Ambient temperature and spontaneous intracerebral haemorrhage: a cross-sectional analysis in Tainan, Taiwan

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ABSTRACT

Objectives: Ambient temperature has been reported to play a role in the occurrence of spontaneous intracerebral haemorrhage (ICH). This study aimed to investigate the relation between ambient temperature of onset time and ICH and the effect of hourly temperature within 72 h before ICH.

Design: This is a cross-sectional case-only study and a retrospective analysis of a prospective database.

Setting: Two medical centres in Southern Taiwan participating a prospective stroke registry.

Participants: A total of 933 patients with ICH registered from August 2006 to July 2008.

Primary and secondary outcome measures: The hourly temperature was collected, and patients were grouped according to the deciles of hourly temperature at onset. Primary outcome was the association between the number of ICH cases and mean temperature (or temperature variation). Secondary outcome was the difference of onset temperature and hourly temperature before onset in patients with known onset time.

Results: Winter (n=282) had significant higher ICH cases than other seasons (n=651; p=0.002). Of those patients with an exact time of onset, the results showed 13% patients occurred at the lowest decile temperature group (<17.4°C) and 8% patients occurred at the highest decile temperature group (>30.8°C). It showed a significant temperature change before onset for these patients (p<0.005).

Conclusions: This study showed that lower ambient temperature and variation of temperatures precipitated ICH in southern Taiwan. Better protecting vulnerable people from cold temperatures may prevent the occurrences of ICH.

BACKGROUND

The relationship of climate and spontaneous intracerebral haemorrhage (ICH) had long been noticed in our clinical experience. There had been many literatures discussing their relationship, with the earliest literature tracing back at least to 1976.[1] The targets of these studies, however, were very diverse. Some studies focused on the association of a specific season.[2–10] Other indicators such

ARTICLE SUMMARY

Article focus
- Ambient temperature and the occurrence of ICH.
- Temperature fluctuation before onset of ICH.

Key messages
- Overall, low temperature in winter has higher number of ICH occurrence than other seasons.
- Fluctuation of temperature before onset is associated with ICH. The earliest time of significance was 4 h before onset.
- Protection methods during these climates may prevent the occurrences of ICH.

Strengths and limitations of this study
- The registry is prospective and recruiting large number of ICH cases.
- The time of onset comes from the statement of the patient or the family members. There may be errors in report.
- The ambient temperature cannot fully represent the temperature the patient was exposed to due to the variance of location, outdoor/indoor and protection gears.

as air pressure,[11 12] air pollution,[13] holidays,[14] typhoons and wind directions,[15] sunshine hours[16] and daylight saving time[17] were all been discussed before. However, the one discussed most and was correlated most is ambient temperature.[4 11 12 15 16 18–20]

The effect of ambient temperature on the body had been discussed before.[21] After 6 h of surface cooling, platelet count, blood viscosity, arterial pressure and plasma cholesterol increased. Even within the same person, arterial blood pressure rose in colder months and decreased in hotter ones.[22] Blood pressure variation due to low ambient temperature had also been proposed as a possible trigger of ICH.[20]

The effect of ambient temperature on ICH, if according to the literature, occurred within 6 h after exposure. The systolic and diastolic pressures, which are thought to be highly associated with the onset of ICH,[20] rise even within 1 h. A literature proposed the

relationship of hourly temperature and ischaemic stroke[23] and indicated a lag period of 24–54 h between the cold exposure and the onset of ischaemic stroke. Thus, the effect of temperature on ICH should range between 6 and 54 h. However, according to known literatures, there had been no study focusing on the association of hourly temperature and ICH or the effect of temperatures within 24 h before ICH.

This study investigated the relationship of ICH with hourly ambient temperature and focused on the temperature within 72 h before onset.

METHODS
Study population
The National Cheng Kung University Hospital (NCKUH) and Chi Mei Medical Center (CMMC) are the only tertiary medical centres in Tainan City, which is located in southern Taiwan. The population in Tainan city was 1.8 million in 2010. From August 2006 to July 2008, patients with ICH were registered in both hospitals according to the description of Taiwan Stroke Registry.[24] Both hospitals' Institutional Review Boards approved the conduct of the registry. In brief, their basic information, including age and gender, was recorded in the emergency room. Imaging studies, either CT or MRI, were required for the diagnosis of spontaneous ICH. The onset time was also recorded according to the description of the patient himself/herself or his/her family members. Patients with ICH due to trauma, tumour or coagulopathy were excluded.

Study design
Part 1. Mean monthly ambient temperature and ICH cases from NCKUH and CMMC
The hourly temperature data were collected from the Southern Regional Weather Center, Tainan, which is only 2 and 4.2 km to NCKUH and CMMC, respectively. The mean monthly temperature was the mean hourly temperature in each month of the study period. The variation of temperature in each month was expressed by the SD of hourly temperature. The year was divided into four seasons: winter was December, January and February; spring was March, April and May; summer was June, July and August, and autumn was September, October and November. The χ^2 test was used to test for differences in the number of ICH cases among seasons. The difference between actual and expected cases in each month was shown. Expected cases were calculated by distributing cases according to the proportion of days in each month within the study period. If χ^2 test is significant, it means that there is a difference among seasons. Primary outcome measure was the association between the number of ICH cases and mean temperature (or temperature variation) and was evaluated by the regression analysis.

Part 2. Temperature of 72 h before onset for ICH patients from NCKUH
The onset time in this study is defined to be the round down the hour of the real onset time. Patients from

NCKUH (n=350) were used to find out the association of ICH and the temperature of onset time. But lack of control group (no ICH) and the cut-off points of temperature for the control period (within 72 h before the onset time) influenced the test result if case-crossover design[23] was used. Furthermore, the mean temperature and fluctuation were indeed strongly negatively correlated in this data set. To avoid the temperature fluctuation may be a confounding factor, we collected the temperatures of the control period and split hourly temperatures from August 2006 to July 2008 into 10 equal groups to reduce the temperature variation of each group. The first group (the lowest hourly temperatures) would be in decile group 1, the second group in decile group 2, up to the 10th highest hourly temperatures being in decile group 10. Hence, the effect of temperatures within 72 h before ICH became the secondary end point. The paired t test is used in each patient to test the significance of the difference between onset temperature of ICH (the case period) and temperature during the hours before onset (the control period). If the paired t test results were significant, it means that the fluctuation of temperature during the hours before onset may be the risk factor for ICH. We then compared characteristics of the group with the lowest/highest hourly temperature and other groups using the Mann–Whitney test of nonparametric statistical method. If it was significant, it would mean that there was a difference between the characteristics of groups. The significance level is set to be 0.05.

RESULTS
Part 1. Average monthly ambient temperature and ICH cases from NCKUH and CMMC
From August 2006 to July 2008, there were 933 patients with spontaneous ICH brought to the two hospitals (350 in NCKUH and 583 in CMMC). Their mean age was 61±15 years and 567 (61%) were men; 744 (80%) had a history of hypertension.

The mean and variation (SD) of temperature is shown in figure 1A according to each month. Highest mean temperature fell in July and lowest in February. January and February had higher monthly observed ICH cases than expected, whereas spring and summer had lower observed cases than expected (figure 1B). Winter (n=282) had significant higher ICH cases than other seasons (n=651; p=0.002). Figure 1C,D showed a trend towards the higher average daily cases for months with lower average temperature and higher temperature variation. The regression analysis showed that average daily cases increased by nearly five persons in 100 persons for a 1°C decrease in monthly average temperature (figure 1C) and decreased nearly 20 persons in 100 persons for a 1°C decrease in monthly temperature SD (figure 1D).

Part 2. Temperature of 72 h before onset for ICH patients from NCKUH
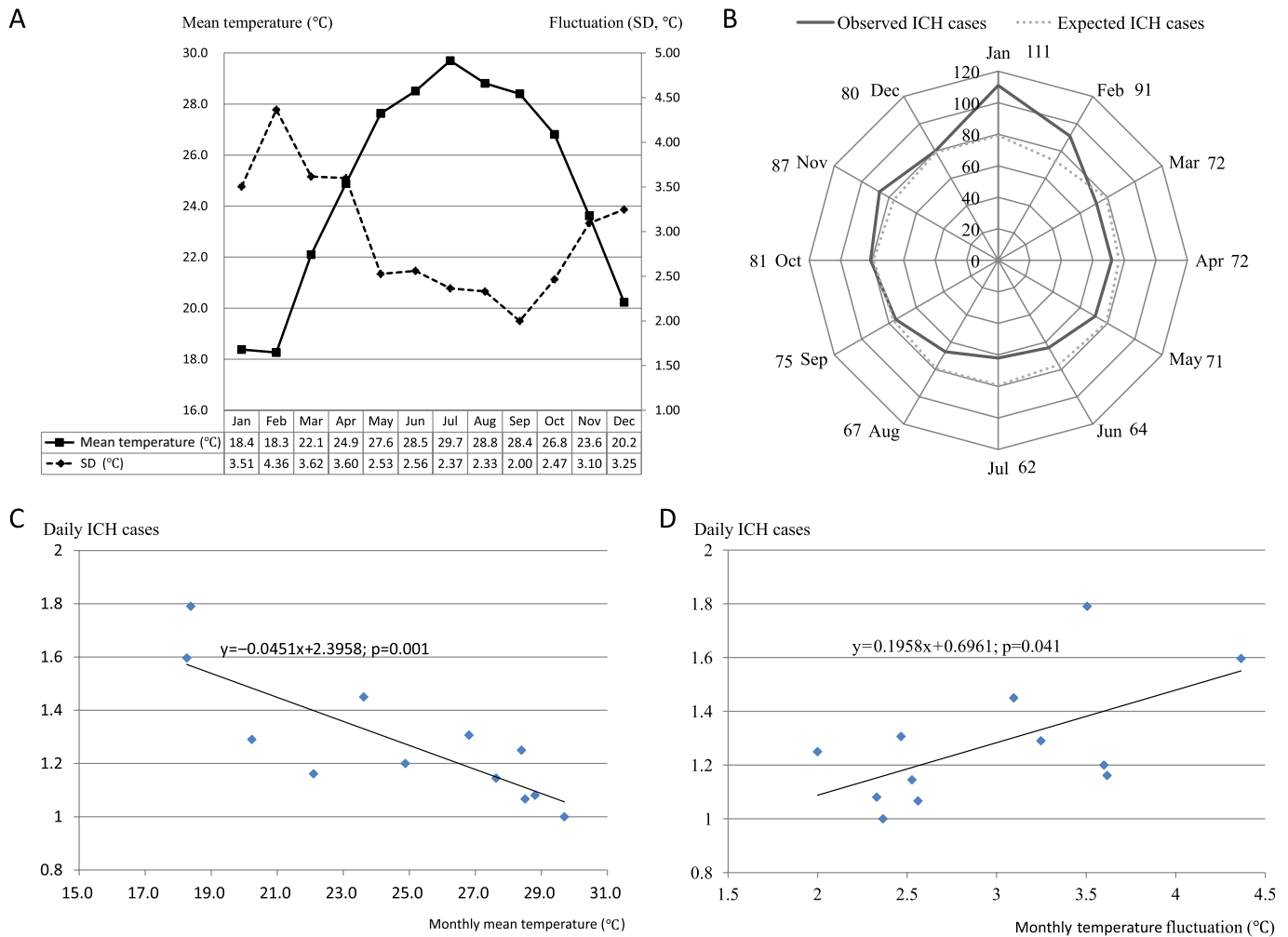At NCKUH, we recruited 350 ICH cases. The mean age was 62±14 years and 215 (61%) were men; 283 (81%)

Figure 1 (A) Mean and fluctuation (SD) of monthly temperature. (B) Radar chart of total observed intracerebral haemorrhage (ICH) cases versus expected. The late fall (November) and winter (December, January and February) clearly exceeded the expected number of ICH cases. (C) Association between monthly mean temperature and daily ICH cases. (D) Association between monthly temperature fluctuation and daily ICH cases.

had a history of hypertension. Initial Glasgow Coma Scale (GCS) was 10.4±4.5. The National Institute of Health Stroke Scale (NIHSS) score was 17.5±12.2. There were 237 patients with known onset time down to hours. The distribution of time is shown in figure 2. The onset hours with highest percentages are 06:00 and 19:00.

The distribution of patients with ICH with known (n=237) and unknown (n=113) onset time is according to decile hourly temperature of 2 years (figure 3). The occurrence of ICH shows a trend towards the lower temperature. Of those patients with known onset time, the results showed 13% patients occurred at the lowest decile temperature group (<17.4°C) and 8% patients occurred at the highest decile temperature group (>30.8°C). The mean age, initial consciousness (GCS) and severity of stroke (NIHSS) were compared between group 1, 10 and other groups (table 1). The mean GCS of patients in groups 1 was significantly lower than groups 2−9 (p=0.02). They tended to be older, but it did not reach statistical significance (table 1).

We further analysed the relationship between ICH and hourly temperature within 72 h before onset. Let the variables be the onset temperature and hourly temperature before onset. We separately tested the temperature differences of past 72 h before onset for patients with known onset time (n=237). For simplification, table 2 shows the p values of paired t tests for temperature difference of onset and past 24 h before onset. Because we simultaneously compared 72 tests, in order to reduce the false discovery rate, here the significance level was set to be 0.005. Except for groups 1, 2, 9 and 10, the temperature difference of other groups was not significant between onset and each hour before onset.

DISCUSSION

This study demonstrates (1) the occurrence of spontaneous ICH in southern Taiwan has higher cases in winter; (2) a negative association between monthly mean temperature and daily ICH cases; (3) a positive association between monthly temperature variation and (4) there was significant difference on temperature of 4 h
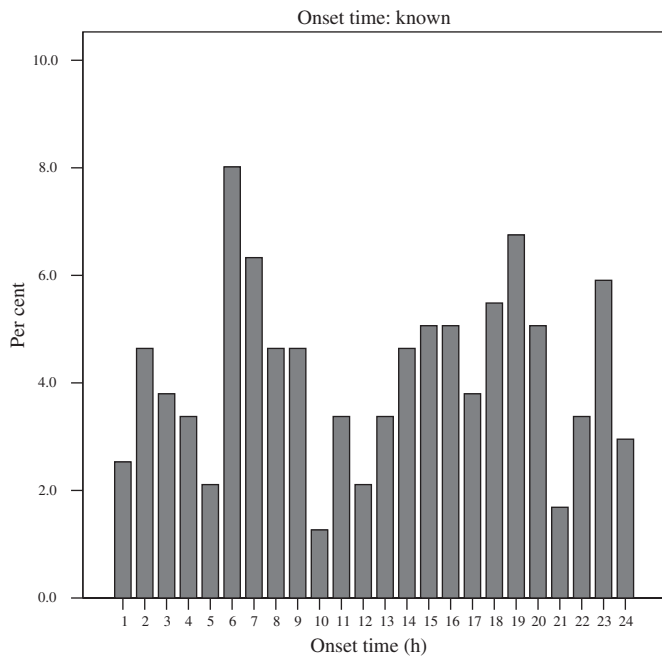
Figure 2 The hourly distribution of intracerebral haemorrhage patients with known onset time (n=237).

before onset and onset temperature in extreme high and low onset temperature group.

Previous studies had long debated about the effect of ambient temperature on ICH. The results were controversial. The most recent large study in Australia[4] with 12 387 stroke admissions in 10 years showed that primary ICH emergency admissions increased by 15% and 12% for a 1°C increase in daily maximum and minimum
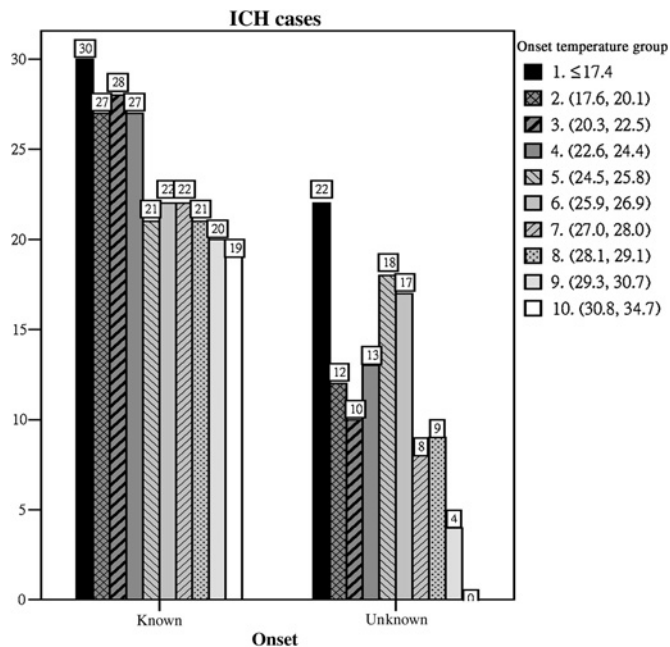

Figure 3 The distribution of patients with intracerebral haemorrhage with known (n=237) and unknown (n=113) onset time according to decile hourly temperature of 2 years.

temperature in summer. Some previous studies suggested an increase in ICH during hot seasons[3] or high temperature as well. Some other studies, however, showed exactly the opposite.[8 10 15 16 18 20] There were also studies indicating no correlation between them at all.[9 11 19] The results were still inconclusive. Some proposed that different geography and climate may be the reason.[24]

The major obstacle to the association between ambient temperature and ICH is that most ICH cases occurred indoors and the use of a heater in the winter season precludes their actual relationships. In Tainan, a subtropical city in the south-western part of Taiwan, even an extremely cold front may bring temperatures of 10°C, a heater is almost never used. Therefore, the ambient temperature in this study can actually represent the onset temperature of ICH.

We found that in Tainan, 13% of ICH cases occurred with lower temperature (<17.4°C) and were associated with fluctuation of temperature in the 72 h before onset. On the contrary, 8% (group 10) had ICH at extreme high temperature. These patients, who suffered ICH in extreme temperatures, are more associated with fluctuation of temperature.

Contrary to the study in Japan,[2] the cooler month or season had higher occurrence of ICH in Taiwan. According to the Köppen–Geiger classification, climate in Taiwan belongs to the Cfa type. Giua et al[25] proposed that in this type of climate, ICH should be 'fall-winter type'. Our data surely found this trend. Although the temperature here was not very extreme in different seasons, the frequency of onset of ICH still correlated well with the monthly average temperature or the variation of temperature.

In figure 2, the proportions of onset hours are significantly uneven. Higher percentages are at 06:00 and 19:00. This time was correlated with the blood pressure surge on awakening. Also, these times are the start of daily activities and thus could be reported with better precision. ICH onset at night might have been occurred while asleep and thus mostly fell into the unknown group.

In table 2, the difference did not reach significance until 4 h before onset. It may indicate that temperature fluctuations, if they cause ICH, need at least 4 h to exert its effect. Changes in temperature, or temperature difference, were less investigated in previous literatures. A study in Scotland showed no changes in risk of ICH with changes in mean temperature of 24 or 48 h before onset.[11] It may be because the mean indicator cannot show the actual fluctuation of temperature. Hong et al[23] noticed an increase in risk with temperature change in winter than in summer and suggested that temperature change as another important indicator of ischaemic stroke. Our data show that most patients of ICH did not correlate with temperature change in the 72 h before onset for patients in groups 2–9. Patients in groups 1 (extreme low) and 10 (extreme high) indicated that they

Table 1 The descriptive statistics of groups 1–10 by mean hourly temperature of 2 years

Group	ICH, n	Mean onset temperature	SD onset temperature	Min	Max	Mean age (years)	Mean GCS	Mean NIHSS
1	30	15.58	1.42	11	17.4	65.30	9.07	19.73
2	27	19.17	0.72	17.6	20.1	63.78	11.26	16.70
3	28	21.53	0.70	20.3	22.5	57.32	10.54	18.37
4	27	23.46	0.64	22.6	24.4	59.56	11.59	14.48
5	21	25.20	0.48	24.5	25.8	63.86	11.48	16.14
6	22	26.43	0.30	25.9	26.9	64.55	11.23	17.32
7	22	27.50	0.31	27	28	62.82	9.82	19.05
8	21	28.59	0.32	28.1	29.1	66.71	10.14	19.71
9	20	29.92	0.40	29.3	30.7	56.85	11.10	14.45
10	19	31.93	0.96	30.8	34.7	64.00	9.95	18.53
2–9 combined	188	24.83	3.51	17.6	30.7	61.79	10.91	17.01
p Value* (groups 2–9 vs group 1)						0.27	0.02	0.19
p Value* (groups 2–9 vs group 10)						0.58	0.28	0.52

*Mann–Whitney test.
GCS, Glasgow Coma Scale; ICH, intracerebral haemorrhage; NIHSS, National Institute of Health Stroke Scale.

were more affected by temperature fluctuation. Patients in lowest temperature group (group 1) tended to be of older age and worse initial GCS and NIHSS.

Previous studies in high-latitude countries may show reduced sensitivity because residents used heating systems. This protection method obscured the effect of ambient temperature such as the study in Siberia[12] showing correlation of ICH with mild temperature (-1.9 to $7.2°C$) compared with high temperature ($\geq 7.3°C$) but no correlation with low temperature ($\leq -2.0°C$) compared with high temperature. Another study tried to compare the patients doing outdoor activities and the patients being indoors.[16] It showed no difference, which may also be attributed to personal protection methods, such as warm clothes or gloves.

There were several limitations. First, the time of onset comes from the statement of the patient or the family members. There may be errors in report. Second, some

Table 2 The p values of paired t tests for temperature at onset and before onset (N=237)

Before onset (h)	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6	Group 7	Group 8	Group 9	Group 10
1	0.291	0.827	0.276	0.844	0.393	0.424	0.129	0.412	0.495	0.153
2	0.071	0.617	0.165	0.745	0.131	0.229	0.271	0.221	0.640	0.083
3	0.012	0.222	0.108	0.728	0.043	0.684	0.675	0.333	0.646	0.017
4	0.004*	0.138	0.073	0.255	0.114	0.788	0.885	0.238	0.677	0.001*
5	0.003*	0.072	0.068	0.298	0.297	0.668	0.799	0.180	0.680	3.9E−05*
6	8.5E−04*	0.036	0.168	0.436	0.237	0.672	0.611	0.186	0.697	2.1E−05*
7	1.3E−03*	0.020	0.362	0.376	0.178	0.911	0.677	0.152	0.952	5.4E−07*
8	0.004*	0.012	0.532	0.319	0.232	0.760	0.718	0.051	0.557	4.5E−07*
9	0.019	0.016	0.562	0.248	0.170	0.469	0.698	0.033	0.099	3.7E−09*
10	0.033	0.023	0.752	0.213	0.198	0.414	0.695	0.047	0.136	4.3E−10*
11	0.054	0.034	0.899	0.185	0.174	0.312	0.635	0.026	0.059	3.3E−10*
12	0.039	0.037	0.899	0.117	0.229	0.227	0.637	0.029	0.003*	3.3E−10*
13	0.031	0.028	0.895	0.107	0.245	0.222	0.492	0.065	6.3E−04*	4.0E−10*
14	0.022	0.026	1.000	0.094	0.264	0.263	0.306	0.261	1.4E−04*	4.9E−10*
15	0.017	0.032	0.888	0.086	0.214	0.374	0.166	0.357	1.0E−04*	9.4E−10*
16	0.013	0.045	0.851	0.075	0.218	0.428	0.190	0.494	3.5E−04*	1.9E−08*
17	0.021	0.030	0.893	0.064	0.249	0.496	0.106	0.782	0.002*	9.1E−08*
18	0.037	0.021	0.866	0.072	0.240	0.707	0.088	0.848	0.010	2.2E−07*
19	0.117	0.021	0.933	0.111	0.265	0.586	0.098	0.792	0.015	2.1E−06*
20	0.391	0.023	0.722	0.150	0.291	0.662	0.114	0.949	0.020	1.9E−05*
21	0.994	0.033	0.638	0.160	0.297	0.640	0.203	0.856	0.081	6.5E−05*
22	0.447	0.064	0.417	0.149	0.355	0.792	0.396	0.768	0.233	4.2E−04*
23	0.191	0.246	0.642	0.085	0.496	0.528	0.569	0.756	0.109	2.4E−04*
24	0.274	0.751	0.982	0.140	0.853	0.609	0.842	0.288	0.178	0.002*

*p<0.005.

patients developed ICH during sleep or time of onset was unknown (32.3%). These events often occur in the late night or early morning, which might underestimate the effects of lower temperature to ICH occurrence. Third, the ambient temperature cannot fully represent the temperature the patient was exposed to due to the variance of location, outdoor/indoor and protection clothing. Fourth, our data did not adjust the temperature according to the humidity. As the study in Australia proposed, adjustment for humidity did not substantially change the stroke emergency admission estimates.[4] Since this study was conducted in a subtropical region, the extension of the study results may not be applicable to other area.

CONCLUSIONS

In southern Taiwan, the onset of ICH is associated with lower temperature and also with temperature fluctuations within the 72 h before onset. Heater/air-conditioner and other protection methods during these climates may prevent the occurrences of ICH.

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