients: a critical analysis in 44 patients over 80 years. Surg Neurol. 1999;52(3): 259–63; discussion 263–4.
- Bateman BT, Pile-Spellman J, Gutin PH, Berman MF. Meningioma resection in the elderly: nationwide inpatient sample, 1998–2002. *Neurosurgery*. 2005;57(5):866–72; discussion 866–72
- 37. Rogne SG, Konglund A, Meling TR, et al. Intracranial tumor surgery in patients >70 years of age: is clinical practice worthwhile or futile? *Acta Neurol Scand.* 2009;120(5):288–94.
- 38. Pirzkall A, Debus J, Lohr F, et al. Radiosurgery alone or in combination with whole-brain radiotherapy for brain metastases. *J Clin Oncol.* 1998;16(11):3563–9.
- 39. Jemal A, Tiwari RC, Murray T, et al. Cancer statistics, 2004. *CA Cancer J Clin.* 2004;54(1):8–29.
- Srivastava G, Rana V, Wallace S, et al. Risk of intracranial hemorrhage and cerebrovascular accidents in non-small cell lung cancer brain metastasis patients. *J Thorac Oncol.* 2009;4(3): 333–7.
- Black P, Kathiresan S, Chung W. Meningioma surgery in the elderly: a case-control study assessing morbidity and mortality. *Acta Neurochir (Wien)*. 1998;140(10):1013–6; discussion 1016–7.
- Eichler AF, Lamont EB. Utility of administrative claims data for the study of brain metastases: a validation study. *J Neurooncol*. 2009;95(3):427–31.
- Leizorovicz A. Epidemiology of postoperative venous thromboembolism in Asian patients. Results of the SMART venography study. *Haematologica*. 2007;92(9):1194–200.
- 44. AHRQ. National Healthcare Disparities Report: US Department of Health and Human Services; July 2005.
- 45. Liu JH, Zingmond DS, McGory ML, et al. Disparities in the utilization of high-volume hospitals for complex surgery. *JAMA*. 2006;296(16):1973–80.
- Mukherjee D, Zaidi HA, Kosztowski T, et al. Predictors of access to pituitary tumor resection in the United States, 1988–2005. Eur J Endocrinol. 2009:161(2):259–65.
- Mehta M, Noyes W, Craig B, et al. A cost-effectiveness and costutility analysis of radiosurgery vs. resection for single-brain metastases. *Int J Radiat Oncol Biol Phys.* 1997;39(2):445–54.
- Woodworth GF, Baird CJ, Garces-Ambrossi G, Tonascia J, Tamargo RJ. Inaccuracy of the administrative database: comparative analysis of two databases for the diagnosis and treatment of intracranial aneurysms. *Neurosurgery*. 2009;65(2):251–6; discussion 256–7.