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Risk Factors Associated With Mortality in Patients With Otogenic Brain Abscess

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Objective: Otogenic brain abscess is a well-recognized clinical condition that describes brain abscess secondary to an ear infection or mastoiditis. Current evidence remains limited on risk factors associated with mortality as most data are from case series. We aimed to 1) report the mortality rate among patients who did and did not receive mastoidectomy 2) identify factors associated with inpatient mortality.
Study Design: Retrospective cohort study.
Setting: Multi-institutional.
Patients: We identified a cohort of patients for years 2008 to 2014 who in their inpatient hospitalization carried the diagnoses of both brain abscess and infectious ear disease.
Interventions: Inpatient neurotology and neurosurgical procedures.
Main Outcome Measures: A multivariable logistics regression model was built to identify the factors associated with inpatient mortality.
Results: The final analysis included 252 patients, of which 84 (33.3%) underwent mastoidectomy. The rate of inpatient morbidity and mortality were 17.5% and 4.0%, respectively. The rate of mortality in patients without mastoidectomy versus those with mastoidectomy was 4.2% versus 3.6%, respectively ($p > 0.99$). The odds of inpatient mortality were significantly increased for every 10-year increase in age (odds ratio [OR] 2.73, 95% confidence interval [CI]: 1.39–7.01, $p = 0.011$) and for Black compared to White patients (OR: 45.81, 95% CI: 4.56–890.92, $p = 0.003$).
Conclusion: Older age and Black race were associated with increased odds of inpatient mortality and there were no significant differences in mortality between mastoidectomy cohorts. This research serves to generate further hypotheses for larger observational studies to investigate the association between sociodemographic factors and surgical variables with outcomes among this surgical population. **Key Words:** brain abscess—disparity—mastoiditis—mortality—national inpatient sample—race.

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Acute otitis media leading to mastoiditis and intracranial complications is a rare but often a life-threatening condition (1). Acute mastoiditis is a suppurative infection of the mastoid air cells with symptomology of less than 4 weeks and is one of the most prevalent complications of acute otitis media (2). The continuous anatomical relationship of the middle ear with the mastoid air cells provides the conduit for acute otitis media to progress to mastoiditis and cranial complications (Fig. 1) (1). Not only may mastoiditis develop if infection persists but also nearby structures, namely the middle and posterior cranial fossa and lateral venous sinuses, may become involved (1). While meningitis is the leading cause of complications in otogenic mastoiditis, with a mortality rate of 14%, brain abscess is the second most prevalent (3,4). Before widespread use of antibiotics, up to 6% of patients experienced intracranial complications (i.e., brain abscess, venous sinus thrombosis, or meningitis) (2,5).

Standard of care of otogenic brain abscess includes early computed tomographic or magnetic resonance imaging with intravenous antibiotics with activity against *Streptococcus pneumoniae* and *Haemophilus influenzae* (6,7). Treatment may also involve neurosurgical craniotomy with drainage of the abscess followed by mastoidectomy to remove the source of infection (4). The advancement of technology has allowed modern neurosurgical approaches to emerge such as image-guided drainage of brain abscesses (8,9). However, current evidence on best surgical management and practice remains unclear. The choice of conservative medical management versus surgical abscess drainage with or without mastoidectomy is guided by physician experience and the

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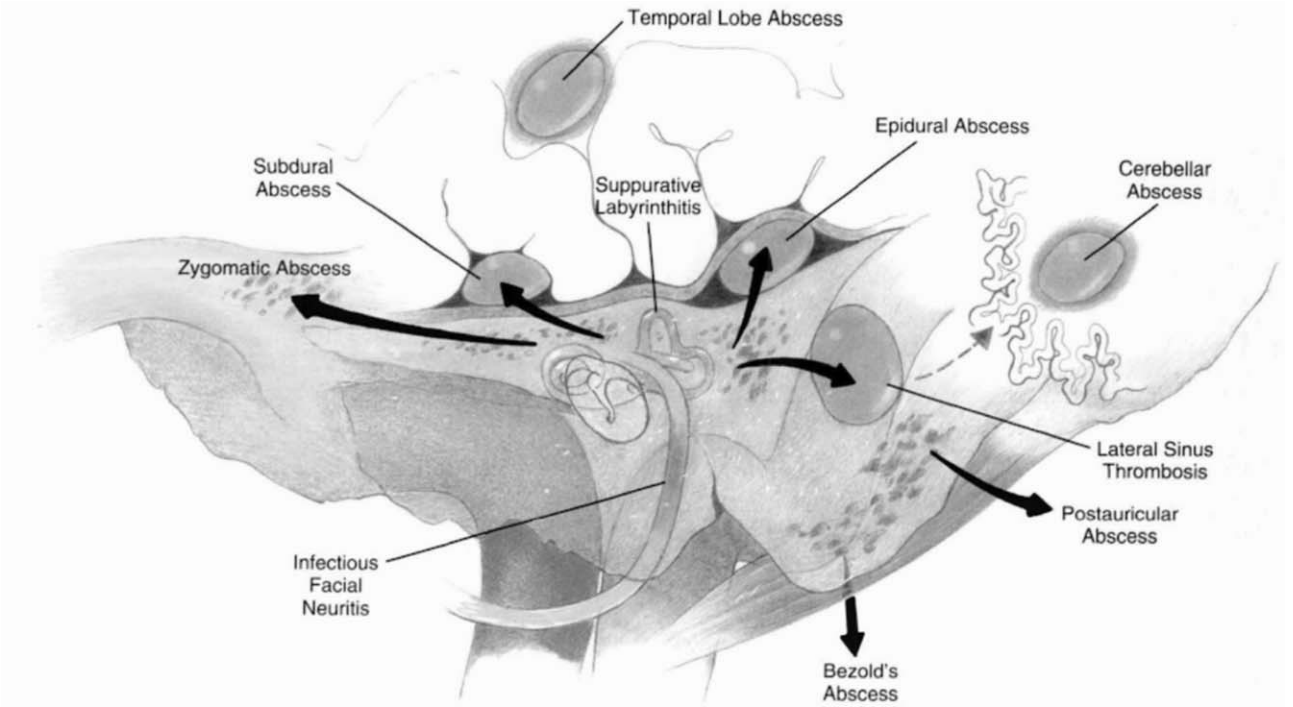

FIG. 1. Complications of otitis media.

patient's clinical presentation. While mastoidectomy is often performed, it remains unclear if mastoidectomy reduces postoperative morbidity and mortality. The rare nature of otogenic brain abscess makes large sample size studies challenging to execute, and current management is based on pooled analysis of single institution retrospective reports and case series. The primary aim of the present study is to use a large administrative database (i.e., National Inpatient Sample database) to 1) report the mortality rate among patients who did and did not receive mastoidectomy, 2) identify factors associated with inpatient mortality in patients with otogenic brain abscess.

MATERIALS AND METHODS

Data Source

Data were obtained from the publicly available dataset, the National (Nationwide) Inpatient Sample (NIS) database of the Healthcare Cost and Utilization Project (HCUP) (10). NIS is the largest inpatient health care database in United States and approximates a 20% stratified sample of medical records from the United States hospitals (11). NIS includes de-identified data and meets the criteria of the Health Insurance Portability and Accountability Act to protect personal information and, therefore, was exempt from the consent requirement by the University of California, San Diego institutional review board.

Patient Population

We defined otogenic brain abscess as patients with hospitalizations with a concurrent diagnosis of acute otitis media, acute mastoiditis, and brain abscess. We used the International Classification of Disease, Ninth Revision, Clinical Modification (ICD9) to identify patients, as well as patient comorbidities and inpatient interventions. We included sociodemographic variables supplied in the database such as: race (White [reference group], Black, Hispanic, Other, i.e., Asian or Pacific Islander, Native American, Other), sex, age, insurance status, and weekend hospital admission. Postoperative inpatient morbidity was defined as any of the following postoperative complications: any postoperative infection, persistent postoperative fistula, internal and external wound disruption, cerebrospinal fluid leak, arrhythmias or myocardial infarction, bleeding complications including hemorrhage/hematoma complicating a procedure and acute post-hemorrhagic anemia, and respiratory complications including acute respiratory failure, pulmonary insufficiency following trauma and surgery, acute respiratory failure following trauma and surgery, other pulmonary insufficiency, post-procedural aspiration pneumonia, iatrogenic pneumothorax, and acute edema of lung. Mortality was the primary outcome of interest and defined as death during same hospitalization. Table 1 lists the ICD9 codes used to identify the patient population and medical history for each case.

Statistical Analysis

R version 3.3.2 was used to perform all statistical analysis. Pearson chi-square and Wilcoxon rank-sum test were used to compare sociodemographic and clinical differences among patients who did not receive mastoidectomy versus those who received mastoidectomy. To evaluate factors associated with inpatient mortality in our study sample, we first conducted a univariable analysis. Next, we performed a multivariable analysis. The odds ratio (OR) with associated 95% confidence interval (CI) were reported for each covariate. Two-tailed significance level was set at $p \leq 0.05$.

TABLE 1. *International classification of diseases, ninth revision, clinical modification codes used to extract medical cases*

Variables	ICD9 Codes
Acute otitis media	381.0, 381.00, 381.01, 381.02, 381.03, 381.04, 381.05, 381.06, 382.0, 382.00, 382.01, 382.02
Acute mastoiditis	383.0, 383.00, 383.01, 383.02, 383.1, 383.9
Brain abscess	324.0, 324.9
Cavernous sinus thrombosis	671.5, 325, 437.6, 674.0
Asthma	493.00, 493.01, 493.02, 493.10, 493.11, 493.12, 493.20, 493.21, 493.22, 493.81, 493.82, 493.90, 493.91, 493.92
Diabetes mellitus	250, 250.0, 250.1, 250.2, 250.3, 250.4, 250.5, 250.6, 250.7, 250.8, 250.9, 250.00, 250.01, 250.02, 250.03, 250.10, 250.11, 250.12, 250.13, 250.40, 250.41, 250.42, 250.43, 2505.0, 250.51, 250.52, 250.53, 250.60, 250.61, 250.62, 250.63, 250.20, 250.21, 250.22, 250.23, 250.30, 250.31, 25032, 250.33, 250.70, 250.71, 250.72, 250.73, 250.80, 250.81, 250.82, 250.83, 250.90, 250.91, 250.92, 250.93
Hypertension	401, 401.0, 401.1, 401
Sinusitis	473.8, 473.2, 473.0, 473.9, 473.1, 473.3, 461.8, 461.2, 461.0, 461.1, 461.9, 461.3
Bacterial meningitis	320.0, 320.1, 320.2, 320.3, 320.81, 320.82, 320.89, 320.9, 322.9
Mastoidectomy	20.4, 20.41, 20.42, 20.49
Intracranial abscess	32.40, 32.49
Craniotomy	01.2, 01.21, 01.24, 01.25
Myringotomy	20.0, 20.01, 20.09
Morbidity	998.5, 998.51, 998.59, 99.86, 998.31, 998.32, 997.09, 997.1, 998.11, 998.12, 998.13, 349.81, 518.81, 997.3, 415.1, 518.5, 997.39, 518.51, 518.4, 518.52, 518.53, 997.32, 512.1, 285.1

ICD9 indicates International Classification of Disease, Ninth Revision.

RESULTS

We identified 252 patients with otogenic brain abscess, of which 69 (33.3%) received mastoidectomy. Among the entire cohort, the rate of inpatient morbidity and mortality were 17.5 and 4.0%, respectively. Table 2 outlines the demographics and perioperative factors of the overall study population. The median age was 31 years old, 94 (37.3%) were women, and 136 (54.0%) were White. Private insurance (40.9%) was the most common primary payer. Meningitis (27.4%), hypertension (23%), and cavernous sinus thrombosis (16.7%) were the most common perioperative conditions.

Table 3 illustrates the differences in patient characteristics between mastoidectomy cohorts. Patients without mastoidectomy were significantly older than the mastoidectomy group (median age of 39 versus median age of 13, $p > 0.001$). Compared with patients without mastoidectomy, patients who underwent mastoidectomy had a higher rate of cavernous sinus thrombosis (33.3% versus 8.3%, $p < 0.001$). Patients in the mastoidectomy group had lower rates of sinusitis, hypertension, and meningitis (all $p < 0.05$). The rate of morbidity and median days of hospital stay were no different among mastoidectomy cohorts ($p > 0.05$). Patients with mastoidectomy versus those without had higher rates of inpatient procedures (median of 5 versus median of 3, $p < 0.001$). The rate of mortality in patients without mastoidectomy versus those with mastoidectomy was 4.2% versus 3.6%, $p > 0.99$.

Table 4 shows the results of the adjusted logistic regression analysis evaluating the association between mastoidectomy and inpatient mortality. The odds of inpatient mortality were significantly increased for every 10-year increase in age (OR 2.73, 95% CI: 1.39–7.01, $p = 0.011$). The odds of inpatient mortality were significantly increased for Black compared with White patients (OR: 45.81, 95% CI: 4.56–890.92, $p = 0.003$). The odds of mortality were not significantly higher for female patients and patients with weekend hospital admission, diabetes mellitus, asthma, cavernous sinus thrombosis, hypertension, sinusitis, meningitis, mastoidectomy, craniotomy, and myringotomy (all $p > 0.05$).

DISCUSSION

Using the NIS dataset, our analysis demonstrated no significant differences in the rates of inpatient mortality among patients who underwent mastoidectomy versus those who did not. We have demonstrated a 2.7-fold increase in inpatient mortality for every 10-year increase in age. In addition, we found a 45-fold increase in mortality for Black versus White patients. Identifying differences in rates of mortality and these factors associated with mortality may help to further risk stratify and appropriately allocate resources to vulnerable populations.

Mastoiditis may affect any age group; however, mastoiditis is more commonly diagnosed in children and therefore most studies are derived from small cohort single institution experiences in the pediatric population (12,13). The rate of morbidity and mortality associated with otogenic intracranial complications has dramatically decreased with broad-spectrum antibiotics and neurosurgical and otologic intervention (14,15). Intracranial complications are rare in developed countries and therefore make establishing the standard of care challenging; however, the incidence continues to be unacceptably high in developing countries. Contrary to our a priori assumptions, this analysis showed no difference in the unadjusted mortality rate among mastoidectomy

TABLE 2. *Overall characteristics of patients with otogenic mastoiditis complicated by brain abscess*

	Overall Study Population
Total, n	252
Age (yr), (median [IQR])	31 [8, 53]
Age, n (%)	
<18	97 (38.5)
18–49	81 (32.1)
>50	74 (29.4)
Female gender, n (%)	94 (37.3)
Race, n (%)	
White	136 (54.0)
Black	27 (10.7)
Hispanic	44 (17.5)
Other	45 (17.9)
Weekend hospital admission, n (%)	60 (23.8)
Elective hospital admission, n (%)	30 (11.9)
Insurance status, n (%)	
Medicare	36 (14.3)
Medicaid	67 (26.6)
Private Insurance	103 (40.9)
Other	46 (18.3)
Inpatient diagnoses, (median [IQR])	10 [7, 15]
Cavernous sinus thrombosis, n (%)	42 (16.7)
Asthma, n (%)	[a]
Diabetes mellitus, n (%)	35 (13.9)
Hypertension, n (%)	58 (23.0)
Chronic sinusitis, n (%)	38 (15.1)
Bacterial meningitis, n (%)	69 (27.4)
Inpatient procedures, n (median [IQR])	4 [2, 6]
Craniotomy, n (%)	53 (21.0)
Myringotomy, n (%)	115 (45.6)
Morbidity, n (%)	44 (17.5)
Mortality, n (%)	[a]
Length of hospital stay (d), (median [IQR])	9 [6, 16.25]

IQR indicates (interquartile range).
[a]Data with cell counts less than or equal to 10 were suppressed per HCUP guidelines to protect patient identity.

cohorts. While we did not demonstrate a mortality benefit, in addition to broad-spectrum antibiotics, mastoidectomy has a role in the treatment of otogenic intracranial abscesses in specific patients. In a case series of 30 pediatric patients with otogenic intracranial complications, 80% underwent a canal wall up mastoidectomy, 10% received craniotomy alone, and 10% were treated with antibiotics. In this review, all the patients survived although the management varied at the discretion of the provider (16). Mastoidectomy is an important surgical intervention as it removes the source of infection, which is particularly important in the setting of antimicrobial resistance, emerging more virulent strains of bacteria such as Fusobacterium, and insufficient antibiotic penetration of bony tissue (17,18). Yarden-Bilavsky et al. (19) report a case series of seven pediatric patients with Fusobacterium otogenic subperiosteal abscess in which 50% had osteomyelitis beyond the mastoid bone. They show that all patients received cortical mastoidectomy with tympanostomy tubes and no deaths were reported at the 19-month follow-up (18). Taken together, while strategies of otogenic brain abscess management vary by institution and clinician, there is a role for mastoidectomy. Further observational prospective studies are needed to evaluate the impact of mastoidectomy on outcomes in these patients.

To our knowledge, this is the first study using a nationally representative database to evaluate risk factors of mortality in otogenic brain abscess. Here, we show that Black patients have roughly a 7-fold increase in inpatient mortality after controlling for clinical conditions. Racial disparities result in less equitable care, which contributes to higher rates of postoperative morbidity and mortality (20,21). Previous research has shown that Black patients have higher rates of poor postoperative outcomes. In the neurotology literature, health equity data remain sparse, however researchers have evaluated the impact of racial disparities in pediatric population (12,22–24). Compared with white children, black children are significantly less likely to be referred for subspecialty care for further acute otitis media management (25,26). In a prospective cohort study of 240 pediatric patients with acute otitis media, Ambrosio and Brigger (27) show that Black children were 87% less likely to undergo bilateral myringotomy and tube placement compared with non-Hispanic Caucasian children and that surgery was associated with improved quality of life. In a cross-sectional analysis of 25,497 children with frequent ear infections, after adjusting for sociodemographic factors and health insurance status, Black children were 51% less likely to receive subspecialty care and 61% less likely surgery versus White children (26). Similarly, Simon et al. (23) demonstrated that non-Hispanic Caucasian children were significantly more likely to receive pressure equalization tubes than Black and Hispanic children. These disparities are multifactorial and maybe explained by differential access to care, less diagnostic testing and medical treatment in minority groups, and bias and barriers to patient–physician relationship (27,28). Although majority of the literature regarding racial disparities is in the pediatric population, this work highlights the continued need to address the impact of racial disparities on health outcomes. Further studies are needed to evaluate the association of racial differences with outcomes in neurotologic surgery.

In a systematic review of otogenic brain abscess, Duarte et al. (29) show the pediatric population to be overrepresented in most studies meeting inclusion criteria, and therefore it is likely that either otogenic brain abscess and associated complications more frequently occur in the pediatric population or children more commonly present with overt signs and symptoms of intracranial complications. In a case series of 47 patients with otogenic intracranial complications, Van der Pol et al. (15) show 95% of pediatric patients underwent mastoidectomy, however only 57% of adults received mastoidectomy. These findings may be explained by the fact that providers may more aggressively treat conditions in pediatric population, children more commonly present

TABLE 3. *Characteristics of patients with otogenic mastoiditis complicated by brain abscess*

	No Mastoidectomy	Mastoidectomy	*p* Value
Total, n	168	84	
Age (yr), (median [IQR])	39 [13.5, 57.25]	13 [5.75, 43]	<0.001
Age, n (%)			<0.001
<18	49 (29.2)	48 (57.1)	
18–49	59 (35.1)	22 (26.2)	
>50	60 (35.7)	14 (16.7)	
Female Gender, n (%)	67 (39.9)	27 (32.1)	0.289
Race, n (%)			0.791
White	89 (53.0)	47 (56.0)	
Black	20 (11.9)	[a]	
Hispanic	28 (16.7)	16 (19.0)	
Other	31 (18.5)	14 (16.7)	
Weekend hospital admission, n (%)	36 (21.4)	24 (28.6)	0.272
Elective hospital admission, n (%)	23 (13.7)	7 (8.3)	0.302
Insurance status, n (%)			0.324
Medicare	28 (16.7)	[a]	
Medicaid	40 (23.8)	27 (32.1)	
Private insurance	69 (41.1)	34 (40.5)	
Other	31 (18.5)	15 (17.9)	
Inpatient diagnoses, (median [IQR])	11 [7, 15]	9 [7, 13]	0.066
Cavernous sinus thrombosis, n (%)	14 (8.3)	28 (33.3)	<0.001
Asthma, n (%)	[a]	[a]	1.00
Diabetes mellitus, n (%)	25 (14.9)	[a]	0.652
Hypertension, n (%)	46 (27.4)	12 (14.3)	0.030
Chronic sinusitis, n (%)	32 (19.0)	[a]	0.021
Bacterial meningitis, n (%)	55 (32.7)	14 (16.7)	0.011
Inpatient procedures, n (median [IQR])	3 [2, 5]	5 [4, 7]	<0.001
Craniotomy, n (%)	21 (12.5)	32 (38.1)	<0.001
Myringotomy, n (%)	64 (38.1)	51 (60.7)	0.001
Morbidity, n (%)	32 (19.0)	12 (14.3)	0.446
Mortality, n (%)	[a]	[a]	1.00
Length of hospital stay (d), (median [IQR])	9 [6, 16]	8.5 [6, 19]	0.40

IQR indicates (interquartile range).
Insurance status other, uninsured, worker's compensation, Indian health service, other government.
Race other, Asian or Pacific Islander, Native American, Other.
[a]Data with cell counts less than or equal to 10 were suppressed per HCUP guidelines to protect patient identity.

TABLE 4. *Factors associated with mortality in otogenic mastoiditis complicated by brain abscess*

	Univariable		Multivariable	
	OR (95% CI)	*p* Value	OR (95% CI)	*p* Value
Black Race	3.3 (0.75–14.53)	0.102	45.81 (4.56–890.92)	0.003
Female	2.62 (0.73–10.5)	0.143	2.48 (0.45–17.2)	0.313
Age (per decade)	1.54 (1.08–2.31)	0.023	2.73 (1.39–7.01)	0.011
Weekend hospital admission	1.39 (0.29–5.18)	0.640	3.5 (0.35–53.18)	0.306
Diabetes mellitus	1.58 (0.23–6.66)	0.572	0.15 (0.01–1.72)	0.170
Asthma	3.25 (0.17–20.73)	0.290	9.65 (0.33–195.9)	0.128
Cavernous sinus thrombosis	1.26 (0.19–5.27)	0.773	16.81 (0.98–364.76)	0.051
Hypertension	5.48 (1.51–22.12)	0.010	5.87 (0.81–68.05)	0.106
Sinusitis	1.43 (0.21–6.00)	0.659	1.3 (0.12–10.62)	0.809
Bacterial meningitis	1.82 (0.45–6.56)	0.367	2.66 (0.39–20.65)	0.317
Mastoidectomy	0.85 (0.18–3.15)	0.820	1 (0.08–9.56)	0.999
Craniotomy	0.41 (0.02–2.23)	0.398	1.04 (0.03–17.36)	0.980
Myringotomy	0.29 (0.04–1.17)	0.117	0.12 (0.01–0.88)	0.076

The reference for Black Race is White Race.
CI indicates confidence interval; OR, odds ratio.
Underlined values indicate significance $p < 0.05$.

with classic findings of intracranial complications, or children present with additional intracranial complications such as cavernous sinus thrombosis. As such, much of the clinical practice and current guidelines are derived from pediatric data. Here, we show a 2.7-fold increase in mortality for every 10-year increase in age, such disparity in mortality may be explained by either the conservative management approach for adults compared with children or a higher comorbidity burden in adult patients. Other studies have shown that when otogenic mastoiditis occurs in adults it tends to be associated with increased morbidity and mortality (30). The adult population data evaluating the impact of age on mortality is limited to non-nationally representative data. In a retrospective study of 224 adult patients treated at Istanbul Medical Faculty Department of Neurosurgery, otitis media and mastoiditis were the leading causes of brain abscess (31). The authors demonstrate that mortality was higher among older (mean age 38 yr) versus younger (mean age 24 yr) patients (31). Moreover, data are also limited to case series and thus provide only a descriptive analysis of otogenic brain abscess. For example, in a series of 12 adult patients with complicated infective otitis media, six patients experienced intracranial complications, of which 16% were brain abscess (32). While these case studies are descriptive and informative they are not powered to evaluate mortality and populated-based studies may help to evaluate risk factors of poor outcomes in this patient population. Further work is needed to define the differences in clinical presentation and optimal management strategies for adult patients.

Although NIS is an administrative database in which data are derived from billing information, this nationally representative database is excellent for investigating rare diagnoses such as otogenic brain abscess and mortality. However, there are several limitations to utilizing administrative large databases such as the NIS. First, using ICD9 codes may lead to misclassification selection bias that limits the ability to estimate a true association between potential risk factors and postoperative mortality. We are unable to determine the diagnostic criteria used for each ICD9 codes included in our study. The use of NIS precludes the evaluation of temporal relationships with comorbidities and postoperative outcomes. For example, there are no unique ICD9 codes for postoperative meningitis and therefore we are unable to determine with accuracy if this is a complication of surgery or a preoperative diagnosis. With certainty, we can however state there is an association of race and age with mortality, as these variables are patient-specific. The database does not contain intraoperative variables such as operation time, duration of anesthesia, and intraoperative medications which are important in understanding mortality. However, as the NIS is an administrative inpatient database, important clinical data are not available, such as cause-specific mortality, location (i.e., epidural, subdural, intraparenchymal), size, and number of intracranial abscess, the presence or absence of suppurative labyrinthitis, microbiology, specific antibiotics, imaging findings, time from diagnosis to surgical management, markers of clinic improvement, quality of life measures, or events that transpire after discharge. With the limitations of the database it is not possible to determine whether the otological disease was causative of the intracranial infective process or merely an unrelated association. For instance, a patient hospitalized with a brain abscess of other origin could have had unrelated otitis during the hospital course. It is likely that not all the patients included had brain abscesses of otological origin. Lastly, our study may not be adequately powered to detect significant associations. Despite the limitations, this is the largest nationally representative study to report on outcomes in otogenic intracranial complications.

In conclusion, this is the first national study to evaluate risk factors associated with inpatient mortality in patients with otogenic brain abscess. Despite recent changes in health care, we identified Black race and older age as independent risk factors of inpatient mortality. We show that receipt of mastoidectomy was not associated with a significant decrease in the odds of inpatient mortality. However, we agree with current literature that there is a role for mastoidectomy in the treatment of otogenic intracranial complications. This exploratory study should serve to generate hypotheses for future high-quality studies.

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