Demographic and Clinical Characeristics of Seizures in Children at Emergency Room Visits : A Single-Center Study

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Aim : This study aimed to evaluate the demographic and clinical characteristics of children who present to the emergency room with seizures and determine the etiology to appropriately treat these patients.

Methods : This hospital-based retrospective cohort study was conducted using data retrieved from the medical records of 1600 seizure cases treated at the Emergency and Pediatric Departments of Ina Central Hospital from January 2010 to December 2019.

Results : Of the 1600 cases, 1248 (78 %) were associated with fever and 1228 (98.3 %) were diagnosed with febrile seizures. Epilepsy was the most frequent cause of seizures without fever (75 %). A total of 222 patients (17.3 %) visited multiple times (maximum seven times). Complex febrile seizures increased the chances of being diagnosed with epilepsy later. Six cases (0.3 % of all visits) were diagnosed with acute encephalitis/encephalopathy ; however, there were no cases of meningitis. Body temperature at the visit was significantly lower, whereas age and previous occurrence of seizures were significantly higher in the epilepsy group with fever than in the febrile seizure group. In contrast, the recurrent seizure frequency during the same episode was significantly higher in the acute encephalitis/encephalopathy group than in the epilepsy group without fever.

Conclusion : Clinical characteristics and backgrounds such as age, body temperature, seizure history and recurrent episodes can be the important factors to predict the cause of seisures to ensure appropriate treatment of pediatric patients experiencing seizures in an emergency outpatient department. *Shinshu Med J 72 : 39—47, 2024*

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Key words : encephalitis, epilepsy, fever, meningitis, seizures

I Introduction

Childhood seizures are common and frightening disorders that occur in approximately 4 %-10 % of children, accounting for 1 % of all emergency department visits[1]. Several neurological disorders, including febrile seizure (FS), epilepsy, acute encephalitis/encephalopathy, traumatic head injury, and gastroenteritis, may cause pediatric seizures[1]. Our hospital locating in the Kami-Ina area, Nagano, Japan has an emergency department that treats patients of all ages including children, many of whom are evaluated for seizures annually.

FS is a common neurological disorder occurring in 2 %-5 % and 7 %-11 % of children (aged 6-60 months) in the United States and Western Europe[2)-5)] and Japan[6)7)], respectively[5]. It is also reported as the most common disorder in children in out-of-hospital and emergency department settings, with an incidence of 38.5 %-68.6 %[8)-10)]. Although almost pediatric seizure patients have good neurological and developmental prognoses, serious diseases which need prompt diagnosis and intensive care, such as central nervous system infections, including acute meningitis and encephalitis/encephalopathy, should be identified. On the other hand, no study has reported analyzing pe-

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diatric seizures using a large number of cases for years. Therefore, clarification of the clinical differences for each seizure by statistical analysis of a large number of patients is important especially in out-of-hospital and emergency department settings.

Because our hospital is the only center providing emergency medical care 24 h a day, 365 days a year in the Kami-Ina area which has approximately 25,000 children (<15 years old), most pediatric patients from this area are brought here by ambulance or their guardians. Here, we report the prevalence of various seizure etiologies in children who visited the emergency and pediatric departments at Ina Central Hospital during past 10 years.

Ⅱ Methods

This retrospective hospital-based cohort study included all pediatric seizure patients aged <15 years treated at the Emergency and the Pediatric Departments of Ina Central Hospital in Ina, Japan (January 2010-December 2019). The study was approved by the institutional ethics committee of Ina Central Hospital.

We collected demographic and clinical data and history from the electronic medical records of Ina Central Hospital. Each seizure diagnosis was based on the discharge diagnosis or retrospectively identified by reviewing case histories and reported clinical findings. Status epilepticus was defined as a single seizure lasting over 30 min or repeated seizures without full consciousness recovery between ictal events in more than 30 min[11]. FS was defined as a seizure accompanied by fever (temperature ≥ 38 ℃) without a central nervous system infection occurring in infants and children aged 6-60 months[5]. In this study, even if they were >60 months old and fit the definition of FS, except for age, they were defined as FS patients. Simple FS lasts for <15 min, is initially generalized, and occurs once during 24 h. In contrast, complex FS lasts ≥ 15 min, has focal features at any time, and recurs within 24 h. "Fever" was also considered regardless of body temperature at admission if the body temperature before the seizure was ≥ 38 ℃. Epilepsy was defined as a neurological disease with any of the following conditions : 1) at least two unprovoked seizures occurring >24 h apart and 2) one unprovoked seizure and probability of further seizures similar to the general recurrence risk[11]. We defined acute encephalitis/encephalopathy as a condition with acute onset of impaired consciousness lasting more than 24 h. Benign convulsion with mild gastroenteritis (CwG) is a clinical condition characterized by seizures occurring in otherwise healthy children, usually without high fever and with mild acute gastroenteritis[12]. CwG was diagnosed when a patient met these criteria : 1) seizure associated with gastroenteritis without clinical signs of dehydration or electrolyte derangement and 2) body temperature <38 ℃ before and after seizures. Breath-holding spells are episodes where infants excessively cry for up to 1 min while holding their breath to the point of losing consciousness, with a seizure occurring immediately after[13].

Ⅲ Statistical Analysis

Patient and disease characteristics in all cohorts were summarized using descriptive statistics. Comparisons of demographic and clinical data between the groups were performed using Fisher's exact test for categorical variables. Student's *t* or Mann-Whitney *U* tests were used to assess the significance of differences for continuous variables. Statistical analysis was performed using EZR[14], a modified version of R commander designed to add frequently used statistical functions in biostatistics. All reported *p*-values were 2-sided and considered significant if <0.05.

Ⅳ Results

Table 1 shows the entire cohort's demographic and clinical characteristics. Our hospital received 1600 seizure cases (890 males [55.6 %] and 710 females [44.4 %], 1285 patient visits) within the cohort period. The median patient age was 28 months (0-179 months). Overall, 80 % of patients were aged <5 years ; the largest number being patients aged 1 year **(Fig. 1)**. A seizure history was found in 580 (36 %) patients. Although 841 (52.6 %) patients used ambulances, only 64 (4 %) had persistent seizures at the time of arrival. Fever was associated with seizures in 1248 patients (78 %) ; the remaining 352 (22 %) were non-febrile.

Table 1　Clinical characteristics of subject

Parameters	*N* = 1600
Median age at seizure, months (range)	28 (0–179)
Sex	
Male	890 (55.6)
Female	710 (44.4)
Past history of seizure	580 (36.0)
FS	369 (23.4)
Others	201 (12.6)
Use of ambulance	841 (52.6)
Seizure at admission	64 (4.0)
Fever	1248 (78.0)
Median duration of seizure, min (range)	2 (1–120)
Status epilepticus	50 (3.2)
Recurrent seizure during same episode	191 (11.9)
Emergency use of anticonvulsants	103 (6.4)
i.v. diazepam	46 (2.9)
i.v. midazolam	14 (0.9)
Suppository diazepam	38 (2.4)
Others	5 (0.3)
Use of suppository diazepam after seizure	1241 (77.6)
Outcome	
Not hospitalized	1297 (81.1)
Hospitalized in our hospital	280 (17.5)
Transferred to advanced hospitals with pediatric intensive care unit	23 (1.4)

Data presented are number (%) unless otherwise indicated.
i.v., intravenous

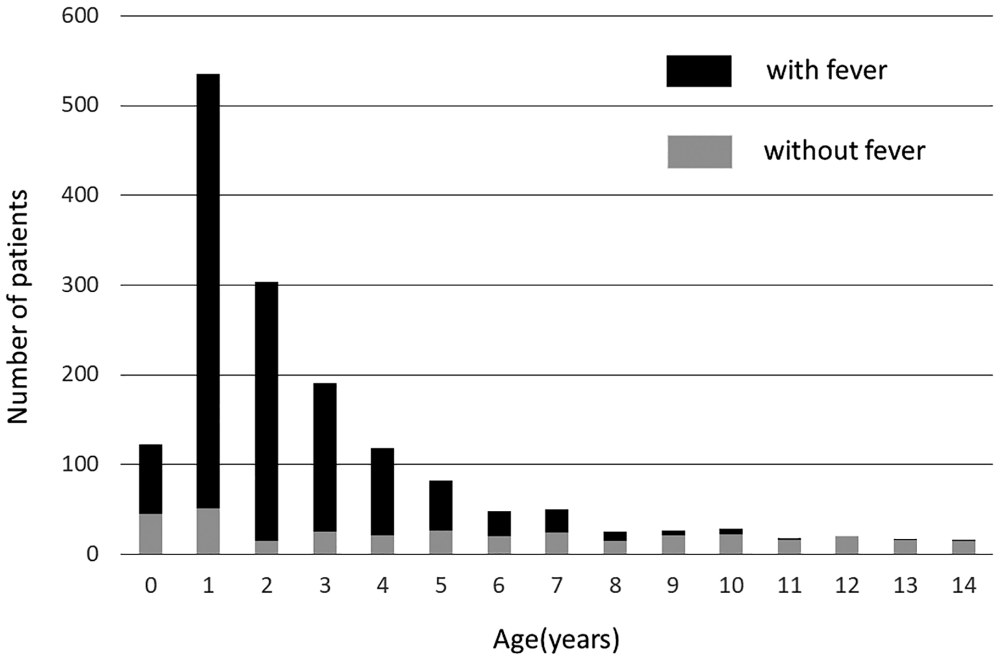

Fig. 1　Age distribution of children with seizures

The number of seizure patients in 1-year age groups. Peaks of age at seizure onset are seen at 1 year in the fever and no fever groups. The number of seizure patients in the with fever group decreases with age, and there are few patients aged over 8 years. There are an almost even number of seizure patients from age 2 to 14 years in the no fever group.

Table 2 Final diagnosis of subjects

Final diagnosis	Total (N = 1600) n (%)	Fever (N = 1248) n (%)	Without fever (N = 352) n (%)
Febrile seizure	1228 (76.8)	1228 (98.4)	0
Simple	1042 (65.1)	1042 (83.5)	–
Complex	186 (11.6)	186 (14.9)	–
Epilepsy	282 (17.6)	18 (1.4)	264 (75.0)
CwG	41 (2.6)	0	41 (11.6)
Breath-holding spell	20 (1.2)	0	20 (5.7)
Acute encephalitis/encephalopathy	6 (0.4)	2 (0.2)	4 (1.1)
Brain tumor	3 (0.2)	0	3 (0.9)
Cerebrovascular disorder	1 (0.1)	0	1 (0.3)
Others†	19 (1.2)	0	19 (5.4)

† Others include hypoglycemia, hypocalcemia, after head injury, after suffocation, and neurally-mediated syncope.
CwG, benign convulsions with mild gastroenteritis.

The median seizure duration was 2 min, and 50 patients (3.2 %) were treated as status epilepticus. Additionally, 191 (11.9 %) patients experienced repeated seizures during the same episode. Although only 106 (6.4 %) patients were administered with acute anticonvulsant drugs to control seizures, suppository diazepam was used after seizures in 1241 (77.6 %) patients to prevent subsequent seizures. After emergency management at the emergency or pediatric department, 1297 (81.7 %) patients were not hospitalized, 280 (17.5 %) were hospitalized in our hospital, and 23 (1.4 %) were transferred to advanced hospitals with pediatric intensive care units.

Table 2 shows the final diagnoses of the patients. FS was the most common cause (76.8 %), followed by epilepsy (17.6 %) and benign CwG (2.6 %). FS accounted for 98.4 % of cases with fever, whereas epilepsy accounted for 75 % of cases without fever. Among the 1228 cases with FS, 186 (15.1 %) showed complex FS patterns. Six cases (0.3 %) were diagnosed with acute encephalitis/encephalopathy **(Table 3)**; of these, only two cases diagnosed as mildly encephalitic/encephalopathic with reversible splenial lesion (MERS) presented with fever, and no cases presented with status epilepticus. However, five of the six patients showed repeated seizures, and all experienced impaired consciousness. Furthermore, magnetic resonance imaging (MRI) showed significant findings in three cases, leading to diagnoses. In contrast to cases with acute encephalitis/encephalopathy, no meningitis case was detected. **Fig. 2** shows the number of patients according to the visit frequency across all patients and FS and/or other diagnoses ratio for each number of visits. In 1600 cases, 1063 patients visited once owing to seizures. However, 222 patients visited multiple times (maximum seven). Although FS occurred majorly in patients who only visited once, the incidence of epilepsy among seizures increased in patients who visited multiple times, especially in those who visited ≥ 3 times. **Table 4** shows the demographic and clinical characteristics of FS in patients grouped according to whether they had developed epilepsy until at least 5 years of age; the target was patients born before December 31, 2014 (n = 926). Complex FS incidence was significantly higher in the group where FS later developed into epilepsy than in the group where FS did not develop into epilepsy ($p = 0.031$), whereas sex, age, body temperature, seizure duration, and seizure recurrence during the same episode were not significantly different between the two groups.

Table 5 shows a comparison of the clinical data of patients with FS and epilepsy with fever at visit. The median body temperature was significantly higher in the FS group (39.4 ℃ vs. 38.75 ℃, $p < 0.001$). In contrast, the median seizure age and the presence of past histry of seisures were significantly higher in the epilepsy group (25.0 months vs. 103.5 months,

Table 3　Detail of clinical data in 6 patients with encephalitis/encephalopathy

No.	Age	Sex	Fever	Duration of first seizure (minutes)	Number of seizures	Loss of consciousness at admission : GCS	CSF findings on admission	Brain MRI results	Final diagnosis	Past history
1	1y11m	M	+	1	13	E4V4M6	not examined	splenic lesion†	MERS	FS
2	3y8m	M	+	1	10	E4V4M6	normal	splenic lesion†	MERS	None
3	3y11m	M	−	2	3	E4V4M5	not examined	bright tree appearance in white matter	AESD	FS
4	5y6m	F	−	1	1	E4V4M5	normal	normal	unclassified encephalopathy	acute encephalopathy
5	12y1m	F	−	1	3	E4V4M6	WBC 32/μL	normal	non-herpetic lymbic encephalitis	None
6	12y10m	M	−	1	6	E4V4M6	not examined	normal	non-herpetic lymbic encephalitis	FS

† high-signal-intensity on DWI in the midline of the splenium of the corpus callosum
y, years ; m, months ; GCS, Glasgow Coma Scale ; CSF, cerebral spinal fluid ; MRI, magnetic resonance imaging ; F, female ; M, male ; WBC, white blood cells ; DWI, diffusion-weighted images ; MERS, mild encephalitis/encephalopathy with a reversible splenial lesion ; AESD, acute encephalopathy with biphasic seizures and late reduced diffusion.

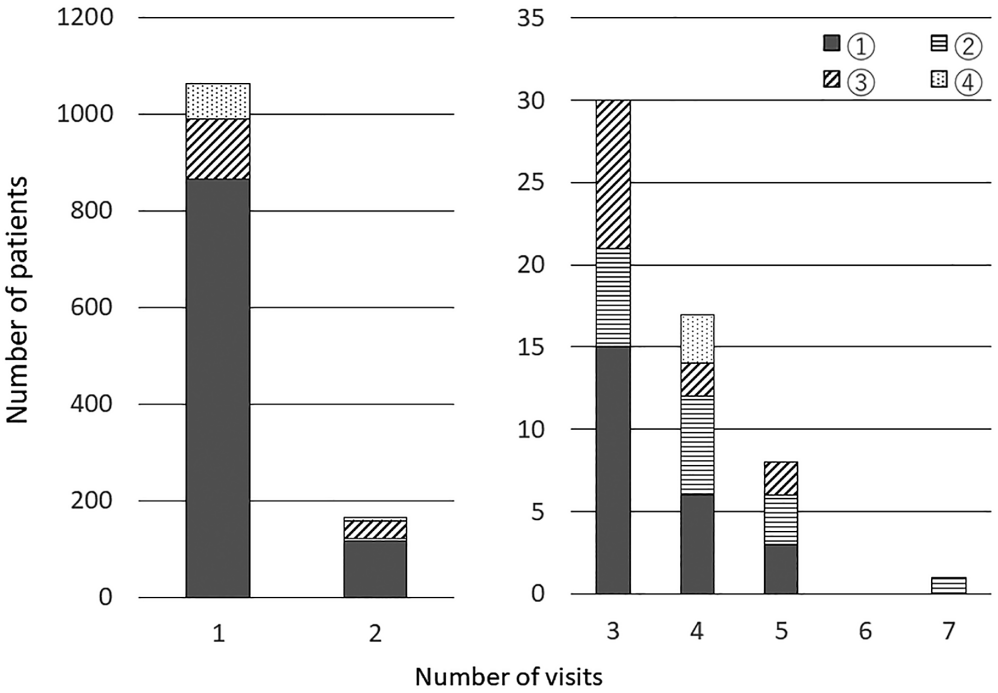

Fig. 2　Distribution of the number of visits and each diagnosis
The number of visits ranges from 1 to 7 times ; 1063 of 1285 patients visited our emergency room only once. In the image, ① indicates the group of febrile seizure diagnoses only, ② indicates the group of diagnoses of febrile seizure and epilepsy, ③ indicates the group of epilepsy diagnoses only, and ④ indicates the group of other diagnostic combinations.

Table 4　Clinical characteristics of patients with FS according to whether they exhibited or not epilepsy

	FS only (N＝902)	FS later developed epilepsy(N＝26)	*p*-value
Sex(male/female)	529/373	13/13	0.422
Body temperature at visit (℃), mean ± SD	39.34 ± 0.87	39.26 ± 0.74	0.670
Age at seizure (months), mean ± SD	34.78 ± 21.99	28.85 ± 15.85	0.172
Duration of seizure, minutes†	2.0 [1, 4]	2.5 [1, 5]	0.385
Recurrence of seizures during same episode‡	79 (8.8)	2 (7.7)	1.000
Complex FS‡	109 (12.1)	7 (26.9)	0.031

† median [25 %, 75 %], ‡ number (%), SD, standard deviation.

Table 5　Comparison between FS and epilepsy with fever at visit

	Febrile seizure (N＝1228)	Epilepsy (N＝18)	*p*-value
Body temperature at visit (℃), mean ± SD	39.37 ± 0.85	38.81 ± 0.57	0.005
Age at seizure (months), mean ± SD	31.63 ± 20.25	96.72 ± 41.99	＜0.001
Past history of seizures‡	380 (30.9)	17 (94.4)	＜0.001
Duration of seizure, minutes†	2 [1, 5]	3 [1, 5]	0.200
Recurrence of seizures during same episode‡	124 (10.1)	3 (16.7)	0.418
Use of anticonvulsants‡	30 (2.4)	2 (11.1)	0.076

† median [25 %, 75 %], ‡ number (%), SD, standard deviation.

Table 6　Comparison between epilepsy and acute encephalitis/encephalopathy without fever at visit

	Epilepsy (N＝264)	Acute encephalitis/encephlopathy (N＝4)	*p*
Age at seizure (months), mean ± SD	86.60 ± 50.76	103.00 ± 54.38	0.522
Past history of seizure‡	154 (58.3)	3 (75.0)	0.644
Duration of seizure, minutes†	3 [1, 5.5]	1 [1, 1.5]	0.138
Recurrence seizures during same episode‡	36 (13.6)	3 (75.0)	0.010
Use of anticonvulsants‡	30 (11.4)	1 (25.0)	0.390

† median [25 %, 75 %], ‡ number, (%), SD, standard deviation.

$p<0.001$; 94.4 % vs. 30.9 %, $p<0.001$, respectevely). However, the differences in the median seizure duration and proportion of cases with seizure recurrence during the same episode between the two groups were not statistically significant. **Table 6** presents a comparison of the clinical data of patients with epilepsy and acute encephalitis/encephalopathy without fever at visit. The recurrent seizure frequency during the same episode was higher in the acute encephalitis/encephalopathy group than in the epilepsy group (75 % vs. 13.6 %, $p=0.010$). The median seizure age, seizure duration, and anticonvulsant use did not reach statistical significance.

V　Discussion

We analyzed the characteristics of 1600 pediatric seizure cases admitted to the emergency and pediatric departments. To the best of our knowledge, no study has analyzed pediatric seizures using such a large number of cases over the past 10 years.

Overall, 1285 patients, representing 5.4 % of the population aged ＜15 years in our medical block

(Kami-Ina area, Nagano Prefecture), visited our hospital owing to seizures in 10 years, although this might be a little higher because of some patients who were treated by family physicians. Similar to previous reports, FS was the most frequent cause of seizures in patients admitted to the emergency and pediatric departments, accounting for a higher proportion of all seizures (76.8 %) in our study than in other studies. Studies conducted by Berksoy et al.[9], Abbasi et al.[10], and Ojha et al.[8] reported 38.5 %, 46.8 %, and 68.6 % of children with FS in Turkey, Pakistan, and Nepal, respectively. The high FS rate in our study may be because FS incidence is higher in East Asia, especially in Japan, than in European countries[2)-7)]. Consistent with previous findings that simple FS accounts for 80 %-85 % of FS[5)15)16)], approximately 85 % of FS were simple FS in our study. Furthermore, our data indicated that complex FS is associated with the risk of developing epilepsy later, consistent with previous findings[17)18)]. Additionally, epilepsy was the most frequent cause of seizures in cases without fever, which was according to previous findings[9]. However, our data showed that 17.3 % of patients visited multiple times who showed a higher chance of being diagnosed with epilepsy. These data are important for treating patients with a seizure history.

Notably, although FS accounted for 98.4 % of cases with fever, no case was diagnosed as meningitis. The wide use of *Haemophilus influenzae* type b (Hib) and pneumococcal conjugate vaccines since 2010 might have reduced the overall incidence of bacterial meningitis in Japan[19]. We encountered ≥ 10 meningitis cases, including several with acute purulent meningitis, during the cohort period, although seizure did not accompany any on admission. The American Academy of Pediatrics does not recommend performing routine evaluation with neuroimaging, electroencephalography, and electrolyte serum tests for simple FS[20]. Our data indicate that seizures are not necessarily essential symptoms directly leading to meningitis diagnosis by themselves when treating outpatient children with fever. However, six cases diagnosed as acute encephalitis/encephalopathy were detected among all our patients, wherein only two cases had fever, suggesting that acute encephalitis/encephalopathy cannot be ruled out even if fever is not followed by seizures. Although long-lasting seizures were not present in these six cases, seizures occurred ≥ thrice in five cases, and all patients showed mildly impaired consciousness. Nishiyama et al.[21] reported that 9.1 % of 120 status epilepticus cases had acute encephalitis/encephalopathy, and in Japan, status epilepticus is considered a risk factor associated with developing acute encephalitis/encephalopathy. Our results indicate that seizure recurrence, in addition to seizure duration, is also an important factor in patients with impaired consciousness for predicting acute encephalitis/encephalopathy and is an important factor for deciding whether to perform additional neurological tests, such as MRI and electroencephalography. We further analyzed several statistical differences to clarify the factors essential for distinguishing epilepsies from FS in cases with fever and found significant differences in body temperature, age, and history, whereas seizure duration and recurrence showed no significance. These findings indicate that patients with relatively low fever, older age, and past seizures are more likely to be diagnosed with epilepsy than FS. In contrast, in cases without fever, seizure recurrence during the same episode was more significant for distinguishing acute encephalitis/encephalopathy from epilepsy compared with age and history. These findings have never been reported previously and will greatly help in treating pediatric seizure patients.

Our study has some limitations, mainly due to its retrospective nature in a single institution. First, because most of the included children were lost to follow-up after their seizure episodes, their long-term prognosis was not fully evaluated. Epilepsy might develop in more children with seizures than reported here. Second, as not all patients underwent neuroimaging, electroencephalography, or lumbar punctures, some patients with clinically diagnosed FS might have had a mild central nervous system infection.

Taken together, our study showed that understanding the patient demographics and assessing patient backgrounds and clinical characteristics will help us to predict the cause of seizures for providing

more appropriate treatment and avoiding unnecessary examinations.

Ⅵ Conclusion

We evaluated seizures in a sizable number of children, revealing a higher rate of FS in cases with fever and epilepsy as the major cause of seizures in cases without fever. We also revealed several new findings. First, patients with complex FS or visited multiple times have a higher chance of being diagnosed with eplepsy. In adission, in the case of patients with fever, relatively low fever, older age, and past seizures are more likely to be diagnosed with eplilepsy than FS. Furthermore, in the case without fever, seizure recurrence during the same episode was more significant in acute encephalitis/encephalopathy as compared with eplilepsy.

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Approval of the research protocol : This study was approved by the institutional ethics committee of Ina Central Hospital (No. 20-21) on October 21, 2020, and was performed according to the ethical guidelines of the Declaration of Helsinki.

Informed consent : The institutional ethics committee of Ina Central Hospital waived informed consent because we collected and analyzed demographic and clinical data in an anonymized manner

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