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# The incidence of peri-ictal prone position in patients with generalized convulsive seizures



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#### ABSTRACT

*Objective:* The objectives of this study were to determine the incidence of peri-ictal prone position in patients with generalized convulsive seizures (GCS) and to further assess the risk of sudden unexpected death in epilepsy (SUDEP) associated with the prone position.

*Method:* We retrospectively reviewed the video-EEG data of 308 GCS in 193 patients who underwent long-term video-EEG monitoring in two epilepsy centers. We determined the peri-ictal (preictal, ictal, and/or postictal) body positions.

*Results*: A peri-ictal prone position was observed in 12 (6.2%) of 193 patients and 13 (4.2%) of 308 GCS. In 5 (1.6%) of 308 GCS, patients in nonprone positions at seizure onset turned into the prone position during versive seizures. In 8 (2.6%) of 308 GCS, patients were sleeping prone at seizure onset. Peri-ictal intervention with body repositioning was provided in 11 of 12 patients and 12 of the 13 GCS. Repositioning was not provided during the remaining seizure; the patient died in the prone position. In the subset of 96 GCS without ictal intervention, patients in a supine position at seizure onset remained in the supine position at seizure termination in 57 (98.3%) of 58 GCS. Patients sleeping prone at seizure onset remained in the prone position at seizure termination in 4 (80%) of 5 GCS.

*Conclusion:* Our data suggest that the incidence of peri-ictal prone position in patients with GCS is low. Both prone sleeping and forced ictal version may result in postictal prone position. Although avoiding prone sleeping may reduce the SUDEP risk, influencing forced ictal version may be difficult in the absence of supervision.

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#### 1. Introduction

Sudden unexpected death in epilepsy (SUDEP) is a leading cause of premature mortality in patients with chronic uncontrolled epilepsy [1]. Comparing years of potential life lost from SUDEP with other neurological diseases, SUDEP ranks second only to stroke [2]. Sudden unexpected death in epilepsy commonly occurs during sleep, in bed, and unwitnessed [3,4]. A recent systematic review showed that 73% of all reported SUDEP patients were found in a prone position at the time of death [5], suggesting that sleeping prone might be a risk factor for SUDEP. Although the mechanism of SUDEP remains unclear [6], SUDEP commonly occurs in patients with uncontrolled generalized convulsive seizures (GCS) [7,8]. Postictal generalized EEG suppression (PGES) is a common EEG pattern associated with the GCS [9] and is

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consistently correlated with postictal coma [10,11]. The impaired arousal in postictal patients may compromise the brainstem autoresuscitation mechanism and prevent them from lifting or turning their heads, at a time when their airways are obstructed by soft bedding in the prone position [12,13]. Among the 11 published video-EEG-monitored SUDEP cases, GCS, PGES, and prone position were observed in all the victims [5]. Therefore, the cascade of GCS, PGES, and prone position may be an important mechanism of SUDEP.

Similar to sudden infant death syndrome (SIDS), a "Back to Sleep" campaign has been advocated for SUDEP prevention [5,14]. However, prone sleeping immediately prior to the agonal seizures has rarely been reported in SUDEP studies. The dynamics of spontaneous body positions during convulsive seizures are poorly characterized. As such, the utility of a "Back to Sleep" campaign for SUDEP prevention is unknown. Among the monitored SUDEP cases in the study of Mortality in Epilepsy Monitoring Unit (MORTEMUS), 4 of 11 patients were sleeping prone prior to seizures, while 5 of 11 patients turned into prone position from nonprone positions during versive seizures [15,16]. This finding led to the argument that forced ictal version, rather than prone sleeping,



might be an important SUDEP risk factor. The aims of this study were to determine the incidence of the peri-ictal prone position in patients with GCS and to further assess the SUDEP risk associated with the prone position.

#### 2. Methods

We retrospectively reviewed the medical records and video-EEG recordings of patients who underwent long-term video-EEG monitoring in adult epilepsy centers at the University of Chicago, IL, USA and Zhejiang University, Hangzhou, China. The patients from both centers were included in previously published reports [10,17].

Video-EEG recordings were performed using 26 channels with electrodes placed in the international 10–20 system and a single channel of EKG. During video-EEG monitoring, antiepileptic drugs (AEDs) were reduced or discontinued to facilitate the recording of habitual seizures at the discretion of the attending physicians. Nursing interventions such as nasal oxygen treatment, oral suctioning, and body repositioning were performed at the discretion of the nursing staff. Data were acquired by two clinical neurophysiologists in each center (SG and JXT in USA and JX and SW in China). The institutional review board approved the study in each center.

We collected the following variables: age, sex, age at seizure onset, epilepsy duration, epilepsy syndrome (partial or generalized), and state of wakefulness (awake or asleep) at seizure onset. The body positions were categorized into the following: 1) supine: lying on the back with the upper body elevated less than 60° from the horizontal plane; 2) prone: lying on the abdomen with the upper body elevated less than 60° from the horizontal plane; 3) lateral: lying on the left or right side with the upper body elevated less than 60° from the horizontal plane; 4) sitting: the upper body elevated more than 60° from the horizontal plane; 5) and standing.

Peri-ictal body position is defined as the position starting at 2 min before, during, and ending at 2 min after the clinical seizure. Preictal body position is defined as the body position at the time of clinical seizure onset. Postictal body position is defined as the body position at the time of clinical seizure termination. Ictal intervention is defined as any direct body contact (e.g., oxygen administration, oral suctioning, or body repositioning) between nurses and a patient during the ictal phase, which would prevent spontaneous changes of a patient's body position during a seizure. Verbal communication is not considered ictal nursing intervention in this study.

#### 3. Results

A total of 193 patients with 308 GCS were included from two centers, 109 patients with 150 GCS from the University of Chicago epilepsy center and 84 patients with 158 GCS from the Zhejiang University epilepsy center. Patient and seizure characteristics are summarized in Table 1.

Table 1	
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Characteristics of patients and generalized convulsive seizures.

Number of patients (n)	193
Number of seizures (n)	308
Age, years $\pm$ sd	$30.2 \pm 12.7$
Gender (%)	Female (52.3); Male (47.7)
Age of onset, years $\pm$ sd	$12.6 \pm 9.7$
Epilepsy duration, years $\pm$ sd	$16.4 \pm 11.3$
Epilepsy syndromes (%)	
Generalized	25 (13)
Partial	178 (87)
State of wakefulness (%)	
Awake	177 (57.5)
Sleep	131 (42.5)
Ictal intervention (%)	
Yes	212 (68.6)
No	96 (31.4)

Fourteen GCS were excluded from the study because the video recording was obscured in the peri-ictal period and body positions could not be assessed.

Pre- and postictal body positions of patients were assessed in the 308 GCS with and without nursing intervention during the ictal phase. At the time of seizure onset, a supine position was observed in 155 (50.3%) seizures, a lateral position was observed in 74 (24%) seizures, a sitting position was observed in 69 (22.4%) seizures, a prone position was seen in 8 (2.6%) seizures, and a standing position was observed in 2 (0.6%) seizures. At the time of seizure termination, a supine position was observed in 80 (26%) seizures, a sitting position was observed in 8 (2.6%) seizures, a lateral position was observed in 80 (26%) seizures, a sitting position was observed in 8 (2.6%) seizures, a prone position was observed in 4 (1.2%) seizures, and a standing position was not observed in any seizures.

Further analysis revealed that a peri-ictal prone position was observed in 12 (6.2%) of 193 patients and in 13 (4.3%) of 308 GCS. Because of the SUDEP risk associated with the prone position, we assessed how the 12 patients in the peri-ictal prone position transitioned into and out of prone position during their 13 seizures (Table 2). We initially consider the patients who were prone sleeping at the time of seizure onset, which was the case in 8 (2.6%) of 308 GCS. Patients in 3 of these seizures were repositioned to a lateral position by the nursing staff during the seizures. During one GCS, the patient turned into a lateral position spontaneously. In 3 additional seizures, patients were repositioned by the nurses to a lateral position soon after seizure termination. Unfortunately, nursing intervention was not provided in the remaining agonal seizure, and the patient subsequently died in the prone position.

We next consider the patients who were not sleeping in a prone position at the time of seizure onset but turned into the prone position during the ictal phase; this was the case in 5 (1.7%) of 308 GCS. Three of these patients turned into the prone position from a lateral position during versive seizures. One patient turned into a prone position from a supine position during a versive seizure. One patient flipped into the prone position from the supine position during a hypermotor seizure. All 5 patients were repositioned by the nursing staff during their seizures.

The dynamics of spontaneous body position changes were investigated in the subset of 96 GCS without ictal intervention. At the time of seizure onset, the supine position was the most frequent (58 of 96; 60.4%), followed by the lateral position (20; 20.8%), the sitting position (13; 13.5%), and the prone position (5; 5.2%). The vast majority of patients in the preictal supine or prone position remained in the same position at the time of seizure termination, while only a minority of patients in a preictal lateral and sitting position remained in the same position. At the time of seizure termination, the supine position was again the most frequently observed (79 of 96; 82.3%), followed by the lateral position (10; 10.4%), the prone position (4; 4.2%), and the sitting position (3; 3.1%). Patients in a supine position at seizure onset

Table 2	
Peri-ictal prone position in 13 generalized convulsive seizures	s.

Patient	Age/sex	Seizure	Preictal position	Ictal position	Postictal position	Peri-ictal intervention
1	24/F	1	р	$P \rightarrow L$	L	Ictal
2	27/M	2	Р	$P \rightarrow L$	L	Ictal
		3	Р	Р	Р	Postictal
3	50/F	4	S	$S \rightarrow P \rightarrow L$	L	Ictal
4	45/M	5	L	$L \rightarrow P \rightarrow L$	L	Ictal
5	36/M	6	S	$S \rightarrow P \rightarrow L$	L	Ictal
6	44/F	7	Р	Р	Р	No
7	30/M	8	Р	$P \rightarrow L$	L	Ictal
8	44/F	9	Р	Р	Р	Postictal
9	18/M	10	Р	$P \rightarrow L$	L	Postictal
10	14/F	11	Р	Р	Р	Postictal
11	21/F	12	L	$L \rightarrow P \rightarrow S$	S	Ictal
12	36/M	13	L	$L \rightarrow P \rightarrow S$	S	Ictal

S: supine position; L: lateral position; P: prone position. F: Female; M: male.

### Table 3

Dynamic body positions in unsupervised generalized convulsive seizures.

Preictal body position		Postictal body position				
Position	# of GCS	Supine	Lateral	Sitting	Prone	
Supine	58	57	1	0	0	
Lateral	20	12	8	0	0	
Sitting	13	10	0	3	0	
Prone	5	0	1	0	4	
Total	96	79	10	3	4	

remained in the supine position at seizure termination in 57 (98.3%) of 58 GCS without ictal intervention. Patients sleeping prone at seizure onset remained in the prone position at seizure termination in 4 (80%) of 5 GCS without ictal intervention (Table 3).

#### 4. Discussion

Sudden unexpected death in epilepsy often occurs in sleep when someone is alone and unsupervised, and the victim is commonly found prone [5,18]. Our study demonstrates that the peri-ictal prone position occurs rarely in the epilepsy monitoring unit where close supervision is provided. This may explain why SUDEP has been rarely witnessed. Sharing a room or a bed with someone or using nocturnal audio-visual monitoring has been considered for reducing SUDEP risk, suggesting that simple measures such as body repositioning or shaking during and following a seizure may be lifesaving [19,20]. In this study, the peri-ictal intervention was provided in 12 of 13 convulsive seizures when patients were either sleeping prone at seizure onset or turned into prone during versive seizures. Unfortunately, it was not provided in one seizure, and the patient was sleeping prone and died in the prone position. These data further highlight the potential role of nocturnal supervision for SUDEP prevention.

Patients sleeping prone at the time of seizure onset commonly ended up in a postictal prone position in the absence of ictal intervention. In 4 of the 5 seizures in this study, patients sleeping prone at the time of seizure onset ended up in a postictal prone position. When combined with the cases reported in the MORTEMUS study, 8 of 9 patients sleeping prone at the onset of seizures ended up in a postictal prone position in the absence of nursing intervention. These data suggest that prone sleeping might be an important risk factor for SUDEP. A limitation in this study is that sleeping prone might have been discouraged by medical staff in the EMU because of the increased SUDEP awareness and the SUDEP risk associated with epilepsy monitoring [15,21]. Prone sleeping constitutes approximately 10% of total sleep time among young healthy adults sleeping at home in their own bed [22]. As such, the low incidence of prone sleeping in this study may underestimate the incidence of prone sleeping in the general patient population with epilepsy.

Both prone sleeping and forced ictal version may result in a postictal prone position. In our study, prone sleeping (8/13 cases) was a more common risk factor than forced ictal version (5/13 cases) for the postictal prone position. However, forced ictal version (5/11 cases) was a slightly more common risk factor than prone sleeping (4/11 cases) for the postictal prone position in the MORTEMUS [16]. Given the limited case number in both studies, it is premature to determine whether prone sleeping or forced ictal version is a more significant risk factor. More likely, both prone sleeping and forced ictal version are significant risk factors for SUDEP.

The "Back to Sleep" campaign has been remarkably successful in preventing SIDS, reducing the mortality of SIDS by approximately 60% [12]. Given the similarity between SUDEP and SIDS, a "Back to Sleep" campaign may also be an effective measure to reduce SUDEP risk, particularly in those with a tendency to sleep prone. Our data showed that patients in 57 (98.3%) of 58 unsupervised GCS in the supine position at the time of seizure onset remained in a supine position at the

time of seizure termination. This argues for potential effectiveness of the SIDS-like prevention. Nevertheless, a "Back to Sleep" campaign for SUDEP prevention is unlikely to achieve the same success as it did for SIDS prevention for the following reasons. First, infants are not able to change body position when being placed in a supine sleeping position, while children or adults may change sleeping position many times over the course of a night [22]. Second, supine sleeping may not prevent patients from turning into the prone position during versive seizures. Forced ictal version in secondarily GCS is frequently in a direction contralateral to the side of seizure onset [23,24]. As such, patients may be less likely turning into prone from a supine position compared with a lateral position.

A "Back to Sleep" campaign may increase the risk of aspiration pneumonia in patients with epilepsy, undermining its potential benefit for SUDEP prevention [25]. Fortunately, the risk of aspiration during seizures is relatively low, particularly when patients are not eating or drinking at the time of seizures [26]. The risk of aspiration in the EMU appears to be less than 1% of patients with GCS [27]. Our data showed that patients in 79 (82.3%) of 96 unsupervised GCS ended up in a postictal supine position regardless of preictal body position, and the risk of aspiration may be difficult to influence in the absence of supervision. While a supine position may risk aspiration, a prone position may risk suffocation in postictal unresponsive patients. Therefore, the limited risk of aspiration should not deter physicians from advising those with uncontrolled GCS to avoid sleeping in a prone position.

In summary, we conclude that the incidence of the peri-ictal prone position is low in an epilepsy monitoring environment, which underscores the importance of peri-ictal supervision for SUDEP prevention. Both prone sleeping and forced ictal version may result in a postictal prone position and therefore increase SUDEP risk. Although avoiding prone sleeping may have the potential for reducing the SUDEP risk, influencing forced ictal version may be difficult in the absence of supervision. Future studies are warranted to develop effective measures to prevent the postictal prone position and thus mitigate the SUDEP risk.

#### Disclosure and conflicts of interest

NPI is a shareholder in the for-profit company Medical Resource Group, LLC that receives advertising revenue from various entities including pharmaceutical companies. All other authors have nothing to disclose and no conflict of interest to report. The study is not funded by any private or federal grants.

#### References

- [1] Devinsky O. Sudden, unexpected death in epilepsy. N Engl J Med 2011;365:1801-11.
- [2] Thurman DJ, Hesdorffer DC, French JA. Sudden unexpected death in epilepsy: assessing the public health burden. Epilepsia 2014;55:1479–85.
- [3] Lamberts RJ, Thijs RD, Laffan A, Langan Y, Sander JW. Sudden unexpected death in epilepsy: people with nocturnal seizures may be at highest risk. Epilepsia 2012; 53:253–7.
- [4] Nobili L, Proserpio P, Rubboli G, Montano N, Didato G, Tassinari CA. Sudden unexpected death in epilepsy (SUDEP) and sleep. Sleep Med Rev 2011;15:237–46.
- [5] Liebenthal JA, Wu S, Rose S, Ebersole JS, Tao JX. Association of prone position with sudden unexpected death in epilepsy. Neurology 2015;84:703–9.
- [6] Bermeo-Ovalle AC, Kennedy JD, Schuele SU. Cardiac and autonomic mechanisms contributing to SUDEP. J Clin Neurophysiol 2015;32:21–9.
- [7] Tomson T, Nashef L, Ryvlin P. Sudden unexpected death in epilepsy: current knowledge and future directions. Lancet Neurol 2008;7:1021–31.
- [8] Hesdorffer DC, Ishihara L, Mynepalli L, Webb DJ, Weil J, Hauser WA. Epilepsy, suicidality, and psychiatric disorders: a bidirectional association. Ann Neurol 2012; 72:184–91.
- [9] Lhatoo SD, Faulkner HJ, Dembny K, Trippick K, Johnson C, Bird JM. An electroclinical case–control study of sudden unexpected death in epilepsy. Ann Neurol 2010;68: 787–96.
- [10] Tao JX, Yung I, Lee A, Rose S, Jacobsen J, Ebersole JS. Tonic phase of a generalized convulsive seizure is an independent predictor of postictal generalized EEG suppression. Epilepsia 2013;54:858–65.
- [11] Rajakulendran S, Nashef L. Postictal generalized EEG suppression and SUDEP: a review. J Clin Neurophysiol 2015;32:14–20.
- [12] Kinney HC, Thach BT. The sudden infant death syndrome. N Engl J Med 2009;361: 795–805.

- [13] Dlouhy BJ, Gehlbach BK, Richerson GB, Sudden unexpected death in epilepsy: basic mechanisms and clinical implications for prevention. J Neurol Neurosurg Psychiatry 2016;87:402-13.
- [14] Tao JX, Sandra R, Wu S, Ebersole JS. Should the "back to sleep" campaign be advocated for SUDEP prevention? Epilepsy Behav 2015;45:79-80.
- [15] Ryvlin P, Nashef L, Lhatoo SD, Bateman LM, Bird J, Bleasel A, et al. Incidence and mechanisms of cardiorespiratory arrests in epilepsy monitoring units (MORTEMUS): a retrospective study. Lancet Neurol 2013;12:966-77.
- [16] Lhatoo SD, Nashef L, Tomson T, Ryvlin P. Mortality on epilepsy monitoring units. Association of prone position with sudden unexpected death in epilepsy. Neurology 2015-85-1185
- [17] Xu J, Jin B, Yan J, Wang J, Hu J, Wang Z, et al. Postictal generalized EEG suppression after generalized convulsive seizures: a double-edged sword. Clin Neurophysiol 2016:127:2078-84.
- [18] Kloster R, Engelskjon T. Sudden unexpected death in epilepsy (SUDEP): a clinical perspective and a search for risk factors. J Neurol Neurosurg Psychiatry 1999;67: 439-44
- [19] Nashef L, Fish DR, Garner S, Sander JW, Shorvon SD. Sudden death in epilepsy: a study of incidence in a young cohort with epilepsy and learning difficulty. Epilepsia 1995:36:1187-94.

- [20] Langan Y, Nashef L, Sander JW. Case-control study of SUDEP. Neurology 2005;64: 1131-3.
- [21] 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.
- [22] De Koninck J, Gagnon P, Lallier S. Sleep positions in the young adult and their relationship with the subjective quality of sleep. Sleep 1983;6:52–9. [23] Wyllie E, Luders H, Morris HH, Lesser RP, Dinner DS. The lateralizing significance of
- versive head and eye movements during epileptic seizures. Neurology 1986;36: 606-11
- [24] Remi J, Wagner P, O'Dwyer R, Silva Cunha JP, Vollmar C, Krotofil I, et al. Ictal head turning in frontal and temporal lobe epilepsy. Epilepsia 2011;52:1447–51.
  [25] Sethi NK. Association of prone position with sudden unexpected death in epilepsy.
- Neurology 2015;85:1185.
- [26] DeToledo JC, Lowe MR, Gonzalez J, Haddad H. Risk of aspiration pneumonia after an epileptic seizure: a retrospective analysis of 1634 adult patients. Epilepsy Behav 2004.5.593-5
- [27] Noe KH, Tapsell LM, Drazkowski JF. Risk of choking and aspiration during inpatient video-EEG monitoring. Epilepsy Res 2011;93:84-6.