Outcomes of endoscopic sinus surgery for sinusitis-induced intracranial abscess in patients undergoing neurosurgery

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OBJECTIVE Although sinusitis-induced intracranial complications rarely occur in the current era of antibiotics, they can induce neurological symptoms or death. The authors of this study investigated the association between endoscopic sinus surgery (ESS) and outcomes in patients who had undergone neurosurgical procedures for sinusitis-induced intracranial abscess.

METHODS The authors obtained data on patients with sinusitis-induced intracranial abscess from the Japanese Diagnosis Procedure Combination inpatient data for the period from 2010 to 2017. They excluded patients with fungal sinusitis, orbital complications, immunodeficiency, and malignant disease. They also excluded patients who had received antifungal agents, chemotherapy, immunosuppressants, and antidiabetic drugs. Eligible patients were divided into those with and those without neurosurgical procedures. Propensity score–adjusted regression analyses were performed to examine the association between ESS within the same hospitalization and outcomes (mortality, blood transfusion, readmission, revision neurosurgery, and length of stay).

RESULTS Of the 552 potentially eligible patients, 255 were treated with neurosurgical procedures, including 104 who underwent ESS within the same hospitalization and 151 who did not. ESS was not significantly associated with mortality (OR 0.54, 95% CI 0.05–5.81, $p = 0.61$), blood transfusion (OR 1.95, 95% CI 0.84–4.51, $p = 0.12$), readmission (OR 0.86, 95% CI 0.34–2.16, $p = 0.75$), revision neurosurgery (OR 0.65, 95% CI 0.24–1.74, $p = 0.39$), or length of stay (percent difference –10.8%, 95% CI –24.4% to 5.1%, $p = 0.18$).

CONCLUSIONS The present study suggests that ESS may not have significant benefits with respect to reducing mortality, blood transfusion, readmission, revision neurosurgery, or length of stay.

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KEYWORDS intracranial complication; endoscopic sinus surgery; mortality; neurosurgical reoperation; retrospective database study; propensity score

ACUTE and chronic bacterial sinusitis are common in both adult and pediatric patients. However, serious intracranial complications of sinusitis rarely occur. Previous studies have shown that the incidence of intracranial complications ranges from 3.7% to 14.6%^{1,4,13} and that the mortality rate ranges from 0% to 20%.^{2,5,6,7,12,17} Potential intracranial complications include brain abscess, epidural abscess, subdural abscess, meningitis, cerebral venous sinus thrombosis, and cerebritis.^{10,18} Long-term neurological deficits, such as hemiparesis, aphasia, epilepsy, hydrocephalus, and visual deficits, occur in 13%–35%

of patients with bacterial sinusitis.^{6,7,9} Treatments for these life-threatening conditions include intensive intravenous antibiotic therapy, neurosurgical procedures to remove central nervous system abscesses, and sinus surgery to remove paranasal sinus abscesses.¹⁰

Most patients with sinusitis-induced intracranial complications reportedly undergo sinus surgery. A previous study showed that endoscopic sinus surgery (ESS) has a key role in controlling infection,⁸ while another study indicated that the role of ESS in intracranial complications of sinusitis is not clear.² ESS for acute sinusitis can be chal-

ABBREVIATIONS BMI = body mass index; CCI = Charlson Comorbidity Index; ESS = endoscopic sinus surgery; JCS = Japan Coma Scale.

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FIG. 1. Flowchart of the patient selection process.

lenging because of bleeding caused by mucosal inflammation.² With respect to neurosurgical procedures, previous studies have shown that patients with meningitis and a small intracranial abscess (< 1 cm) without significant mass effect can be managed by antibiotics without neurosurgical procedures.^{2,18}

A systematic review involving 16 studies and 180 pediatric patients (age < 18 years) did not reveal the outcomes of ESS.¹⁰ Large studies are necessary to evaluate the role of ESS in the intracranial complications of sinusitis. A practical guideline for the management of acute rhinosinusitis in Japan¹⁶ states that treatments for rhinosinusitis-induced orbital or intracranial complications are slightly different among hospitals and countries. In this Japanese guideline, the level of evidence of treatment for orbital and intracranial complications is III (at least one well-designed nonexperimental descriptive study).

In the present retrospective observational study, we investigated the outcomes of ESS in terms of mortality, blood transfusion, readmission, revision neurosurgery, and length of stay and examined the association between ESS within the same hospitalization and these outcomes using a national inpatient database in Japan.

Methods

Data Source

We used the Diagnosis Procedure Combination database, which is a national inpatient database in Japan. The database includes administrative claims data and discharge abstract data. The database collects information from more than 1000 participating acute-care hospitals across Japan and includes approximately 7 million patients per year. The database contains information regarding patient age, sex, height, weight, smoking status, state

of consciousness at admission, length of stay, discharge status, main diagnosis at admission, comorbidities at admission, complications after admission, dates of admission and operation, surgical procedures, drugs and devices used, and hospital codes.

Because of the anonymous nature of the data, the requirement for informed consent was waived. Study approval was obtained from the institutional review board of The University of Tokyo.

Patient Sample

We included patients who had had acute or chronic sinusitis and a brain, epidural, or subdural abscess in the period from July 2010 to March 2017. We obtained data on patients using the *International Statistical Classification of Diseases and Related Health Problems, 10th Revision* (ICD-10) codes of brain abscess (G060), epidural or subdural abscess (G062), acute sinusitis (J01), and chronic sinusitis (J32). We excluded patients with codes for an orbital abscess (H050), fungal sinusitis (B49), immunodeficiency (D70, D71, D76, D80–D84), acquired immune deficiency syndrome (B20–B24), and malignant lymphoma or leukemia (C81–C96), as well as patients who had received antifungal agents, antineoplastic agents and immunosuppressants, and antidiabetic drugs or insulin because these patients were likely to undergo ESS. We also excluded patients who had died within 3 days of admission to account for immortal time bias. We selected patients who had undergone neurosurgery and divided them into those who did and those who did not undergo ESS within the same hospitalization.

Variables

We obtained the following patient data from the data-

TABLE 1. Summary of patient characteristics

Variable	ESS Group	Control Group	p Value
No. of patients	104	151	
Sex			0.62
Male	76 (73.1)	106 (70.2)	
Female	28 (26.9)	45 (29.8)	
Age in yrs			0.07
0–19	28 (26.9)	24 (15.9)	
20–39	20 (19.2)	20 (13.2)	
40–59	24 (23.1)	39 (25.8)	
60–79	28 (26.9)	57 (37.7)	
≥80	4 (3.8)	11 (7.3)	
BMI in kg/m ²			0.20
<18.5	29 (27.9)	27 (17.9)	
18.5–24.9	50 (48.1)	83 (55.0)	
25.0–29.9	15 (14.4)	24 (15.9)	
≥30.0	6 (5.8)	5 (3.3)	
Missing data	4 (3.8)	12 (7.9)	
Smoking			0.33
Nonsmoker	58 (55.8)	84 (55.6)	
Current/past smoker	26 (25.0)	47 (31.1)	
Unspecified	20 (19.2)	20 (13.2)	
CCI			0.35
0	85 (81.7)	130 (86.1)	
≥1	19 (18.3)	21 (13.9)	
JCS score			0.63
0	52 (50.0)	83 (55.0)	
1–3	34 (32.7)	50 (33.1)	
10–30	13 (12.5)	14 (9.3)	
100–300	5 (4.8)	4 (2.6)	
Type of hospital			0.05
Academic	30 (28.8)	28 (18.5)	
Nonacademic	74 (71.2)	123 (81.5)	

Data are presented as number (%).

base: sex, age (≤ 19 , 20–39, 40–59, 60–79, or ≥ 80 years), body mass index (BMI; < 18.5 , 18.5–22.9, 23.0–24.9, 25.0–29.9, or ≥ 30.0 kg/m²), smoking status (nonsmoker or current/past smoker), Charlson Comorbidity Index (CCI; 0 or ≥ 1), fiscal year of admission (2010, 2011, 2012, 2013, 2014, 2015, or 2016), Japan Coma Scale (JCS) score on admission (0, 1–3, 10–30, or 100–300), and type of hospital (academic or nonacademic). The JCS is a one-axis coma scale.¹¹ JCS scores of 0, 1–3, 10–30, and 100–300 represent alert consciousness, drowsiness, somnolence, and coma, respectively.¹⁴ We categorized BMI according to the definition established by the World Health Organization.¹⁵

The outcomes included in-hospital mortality, blood transfusion, readmission, reoperation of neurosurgical procedures, and length of stay.

Statistical Method

We compared the proportions of in-hospital deaths, re-

TABLE 2. Factors in crude comparison

Factor	ESS Group	Control Group	p Value
Mortality	1 (1.0)	3 (2.0)	0.92
Blood transfusion	16 (15.4)	12 (7.9)	0.10
Readmission	8 (7.7)	18 (11.9)	0.38
Revision neurosurgery	9 (8.7)	12 (7.9)	1.01
Length of stay	45.1 $\pm$ 28.3	49.9 $\pm$ 34.3	0.44

Data are presented as number (%) or mean $\pm$ standard deviation.

admissions, blood transfusions, or revision neurosurgery between the two groups using the chi-square test. We also compared the length of stay between the two groups using the Mann-Whitney U-test. We calculated propensity scores using a logistic regression analysis to adjust for the characteristics of patients. We estimated propensity scores using the following eight variables: sex, age, BMI, smoking status, CCI, fiscal year, JCS score, and type of hospital. We calculated the C-statistics and then performed logistic regression analyses to evaluate the association of ESS with in-hospital mortality, blood transfusion, readmission, or revision neurosurgery with adjustment for propensity scores. We also performed a multiple linear regression analysis with propensity score adjustment to assess the association between ESS and length of stay. Length of stay was log transformed. For a sensitivity analysis, we investigated the association between the outcomes and ESS performed within 3 days of admission using the same analyses described above. We performed subgroup analyses by stratifying patients into a brain abscess group and subdural/epidural abscess group. These analyses were performed using the same methods as described above. In these subgroup analyses, we excluded patients who had both diagnoses. The threshold for significance was $p < 0.05$. We used Stata version 15.0 (StataCorp LLC) for all analyses.

Results

We identified 552 patients with a main diagnosis of sinusitis-induced brain abscess (G060) or epidural/subdural abscess (G062) in the period from July 1, 2010, to March 31, 2017. Figure 1 is a flowchart of the patient selection process. Of the 255 eligible patients, 104 underwent ESS and 151 did not. Of the 255 patients, 247 received intravenous antibiotics, 3 took antibiotic tablets, and 5 received no antibiotics. The median interval from admission to starting antibiotics was 1 day (IQR 1–2 days). Neurosurgical procedures included drainage alone (119 patients), craniotomy alone (117), and both (19). The median interval from admission to starting ESS was 3 days (IQR 2–8 days).

Table 1 shows the characteristics of the patients. Those with a sinusitis-induced intracranial abscess were more frequently male and elderly. There was no significant difference in the characteristics of patients between the ESS and control groups. There was a nonsignificant difference in in-hospital mortality, blood transfusion, readmission, revision neurosurgery, and length of stay between the two groups in the crude data comparisons (Table 2).

In the propensity score-adjusted analyses, the C-sta-

TABLE 3. Multivariable logistic regression and multivariable linear regression for propensity score–adjusted analysis

Variable	OR (95% CI)	p Value
Mortality		
ESS group	0.54 (0.05–5.80)	0.61
Control group	Reference	
Blood transfusion		
ESS group	1.95 (0.84–4.51)	0.12
Control group	Reference	
Readmission		
ESS group	0.86 (0.34–2.16)	0.75
Control group	Reference	
Revision neurosurgery		
ESS group	0.65 (0.24–1.74)	0.39
Control group	Reference	
Length of stay		
ESS group	–10.8%* (–24.4% to 5.1%)	0.18
Control group	Reference	

Propensity scores were calculated with consideration of sex, age, BMI, smoking status, comorbidity at admission, fiscal year of admission, JCS score, and type of hospital.

* Percent difference.

tistic was 0.7. Logistic regression analyses with propensity score adjustment showed no significant association of ESS with mortality (OR 0.54, 95% CI 0.05–5.80, $p = 0.61$), blood transfusion (OR 1.95, 95% CI 0.84–4.51, $p = 0.12$), readmission (OR 0.86, 95% CI 0.34–2.16, $p = 0.75$), or re-

vision neurosurgical procedures (OR 0.65, 95% CI 0.24–1.74, $p = 0.39$). Multiple linear regression after propensity score adjustment showed that ESS was not significantly associated with length of stay (percent difference –10.8%, 95% CI –24.4% to 5.1%, $p = 0.18$; Table 3).

The sensitivity analyses showed trends similar to those for the main analyses. The subgroup analyses also showed trends similar to those for the main analyses (Table 4).

Discussion

There was a nonsignificant association between ESS for the treatment of sinusitis-induced intracranial abscess and outcomes in patients who underwent neurosurgery. This may be explained by how inflammation extends to the central nervous system. Infection of a sinus spreads mostly by progression of septic thrombi through the valveless diploic veins of the skull base that penetrate the dura mater. Direct extension via osteomyelitis of the sinus walls or bony defects (congenital or posttraumatic) is uncommon.^{6,18} Thus, the effect of drainage from the sinus may be limited. The present study showed no significant benefit of ESS in terms of reducing in-hospital mortality, blood transfusion, readmission, revision neurosurgery, or length of stay. This finding will help physicians make treatment decisions for patients with a sinusitis-induced intracranial abscess.

A previous study showed that early ESS tended to reduce revision neurosurgery.⁹ In the present study, approximately 80% of ESS procedures were performed within 8 days of admission. We, therefore, assessed ESS within 3 days of admission as a sensitivity analysis. The results were similar to those in the main analyses. These data indicate the robustness of our results.

We found that male and elderly patients accounted for

TABLE 4. Multivariable logistic regression and multivariable linear regression for subgroup analysis

Variable	Brain Abscess Group		Subdural/Epidural Abscess Group	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Mortality*				
ESS group	—		1.59 (0.07–35.2)	0.77
Control group	—		Reference	
Blood transfusion				
ESS group	2.50 (0.68–9.22)	0.17	1.71 (0.51–5.72)	0.39
Control group	Reference		Reference	
Readmission				
ESS group	1.45 (0.37–5.70)	0.60	0.71 (0.19–2.74)	0.62
Control group	Reference		Reference	
Revision neurosurgery				
ESS group	0.83 (0.22–3.19)	0.79	0.50 (0.10–2.52)	0.40
Control group	Reference		Reference	
Length of stay				
ESS group	–12.5%† (–29.7% to 8.9%)	0.23	–5.6%† (–28.1% to 23.6%)	0.67
Control group	Reference		Reference	

Propensity scores were calculated with consideration of sex, age, BMI, smoking status, comorbidity at admission, fiscal year of admission, JCS score, and type of hospital.

* Mortality was 0% in the ESS group within the brain access group.

† Percent difference.

the highest proportion of patients in this study. Male patients have been dominant in many previous studies, and our results are consistent with those findings. Several studies have shown that sinusitis-induced intracranial abscesses occur more commonly among adolescents and young adults in their 20s and 30s.^{3,12,17,18} Our results are inconsistent with those of previous studies; we found that abscesses occur at any age, although the reason remains unclear.

The main strength of this study is the large number of patients; previous studies have evaluated fewer than 100 patients. Another strength is our inclusion of patients who did and who did not undergo ESS, whereas most previous studies have included only patients who underwent ESS without a control group. The present study showed similar trends in the subgroup analyses and sensitivity analyses. We consider that the robustness of our results is also a strength of our study.

Study Limitations

We acknowledge three main limitations to this study. First, we could not obtain information on the size of the intracranial abscess or severity of sinusitis. Second, we could not identify patients with direct extension of inflammation via a bony defect near the intracranial abscess because of the lack of imaging data. Third, information on the causative microorganism was lacking. These limitations have the potential to impact the treatment decision-making process; however, the patients' characteristics and backgrounds were not significantly different. We, therefore, consider these impacts to be small.

Conclusions

Our analysis suggests that ESS may not always be necessary for patients with a sinusitis-induced intracranial abscess requiring neurosurgery.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Koizumi. Acquisition of data: Koizumi, Ishimaru, Matsui, Fushimi, Yasunaga. Analysis and interpretation of data: Koizumi, Ishimaru, Yamasoba, Yasunaga. Drafting the article: Koizumi, Yasunaga. Critically revising the article: Yamasoba, Yasunaga. Approved the final version of the manuscript on behalf of all authors: Koizumi. Statistical analysis: Koizumi, Ishimaru, Yasunaga. Administrative/technical/material support: Ishimaru, Matsui, Fushimi, Yamasoba, Yasunaga. Study supervision: Yamasoba, Yasunaga.

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