



## Sudden unexpected death in epilepsy in the bathtub

Kino Hayashi <sup>a</sup>, Kazutaka Jin <sup>b,\*</sup>, Chizuko Nagamori <sup>c</sup>, Kazuo Okanari <sup>d</sup>, Tohru Okanishi <sup>e</sup>, Yoichiro Homma <sup>f</sup>, Yasushi Iimura <sup>c</sup>, Takehiro Uda <sup>c</sup>, Lynne Takada <sup>c</sup>, Hiroshi Otsubo <sup>c</sup>

<sup>a</sup> Tokyo Medical Examiner's Office, Tokyo, Japan

<sup>b</sup> Department of Epileptology, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan

<sup>c</sup> Division of Neurology, The Hospital for Sick Children, Toronto, Ontario, Canada

<sup>d</sup> Department of Pediatrics, Oita University Faculty of Medicine, Oita, Japan

<sup>e</sup> Department of Child Neurology, Seirei-Hamamatsu General Hospital, Hamamatsu, Shizuoka, Japan

<sup>f</sup> Department of General Internal Medicine, Seirei-Hamamatsu General Hospital, Hamamatsu, Shizuoka, Japan

### ARTICLE INFO

#### Article history:

Received 31 January 2019

Revised 8 April 2019

Accepted 8 April 2019

Available online 9 May 2019

#### Keywords:

Sudden unexpected death in epilepsy

Drowning

Bathtub

Autopsy

### ABSTRACT

**Objective:** Sudden death in the bathtub occurs relatively frequently in Japan, particularly among elderly people. We hypothesize that sudden death in epilepsy occurring in the bathtub (SDEPB) can be distinguished from sudden death in nonepilepsy occurring in the bathtub (SDnonEPB), but is identical to sudden unexpected death in epilepsy (SUDEP).

**Methods:** Tokyo Medical Examiner's Office conducts postmortem examinations for all sudden and unexpected deaths in Tokyo. Clinical, social, and autopsy findings of 43 SDEPB were compared with 76 SDnonEPB, 50 SUDEP outside the bathtub, and Japanese forensic autopsy data as controls.

**Results:** Extension of the leg(s) outside the bathtub was seen in 33% of SDEPB, but none of SDnonEPB. Sitting position was seen less frequently in SDEPB (37%) than in SDnonEPB (64%). Lung weight and pleural effusion volume were significantly lower in SDEPB than in SDnonEPB. Age at death in SDEPB was significantly younger than that in SDnonEPB. Sudden death in epilepsy occurring in the bathtub showed no differences in lung weight and pleural effusion volume from SUDEP. Living with family was more frequent in SDEPB (73%) than in SUDEP (48%). Few antiepileptic drugs, infrequent seizures, and low rate of mental retardation were identical between SDEPB and SUDEP. Lung weight was significantly heavier in all three groups than in age- and sex- matched autopsy controls.

**Conclusions:** Leg extension outside the bathtub, lower lung weight, and absence of pleural effusion distinguish SDEPB from SDnonEPB in elderly people. Sudden death in epilepsy occurring in the bathtub may represent a form of SUDEP occurring in the bathtub, rather than drowning despite submergence in the bathtub at discovery. Conditions for bathing require careful attention from physicians and relatives, even for patients with epilepsy with few medications and infrequent seizures, and without mental retardation.

© 2019 Elsevier Inc. All rights reserved.

### 1. Introduction

The incidence of sudden unexpected death in epilepsy (SUDEP) in young adults (aged 20–45 years) is 27 times higher than that of sudden death in control populations [1]; SUDEP is a leading cause of death in the population with epilepsy. A systematic international survey of cardiorespiratory arrests in epilepsy monitoring units revealed physiological characteristics suggestive of SUDEP in 16 cases, although the primary

cause of SUDEP was not found [2]; SUDEP in epilepsy monitoring units primarily resulted from early postictal neurovegetative breakdown induced by generalized tonic-clonic seizures (GTCs) in all 16 cases. The GTCs lead to immediate death or a short period of partly restored cardiorespiratory function followed by terminal apnea and then cardiac arrest. A history of primary or secondary GTCs is the strongest risk factor for SUDEP, but other risk factors have also been reported [3,4].

Drowning is considered to be one of the exclusion criteria for SUDEP [5]. Death by drowning in bathtubs, swimming pools, hot tubs, and natural waters occurs frequently in patients with epilepsy [6]. Patients with epilepsy found dead submersed in bathtub water are considered to have died of drowning, so never lead to a diagnosis of SUDEP. A few recent reports describe sudden death in epilepsy occurring in the bathtub (SDEPB). Sixteen (10%) of 167 definite SUDEPs occurred in a bathroom, which included death while showering as well as soaking in a bathtub,

*Abbreviations:* GTCs, generalized tonic-clonic seizure; PGES, postictal generalized electroencephalographic suppression; SD, standard deviation; SDEPB, sudden death in epilepsy occurring in the bathtub; SDnonEPB, sudden death in nonepilepsy occurring in the bathtub; SUDEP, sudden unexpected death in epilepsy.

\* Corresponding author at: Department of Epileptology, Tohoku University Graduate School of Medicine, 2-1 Seiryomachi, Aoba-ku, Sendai, Miyagi 980-8575, Japan.

E-mail address: [jink@med.tohoku.ac.jp](mailto:jink@med.tohoku.ac.jp) (K. Jin).

in a nationwide population-based case series [7]. No autopsy findings were found to distinguish between 47 epilepsy-related drowning deaths, 72% of which occurred in a bathtub, and 92 SUDEP [8]. However, the diagnosis of SDEPB is still ambiguous and whether SDEPB is drowning or SUDEP is often difficult to determine.

The Japanese love to bathe in bathtubs filled with enough water to cover the entire body. A survey of Japanese undergoing routine medical checkups found that 401 (65%) of 617 individuals bathed in a bathtub seven or more times a week [9]. The Japanese take baths more frequently in the winter than in other seasons, because of the cold climate. However, such winter bathing can increase the risks of physiological changes associated with sudden death in the elderly population [10]. The Tokyo Medical Examiner's Office reported 550 autopsied cases of sudden bath-related deaths [11]. The major pathological findings were circulatory system diseases in 300 (55%) cases. These results suggest that drowning is important in the final cause of bath-related death, although circulatory system diseases may be the primary underlying pathology.

To clarify whether SDEPB is drowning or an overlapping entity of SUDEP, we compared clinical, social, and autopsy findings of SDEPB, with those of sudden death in nonepilepsy occurring in the bathtub (SDnonEPB) and SUDEP outside the bathtub. We hypothesize that SDEPB could be distinguished from drowning deaths in the bathtub, and so diagnosed as SUDEP in the bathtub.

## 2. Methods

### 2.1. Tokyo Medical Examiner's Office

Tokyo Medical Examiner's Office is a similar organization to the coroner system of the United States. Police officers investigate all cases of unexpected and unnatural deaths, and then they request a medical examiner to inspect the body to determine the cause of the death except in criminal cases. An inspection team is dispatched to the location of the body, such as a police station, hospital, or residence of the deceased. The inspection team conducts an external examination of the body with the assistance of the police officers who provide investigative information. If the cause of death cannot be determined by external examination, the body is transported to the Medical Examiner's Office for autopsy.

The autopsy international code (ICD-10) for diseases and crimes has been applied at the Tokyo Medical Examiner's Office since 1995. The present study examined 364 consecutive cases with the epilepsy code (G40.0–47.9) among 245,591 cases classified with ICD-10 between 1995 and 2015.

We analyzed the autopsy cases among the 364 cases with the epilepsy code. The first group consisted of patients with epilepsy who suffered sudden death in a bathtub filled with water, defined as the SDEPB group. The second group consisted of patients with epilepsy who suffered definite SUDEP outside the bathtub, as the SUDEP group. We excluded cases of SUDEP during showering in the bathroom. The third group consisted of people without epilepsy who suffered sudden death in a bathtub filled with water and underwent autopsy by a medical examiner (KH) between 2009 and 2017, as the SDnonEPB group. We excluded cases with evidence of high ethanol level for this study.

### 2.2. Standard protocol approval, registration, and patient consent

The institutional review boards of Tokyo Medical Examiner's Office approved this retrospective study. Opt-out consent of the bereaved family was obtained in this study, because all target patients were dead.

### 2.3. Part 1

Age at death, sex, posture at death, living situation ( $\geq 18$  years old), season at death, frequency of bathing, and bathing time at death were compared between SDEPB and SDnonEPB. Body height, body weight,

and weights of the heart and lungs obtained from the autopsy findings were compared between the two groups, using the standardized score of each variable based on a score of 50 representing the mean for the age- and sex-standardized autopsy control group (see part 2.5 for details) [12]. We also compared the volume of pleural effusion between the two groups.

### 2.4. Part 2

Age at death, sex, posture at death, living situation ( $\geq 18$  years old), season at death, and presence of tongue bites and convulsive seizures found by witnesses were compared between SDEPB and SUDEP. Body height, body weight, and weights of the heart and lungs obtained from the autopsy findings were compared between the two groups, using the standardized score of each variable based on a score of 50 representing the mean for the age- and sex-standardized autopsy control group (see part 2.5 for details) [12]. Volume of pleural effusion was also compared between the two groups. History of epilepsy, number of antiepileptic drugs, seizure type, seizure frequency, and presence of mental retardation were compared between the two epilepsy groups.

### 2.5. Statistical analysis

The chi-square independence test, Fisher exact probability test, Student *t*-test, Welch *t*-test, and Mann–Whitney *U* test were used to analyze each category, as appropriate (BellCurve for Excel version 2.00; Social Survey Research Information Co., Ltd. and R version 3.3.2). Unknown data were excluded from the statistical analysis. Residual analysis was performed on the factors with significant difference after the chi-square test. The significance level was set at  $<0.05$ . To standardize the autopsy findings in each group, appropriate data of the mean and standard deviation (SD) were obtained from more than 6000 forensic autopsy cases as a normal control, excluding cases of edema, injury, and decomposition in Japan between 2009 and 2013 [12]. The standardized score of the autopsy findings in each group was based on a score of 50 representing the mean for the age- and sex-standardized autopsy control group. The Student *t*-test was applied to compare the standardized score of the three groups with that of normal control data. The standardized score of weight of both lungs was calculated from the root mean square of the left and right lung standardized score. The post-mortem time in the three groups was analyzed with one-way analysis of variance. The Welch *t*-test was applied to compare the raw data of pleural effusion volume.

## 3. Results

### 3.1. Part 1. Sudden death occurring in the bathtub: comparison between epilepsy (SDEPB) and nonepilepsy (SDnonEPB)

#### 3.1.1. Clinical characteristics (Table 1A)

Age at death was significantly younger in the SDEPB group (mean  $\pm$  SD,  $42 \pm 18$  years) than in the SDnonEPB group ( $74 \pm 11$  years) ( $p = 0.011$ ) (Fig. 1). There was no sex difference. All patients in both the SDEPB and SDnonEPB groups had the face submersed in the bathtub.

Posture at death showed a significant difference between the SDEPB and SDnonEPB groups ( $p < 0.01$ ). Leg extension outside the bathtub along with the face and upper body in the bathtub was seen in 14 (33%) of 43 cases in the SDEPB group (Fig. 2), but in none of the 76 cases in the SDnonEPB group. Sitting position was more common in the SDnonEPB group (49, 64%) than in the SDEPB group (16, 37%).

Comparison of living situations of patients aged 18 years or over between 41 SDEPB and 76 SDnonEPB found no significant difference. There was no difference in season at death. However, both SDEPB (17, 40%) and SDnonEPB (35, 46%) occurred most frequently in the winter season.

**Table 1A**  
Comparison of clinical characteristics between sudden death in epilepsy occurring in the bathtub (SDEPB) and sudden death in nonepilepsy occurring in the bathtub (SDnonEPB).

	SDEPB (N = 43)	SDnonEPB (N = 76)	p-Value
Age at death (years)			0.011
Mean $\pm$ SD	42 $\pm$ 18	74 $\pm$ 11▲	
Sex			0.070
Male	21 (49)	50 (65)	
Female	22 (51)	26 (34)	
Posture at death in the bathtub			<0.01
Extension of leg(s) outside the bathtub	14 (33)▲	0 (0)	
Sitting	16 (37)	49 (64)▲	
Supine	3 (7)	6 (8)	
Lateral	2 (5)	10 (13)	
Prone	6 (14)	7 (9)	
Unknown	2 (5)	4 (5)	
Living situation (>18 years) <sup>a</sup>	N = 41		0.297
One-person household	8 (20)	23 (30)	
With family	30 (73)	53 (70)	
Unknown	3 (7)	0 (0)	
Season at death			0.839
Spring	12 (28)	22 (29)	
Summer	8 (19)	11 (14)	
Autumn	6 (14)	8 (11)	
Winter	17 (40)	35 (46)	
Frequency of bathing			0.602
Everyday	35 (81)	52 (68)	
Few days a week	0 (0)	1 (1)	
Unknown	8 (19)	23 (30)	
Bathing time at death			0.677
24:00–3:00	12 (28)	19 (25)	
3:00–7:00	2 (5)	4 (5)	
7:00–12:00	2 (5)	6 (8)	
12:00–16:00	4 (9)	3 (4)	
16:00–19:00	4 (7)	11 (14)	
19:00–24:00	19 (44)	24 (32)	
Unknown	0 (0)	9 (12)	

Data are numbers of patients (%).

<sup>a</sup> Two patients in SDEPB aged under 18 years old were excluded.

Most patients in both the SDEPB (35, 81%) and SDnonEPB (52, 68%) groups took baths every day. The bathing time at death showed no difference between the two groups. The most common bathing time was 19:00–24:00 before sleep.

### 3.1.2. Autopsy findings (Table 1B)

Postmortem time showed no significant difference between the SDEPB (mean  $\pm$  SD, 34.7  $\pm$  24.5 h) and SDnonEPB (29.2  $\pm$  25.6 h) groups. Body height and weight and weight of heart also showed no significant difference. Structural heart diseases including coronary sclerosis with more than 75% stenosis, old myocardial infarction, and hypertensive cardiomyopathy were seen in 2 (5%) out of 43 SDEPB and 18 (24%) out of 76 SDnonEPB.

The standardized score of lung weight of the SDEPB group (mean  $\pm$  SD, 57.7  $\pm$  11) was significantly lower than that of the SDnonEPB group (64.7  $\pm$  15.5), based on the autopsy control data ( $p = 0.010$ ). Real lung weight showed no difference between 41 SDEPB (mean  $\pm$  SD, 1120.9  $\pm$  294.4 g) and 76 SDnonEPB patients (1199.8  $\pm$  369.1 g) over 18 years old without standardization of age and sex.

The volume of pleural effusion in the SDEPB group (mean  $\pm$  SD, 56.4  $\pm$  90.3 mL) was significantly less than that in the SDnonEPB group (121.1  $\pm$  163.4 mL) ( $p < 0.01$ ). No pleural effusion was confirmed in 10 (23.2%) of 43 SDEPB and seven (9.2%) of 76 SDnonEPB (Fig. 1). The volume of pleural effusion showed significant correlation with the weight of the lungs in both the SDEPB (RS = 0.648;  $p < 0.01$ ) and SDnonEPB (RS = 0.338;  $p < 0.01$ ) groups. Structural lung diseases including emphysema, pleural adhesions due to pleuritis, and

interstitial pneumonia were seen in 2 (5%) out of 43 SDEPB and 14 (18%) out of 76 SDnonEPB.

### 3.2. Part 2. Sudden death of patients with epilepsy: comparison between death in the bathtub (SDEPB) and outside the bathtub (SUDEP)

#### 3.2.1. Clinical characteristics (Table 2A)

Age at death in the SDEPB group (mean  $\pm$  SD, 42  $\pm$  18 years) was significantly older than in the SUDEP group (35  $\pm$  18 years) ( $p = 0.044$ ). There was no sex difference.

Posture at death showed a significant difference between the SDEPB and SUDEP groups ( $p < 0.01$ ). Prone position was more common in the SUDEP group (26, 52%) than in the SDEPB group (6, 14%). Supine position was also more common in the SUDEP group (16, 32%) than in the SDEPB group (3, 7%).

Comparison of living situations of patients aged 18 years or over between 41 SDEPB and 41 SUDEP showed a significant difference between the SDEPB and SUDEP groups ( $p = 0.016$ ). The rate of one-person households in the SUDEP group (18/41, 44%) was significantly higher than that in the SDEPB group (8/41, 20%). The rate of living with family in the SDEPB group (30/41, 73%) was significantly higher than in the SUDEP group (20/41, 49%).

Season at death showed no significant difference between the two groups. However, the most common season at death was winter in SDEPB (17, 40%) and summer in SUDEP (17, 34%).

Tongue bites were found in three (7%) of 43 SDEPB and in seven (14%) of 50 SUDEP. The witnesses reported convulsive seizures at the time of death in three (6%) of 50 SUDEP.

#### 3.2.2. Autopsy findings (Table 2B)

Postmortem time showed no difference between the SDEPB (mean  $\pm$  SD, 34.7  $\pm$  24.5 h) and SUDEP (39.3  $\pm$  24.6 h) groups. Body height and weight and weight of heart also showed no significant difference. Structural heart diseases including coronary sclerosis with more than 75% stenosis, old myocardial infarction, and hypertensive cardiomyopathy were seen in 2 (5%) out of 43 SDEPB and 1 (3%) out of 39 SUDEP.

The standardized score of lung weight showed no difference between the SDEPB (mean  $\pm$  SD, 57.7  $\pm$  11) and SUDEP (55.7  $\pm$  14.2) groups for all ages, based on the autopsy control data. Real lung weight showed no difference between 41 SDEPB (mean  $\pm$  SD, 1120.9  $\pm$  294.4 g) and 41 SUDEP (1184.6  $\pm$  350.9 g) over 18 years without standardization of age and sex.

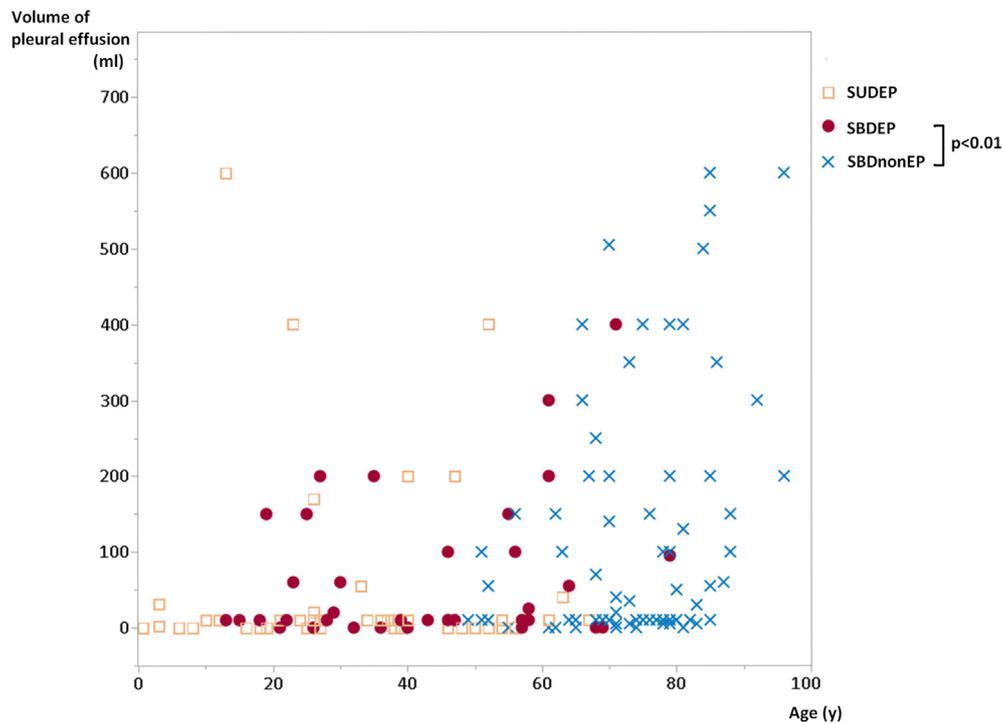
Pleural effusion volume showed no difference between SDEPB (mean  $\pm$  SD, 56.4  $\pm$  90.3 mL) and SUDEP (45.7  $\pm$  117.5 mL). No pleural effusion was confirmed in 10 (23.2%) SDEPB and 16 (32%) SUDEP (Fig. 1). Structural lung diseases including emphysema, pleural adhesions due to pleuritis, and interstitial pneumonia were seen in 2 (5%) out of 43 SDEPB and 1 (3%) out of 39 SUDEP.

#### 3.2.3. Epilepsy profiles (Table 2C)

Epilepsy profiles showed no difference between the SDEPB and SUDEP groups, except for seizure types based on history taken from their families ( $p < 0.01$ ). Five (12%) of 43 SDEPB patients had absence or myoclonic seizures, compared to none of the SUDEP patients. Six (14%) of 43 SDEPB and six (12%) of 50 SUDEP patients took no medication. Eighteen (42%) of SDEPB and 22 (44%) of SUDEP patients had received antiepileptic drug monotherapy. Approximately half of both SDEPB (22, 51%) and SUDEP (26, 52%) patients had seizures less than once a month. Mental retardation was seen in 5 (12%) of SDEPB and 10 (20%) of SUDEP patients.

### 3.3. Part 3. Comparison to the Japanese autopsy controls

The SDnonEPB patients had significantly taller ( $p < 0.01$ ) and heavier ( $p = 0.013$ ) bodies than the Japanese autopsy controls. The SUDEP



**Fig. 1.** Age at death and volume of pleural effusion in the SDEPB, SDnonEPB, and SUDEP groups. Age at death was significantly younger in the SDEPB group (mean  $\pm$  SD, 42  $\pm$  18 years) than in the SDnonEPB group (74  $\pm$  11 years ( $p < 0.01$ )). Age at death in the SDEPB group was significantly older than in the SUDEP group (35  $\pm$  18 years) ( $p = 0.044$ ). The volume of pleural effusion in the SDEPB group (mean  $\pm$  SD, 56.4  $\pm$  90.3 mL) was significantly less than that in the SDnonEPB group (121.1  $\pm$  163.4 mL) ( $p < 0.01$ ). No pleural effusion was confirmed in 10 (23.2%) of 43 SDEPB and seven (9.2%) of 76 SDnonEPB. Volume of pleural effusion showed no difference between SDEPB (56.4  $\pm$  90.3 mL) and SUDEP (45.7  $\pm$  117.5 mL). No pleural effusion was confirmed in 10 (23.2%) SDEPB and 16 (32%) SUDEP. SDEPB = sudden death in epilepsy occurring in the bathtub; SDnonEPB = sudden death in nonepilepsy occurring in the bathtub; SUDEP = sudden unexpected death in epilepsy outside the bathtub.

patients had significantly shorter bodies than the controls ( $p < 0.01$ ). The heart was significantly heavier in the SDEPB than in the controls ( $p = 0.041$ ). All three groups had significantly heavier lungs than the controls ( $p < 0.01$ ).

#### 3.4. Part 4. Comparison between patients with and without leg extension outside the bathtub in sudden death in epilepsy occurring in the bathtub (SDEPB) (Table 3)

Fourteen (33%) of 43 SDEPB patients were found supine with leg extension outside the bathtub. The body height of these 14 patients (mean  $\pm$  SD, 168.6  $\pm$  10.8 cm) was taller than that of 28 patients without leg extension (160.6  $\pm$  30.4 cm) ( $p = 0.029$ ). Other clinical characteristics, autopsy findings, and epilepsy profiles showed no significant differences between the two groups of SDEPB with and without leg extension.

## 4. Discussion

### 4.1. Summary of findings

The age at death in SDEPB was significantly younger than that in SDnonEPB. All patients in both the SDEPB and SDnonEPB groups had the face submersed in the bathtub. Extension of the leg(s) outside the bathtub was seen in 33% of SDEPB, but none of SDnonEPB. Sitting position was seen less frequently in SDEPB (37%) than in SDnonEPB (64%). The lung weight and pleural effusion were significantly lower in SDEPB than in SDnonEPB. Living with family was more frequent in SDEPB (73%) than in SUDEP (48%). Compared with SUDEP, SDEPB showed no differences in the lung weight and pleural effusion. Few anti-epileptic drugs, infrequent seizures, and low rate of mental retardations were identical between SDEPB and SUDEP. Lung weights were

significantly heavier in all three groups than in age- and sex-matched autopsy controls.

### 4.2. Extension of the leg(s) outside the bathtub

Extension of the leg(s) outside the bathtub was a unique posture seen in SDEPB, but never seen in SDnonEPB in this study. The most common posture in SDnonEPB was sitting position. Leg extension is considered to be part of the semiology of GTCs. Both leg extensions could be a part of symmetric tonic extension postures. In 40 children with generalized convulsive seizures, ictal symmetric tonic extension postures significantly increased the odds of postictal generalized electroencephalographic suppression (PGES) [13]. Ictal decerebrate-like symmetric tonic extension posture with shorter clonic phase and a terminal burst-suppression pattern indicate malignant generalized convulsive seizures, associated with PGES. In 69 of 99 generalized convulsive seizures in adult patients, typical GTCs with bilateral and symmetric tonic arm extension at the onset were significantly associated with PGES [14]. Postictal generalized electroencephalographic suppression was observed in all 16 patients who were with diagnosed definite SUDEP during long-term video-electroencephalographic monitoring [2].

Leg extension outside the bathtub associated with SDEPB is considered to be a feature of GTCs. If patient with epilepsy is found dead with the leg(s) extending outside the bathtub, the patient presumably had GTCs preceding sudden death during bathing.

The epidemiological study found that 120 of 195 households in Japan had narrower and deeper bathtub sizes (depth 60 cm, length 80–120 cm) than the recommended size for safety [15]. Japanese bathtubs are not designed for washing the body with soap, nor for bubble baths as in western culture, but are narrow



**Fig. 2.** Illustration of sudden unexpected death in epilepsy (SUDEP) in the bathtub. This illustration was drawn from the sketch by a medical examiner of Tokyo Medical Examiner's Office. The patient was found extending the right arm and both legs outside the bathtub while the face was submerged in the filled water of the bathtub. Illustrated by Mr. Mitsuru Satomi and Mr. Kotobuki Shiriagari.

and deep, and filled to the top with plenty of water to soak the whole body. The sitting position in SDnonEPB is a Japanese standard position of bathing.

#### 4.3. Drowning vs. SUDEP

Lung weight and volume of pleural effusion in the SDEPB group were significantly lower than those in the SDnonEPB group, but similar to

**Table 1B**

Autopsy findings between sudden death in epilepsy occurring in the bathtub (SDEPB) and sudden death in nonepilepsy occurring in the bathtub (SDnonEPB) (comparison to age and sex standardized autopsy control group) (mean = 50).

	SDEPB (N = 43)	SDnonEPB (N = 76)	p-Value
Body height <sup>a</sup>	N = 42		0.069
Mean ± SD	50.5 ± 11.5	54.1 ± 9.6	
Body weight			0.94
Mean ± SD	52.7 ± 10.5	52.9 ± 9.3	
Weight of heart			0.64
Mean ± SD	53.1 ± 9.5	52.1 ± 11.9	
Weight of lungs			0.01
Mean ± SD	57.7 ± 11	64.7 ± 15.5▲	
Volume of pleural effusion (mL) <sup>b</sup>			<0.01
Mean ± SD	56.4 ± 90.3	121.1 ± 163.4▲	

<sup>a</sup> Body height was not specified for one patient in SDEPB.

<sup>b</sup> Pleural effusion was exact volume.

**Table 2A**

Clinical characteristics between sudden death in epilepsy occurring in the bathtub (SDEPB) and sudden unexpected death in epilepsy (SUDEP) outside the bathtub.

	SDEPB (N = 43)	SUDEP (N = 50)	p-Value
Age at death (years)			0.044
Mean ± SD	42 ± 18 ▲	35 ± 18	
Sex			0.377
Male	21 (49)	29 (57)	
Female	22 (51)	21 (42)	
Posture at death			<0.01
Extension of leg(s) outside the bathtub	14 (33) ▲	0 (0)	
Sitting	16 (37) ▲	7 (14)	
Supine	3 (7)	16 (32) ▲	
Lateral	2 (5)	1 (2)	
Prone	6 (14)	26 (52) ▲	
Unknown	2 (5)	0 (0)	
Living situation (>18 years) <sup>a</sup>	N = 41	N = 41	0.016
One-person household	8 (20)	18 (44) ▲	
With family	30 (73) ▲	20 (49)	
Unknown	3 (7)	3 (7)	
Season at death			0.0813
Spring	12 (28)	13 (26)	
Summer	8 (19)	17 (34)	
Autumn	6 (14)	11 (22)	
Winter	17 (40)	9 (18)	
Tongue bites	3 (7)	7 (14)	0.227
Convulsive seizures found by witness	0 (0)	3 (6)	0.151

Data are numbers of patients (%).

<sup>a</sup> Two patients in SDEPB and 9 patients in SUDEP aged under 18 years were excluded.

those in the SUDEP group. The comparisons of lung weight were performed with the standardized scores using the age- and sex-matched autopsy control data, because the ages were significantly different between three groups.

Lung weight and volume of pleural effusion are basically increased in drowning cases, although a longer time interval in the water results in decreased lung weight and increased volume of pleural effusion [16]. Postmortem time showed no significant difference between the SDEPB and SDnonEPB groups. In Japan, SDnonEPB was frequently seen in the elderly group older than 65 years [11]. Most Japanese elderly people are shorter and smaller than young people. Even the real lung weight was similar between SDEPB and SDnonEPB, but the standardized data showed heavier lung weights in the elderly SDnonEPB group due to drowning than in the young SDEPB. Drowning was strongly associated with the final process of SDnonEPB, although cardiac lesions were the most common pathological findings that may have contributed significantly to death [11]. The present results suggest no aspiration of water before SDEPB, regardless of the location of the body in water. Analysis of the classification of SUDEP cases based on a review of

**Table 2B**

Autopsy findings between sudden death in epilepsy occurring in the bathtub (SDEPB) and sudden unexpected death in epilepsy (SUDEP) outside the bathtub (comparison to age and sex-standardized autopsy control group) (mean = 50).

	SDEPB (N = 43)	SUDEP (N = 50)	p-Value
Body height <sup>a</sup>	N = 42		0.15
Mean ± SD	50.5 ± 11.5	46.2 ± 16.1	
Body weight			0.63
Mean ± SD	52.7 ± 10.5	51.3 ± 16.3	
Weight of heart			0.11
Mean ± SD	53.1 ± 9.5	49.2 ± 13.7	
Weight of lungs			0.47
Mean ± SD	57.7 ± 11	55.7 ± 14.2	
Volume of pleural effusion (ml) <sup>b</sup>			0.62
Mean ± SD	56.4 ± 90.3	45.7 ± 117.5	

<sup>a</sup> Body height was not specified for one patient in SDEPB.

<sup>b</sup> Pleural effusion was exact volume.

**Table 2C**

Epilepsy profiles between sudden death in epilepsy occurring in the bathtub (SDEPB) and sudden unexpected death in epilepsy (SUDEP) outside the bathtub.

	SDEPB (N = 43)	SUDEP (N = 50)	p-Value
History of epilepsy (years), mean ± SD	18 ± 15	15 ± 13	0.299
<10	16 (37)	20 (40)	
11–20	10 (23)	14 (28)	
21–30	4 (9)	5 (10)	
31–40	6 (14)	4 (8)	
41–50	0 (0)	2 (4)	
>50	2 (5)	0 (0)	
Unknown	5 (12)	5 (10)	
Number of antiepileptic drugs, mean ± SD	1.3 ± 0.9	1.4 ± 0.9	0.802
0	6 (14)	6 (14)	
1	18 (42)	22 (44)	
2	10 (23)	14 (28)	
3	4 (9)	3 (6)	
4	0 (0)	1 (2)	
5	0 (0)	0 (0)	
Unknown	5 (12)	4 (8)	
Seizure type			<0.01
Generalized convulsive seizure	6 (14)	15 (30)	
Absence/myoclonic seizure	5 (12) ▲	0 (0)	
Focal seizure	10 (23)	23 (46)	
Others	2 (5)	0 (0)	
Unknown	20 (47) <sup>a</sup>	12 (24)	
Seizure frequency			0.318
Daily, ≥1/day	1 (2)	2 (4)	
Weekly, 1–6/week	0 (0)	4 (8)	
Monthly, 1–3/month	6 (14)	7 (14)	
Yearly, ≤11/year	22 (51)	26 (52)	
Unknown	14 (33)	11 (22)	
Mental retardation			0.255
Yes	5 (12)	10 (20)	
No	38 (88)	39 (78)	
Unknown	0 (0)	1 (2)	

<sup>a</sup> Sixteen (80%) of the 20 SDEPB with unknown seizure type were taking antiepileptic drugs, which confirmed the diagnosis of epilepsy.

>1500 epilepsy deaths revealed ambiguities [17]. The significant lower lung weight and volume of pleural effusion in SDEPB than SDnonEPB suggest that SDEPB was not caused by drowning.

In addition, the lung weights and volume of pleural effusion in SDEPB were identical to those in SUDEP outside the bathtub. Age- and sex-matched standardized scores of lung weight were used in the SDEPB and SUDEP groups, because the age at SUDEP was younger than at SDEPB. Therefore, the autopsy findings of lower lung weight and pleural effusion volume support the diagnosis of SUDEP in a bathtub rather than drowning death in a bathtub.

Suffocation followed by respiratory arrest is one of the mechanisms of SUDEP [18]. If a patient with epilepsy suffocates because of GTCs in the bathtub, the patient may not aspirate water even with the face submerged in the water. Sudden death occurring in the bathtub in epilepsy may be identical to SUDEP in the bathtub, but not to drowning in the bathtub.

On the other hand, patients could have died of drowning in the bathtub in the postictal state, when water inhalation might be less likely to occur due to impaired respiration/consciousness. This alternate explanation may also be compatible with the lower lung weight and volume of pleural effusion observed in SDEPB. Respiration/consciousness has never been evaluated if the patient had the seizure before death. However, seizures could have caused submersion of the face into water followed by death of drowning during the postictal state.

The SDEPB, SDnonEPB, and SUDEP groups had significantly heavier lungs than the controls. The higher lung weight of SUDEP can be explained by the presence of neurogenic pulmonary edema [19]. Lung weight showed no difference between the SDEPB and SUDEP groups. The higher lung weight of SDEPB can be caused by the same mechanism as SUDEP, even in the water of the bathtub.

**Table 3**

Clinical characteristics of patients with and without leg extension in sudden death in epilepsy occurring in the bathtub (SDEPB).

	Leg extension (N = 14)	No leg extension (N = 29)	p-Value
Age at death (years)			0.266
Mean ± SD	38 ± 14	44 ± 19	
Sex			0.232
Male	9 (64)	13 (45)	
Female	5 (36)	16 (55)	
Living situation (>18 years) <sup>a</sup>		N = 27	0.257
One-person household	4 (29)	4 (15)	
With family	9 (64)	21 (78)	
Unknown	1 (7)	2 (7)	
Bathing time at death			0.526
24:00–3:00	1 (7)	10 (34)	
3:00–7:00	1 (7)	1 (3)	
7:00–12:00	1 (7)	1 (3)	
12:00–16:00	2 (14)	2 (7)	
16:00–19:00	1 (7)	2 (7)	
19:00–24:00	8 (57)	13 (45)	
Unknown	0 (0)	0 (0)	
Tongue bites	1 (7)	2 (7)	0.704
Body height (cm) <sup>b</sup>		N = 28	0.029
Mean ± SD	168.6 ± 10.8 ▲	160.6 ± 30.4	
Body weight (kg)			0.276
Mean ± SD	62.6 ± 14.9	57.5 ± 10.7	
Weight of heart (g)			0.577
Mean ± SD	338.5 ± 77.3	324.7 ± 61.7	
Weight of lungs (g)			0.576
Mean ± SD	(left) 556.7 ± 156.4 (right) 598.6 ± 141.3	512.6 ± 134.7 587.9 ± 59.1	
Volume of pleural effusion (mL)			0.891
Mean ± SD	(left) 26.4 ± 34.2 (right) 27.5 ± 33.7	26.0 ± 48.9 31.6 ± 51.3	
History of epilepsy (years), mean ± SD	15 ± 12	20 ± 16	0.210
<10	8 (57)	8 (28)	
11–20	2 (14)	8 (28)	
21–30	0 (0)	4 (14)	
31–40	3 (21)	2 (7)	
41–50	0 (0)	1 (3)	
>50	0 (0)	2 (7)	
Unknown	1 (7)	4 (14)	
Number of antiepileptic drugs, mean ± SD	1.2 ± 0.7	1.4 ± 1.0	0.644
0	2 (14)	4 (14)	
1	6 (43)	12 (41)	
2	5 (36)	5 (17)	
3	0 (0)	4 (14)	
4	0 (0)	0 (0)	
5	0 (0)	0 (0)	
Unknown	1 (7)	4 (14)	
Seizure type			0.662
Generalized convulsive seizure	2 (14)	4 (14)	
Absence/myoclonic seizure	1 (7)	4 (14)	
Focal seizure	4 (29)	6 (21)	
Others	0 (0)	2 (7)	
Unknown	7 (50)	13 (45)	
Seizure frequency			0.096
Daily, ≥1/day	0 (0)	1 (3)	
Weekly, 1–6/week	0 (0)	0 (0)	
Monthly, 1–3/month	1 (7)	5 (17)	
Yearly, ≤11/year	11 (79)	11 (38)	
Unknown	2 (14)	12 (41)	
Mental retardation			0.469
Yes	1 (7)	4 (14)	
No	13 (93)	25 (86)	
Unknown	0 (0)	0 (0)	

Data are numbers of patients (%).

<sup>a</sup> Two patients without leg extension aged under 18 years were excluded.

<sup>b</sup> Body height was not specified for one patient without leg extension.

#### 4.4. Overweight hearts

Higher heart weight than the controls was found in the SDEPB group, but not in the SUDEP and SDnonEPB groups. Overweight heart was found in all 14 patients with epilepsy who suffered cardiovascular death, and in 19 of 40 SUDEP patients [20]. Heart weight showed no significant difference between SUDEP and non-SUDEP patients with epilepsy [21]. Overweight heart may be a specific finding in SDEPB, but not in SUDEP. This finding may indicate the presence of chronic cardiovascular abnormality, although specific abnormalities in the cardiac muscles and coronary arteries were identified in 5% of SDEPB and 3% of SUDEP cases.

Significant increase of heart weight was found in patients who suffered sudden unexplained nocturnal death syndrome including sodium channelopathy compared to controls [22]. Abnormal heart rate variability was more frequently found in patients with epilepsy than in controls [23]. Sympathovagal imbalance tended to correlate with epilepsy and antiepileptic drugs. Epilepsy and the Brugada syndrome coexist in families with channelopathy including SCN5A mutation [24]. Patients with Dravet syndrome, a well-known sodium channelopathy, have the risk of seizures during bathing and SUDEP [25]. A Japanese study of biodynamics and electrocardiographic findings during bathing suggested myocardial oxygen consumption, supraventricular extrasystole, or ventricular tachycardia are related to sudden death in the Japanese senior population in the winter season [10]. We speculate that chronic cardiovascular abnormality associated with sympathovagal imbalance and channelopathy may be one of the causes of SUDEP in the bathtub.

#### 4.5. Prevention of SUDEP in the bathtub

The rate of one-person households in the SDEPB group (20%) was significantly lower than that in the SUDEP group (45%) in this study, and also lower than that in the general population (35%), according to the national census in 2015 [26]. The SUDEP cases are more likely to live alone than non-SUDEP cases, but the living arrangements of SDEPB cases are unknown [7].

The Japanese custom is to retain water in the bathtub for one day to share with the family by reheating, so SDEPB patients, who tend to live with family, seem more likely to take baths than SUDEP patients.

Thirty-five (81%) of 43 SDEPB patients and 52 (68%) of 76 SDnonEPB bathed every day in the present study. Another Japanese study reported that 401 (65%) of 617 patients in clinics bathed in a bathtub seven or more times a week [9]. These patients claimed that bathing in the bathtub kept them healthy and ensured good sleep. The Japanese custom of bathing in hot water is common even among patients with epilepsy. However, families did not notice the occurrence of seizures in the bathtub, even GTCs as indicated by leg extension outside the bathtub.

Thirty-one (53%) of 59 patients dying with Dravet syndrome in Japan suffered SUDEP [24]. Six (10%) died of drowning, five of whom died in the hot bathtub (personal communication). The parents of children with Dravet syndrome are informed about SUDEP by pediatricians, especially pediatric neurologists. Neither SUDEP nor SUDEP in the bathtub in Dravet syndrome was included in this study, because those patients were considered as either SUDEP or drowning-related death and not reported to the medical examiner's office. The incidence of SUDEP in and out of bathtub in Japan could be higher than that reported in the present study.

Japanese physicians should always instruct patients with epilepsy at the clinic to take showers instead of baths. This instruction should be emphasized to all patients with epilepsy and their families to prevent SUDEP in the bathtub. Installation of a seizure detection system in the bathroom would be effective for patient safety.

## 5. Conclusion

Leg extension outside the bathtub, lower lung weight, and absence of pleural effusion distinguish SDEPB from SDnonEPB in elderly people. Sudden death occurring in the bathtub in epilepsy can be identified as SUDEP in the bathtub, not drowning despite submergence in the bathtub at discovery. Conditions for bathing require careful attention from physicians and relatives, even for patients with epilepsy with few medications and infrequent seizures, and without mental retardation.

## Disclosures and funding

This work was supported by Grants-in-Aid for Scientific Research (No. JP16K09708) from the Japan Society for the Promotion of Science, Japan, and Grants-in-Aid from the Research Committee of Rare Epilepsy Syndromes, Research on Policy Planning and Evaluation for Rare and Intractable Diseases, Health, Labour and Welfare Sciences Research Grants, the Ministry of Health, Labour and Welfare, Japan.

KJ has received honoraria for presentations from UCB Japan Co., Ltd.; Otsuka Pharmaceutical Co., Ltd.; Daiichi Sankyo Co., Ltd.; and Eisai Co., Ltd. YI and HO have been supported by EpLink — the Epilepsy Research Program of the Ontario Brain Institute, Canada. The remaining authors have no conflicts of interest. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

## References

- [1] Holst AG, Winkel BG, Risgaard B, Nielsen JB, Rasmussen PV, Haunsø S, et al. Epilepsy and risk of death and sudden unexpected death in the young: a nationwide study. *Epilepsia* 2013;54:1613–20.
- [2] Ryvlin P, Nashef L, Lhatoo SD, Bateman LM, Bird J, Blease A, et al. Incidence and mechanisms of cardiorespiratory arrests in epilepsy monitoring units (MORTEMUS): a retrospective study. *Lancet Neurol* 2013;12:966–77.
- [3] Langan Y, Nashef L, Sander JW. Case-control study of SUDEP. *Neurology* 2005;64:1131–3.
- [4] Devinsky O, Hesdorffer DC, Thurman DJ, Lhatoo S, Richerson G. Sudden unexpected death in epilepsy: epidemiology, mechanisms, and prevention. *Lancet Neurol* 2016;15:1075–88.
- [5] Nashef L, So EL, Ryvlin P, Tomson T. Unifying the definitions of sudden unexpected death in epilepsy. *Epilepsia* 2012;53:227–33.
- [6] Leestma JE. Forensic considerations and sudden unexpected death in epilepsy. In: Lathers CM, Schraeder PL, Bungo MW, et al, editors. *Sudden death in epilepsy: forensic and clinical issues*. Boca Raton, FL: CRC Press; 2011. p. 37–55.
- [7] Sveinsson O, Andersson T, Carlsson S, Tomson T. Circumstances of SUDEP: a nationwide population-based case series. *Epilepsia* 2018;59:1074–82.
- [8] Cihan E, Hesdorffer DC, Brandsoy M, Li L, Fowler DR, Graham JK, et al. Dead in the water: epilepsy-related drowning or sudden unexpected death in epilepsy? *Epilepsia* 2018;59:1966–72.
- [9] Hayasaka S, Shibata Y, Goto Y, Noda T, Ojima T. Bathing in a bathtub and health status: a cross-sectional study. *Complement Ther Clin Pract* 2010;16:219–21.
- [10] Chiba T, Yamauchi M, Nishida N, Kaneko T, Yoshizaki K, Yoshioka N. Risk factors of sudden death in the Japanese hot bath in the senior population. *Forensic Sci Int* 2005;149:151–8.
- [11] Suzuki H, Hikiji W, Tanifuji T, Abe N, Fukunaga T. Characteristics of sudden bath-related death investigated by medical examiners in Tokyo, Japan. *J Epidemiol* 2015;25:126–32.
- [12] Planning and Investigation Committee of the Japanese Society of Legal Medicine. [Weights and sizes of internal organs measured in forensic autopsy cases from 2009 to 2013 in Japan. Questionnaire research performed by the Japanese Society of Legal Medicine; October 15, 2015] Japanese. Available from: <http://www.jslm.jp/problem/zouki.pdf>, Accessed date: 25 February 2018.
- [13] Okanari K, Otsubo H, Kouzmitcheva E, Rangrej J, Baba S, Ochi A, et al. Ictal symmetric tonic extension posturing and postictal generalized EEG suppression arising from sleep in children with epilepsy. *Pediatr Neurol* 2017;76:54–9.
- [14] Alexandre V, Mercedes B, Valton L, Maillard L, Bartolomei F, Szurhaj W, et al. REPO<sub>2</sub>MSE study group. Risk factors of postictal generalized EEG suppression in generalized convulsive seizures. *Neurology* 2015;85:1598–603.
- [15] Kubota K, Shoyama S, Tochihara Y, Ohnaka T, Yositate M. State of the bathroom environment in houses of elderly people: from the viewpoint of household composition, heights and ages. *Ningen To Seikatsu Kanryo* 2004;11:63–71 Japanese. Available at [https://www.jstage.jst.go.jp/article/jhesj/11/2/11\\_KJ00007030301/\\_pdf-char/ja](https://www.jstage.jst.go.jp/article/jhesj/11/2/11_KJ00007030301/_pdf-char/ja).
- [16] Kringsholm B, Filskov A, Kock K. Autopsied cases of drowning in Denmark 1987–1989. *Forensic Sci Int* 1991;52:85–92.
- [17] Devinsky O, Bundock E, Hesdorffer D, Donner E, Moseley B, Cihan E, et al. Resolving ambiguities in SUDEP classification. *Epilepsia* 2018;59:1220–33.

- [18] Tao JX, Qian S, Baldwin M, Chen XJ, Rose S, Ebersole SH, et al. SUDEP, suspected positional airway obstruction, and hypoventilation in postictal coma. *Epilepsia* 2010;51:2344–7.
- [19] Kloster R, Engelskjøn T. Sudden unexpected death in epilepsy (SUDEP): a clinical perspective and a search for risk factors. *J Neurol Neurosurg Psychiatry* 1999;67:439–44.
- [20] Esen Melez I, Arslan MN, Melez DO, Şanlı AN, Koç S. Sudden unexpected death in epilepsy: a retrospective autopsy study of 112 epileptic patients. *Noro Psikiyatr Ars* 2017;54:225–33.
- [21] Davis GG, McGwin Jr G. Comparison of heart mass in seizure patients dying of sudden unexplained death in epilepsy to sudden death due to some other cause. *Am J Forensic Med Pathol* 2004;25:23–8.
- [22] Zhang L, Tester DJ, Lang D, Chen Y, Zheng J, Gao R, et al. Does sudden unexplained nocturnal death syndrome remain the autopsy-negative disorder: a gross, microscopic, and molecular autopsy investigation in Southern China. *Mayo Clin Proc* 2016;91:1503–14.
- [23] Lotufo PA, Valiengo L, Benseñor IM, Brunoni AR. A systematic review and meta-analysis of heart rate variability in epilepsy and antiepileptic drugs. *Epilepsia* 2012;53:272–82.
- [24] Parisi P, Oliva A, Coll Vidal M, Partemi S, Campuzano O, Iglesias A, et al. Coexistence of epilepsy and Brugada syndrome in a family with SCN5A mutation. *Epilepsy Res* 2013;105:415–8.
- [25] Sakauchi M, Oguni H, Kato I, Osawa M, Hirose S, Kaneko S, et al. Retrospective multiinstitutional study of the prevalence of early death in Dravet syndrome. *Epilepsia* 2011;52:1144–9.
- [26] Statistics Bureau, Ministry of Internal Affairs and Communications. [2015 Population census in Japan Basic complete tabulation on population and households; September 27, 2017] Japanese. Available from <http://www.stat.go.jp/data/kokusei/2015/kekka/kihon3/pdf/gaiyou.pdf>. Accessed date: 25 February 2018.