RHINOLOGY Corrected Proof SYSTEMATIC REVIEW

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Risk factors in patients treated with surgical drainage for rhinogenic intracranial complications: a nationwide study

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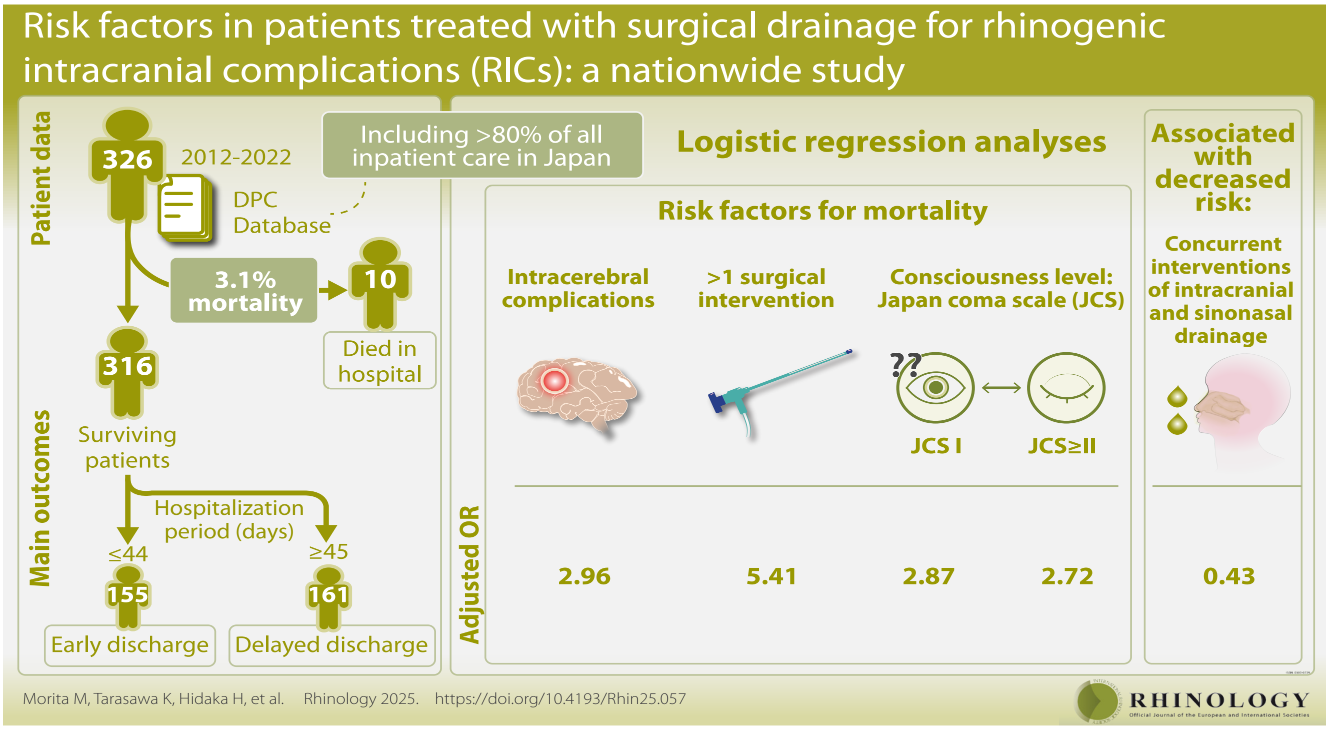

Abstract

Background: Data on risk factors for rhinogenic intracranial complications (RICs) including cerebral abscess have been limited. Using a nationwide database, the aim was to identify the factors related to mortality and delayed discharge.

Methodology: Data of 326 patients between 2012 and 2022 were extracted from a Japanese inpatient database. The main outcome was survival at discharge. In a subgroup analysis of the 316 surviving patients, the outcome was delayed discharge.

Results: The mortality rate was 3.1%. Logistic regression analyses identified intracerebral complications more than one surgical intervention and consciousness level evaluated by the Japan Coma Scale (JCS): JCS I and JCS≥ II as risk factors for mortality. Concurrent interventions of intracranial and sinonasal drainage was identified as a factor associated with decreased risk.

Conclusions: Although RICs are rare, with decreasing mortality due to progress in imaging and clinical strategies, they remain the most severe complications of rhinosinusitis. Subdural and/or intracerebral abscess, consciousness level at admission, and more than one surgical intervention were found to be risk factors for mortality. Conversely, concurrent interventions, intracranial and sinonasal drainage, contributed to reducing this risk.

Key words: DPC database, intracranial complications, Japan Coma Scale (JCS), mortality, rhinosinusitis

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Introduction

Rhinosinusitis is one of the most common diseases, and most cases improve with observation or appropriate conservative treatment, but in rare cases, the inflammation can spread to adjacent structures such as the orbit or skull base, causing serious complications [1-5].

Although rhinogenic intracranial complications (RICs) are decreasing due to advances in antimicrobial agents, they remain the most severe complications of rhinosinusitis and affect life expectancy. Long-term neurological sequelae such as paresis, aphasia, and seizures remain a concern. Further, patients with RICs have long hospital admissions, with reported hospitalization times over the past 10 years of up to 40 days [6-8].

Despite improvements in diagnostic methods, surgical technique, and intensive care protocols, RICs have been reported to be life-threatening, with mortality rates ranging from 2% to 27% [2-4,9,10]. Although the aetiology and clinical outcomes of their treatment have been extensively reported, almost all of these were case series from a single institution, with several limitations due to their relatively small sample sizes from single medical centres. In addition, their rarity has been one of the reasons for the difficulties in prospective investigations of these patients. Although clinical factors related to mortality and therapeutic schema have been proposed, optimal surgical strategies, including delaying surgery until the patients stabilize, are controversial [5,8].

The present report describes a study that used a nationwide inpatient database in Japan to investigate the factors associated with mortality and prolonged hospitalization in patients who underwent surgical drainage for RICs.

Materials and methods

Data source

Data were extracted from the Diagnosis Procedure Combination (DPC) database, a national inpatient database in Japan. The DPC database includes approximately 1,100 hospitals and more than 7 million inpatient cases per year and is representative of acute inpatient care in Japan due to its scale. The details of the DPC database have been described previously [11-14]. Briefly, the DPC database includes administrative claims data and detailed medical data collected for all inpatients discharged from participating hospitals. More than 80% of acute inpatient care in Japan is included in the DPC system [11,12,15-17]. The dates of hospital admission, surgery, discharge, bedside procedures, and drugs administered are recorded using a uniform data submission format [12].

All patient identifiers were removed from this database. Because of the anonymous nature of the data, the need for informed consent was waived. Study approval was obtained from the Institutional Review Board of the Tokyo Medical and Dental University (protocol Number: M2000-788-15) and Kansai Medical University (protocol Number: 2019316).

Patient selection and characteristics

Of the 78.3 million inpatients in the DPC database over a total of 10 years (between April 2012 and March 2022), patients satisfying the following inclusion criteria according to surgical interventions encoded with original Japanese codes were selected: craniotomy (Japanese code: K147) or exploratory craniotomy (Japanese code: K148) or drainage of brain abscess (Japanese code: K150) or surgery for rhinogenic intracranial complications (Japanese code: K153).

The following background characteristics of the patients were assessed: age; sex; main diagnosis; comorbidities at admission including level of consciousness evaluated by the Japan Coma Scale (JCS), and sepsis (ICD-10 codes: A40-A41) classified according to the International Classification of Diseases, 10th Revision (ICD-10) and test data in Japan [11-17]; diabetes mellitus (DM) classified according to whether diabetes medication was used during the hospital stay; number of surgical interventions; length of stay; and discharge status. The JCS is one of the most widely used grading scales for assessing impaired consciousness, consisting of four main categories: 0, alert consciousness; 1–3 (single-digit), awake without any stimuli; 10–30 (double-digits), arousable by some stimuli but reverts to previous state if stimulus stops; and 100–300 (triple-digits), unarousable by any stimuli [18-20].

Outcome measurement

The primary outcome was survival at discharge, as well as length of hospitalization of surviving patients. The patients who were alive at discharge were divided into two groups according to the median interval between admission and discharge. The patients were then categorized into three groups: in-hospital death, longer hospitalization, and shorter hospitalization.

Statistical analysis

Differences in frequencies between the groups were evaluated using Fisher's exact test. Multiple logistic-regression analysis was performed to compare multiple outcome categories, assessing the independent effect on the severity of intracranial complications. Inclusion of independent variables in the model was based on earlier research and existing knowledge in terms of the following risk factors for aggravation of intracranial complications and abscesses in the head and neck region [1-10,13,14]: age; sex; type of complication (subdural abscess including cerebral abscess or other intracranial complications such as epidural abscess or meningitis); level of consciousness evaluated by the JCS; comorbid DM and sepsis; with or without concurrent neurosurgical and sinonasal procedure; and repeated surgical interventions.

A p-value < 0.05 was considered significant. All statistical analyses were conducted using EZR software [21].

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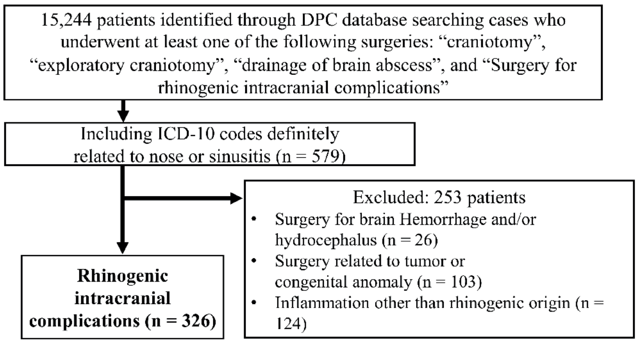

Figure 1. Schematic illustration of patient selection. DPC, Diagnostic Procedure Combination.

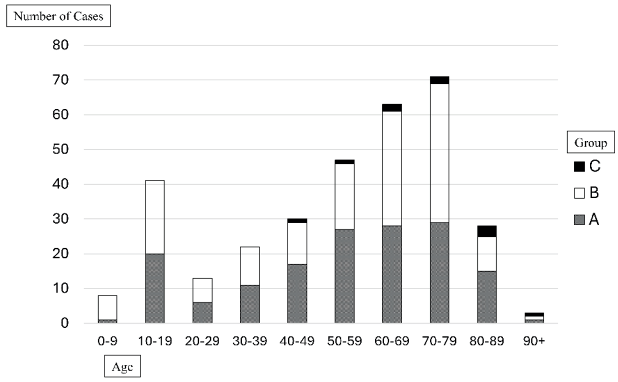

Figure 2. Age distribution according to outcomes related to survival at discharge and prolonged hospitalization categorized as in Table 1. Group A: Short-term hospitalization group. Group B: Long-term hospitalization group. Group C: Died in hospital group.

Results

Demographic data

During the study period, a total of 15,244 cases fulfilled the inclusion criteria for surgical screening, as shown in Figure 1. Of these cases, 14,665 were excluded because of no ICD-10 codes including nose and/or sinusitis. Of the remaining 579 patients, 253 were excluded because their surgeries were attributed to reasons other than rhinogenic complications, as follows: brain haemorrhage and/or hydrocephalus in 26 cases; tumour or congenital anomaly in 103 cases; and inflammation of other than rhinogenic origin in 124 cases. The resulting 326 patients were selected for inclusion in the qualitative analyses.

Of the total 326 patients, the 316 patients who were alive at discharge were divided into two groups according to the median interval (45 days) between admission and discharge. Namely, the short-term hospitalization group (group A) and the long-term hospitalization group (group B) included cases with intervals less than <45 days and ≥45 days, respectively (Figure S1, representing the distribution of length of hospitalization by group). Another 10 patients who died in hospital were assigned to the died in hospital group (group C). Table 1 summarizes the baseline characteristics of each group of patients. Figure 2 shows the age distribution of each patient group. Although the most common age of the patients with RICs was in the 70s, followed by the 60s, the graph shows another peak in the 20s. The median ages of groups A, B, and C were 58, 61, and 75 years, respectively. Group C showed a higher interquartile range for age (48-95 years) than the other groups (p =0.03, Kruskal-Wallis test). Conversely, the male to female ratios of the three groups were not significantly different.

Regarding intracranial complications, the patients were classified into two groups: 1) subdural and/or intracerebral abscess; and 2) other complications without these two ICD-10 codes, mainly representing epidural abscess. The prevalences of subdural complications of groups A, B, and C were 42.6%, 78.8%, and 60%, respectively. Group A showed a significantly lower prevalence of subdural and/or intracerebral abscesses (p < 0.001).

Impaired consciousness evaluated by the JCS score showed a significant difference among the groups. Specifically, the prevalence of a score > I was only 7.1% (11 of 155) in group A compared with both group B (18.6%: 30 of 161) and group C (20%: 2 of 10). Only one patient in group C showed a JCS score of zero. Concerning disease comorbidity, the prevalence of DM was higher in group C (50%) than in group A (13.5%) and group B (23%) (P = 0.005). In addition, comorbid sepsis was significantly higher in group C (20%) than in group A (1.9%) and group B (8.7%) (p = 0.004).

Regarding surgical interventions, the median duration from admission to surgery was four days, and this was used as the cutoff (Figure S2 for details, showing the distribution of days from admission to first surgery in each group). Namely, the prevalence of delayed surgery (>4 days after admission) was higher in group B (55.9%) than in the other groups (p = 0.005). Conversely, the prevalence of undergoing concurrent sinonasal and brain surgery was higher in group A (49.7%) than in group B (19.9%) and group C (30%) (p < 0.001). Further, the prevalence of repeated surgical interventions (more than one surgical drainage) was lower in group A (3.9%) than in group B (18%) and group C (20%) (p = 0.001).

Risk factors contributing to prolonged hospitalization or mortality

As shown in Table 1, group C consisted of only 10 cases, with a few cells of independent variables with low counts including zero. Moreover, none of the group C patients showed a JCS score of III (Table 1). To avoid separation and convergence failure in the logistic regression, groups B and C, comprising cases with prolonged hospitalization or mortality, were combined, similar to our previous study addressing otogenic intracranial complications (OICs) [14]. Therefore, patients in group B (longer hospitalization) and group C (in-hospital death) were defined as

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Table 1. Baseline characteristics of patients categorized by survival at discharge and prolonged hospitalization by rhinogenic intracranial complication.

	Group			
	A (No. =155)	B (No. =161)	C (No. =10)	P value
Age (years)				0.028 *
Median	58	61	75	
Range	7–90	0–91	48–95	
Interquartile range	40–71	37–72	65–83.5	
Sex				0.062 #
Male	94 (60.6%)	117 (72.7%)	8 (80%)	
Female	61 (27.3%)	44 (27.3%)	2 (20%)	
Intracerebral complications				< 0.001 #
No	89 (57.4%)	34 (21.2%)	4 (40%)	
Yes	66 (42.6%)	127 (78.8%)	6 (60%)	
Consciousness level (JCS)				< 0.001 #
0	115 (74.2%)	68 (42.2%)	1 (10%)	
I	29 (18.7%)	63 (39.1%)	2 (20%)	
II	7 (4.5%)	21 (13.0%)	2 (20%)	
III	4 (2.6%)	9 (5.6%)	0	
Unknown	0	0	5 (50%)	
Diabetes mellitus				0.005 #
No	134 (86.5%)	124 (77.0%)	5 (50%)	
Yes	21 (13.5%)	37 (23.0%)	5 (50%)	
Sepsis				0.004 #
No	152 (98.1%)	147 (91.3%)	8 (80%)	
Yes	3 (1.9%)	14 (8.7%)	2 (20%)	
Delay of 1st surgery after admission				0.005 #
≤4	95 (61.3%)	71 (44.1%)	7 (70%)	
>4	60 (38.7%)	90 (55.9%)	3 (20%)	
Concurrent sinonasal and brain surgery [a)]				< 0.001 #
No	78 (50.3%)	129 (80.1%)	7 (70%)	
Yes	77 (49.7%)	32 (19.9%)	3 (30%)	
Surgical intervention / more than once				< 0.001 #
No	149 (96.1%)	132 (82.0%)	8 (80%)	
Yes	6 (3.9%)	29 (18.0%)	2 (20%)	

Patients were categorized into three groups according to outcomes related to survival at discharge and prolonged interval for hospitalization, as follows: A) Short-term hospitalization group (alive at discharge 44 days after admission); B) Long-term hospitalization group (alive at discharge for more than or equal to 45 days after admission); and C) Died in hospital group. [a)]: Concurrent surgery was defined as cases in which both sinonasal and neurosurgical surgery were performed on the same day. Specifically, "*Concurrent sinonasal and brain surgery*" included cases in which "*surgery for rhinogenic intracranial complications*" was performed, and those in which sinonasal and neurosurgical surgery were performed on the same day. # Ficher's exact test, conducted for other than unknown cases for each characteristic. * Kruskal-Wallis test. Abbreviations: No., number of patients; JCS, Japan Coma Scale.

the "prolonged hospitalization or mortality" group, resulting in categorizing the outcomes into two groups. The cases with JCS scores of II and III were also combined, constituting the group with JCS score ≥ II.

Logistic regression analysis showed that the following factors were significant with respect to prolonged hospitalization or mortality: intracerebral complications, comprising cerebral and/or subdural abscess, JCS score, DM, sepsis, repeated surgery, more than a 4-day interval between admission and the first surgery, and intervention with concurrent neurosurgical and sinonasal surgery as the first procedure, with the crude odds ratios (ORs) shown in Table 2. Of these factors, the following were significant with ORs adjusted by the other variables (adjusted ORs): intracerebral complications comprising cerebral and/or subdural abscess, OR of 2.96 (95% confidence interval [CI], 1.63-5.39); JCS score I, OR of 2.87 (95%CI, 1.58-5.22); JCS score ≥ II, OR of 2.72 (95%CI, 1.18-6.30); concurrent brain and sinonasal surgery at the 1st procedure, OR of 0.43 (95%CI, 0.23-0.81); and repeated surgery, OR of 5.41 (95%CI, 1.84-15.6).

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Table 2. Multiple logistic regression analysis of risk factors for prolonged hospitalization or mortality in patients who underwent surgical intervention for rhinogenic intracranial complications.

	Crude OR (95% CI)	Adjusted OR (95% CI)
Age (years)		
<50	1.00	1.00
50≤, <75	1.07 (0.66–1.75)	1.13 (0.61–2.09)
75≤	0.99 (0.54–1.82)	1.00 (0.46–2.17)
Sex: female (vs. male)	0.57 (0.35–0.90)	0.69 (0.39–1.22)
Intracerebral complications		
No	1.00	1.00
Yes	4.72 (2.92–7.63)	2.96 (1.63–5.39)
Consciousness level (JCS)		
0	1.00	1.00
I	3.74 (2.20–6.35)	2.87 (1.58–5.22)
≥II	4.85 (2.30–10.20)	2.72 (1.18–6.30)
Diabetes mellitus	2.08 (1.17–3.70)	1.44 (0.71–2.94)
Sepsis	5.23 (1.49–18.3)	3.69 (0.95–14.3)
Delay of 1st surgery after admission		
≤4	1.00	1.00
>4	1.89 (1.21–2.94)	1.63 (0.94–2.83)
Concurrent sinonasal and brain surgery		
No	1.00	1.00
Yes	0.25 (0.16–0.41)	0.43 (0.23–0.81)
Surgical intervention / more than once	5.50 (2.23–13.6)	5.41 (1.84–15.6)

Abbreviations: CI = confidence interval; OR = odds ratio; JCS= Japan Coma Scale.

Discussion

Intracranial complications of acute sinusitis remain life-threatening. Complications include cerebral sequelae, which can be disabling in 25% of cases and may cause death in 10% [22-24]. In this study, a total of 326 patients throughout Japan who underwent drainage surgery for RICs were investigated using a Japanese nationwide inpatient database. Because the database was screened according to intracranial surgery, almost all of them would be classified as intracranial abscesses, similar to our previous study focusing on otogenic intracranial complications (OICs) [14]. Although a recent systematic review reported that approximately 10% of brain abscess cases had predisposing conditions related to sinusitis [25], previous studies of RICs were based on retrospective designs from a few institutions. To the best of our knowledge, this is the first study to investigate the factors related to prolonged hospitalization or mortality in patients with RICs including intracranial abscesses in a nationwide clinical setting. In the present study, the mortality rate was 3.1% (10 of 326), showing similar rates to the recent reports [3,9,26]. This rate was also slightly lower than that of OICs (9%; 8/88) according to our previous results using the DPC database [14]. These results are consistent with a previous observation that the prognosis for morbidity and mortality in cases with RICs is generally good when compared with intracranial infections from other causes [22].

In the present study, the average length of hospital stay was 49.6 days (Figure S1), which was longer than in previous studies [6-8]. Several possible reasons for this are presumed to be related to the unique characteristics of the Japanese healthcare system. One is that, since the number of hospital beds per population is high, it is easier to secure a longer length of stay than in other countries. Another is that the length of stay in this DPC database includes the period for cases transferred to non-acute care units (such as convalescent wards).

Data in the literature mention that adolescents carry a greater risk of RICs because of the highly vascularized diploic venous system and development of the frontal sinuses in this age group [3]. In the present study, the prevalence of age < 30 years was 19% (62/362), and a second peak in the incidence was observed in patients at age ≥ 75 years, comprising 20% (66/326). The results are consistent with the previous reports and are explained by the decline of immune functions and other comorbidities with advanced age [26]. Although higher age tended to increase mortality of RICs, the present study failed to identify age as an independent risk factor in the age group ≥75 years. These results are similar to those for OICs [14], contrasting with those of our nationwide study addressing deep neck infection, in which advanced age (≥75 years) was significantly associated with mortality [13]. These differences might be attributed to a relatively higher prevalence of adolescents among cases of both RICs and OICs than among those with deep neck infection. Other series have reported a male predominance in RIC cases [6-8,22-24], and this was also seen in the present series. However, sex did not contribute to morbidity and mortality, similar to the results for OICs [14] and deep neck infection [13].

Regarding the types of RICs, the prevalence of subdural or intracerebral abscess was less than 43% in the group with shorter hospitalization. These complications were the most severe types of intracranial complications other than meningitis [10,14,22,25], and it is plausible that patients with subdural and/or intracranial abscesses showed severe mortality and morbidity. This factor was shown to be a significant risk factor, with an adjusted OR of 2.96 (95% CI, 1.63-5.39). These results were similar to the results for OICs (adjusted OR of 3.09) [14].

The clinical presentation of an RIC incudes acute or chronic sinonasal complaints, along with fever and symptoms of increased intracranial pressure, such as headache, nausea and vomiting, altered mental status, seizures, and nuchal rigidity [22]. However, the onset of intracranial abscess is variable, and an altered level of consciousness is frequently absent [27]. Only a few reports have evaluated whether the prognosis of RICs correlates with consciousness level, other than a study by Dill and colleagues involving 32 patients with subdural empyema [27]. The DPC database has an advantage of including the JCS score at admission, which has been widely used to assess patients' consciousness level in Japan [18-20]. The JCS consists of four main grades of consciousness based on reactive eye-opening, which was described in the Methods section. Although the JCS and Glasgow Coma Scale (GCS) cannot be seamlessly converted due to inherent differences between the components evaluated, Nakajima et al. have developed a conversion method between the JCS and GCS, with JCS I roughly equivalent to GCS 13-15, JCS II to GCS 9-12, and JCS III to GCS 3-7 [19]. In the present study using the JCS, it was found that the consciousness level was significantly related to prolonged hospitalization or mortality, as compared with patients with JCS score 0 (alert). JCS score I (alert or awake without stimuli) was a significant factor, with an adjusted OR of 2.87 (95% CI, 1.58-5.22). Specifically, JCS score II (arousable by some stimuli but reverts to previous state if stimulus stops) or III (unarousable by any forceful stimuli) was also a significant factor, with an adjusted OR of 2.72 (95% CI, 1.18-6.30). These results contrast with those of our previous study addressing OICs [14], in which mortality was strongly correlated with increases of the JCS, i.e. ORs of scores I and ≥II were 3.4 (95% CI, 1.1-10.5) and 25.1 (95% CI, 2.5-253), respectively. These relatively smaller adjusted ORs that did not correlate with increases of the JCS in RICs might be attributed to their different intracranial sites including frontal lobe versus temporal lobe and/or cerebellum.

The presence of systemic disease is an important predisposing factor for severity of severe infections, including those in the head and neck region [13]. Of them, comorbid DM is a well-known risk factor. Specifically, chronic sinusitis and DM have been reported to be common pre-existing diseases [28]. Although the present study showed a higher prevalence of DM (50%) in patients with in-hospital death, logistic regression analysis failed to identify it as a significant risk factor for prolonged hospitalization or mortality in RICs, different from the results for OICs, with an adjusted OR of 3.85 (95% CI, 1.12-13.2) [14]. One hypothesis for these inconsistencies is that a relatively high prevalence of comorbid DM was present even in the group (A) with a good prognosis (13.5%), which was higher than that of OICs (7.2%) [14]. Of the systemic diseases contributing to mortality, sepsis is also a well-known complication, as in the head and neck region [13]. Although the poorer prognosis group showed a higher prevalence of sepsis, similar to results for OICs [14], the present study also failed to show that sepsis was a significant risk factor for prolonged hospitalization or mortality in RICs. These results were similar to those for OICs, contrasting with the results for deep neck infection [13]. One hypothesis for these inconsistencies is that sepsis, presumably attributed to septic cerebral venous sinus thrombosis [29], is extremely less common in both RICs (1.9-20%) and OICs (1.4-37.5%) [3,14] than in deep neck infection (5.2-21.3%) [13].

Although the treatment for RICs involves surgery, the question of if, when, and which surgery of the paranasal sinuses should be performed has not been definitively addressed [5,30]. Specifically for intracranial abscesses, early treatment combined with abscess drainage and sinus drainage has been shown to decrease the need for repeated craniotomies and is associated with a decreased length of hospital stay [1-3]. Although a 4-day delay to the first surgery after admission was not identified as a risk factor in RICs, there was a trend towards prolonged hospitalization or mortality, with an adjusted OR of 1.63 (95% CI, 0.94-2.83). These results are consistent with the previous report showing that a poor prognosis was associated with a prolonged time interval between the onset of symptoms and the beginning of treatment [10].

Debate also continues for RICs regarding the topics of combined (performed during the same admission) and concurrent (performed under the same general anaesthetic) neurosurgical and otolaryngological (ORL) interventions [5,31-34]. Several reports advocated concurrent intervention to reduce the prevalence of abscess recurrence and revision surgery [1,24,26,32,34]. Conversely, others stated that concurrent sinus surgery is indicated when the paranasal sinus causing the complication is directly connected with the intracranial collection of fluid, in recurrences of intracranial complications after neurosurgical drainage, or persisting sinusitis after healing of the intracranial complication [3,5,30]. The present study showed that concurrent sinonasal and brain surgery was identified as a significant factor, with an adjusted OR of 0.43 (95% CI, 0.23-0.81). In addition, repeated surgery (more than once) was identified as a significant risk factor for prolonged hospitalization or mortality in RICs, with an adjusted OR of 5.41 (95% CI, 1.84-15.6). These results are consistent with a recent reports stating that the use of concurrent interventions produced a lower rate of revision neurosurgery than combined intervention [24,32-34], although the timing of ORL surgery had a lesser impact on the choice of neurosurgical approach. The present study using the DPC database showed that only 11.3% (37/326) of patients underwent more than one surgery, similar to the result for OICs [14]. One of the hypotheses contributing to the small prevalence of repeated surgery is that some patients are discharged after intracranial drainage, and sinus surgery is considered. However, only two patients underwent another sinus surgery after discharge of their first admission. Although there is as yet no routine indication for emergency sinus surgery for the management of RICs, the present results confirm a recent review concluding that combined sinonasal and transcranial approaches achieve definitive control of sinogenic and intracranial disease, whereas either modality alone carries a potential risk for higher morbidity and mortality [34].

Several limitations of this study need to be acknowledged. First, this was a retrospective, cohort study using a national Japanese database, and generalization of the results outside Japan,

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specifically to a country where CT has yet to become available, may not be appropriate. Second, the screening method involved restricting the cases to those that underwent intracranial surgical intervention first, and then narrowing them down to the rhinogenic cases. Similar to the previous study focusing on OICs, this strategy remains a weakness, because RIC patients without neurosurgical interventions, such as those with meningitis or cavernous sinus thrombosis, were not included, since many of these patients would not undergo neurosurgical interventions (4). Third, subcategorization of sinus surgery according to the affected sinus (i.e. frontal sinus and/or ethmoid sinus) are not available from the DPC database. Furthermore, the absence of records of vital signs, blood tests, radiological findings, and bacteriological cultures in the DPC database precluded a more rigorous definition of DM and sepsis [12-14]. Fourth, comorbidities are less accurately recorded in administrative claims databases than planned prospective studies. Moreover, DPC data come from an inpatient database, and it is difficult to evaluate the prognosis of delay from onset to intervention and neurological sequelae at discharge.

Conclusion

Within these limitations, the current study using a nationwide database has several suggestions for the management of RICs. Subdural and/or intracerebral abscess, consciousness level at admission, and more than one surgical intervention were found to be risk factors for mortality. Conversely, concurrent interventions of intracranial and sinonasal drainage reduce this risk.

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None.

Authorship contribution

HH and YY designed and supervised the study. KT, FK, and KF acquired all clinical data. MM, YY, SH, MA, and MY performed data analysis and interpretation. KT and HH assisted in the statistical analyses. MM, HH, and HI wrote the manuscript. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no competing interests.

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Corrected Proof

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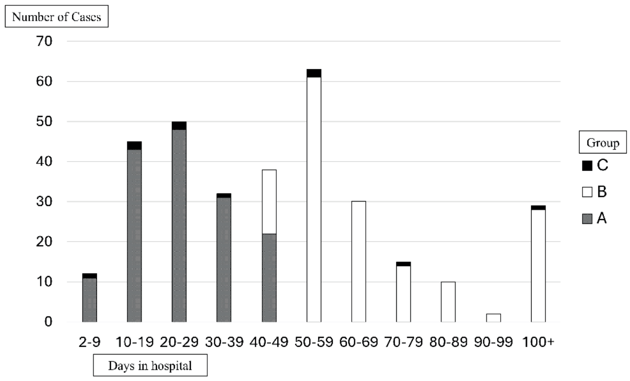

Figure S1. The distribution of the hospitalization period in each group, according to outcomes related to survival at discharge and prolonged hospitalization categorized as in Table 1. Group A: Short-term hospitalization group. Group B: Long-term hospitalization group. Group C: Died in hospital group.

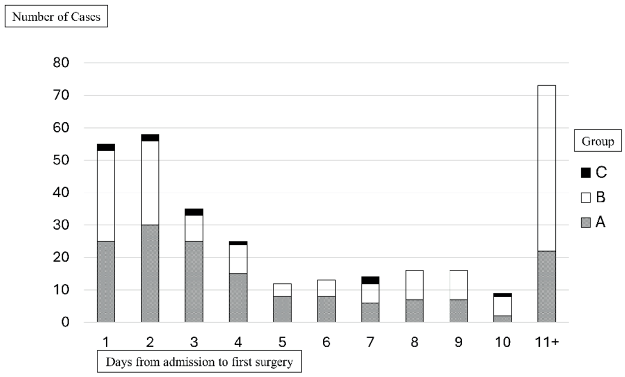

Figure S2. The distribution of days from admission to first surgery, according to outcomes related to survival at discharge and prolonged hospitalization categorized as in Table 1. Group A: Short-term hospitalization group. Group B: Long-term hospitalization group. Group C: Died in hospital group.