Background: Hypertension is one of the most common comorbid conditions of epilepsy. Hypertension and epilepsy may be related to each other. Qigong Bigu practice induces a similar effect as fasting in the first week. As ketogenesis is induced during ketogenic diet therapy, we hypothesize that ketogenesis is detectable and related body weight loss would occur during the first week of Qigong Bigu practice.

Methods: During the prospective observational study, 34 healthy adult participants attended the Qigong Bigu practice for one week. The blood pressure, body weight, calorie consumption, blood glucose and beta-hydroxybutyrate level were measured.

Results: The body weight and body mass index decreased by 2.39 ± 1.34 kg (95%CI 1.92–2.85) and 0.94 ± 0.57 (95%CI 0.73–1.15), respectively, after five days of practice (P < 0.001). The systolic and diastolic blood pressure decreased by 17.86 ± 14.17 mmHg (95%CI 12.36–23.35) and 9.75 ± 7.45 mmHg (95%CI 6.86–12.64), respectively (P < 0.001). The average five-day calorie consumption was 1197.47 ± 569.97 kcal (95%CI 998.60–1396.35). Meanwhile, no symptomatic hypoglycemia or other significant side effects were observed. The blood beta-hydroxybutyrate level increased to a nutritional level of 1.15 ± 1.12 mmol/L (95%CI 0.76–1.62). The calorie consumption negatively correlated to the beta-hydroxybutyrate level in the blood. The loss of body weight and the decrease of body mass index were positively correlated to the blood beta-hydroxybutyrate level.

Conclusions: Qigong Bigu can decrease the blood pressure, the body weight and the body mass index in healthy adult participants. The fasting stage of Qigong Bigu is accompanied by ketogenesis. Clinical trial of Qigong Bigu in hypertension and epilepsy patients might be worthwhile. The blood beta-hydroxybutyrate might be used as a biomarker to evaluate the effect of Qigong Bigu practice during fasting.

Trial registration: ChiCTR1800016923.

Keywords: Blood pressure, Body weight, Body mass index, Epilepsy, Ketogenic diet, Qigong, Bigu, Fasting, Comorbidity, Hypertension, Pigu

Background
Hypertension is the most common comorbidity in epilepsy patients older than 19 years [1]. The blood pressure can increase at the onset of seizure due to the up-regulation of activity of the sympathetic nervous system. On the other hand, the seizure threshold may be decreased due to the high blood pressure insult to the brain, thereby leading to the occurrence of seizures and epilepsy [2]. Seizures may be a result of persistent hypertension [3].
Sudden unexpected death in epilepsy (SUDEP) is an important cause of deaths in patients with epilepsy, therefore more clinical researches are needed to find ways for its treatment [4]. These patients might suffer an over-active status of the sympathetic nervous system [5]. Young age is one of the risk factors for SUDEP [6]. In young adults (aged 20–45 years), the risk of SUDEP is much higher than that in other age groups [7]. Some angiotensin II receptor blockers have both blood-pressure-lowering and neuroprotective effects [8, 9]. Treatment with angiotensin-converting enzyme inhibitors greatly decreases seizures [2]. Accumulative evidence has indicated that the increased activity of the sympathetic nervous system through the renin-angiotensin system (RAS) leads to hypertension [10]. RAS may be related to the pathogenesis of SUDEP. RAS inhibitors have anti-seizure effects and RAS may be a potential target for prevention of SUDEP. Therefore, there may be interactions between epilepsy and high blood pressure [11, 12].

Bigu (which means avoiding grains/cereals, fasting) is one of the common practices for health care of ordinary people and for treating diseases in China. The practice of Bigu can date back to over 2,000 years ago in literature [13, 14]. There are different procedures of Bigu practice, among which the Traditional Qigong Bigu practice (Qigong and Bigu practice together) [15] is the most popular one. At the initiation (usually the first week) of Qigong Bigu practice, although foods are mandatorily decreased (fasting but could take some low calorie of fresh fruits), natural water can be freely taken as needed. Studies have demonstrated that Bigu has many effects such as decreasing body mass index (BMI), reducing blood pressure in hypertension, relieving stiffness of cervical vertebra, etc. [15–17]. But the underlying mechanisms are far from clear. Ketogenic diet therapy (KDT) involves foods with a high proportion of fats, a low proportion of carbohydrates, and adequate proteins and other nutrients [18, 19]. It has long been used to treat epilepsy [20] and other diseases, and its advantages of practicability and low-cost make it popular in the normal population for health care and for treating diseases. From the history of KDT, one could see that KDT was derived from fasting [21], as the protocol decreases food intake but water is freely drunk as needed, thereby treating epilepsy, diabetes mellitus and other diseases. Accompanying short fasting, there is ketosis in the body and research has demonstrated that physiological ketosis of the body may be one of the mechanisms of the anti-seizure effect of KDT. KDT was proposed for the purpose of maintaining the efficacy of short fasting. It is the decomposing process of high proportion of fats that the KDT mimics the metabolic response in the body when hungry, maintaining the physiological ketosis for a long term, even for many years, thereby exerting disease-treating and health caring effects. As the Qigong Bigu protocol includes short fasting in the early stage, we hypothesized that during the initiation of Qigong Bigu, physiological ketosis and blood pressure lowering occur; therefore seizures or epilepsy might be a potential indication of Qigong Bigu.

As part of the national consecutive medical education project of Traditional Qigong Bigu (sponsored by the School of Traditional Chinese Medicine, Ningxia Medical University), this study was aimed to investigate the effects of Qigong Bigu on ketone bodies, body weight, BMI and blood pressure in healthy adult participants.

**Participants and methods**

**Participant recruitment**

The national consecutive medical education program of Traditional Medical Qigong Bigu was permitted by the State Consecutive Education Committee, China. Participants were recruited through Wechat and telephone. Registered participants were recruited according to the inclusion criteria: (1) age of 18–70 years, regardless of sex; (2) normal result of general physical examination; and (3) no diseases of major organs of the body, no intelligence disability. The exclusion criteria were: (1) non-registered consecutive education participants; and (2) having significant disease which makes it unsuitable to practice. The study was approved by the Ethics Committee of Medical Research in Ningxia Medical University. Clinical trial registration number was ChiCTR1800016923. Informed consent was obtained from all participants.

**The protocol of Qigong Bigu practice**

The Qigong Bigu practice consists of three phases [15, 17]: Qigong Bigu fasting phase, dietary regain phase and long-term Qigong practice phase. We studied only the first fasting phase in this work. The Qigong Bigu fasting phase lasted for seven days, during which the participants were organized to a relatively independent and isolated place. The place was relatively quiet, with fresh air and many trees or fruits, and without much traffic or crowded people, which was usually far away from commercial downtown area, ideally with a natural clean water source for drinking. Usually, hotels in a resort are selected as the place for practice. During the first week of Qigong Bigu fasting phase, participants were asked to practice Qigong, Rest Qigong and Movement Qigong, each for at least 1.5 h, in the morning, afternoon and evening, respectively. At the same time, methods and rationale of the Qigong practice were explained by experienced teachers from School of Traditional Chinese Medicine, Ningxia Medical University, and Medical Qigong Institute, Beijing Traditional Chinese Medicine University, Henan Traditional
Chinese Medicine University, and experienced folk Qigong masters. During Qigong training, music specifically designed and recorded was played or a master spoke on site to guide the practice. After each practice, important acupuncture points were patted. When participants had a strong feeling of hunger, they could take fresh fruits or porridge, or have a normal diet. The foods taken were recorded daily for each participant. During the Bigu dietary regain period, the participants gradually regain normal diet according to a special protocol, with gradual increases of calorie and food intake, from foods that are easy to digest to various types of food. The amount and type of food gradually increase to usual. The dietary regain phase usually lasts two weeks. During the dietary regain phase and long-term Qigong practice, the duration of daily Qigong practice was at least 30 min in average, no matter for Rest Qigong or for Movement Qigong or for both.

**Measuring methods**

Blood pressure was measured with a medical mercury sphygmomanometer, desk type (Yuyue, Danyang, Jiangsu Province, China). Body weight was measured with an electronic weighing scale (Type CS20G, Yolanda, Shenzhen, China) on site by research assistants after training. The levels of blood beta-hydroxybutyrate (BHB) and glucose were measured at 7:00, 12:00, 17:00, and 23:00 on the first three days, 7:00 on the next three days and 20:00 on the seventh day after the start of Qigong Bigu practice. The BHB level was measured with Beijing Yicheng Biostrips, Sentest type T1, using finger prick blood. The machine was calibrated before use. The project was performed in Yinchuan City, Ningxia Hui Autonomous Region, China.

**Statistics**

Data were analyzed with paired t-test for comparison of variables at different time points. Chen Qingshan Excel Statistics and software was used to treat our data. Linear regression analysis was performed to determine the relationship of BHB with blood pressure, body weight and BMI. Data are presented as mean ± SD.

**Results**

**Demographics and baseline data of participants**

In August 2017, 34 Chinese participants (16 males and 18 females) participated in the study. They were healthy without major diseases and could perform the Traditional Qigong Bigu practice. The demographic information is provided in Table 1.

**Effects of Qigong Bigu practice on physiological parameters**

Beginning from day 2, ketosis was induced and maintained at a relatively stable level. Table 2 shows the changes of different physiological parameters during the initial stage of Traditional Qigong Bigu practice. The total calorie consumption within the five days was $1197.47 ± 569.97$ kcal (95%CI 998.60–1396.35). The blood level of BHB increased from $0.1 ± 0.14$ mmol/L (95%CI 0.08–0.18) to $1.15 ± 1.12$ mmol/L (95%CI 0.76–1.62). The body weight was significantly decreased from $65.44 ± 11.26$ kg (95%CI 61.51–69.36) to $63.05 ± 10.92$ kg (95%CI 59.24–66.86) ($P < 0.001$). The difference was $2.39 ± 1.34$ kg (95%CI 1.92–2.85). The BMI was significantly decreased from $23.42 ± 3.44$ (95%CI 22.14–24.71) to $22.49 ± 3.36$ (95%CI 21.23–23.74) ($P < 0.001$). The systolic blood pressure was significantly decreased from $124.07 ± 20.66$ mmHg (95%CI 116.06–132.08) to $106.21 ± 15.93$ mmHg (95%CI 100.04–112.39) ($P < 0.001$). Similarly, the diastolic blood pressure was significantly decreased from $81.25 ± 6.88$ mmHg (95%CI 68.58–73.92) ($P < 0.001$). The blood glucose level did not change significantly.

Side effects such as hypoglycemia, hunger, and dizziness were occasionally present during the early stage of Qigong Bigu practice, but no severe side effect was reported by the participants.

**Correlation of blood BHB level with calorie consumption and other parameters**

The blood level of BHB showed significant negative correlation with calorie consumption within two days, three days, and five days of Qigong Bigu practice (Table 3). In addition, the blood BHB level was positively correlated with weight loss and BMI reduction (Table 3, Fig. 1).

**Table 1** The demographic information of participants

| Value, mean ± SD | 95% CI |
|------------------|-------|
| Sex, n (m/f) a   | 16/18 |
| Age, years b     | 41.24 ± 14.63 | 36.13–46.34 |
| Weight, kg c     | 65.44 ± 11.26 | 61.51–69.36 |
| Body mass index d| 23.49 ± 3.45 | 22.28–24.69 |
| Systolic blood pressure, mmHg e | 123.18 ± 19.83 | 116.15–130.21 |
| Diastolic blood pressure, mmHg e | 81.76 ± 9.09 | 78.53–84.98 |
| Height, cm f     | 166.87 ± 8.99 | 163.73–170.00 |
| Blood BHB, mmol/L g | 0.13 ± 0.14 | 0.08–0.18 |
| Blood glucose, mmol/L h | 5.71 ± 0.8 | 5.42–6.00 |

| Data are provided as mean ± SD, a n = 34, b n = 32, c n = 32 |

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Angle brackets are used for quantities in scientific notation.
In this study, we demonstrated that Qigong Bigu practice for five days can lead to body weight loss, reduction of BMI and down-regulation of blood pressure in healthy adult participants. The blood BHB level increased to a physiological level after two days of Qigong Bigu practice (fasting and practice), while no symptomatic hypoglycemia and other significant side effects were observed, which suggests the safety of Qigong Bigu fasting. In addition, the calorie consumption was negatively related to the blood BHB level, while the body weight loss and decrease of BMI were positively related to the level of blood BHB.

The present results provide strong evidence to support our hypothesis that nutritional or physiological ketosis occurs during the initial five days of Qigong Bigu practice. Previous studies seldom showed these similar results. As blood ketone bodies have been demonstrated to have anti-seizure efficacy [19, 22], one could speculate that during the initial stage of Qigong Bigu practice, BHB might have potential to treat patients with epilepsy or other diseases. Further clinical trials in patients with different diseases are needed to verify the clinical use of Qigong Bigu practice.

In this study, Qigong Bigu practice decreased blood pressure in healthy adults, the blood BHB level was negatively associated with calorie consumption while positively correlated to the body weight and BMI loss. The underlying mechanism may be associated with decomposition of fats that produces ketone bodies. The BHB level was neither related to the systolic blood pressure nor the diastolic blood pressure after five days of practice, suggesting that other unknown mechanisms such as the over-activation of sympathetic nervous system might be involved. However, the lowering of blood pressure might contribute to the neuroprotective effect of KDT, since hypertension is one of the important comorbidities in young adult epilepsy patients [1] and may lead to cerebral damage, thus lowering the threshold of seizures [2]. Seizures are accompanied by blood pressure elevation because of increased sympathetic tone [5]. Furthermore, the increased sympathetic tone is associated with SUDEP [12]. If Qigong Bigu practice could lower the blood pressure in patients with epilepsy, then it may be helpful for

| Parameter | Day 1     | Day 5     | Difference | P value |
|-----------|-----------|-----------|------------|---------|
|           | Mean ± SD | 95%CI     | Mean ± SD  | 95%CI   | Mean ± SD | 95%CI   |        |
| Level of blood BHB, mmol/L | 0.13 ± 0.14 | 0.08–0.18 | 1.15 ± 1.12 | 0.76–1.62 | 1.02 ± 1.22 | 0.6–1.45 | <0.001 |
| Weight, kg (n = 34) | 65.44 ± 11.26 | 61.51–69.36 | 63.05 ± 10.92 | 59.24–66.86 | 2.39 ± 1.34 | 1.92–2.85 | <0.001 |
| BMI (n = 30) | 23.42 ± 3.44 | 22.14–24.71 | 22.49 ± 3.36 | 21.23–23.74 | 0.94 ± 0.57 | 0.73–1.15 | <0.001 |
| Systolic blood pressure, mmHg (n = 28) | 124.07 ± 20.66 | 116.06–132.08 | 106.21 ± 15.93 | 100.04–112.39 | 17.86 ± 14.17 | 12.36–23.35 | <0.001 |
| Diastolic blood pressure, mmHg (n = 28) | 81 ± 8.82 | 77.58–84.42 | 71.25 ± 6.88 | 68.58–73.92 | 9.75 ± 7.45 | 6.86–12.64 | <0.001 |
| Blood glucose, mmol/L (n = 29) | 5.80 ± 0.81 | 5.49–6.11 | 5.83 ± 0.83 | 5.52–6.15 | -0.03 ± 0.96 | -0.39–0.34 | 0.8676 |

| BHB and calories consumed within two days | BHB and calories consumed within three days | BHB and calories consumed within five days |
|------------------------------------------|------------------------------------------|------------------------------------------|
| r                                        | -0.5614                                  | -0.6097                                  | -0.6968                                  |
| freedom                                  | 31                                       | 31                                       | 31                                       |
| t value                                  | 3.7767                                   | 4.2832                                   | 5.4089                                   |
| P                                        | 0.0007                                   | 0.0002                                   | <0.0001                                  |
| Five days                                 |                                        |                                        |                                          |
| weight loss and BHB                      | BMI change and BHB                       | BHB and blood pressure/systolic          |
| r                                        | 0.6428                                   | -0.1870                                  | -0.2523                                  |
| freedom                                  | 32                                       | 31                                       | 31                                       |
| t value                                  | 4.7471                                   | 4.748                                    | 1.4518                                   |
| P                                        | <0.0001                                  | <0.0001                                  | 0.1566                                   |

Discussion
In this study, we demonstrated that Qigong Bigu practice for five days can lead to body weight loss, reduction of BMI and down-regulation of blood pressure in healthy adult participants. The blood BHB level increased to a physiological level after two days of Qigong Bigu practice (fasting and practice), while no symptomatic hypoglycemia and other significant side effects were observed, which suggests the safety of Qigong Bigu fasting. In addition, the calorie consumption was negatively related to the blood BHB level, while the body weight loss and decrease of BMI were positively related to the level of blood BHB.

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seizure control in epilepsy, and even for prevention and treatment of SUDEP.

The ketogenesis demonstrated in our study should be investigated further in future studies. Based on the benefits of fasting in patients with diabetes mellitus and epilepsy, the ketogenic diet was proposed in 1920s [23–25]. Now KDT is widely used to treat epilepsy [22, 24, 26–29], to rescue intractable status epilepticus [23, 30], and serves as an addition to control infections and diabetes mellitus [24, 25]. Moreover, ketogenic diet is the first-line therapy for glucose transporter type 1 deficiency syndrome, pyruvate dehydrogenase deficiency syndrome, some mitochondrial diseases and genetic diseases which currently have no treatment available [24]. Although mechanisms remain to be fully revealed, KDT studies have demonstrated that the anti-seizure and neuroprotective effects are related to ketone bodies [31]. Ketogenic diet could postpone aging [32], improving cognition through inhibiting excessive activation of mammalian targeted protein of rapamycin [33]. Therefore, the loss of body weight and BMI index, and nutritional ketosis during Qigong Bigu practice suggest potential application of Bigu to treat various diseases, including metabolic syndromes. The present study also evidenced that Qigong Bigu practice could be a new approach for health care. Our results are consistent with previous finding that intermittent low calorie food intake in a five-day period could stabilize blood pressure, decrease body weight and BMI index, and lead participants into a nutritional ketosis state [34]. One could speculate that ketosis is a common basic mechanism for both Qigong Bigu practice and KDT.

In Qigong Bigu practice the outcomes are mainly evaluated by clinical observation, and rarely by blood biomarkers. As the ketone bodies are negatively related to energy intake while positively related to body weight loss and BMI reduction, they may be a biomarker in the initial stage of Qigong Bigu practice. Thus, the use of ketone bodies as a biomarker may help standardize the protocols of Qigong Bigu practice.

Our research had limitations. The study was carried out in healthy subjects rather than in patients with hypertension or epilepsy or other diseases, and the sample size was small. Although only short period of fasting was employed in our study, during which we found connections between Traditional Bigu and KDT, ketosis might be a common mechanism, regardless of the fasting time. Future multicenter studies with large sample sizes that monitor blood ketone bodies, fatty acid and other biomarkers of Multi-Omics are needed to clarify the efficacy and mechanisms of Traditional Qigong Bigu practice in different diseases. The relationship between Qigong Bigu practice and KDT also deserves further investigation.
Conclusions
The present study demonstrated blood pressure lowering, body weight and BMI loss, combined with ketogenesis in healthy subjects during Qigong Bigu practice. The effects of Qigong Bigu on hypertension and epilepsy should be studied in future. Nutritional ketosis (physiological ketosis) has potential use in epilepsy treatment and prevention. The Qigong Bigu practice may also have use in treatment of other diseases such as metabolic syndromes and even in health care of healthy people.

Abbreviations
SUDEP: Sudden unexpected death in epilepsy; RAS: Renin-angiotensin system; KDT: Ketogenic diet therapy; BMI: Body mass index; BHB: Beta-hydroxybutyrate.

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Authors’ contributions
JXL, KWF and JHG designed the study, and revised the manuscript. Other authors conducted the study. JXL drafted the study. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used in this study are available upon request from the corresponding author.

Declarations
Ethics approval and consent to participate
This study was approved by the Institutional Ethics Committee of Ningxia Medical University. Informed consent was obtained from all participants in this study.

Consent for publication
All authors agreed on the publication of this study.

Competing interests
Authors have no conflicts of interest in regards to this article.

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