

# Proposed safe apnea test using positive end-expiratory pressure valve and short-term blood gas analysis

## Observational study

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### Abstract

The apnea test is an essential examination for the determination of brain death; however, hypotension, hypoxemia, and other complications during the apnea test can affect the stability of brain-dead patients, as well as organ function for recipients. Therefore, it is necessary to establish standard guidelines for apnea testing.

The modified apnea test (MAT) comprises delivery of 100% oxygen through the endotracheal tube connected to manual resuscitator (Ambu bag) with the positive end-expiratory pressure (PEEP) valve after disconnection of the mechanical ventilator for maintenance of PEEP. Forty-nine instances of the conventional apnea test (CAT) were performed in 25 brain-dead patients; 77 instances of the MAT were performed in 39 brain-dead patients.

The mean duration of the apnea test was  $3.5 \pm 1.4$  minutes in the CAT group and  $3.0 \pm 1.2$  minutes in the MAT group. There were no significant changes in PaCO<sub>2</sub>, PaO<sub>2</sub>, or pH between the CAT and MAT groups ( $P = .341$ ,  $.593$ , and  $.503$ , respectively). In overweight patients (body mass index  $\geq 23$  kg/m<sup>2</sup>), MAT prevented dramatic reductions in PaO<sub>2</sub> and SaO<sub>2</sub> ( $P < .05$  for both). In the patients who had hypoxic brain injury due to hanging, differences in PaO<sub>2</sub> and SaO<sub>2</sub> in the MAT group were significantly smaller than in the CAT group ( $P < .05$ ).

Although MAT, which was invented to maintain PEEP, was not efficient for all brain-dead patients, it could be helpful in selected patient groups, such as overweight patients or those who had hypoxic injury due to hanging. And clinicians should consider short-term apnea test to avoid unnecessarily prolonged hypoxemia.

**Abbreviations:** ABGA = arterial blood gas analysis, APACHE = Acute Physiologic Assessment and Chronic Health Evaluation, BMI = body mass index, CAT = conventional apnea test, EEG = electroencephalogram, IRB = institutional review board, MAT = modified apnea test, PaCO<sub>2</sub> = arterial carbon dioxide partial pressure, PaO<sub>2</sub> = arterial partial pressure of oxygen, PEEP = positive end-expiratory pressure, SaO<sub>2</sub> = oxygen saturation, SPECT = single-photon emission computerized tomography.

**Keywords:** apnea test, brain death, organ procurement, positive end-expiratory pressure

## 1. Introduction

Brain death refers to irreversible cessation of whole brain function, in which an individual becomes unresponsive to all stimuli and exhibits no movement, including breathing.<sup>[1]</sup> According to the Korean medical law (specifically, Article 21 of the Act on Organ Transplantation), 2 instances of brain death

investigation, with 6 hours of observation between investigations, should be performed for the determination of brain death. Then, a judgment of brain death can be ascertained by identifying over 30 minutes of flat waves on electroencephalogram (EEG) analysis. Apnea tests are performed during these first and second brain death investigations; these apnea tests are important and essential to evaluate the brain stem reflex. The criterion of the apnea test in Korea is that no self-respiration is observed upon increased arterial carbon dioxide partial pressure (PaCO<sub>2</sub>) of  $> 50$  mmHg after disconnection of the mechanical ventilator.<sup>[2]</sup>

Although the apnea test is mandatory for the diagnosis of brain death, there are no internationally established guidelines for apnea test procedures. Moreover, the apnea test is always accompanied by various complications, ranging from mild to severe, including hypoxemia or fluctuation of vital signs, and even cardiac arrest.<sup>[3–5]</sup> Therefore, several methods have been attempted to reduce the frequency of hypoxemia or other complications and maintain hemodynamic stability.

The modified apnea test (MAT) was designed to maintain positive end-expiratory pressure (PEEP), even after disconnection of the mechanical ventilator. This MAT does not interfere with the provocation of hypercapnia for the judgment of brain death. Additionally, it can prevent the decruitment of lungs and reduce the risk of hypoxemia and fluctuation of blood pressure.<sup>[6,7]</sup>

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The authors declare that they have no competing interests.

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The aim of this study was to verify the efficiency of MAT for the maintenance of hemodynamic stability without disturbance of hypercapnia and self-respiration by comparison with the conventional apnea test (CAT). Ultimately, we suspect that the MAT may substitute for the CAT, and we propose potential guidelines of apnea testing for the determination of brain death.

## 2. Materials and methods

### 2.1. Patients

From August 2013 to December 2016, potential brain-dead patients who planned to donate their organs, with consent from legal guardians, were enrolled in this study in our tertiary teaching hospital. All brain-dead patients who had undergone brain death investigation by the apnea test at least once were also enrolled, even if organ donation could not be accomplished because of a lack of suitability (e.g., undiagnosed malignancy, active hepatitis, or other infectious disease). Brain-dead patients who were younger than 18 years of age ( $n=2$ ) were excluded. Among the enrolled patients, CAT was conducted in 25 patients from August 2013 to May 2015 (CAT group) and MAT was conducted in 39 patients from June 2015 to December 2016 (MAT group).

This study was approved by the institutional review board (IRB) of Ewha Womans University Mokdong Hospital (IRB number: EUMC 2018-04-047-002).

### 2.2. Apnea test protocol

Before all apnea tests, pre-oxygenation with 100% oxygen for 10 minutes, recommended for the safety of brain-dead patients, was performed. The method of CAT was as follows: after disconnection of the mechanical ventilator, 15 L/min of 100% oxygen was supplied through a simple cannula with a 2.9-mm internal diameter, then hypercapnia and self-respiration were observed. Serial arterial blood gas analysis (ABGA) was performed after 2 or 3 minutes. If the results of ABGA did not meet the requirements for determination of brain death, ABGA was repeated every 1 minute. The method of MAT was as

follows: after disconnection of the mechanical ventilator, a manual resuscitator (Ambu bag) with PEEP valve was connected to the brain-dead patient's endotracheal tube and 15 L/min of 100% oxygen was supplied for maintenance of PEEP, then hypercapnia and self-respiration were observed. As mentioned above, serial ABGA was performed after 2 or 3 minutes. If the results of ABGA did not meet the requirements for determination of brain death, ABGA was repeated every 1 minute.

During apnea tests, the results of ABGA and all data regarding monitored vital signs (e.g., systolic/diastolic/mean blood pressure, pulse rate, central venous pressure, and systolic/diastolic/mean pulmonary arterial pressure) were recorded together.

### 2.3. Statistical analysis

All numeric variables, such as age, results of ABGA, and variables related to hemodynamic status, were expressed as "mean  $\pm$  standard deviation." Categorical variables were analyzed by chi-squared tests. The results of ABGA and variables related to hemodynamic status, according to subgroups, were compared by using Student's *t* test, the Mann-Whitney test, or the Kruskal-Wallis test. Statistical analysis was performed by using IBM SPSS version 20.0 (SPSS Inc., Chicago, IL). Additionally, GraphPad Prism version 5.0 (GraphPad Software, La Jolla, CA) was used for statistical analysis and the creation of figures. Statistical significance was designated as a significance level (*P* value) less than .05.

## 3. Results

From August 2013 to December 2016, 64 patients were enrolled in this study (Fig. 1). Among them, 40 were male and 24 were female. The mean length of hospitalization, from admission due to the cause of brain death until the decision for organ donation, was  $8.6 \pm 13.4$  days.

In the CAT group, 49 instances of CAT were performed in 25 brain-dead patients from August 2013 to May 2015. In 1 patient, the first apnea test was not completed due to unstable vital signs; thus, brain single-photon emission computerized tomography

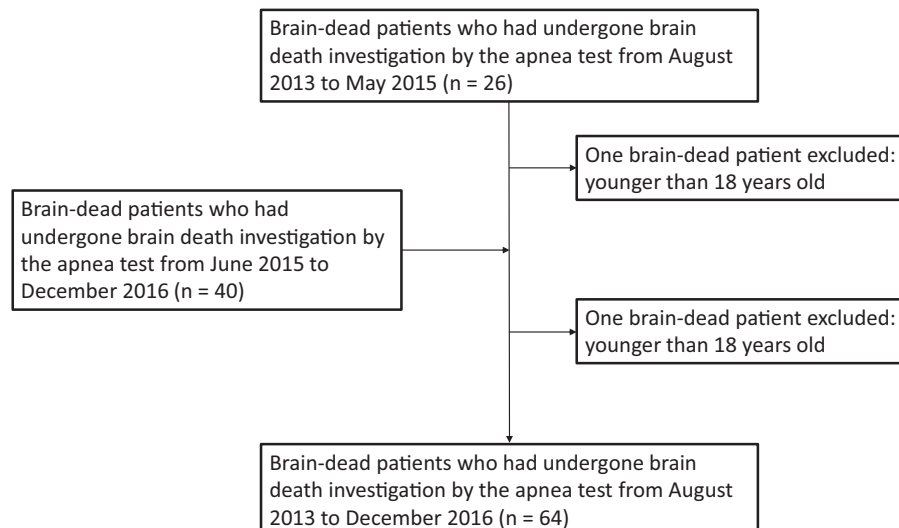


Figure 1. Flow diagram of the study inclusion.

(SPECT) was substituted for the apnea test. Fluid resuscitation, vasopressor, and other conservative treatments were applied to the patient; the patient then completed the second apnea test 24 hours later. In the MAT group, 77 instances of MAT were performed in 39 brain-dead patients from June 2015 to December 2016. There were no failures of apnea tests; however, 1 patient expired during the observational period after the first apnea test, due to abrupt deterioration of general condition. Demographic and clinical characteristics are shown in Table 1.

There were no significant changes in PaCO<sub>2</sub>, arterial partial pressure of oxygen (PaO<sub>2</sub>), or pH between the CAT and MAT groups. Additionally, changes in vital signs or dosages of vasopressor, both during apnea testing and for 30 minutes after apnea testing, were not statistically significant (Table 2, Fig. 2).

Subgroup analysis was also performed. In the subgroup of overweight patients (body mass index, BMI ≥ 23 kg/m<sup>2</sup>, according to east Asian standard, CAT group n=25, MAT

group n=39), the difference of PaO<sub>2</sub> in the MAT group was significantly smaller than in the CAT group (-155.1±123.6 mmHg in CAT group vs -92.9±114.5 mmHg in MAT group, P=.043). Post-apnea test PaO<sub>2</sub> was higher in the MAT group than in the CAT group (151.4±131.1 mmHg in CAT group vs 300.6±143.7 mmHg in MAT group, P<.05). Additionally, the difference of oxygen saturation (SaO<sub>2</sub>) in the MAT group was significantly smaller than in the CAT group (-6.9±8.7 mmHg in CAT group vs -2.3±7.7 mmHg in MAT group, P=.038) (Fig. 3).

Notably, among patients who had hypoxic brain injury due to hanging (CAT group n=14, MAT group n=16), the difference of PaO<sub>2</sub> in the MAT group was significantly smaller than in the CAT group (-178.0±86.0 mmHg in CAT group vs. -51.9±84.7 mmHg in MAT group, P<.05); post-apnea test PaO<sub>2</sub> was higher in the MAT group than in the CAT group (169.3±140.1 mmHg in CAT group vs 397.1±86.0 mmHg in MAT group, P<.05). Moreover, the difference of SaO<sub>2</sub> in the MAT group was significantly smaller than in the CAT group (-6.9±9.1 mmHg in CAT group vs -0.3±0.7 mmHg in MAT group, P=.012) (Fig. 4).

**Table 1**  
Demographic and clinical characteristics.

	CAT* group (n=49)	MAT† group (n=77)	P value
Sex (male:female)	35:14	43:34	.092
Age (yr)	46.1±12.5	49.8±13.7	.715
≤60	45 (91.8%)	61 (79.2%)	.080
>60	4 (8.2%)	16 (20.8%)	
BMI‡ (kg/m <sup>2</sup> )	23.4±4.3	23.2±3.3	.131
<23	24 (49.0%)	35 (46.7%)	.855
≥23	25 (51.0%)	40 (53.3%)	
Hospitalization (days)			
Previous cardiologic disease history	4 (8.3%)	4 (5.2%)	.482
Previous pulmonary disease history	2 (4.2%)	2 (2.7%)	.643
Cause of brain death			.115
Sudden cardiac arrest	6 (12.2%)	18 (23.4%)	
Spontaneous cerebrovascular hemorrhage	14 (28.6%)	31 (40.3%)	
Traumatic brain injury	9 (18.4%)	8 (10.4%)	
Other neurologic diseases	4 (8.2%)	4 (5.2%)	
Hanging-induced hypoxic brain injury	14 (28.6%)	16 (20.8%)	
Near-drawn-induced hypoxic injury	2 (4.1%)	0	
Left ventricular dysfunction on TTE§			1.000
Normal to mild	35 (71.4%)	65 (84.4%)	
Moderate to severe	6 (12.2%)	10 (13.0%)	
Not evaluated	8 (16.3%)	2 (2.6%)	
APACHE   score	34.3±5.6	27.4±6.9	<.05****
Level of lactate (mmol/L)	0.85±1.52	1.20±8.7	.149
Early fluid administration (ml)	10724.4±4222.1	10294.5±4248.8	.605
Dosage of NE¶ (mcg/kg/min)	0.13±0.15	0.06±0.08	.004****
≥0.2 mcg/kg/min	8 (16.3%)	7 (9.1%)	.264
PAP# catheter insertion	46 (93.9%)	52 (89.7%)	.504
Chest PCD** insertion	13 (26.5%)	16 (20.8%)	.517
Number of retrieved organs	3.9±1.5	3.6±1.8	.357
Donation of heart	23 (46.9%)	26 (36.1%)	.261
Donation of lungs	14 (28.6%)	26 (36.1%)	.435

\* CAT = conventional apnea test.

† MAT = modified apnea test.

‡ BMI = body mass index.

§ TTE = transthoracic echocardiogram.

|| APACHE = Acute Physiologic Assessment and Chronic Health Evaluation.

¶ NE = norepinephrine.

# PAP = pulmonary arterial pressure.

\*\* PCD = percutaneous drainage

\*\*\*\* P<.05.

**Table 2**  
Difference between pre- and post-apnea test.

	CAT* group (n=49)	MAT† group (n=77)	P value
Mean duration of apnea test (minutes)	3.5±1.4	3.0±1.2	.061
FiO <sub>2</sub> ‡ of pre-apnea test	0.47±0.15	0.35±0.07	<.05****
PEEP§ of pre-apnea test (mmHg)	10.3±3.3	10.0±1.9	.553
Δ pH	-0.128±0.043	-0.132±0.034	.503
Δ PaCO <sub>2</sub>    (mmHg)	20.15±5.70	19.18±5.51	.341
Δ PaO <sub>2</sub> ¶ (mmHg)	-101.93±125.88	-90.14±115.75	.593
Δ HCO <sub>3</sub> # (mEq/L)	2.29±1.96	1.68±3.95	.314
Δ SaO <sub>2</sub> ** (%)	-4.32±7.60	-1.74±6.50	.059
Δ mean arterial blood pressure (mmHg)	0.5±15.9	-0.9±18.7	.659
Δ systolic arterial blood pressure (mmHg)	2.2±24.4	0.5±26.6	.724
Δ diastolic arterial blood pressure (mmHg)	-0.3±13.3	-1.7±16.0	.609
Δ pulse rate (bpm)	2.1±7.3	1.7±9.2	.812
Δ central venous pressure (mmHg)	-0.3±6.3	-0.1±5.2	.860
Δ mean pulmonary arterial pressure (mmHg)	2.0±8.9	3.5±9.0	.430
Δ systolic pulmonary arterial pressure (mmHg)	2.2±12.8	6.7±15.2	.147
Δ diastolic pulmonary arterial pressure (mmHg)	1.9±8.9	2.2±7.2	.886
Δ SvO <sub>2</sub> †† (%)	7.7±19.8	19.4±35.4	.057
Δ dosage of norepinephrine (mcg/kg/min)	0.012±0.054	0.012±0.041	.938
Δ level of lactate (mmol/L)	-0.31±0.95	1.19±11.31	.356

\* CAT = conventional apnea test.

† MAT = modified apnea test.

‡ FiO<sub>2</sub> = fraction of inspired oxygen.

§ PEEP = positive end-expiratory pressure.

|| PaCO<sub>2</sub> = partial pressure of carbon dioxide.

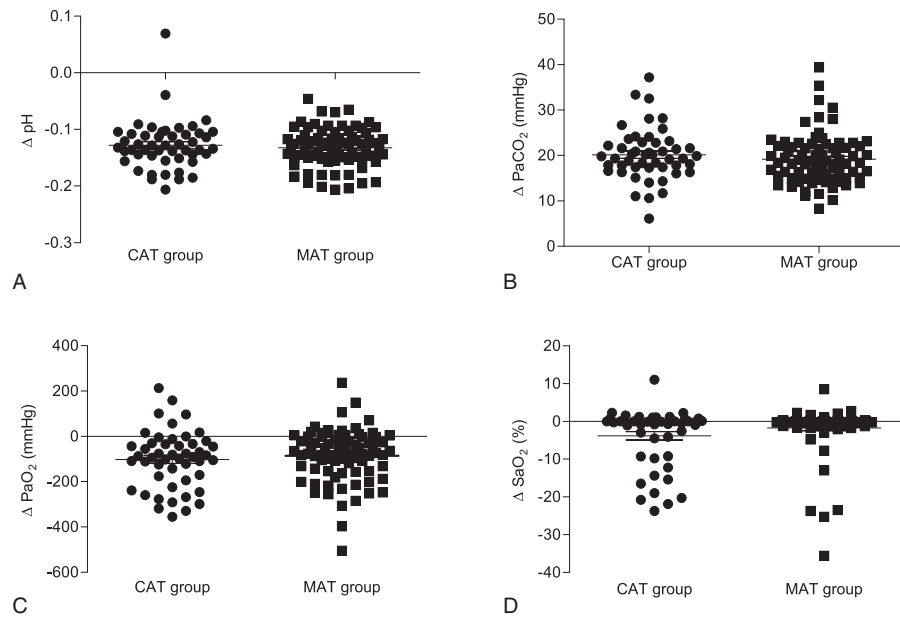
¶ PaO<sub>2</sub> = partial pressure of oxygen,

# HCO<sub>3</sub> = bicarbonate.

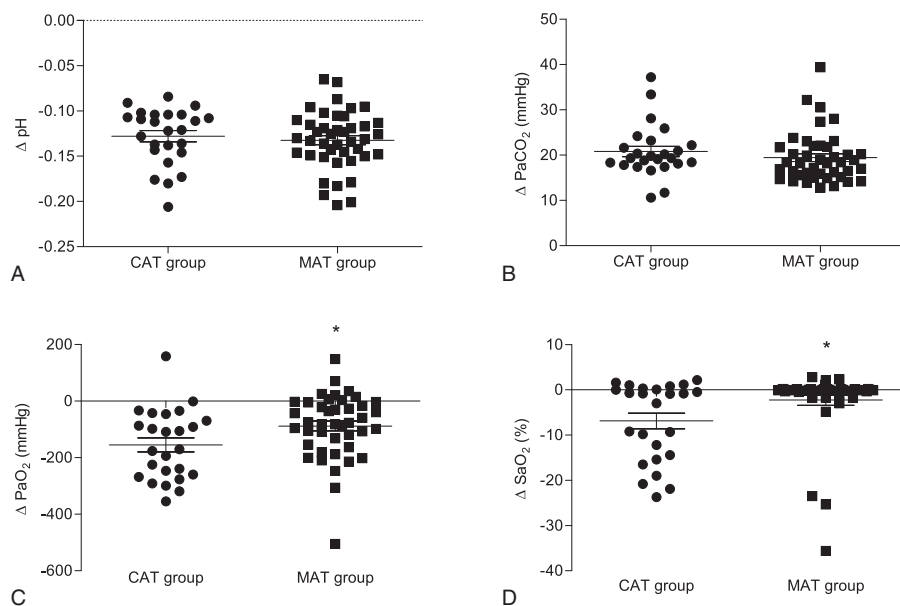
\*\* SaO<sub>2</sub> = oxygen saturation.

†† SvO<sub>2</sub> = mixed venous oxygen saturation.

\*\*\*\* P<.05.



**Figure 2.** Difference of arterial gas analysis results during apnea tests in brain death patients. There were no significances in (A) pH, (B) PaCO<sub>2</sub>, (C) PaO<sub>2</sub> and (D) SaO<sub>2</sub> between conventional apnea test group (CAT group) and modified apnea test group (MAT group).

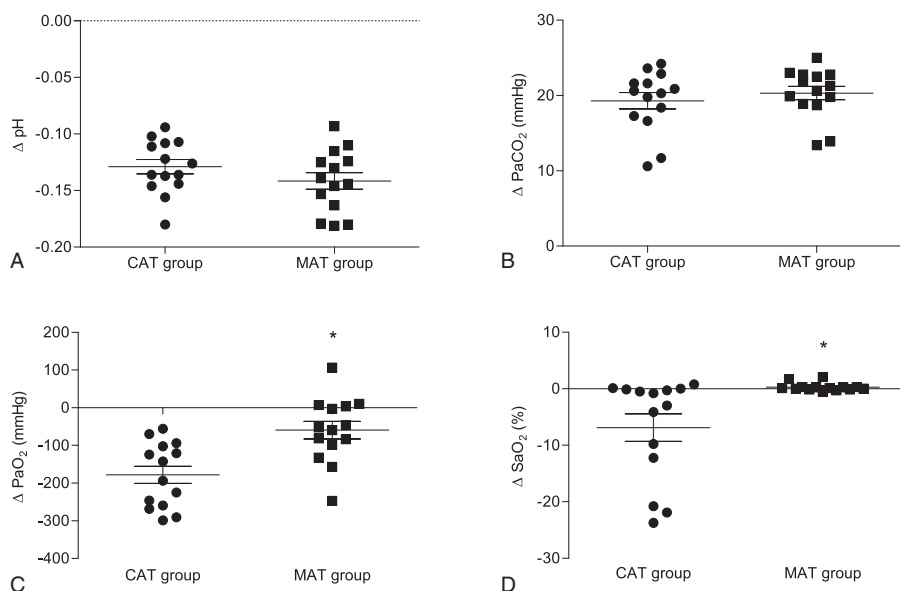


**Figure 3.** Difference of arterial gas analysis results during apnea tests in brain death patients with body mass index (BMI)  $\geq 23$  kg/m<sup>2</sup>. There were no significances in (A) pH and (B) PaCO<sub>2</sub> between conventional apnea test (CAT) group and modified apnea test (MAT) group. Decrease in (C) PaO<sub>2</sub> and (D) SaO<sub>2</sub> was significantly less in MAT group than in CAT group.

#### 4. Discussion

The recognition of brain death enables the initiation of organ transplantation; however, brain-dead donors and deceased donors are in both hemodynamically unstable and pro-inflammatory states. In particular, brain-dead donors continue to exhibit cardiovascular and physiologic instability, due to catecholamine surge, central sympatholysis, and hormonal dysregulation.<sup>[8,9]</sup> During apnea tests in brain-dead patients,

various hemodynamic changes occur;<sup>[10]</sup> therefore, a variety of complications can manifest, such as hypotension, arrhythmia, hypoxemia, acidosis, and even cardiac arrest.<sup>[3,4,11,12]</sup> Reduced blood pressure and hypoxemia affect the stability of brain-dead patients; hypoperfusion of donated organs resulting from these instances of hypotension and hypoxemia can affect the organ function of recipients. Decruitment of lungs due to the removal of PEEP after mechanical ventilator disconnection can hinder the function of the donated lungs and reduce the survival of donated



**Figure 4.** Difference of arterial gas analysis results during apnea tests in brain death patients due to hanging. There were no significances in (A) pH and (B) PaCO<sub>2</sub> between conventional apnea test (CAT) group and modified apnea test (MAT) group. However, MAT prevented the drastic decrease in (C) PaO<sub>2</sub> and (D) SaO<sub>2</sub> than CAT.

lung recipients.<sup>[13,14]</sup> Overall, hypoxemia complications resulting from apnea tests, such as subcutaneous emphysema, pulmonary barotrauma, and tension pneumothorax, can negatively impact brain-dead patients.<sup>[6,15–17]</sup> However, the apnea test is an inevitable and important component for the diagnosis of brain death; thus, it is important to consider when to conduct apnea tests. Therefore, several methods have been attempted to reduce the frequency of hypoxemia and maintain hemodynamic stability.

We hypothesized that the maintenance of PEEP during the apnea test could prevent the decruitment or collapse of lungs, and could help brain-dead patients to preserve lung function and hemodynamic stability. For verification of the efficiency of MAT, we compared variables between CAT and MAT groups. There were more patients with high Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) II score in the CAT group ( $34.3 \pm 5.6$  in CAT group vs  $27.4 \pm 6.9$  in MAT group,  $P < .05$ ). Additionally, patients in the CAT group were administered higher dosages of norepinephrine prior to apnea tests than patients in the MAT group ( $0.13 \pm 0.15$  mcg/kg/min in CAT group vs  $0.06 \pm 0.08$  mcg/kg/min in MAT group,  $P = .004$ ) (Table 1). In this retrospective study, MAT did not negatively affect diagnosis of brain death, with respect to identifying hypercapnia or self-respiratory movement. Contrary to our hypothesis, however, the MAT was not superior to the CAT in terms of hypoxemia, acidosis, or hemodynamic stabilities (Fig. 2). We had expected that the reduction in PaO<sub>2</sub> or frequency of severe hypoxemia would be smaller in the MAT group than in the CAT group, as in previous studies.<sup>[6,18,19]</sup> However, there were no significant differences in PaO<sub>2</sub> or frequency of severe hypoxemia. Further, there were no significant differences in mean arterial blood pressure, pulse rate, central venous pressure, mean pulmonary arterial pressure, and dosage of norepinephrine between the 2 groups (Table 2). Unlike previous studies,<sup>[6,18,19]</sup> these unexpected results were thought to result from shorter durations apnea tests. A longer duration for the apnea test was expected to result in greater collapse of the brain-dead patient's lungs; thus, the gap in PaO<sub>2</sub> might be larger. However, we preferred

to perform short-term apnea tests, such that the reduction of PaO<sub>2</sub> or SaO<sub>2</sub> would not be severe. Kramer and colleagues<sup>[20]</sup> also reported that MAT could be associated with a slightly smaller reduction in PaO<sub>2</sub>, without statistical or clinical significance. The duration of the apnea test in Kramer report was also short: fixed internals of 3 to 5 minutes. Therefore, the short duration of the apnea test might have disturbed interpretation of our results.

Although we could not prove the superiority of MAT over CAT, we observed valuable results in specific subgroups. In overweight patients (BMI  $\geq 23$  kg/m<sup>2</sup>), MAT prevented severe reductions in PaO<sub>2</sub> and SaO<sub>2</sub> ( $P < .05$ ) (Fig. 3C, D). Obesity is associated with a state of chronic systemic inflammation that is driven predominantly by the action of substances released by adipose tissue. Also excess adipose tissue is associated with the production of various proinflammatory cytokines, including tumor necrosis factor- $\alpha$ , interleukin-1- $\beta$ , and interleukin-6.<sup>[21]</sup> Moreover, obese patients are characterized by normal chest-wall elastance and high pleural pressure due to the mass loading effect, subsequently transpulmonary pressure is decreased. And negative end-expiratory transpulmonary pressure is responsible for alveolar collapse in obese patients.<sup>[22]</sup> Therefore, constant application of PEEP using MAT could prevent alveolar collapse and help to sustain PaO<sub>2</sub> and SaO<sub>2</sub> during apnea test.

Additionally, in patients who had hypoxic brain injury due to hanging, MAT was particularly effective. The difference of PaO<sub>2</sub> and SaO<sub>2</sub> in the MAT group was significantly smaller than in the CAT group ( $P < .05$ ) (Fig. 4C, D). Hanging asphyxiation produces significant lung injury in brain deaths. Attempted inspiration against an obstructed upper airway causes a drop in the intrathoracic pressure, resulting in increased venous return and increased pulmonary capillary pressure, with a concomitant decrease in pulmonary interstitial pressure, resulting in pulmonary edema. In addition to increased venous return, decreased left ventricular compliance and increased after load, because of the decrease in negative pressure, increase overall pulmonary blood volume and rise the pulmonary capillary hydrostatic pressure,



further exacerbating the pulmonary edema.<sup>[23]</sup> The acceptable results of MAT in patients who had hypoxic brain injury due to hanging were due to the preservation of PEEP. This PEEP could help to sustain end-expiratory lung volume by opening airways, recruiting alveoli and, possibly, preventing the redistribution of fluid to the lung interstitium. Collectively, these effects nearly always increase the PaO<sub>2</sub> of arterial blood by diminishing intrapulmonary shunting of blood and improving the matching of ventilation and perfusion.<sup>[24]</sup> Therefore, we must select brain-dead patients carefully for the application of PEEP during apnea testing, although MAT is theoretically superior.

Moreover, we would like to note that, during the standard duration apnea test, brain-dead patients tended to be vulnerable to hemodynamic effects resulting from hypercapnia and acidosis.<sup>[10]</sup> Meaningless excessive elevation of PaCO<sub>2</sub> resulted in severe hypercapnia and acidosis; therefore, apnea tests of unnecessarily longer duration could be harmful to brain-dead donors. Nevertheless, many clinicians (90.2%) perform the apnea test for 8 minutes or longer, or as long as the patients can tolerate the test, according to the report of Saritas and colleagues.<sup>[25]</sup> Some respondents (4.9%) reported no established duration. Other previous studies also conducted apnea tests for 10 minutes because such length was a standard recommendation.<sup>[6,19]</sup> However, as mentioned above, we checked ABGAs after 2 or 3 minutes, and then each minute from the start of the

apnea test. If the results of ABGA met the diagnostic criteria for brain death, even after only 2 minutes from the start of the test, we discontinued the apnea test and re-started mechanical ventilation promptly. Thus, the mean duration of apnea tests was  $3.5 \pm 1.4$  minutes in the CAT group and  $3.0 \pm 1.2$  minutes in the MAT group (Table 2). There were 6 brain-dead patients who underwent the apnea test for 6 minutes or more. In those patients, we repeated ABGA every 1 to 2 minutes through arterial cannulation. The level of PaCO<sub>2</sub> met the criteria in all enrolled brain death patients (Fig. 5A). Just after 3 minutes from the start of the apnea test, the mean increase was over 20 mmHg (Fig. 5B). After 2 investigations involving the two instances of short-term apnea tests, we used the EEG as a confirmatory test for final diagnosis of brain death. Although the duration of apnea tests was relatively short, less than 8 to 10 minutes, there was no divergent result between the findings of the apnea test and those of the EEG. No brain-dead patient was misdiagnosed when using the short-term apnea test. Kramer and colleagues<sup>[20]</sup> also reported that regular ABGA, at fixed intervals of 3 to 5 minutes, could help to avoid severe respiratory acidosis and significant hemodynamic complications. Thus, the short-term apnea test is could be one of the options for safe apnea tests.

There were some limitations in this study. The clinical characteristics were not homogenous between the 2 groups; for example, APACHE II score, dosage of norepinephrine, and FiO<sub>2</sub> on pre-apnea test ventilator settings (Table 1). Additionally, there were small number of apnea tests in our study, especially in the subgroup analyses. Therefore, it is necessary to perform subsequent randomized controlled trials with a larger number of brain-dead patients. Further, if it is possible to verify the significance of MAT in various subgroups with additional apnea tests, we can propose credible guidelines for the apnea test.

## 5. Conclusions

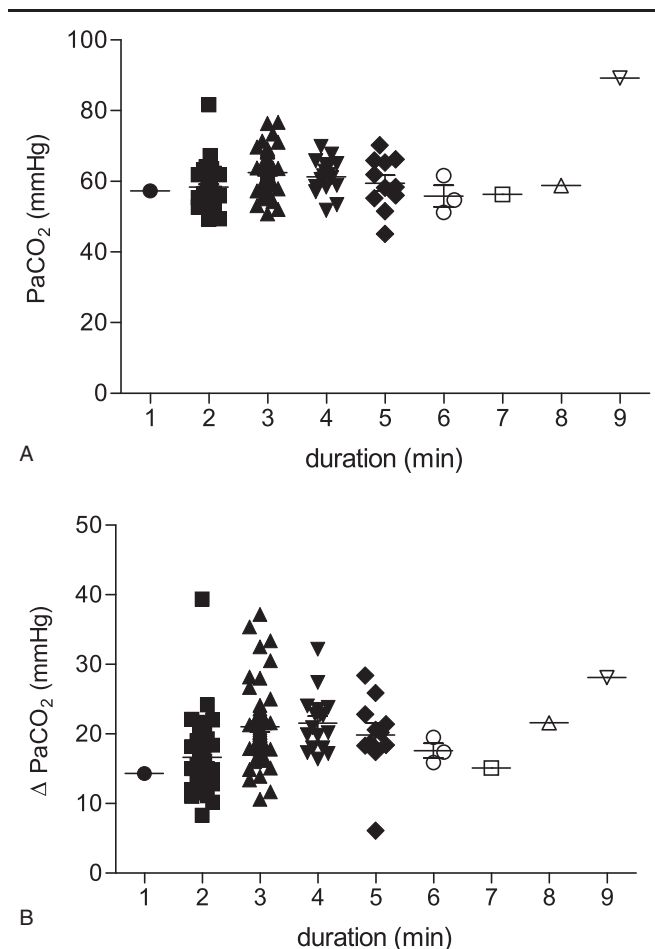
The MAT does not interrupt the determination of brain death and can be efficient for specific brain-dead patients, including those who are overweight or who were injured by hanging. Clinicians who manage brain-dead donors should be aware of the efficiency of MAT in specific subgroups. Further, an extended apnea test duration cannot be the necessary condition for diagnosis of brain death; a duration must be used that is sufficient to meet the diagnostic criteria. The short-term apnea test should be considered during the investigation or diagnosis of brain death.

## Author contributions

**Data curation:** Jin Park, Kyung Sook Hong.  
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**Methodology:** Young-Joo Lee.  
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**Validation:** Kyung Sook Hong.  
**Writing – original draft:** Kyung Sook Hong.  
**Writing – review & editing:** Kyung Sook Hong.  
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**Figure 5.** PaCO<sub>2</sub> and duration of apnea test. (A) The earlier PaCO<sub>2</sub> met the criteria, the earlier apnea test could be ceased. (B) There was no significant relationship between PaCO<sub>2</sub> and duration of apnea test.

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