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Clinical Study

Evaluation of Differences between $PaCO_2$ and $ETCO_2$ by Age as Measured during General Anesthesia with Patients in a Supine Position

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Objective. The aim of this study was to evaluate the arterial to end-tidal partial pressure gradient of carbon dioxide according to age in the supine position during general anesthesia. *Methods*. From January 2001 to December 2013, we evaluated 596 patients aged ≥16 years who underwent general anesthesia in the supine position. The anesthetic charts of these 596 patients, all classified as American Society of Anesthesiologists physical status I or II, were retrospectively reviewed to investigate the accuracy of $PaCO_2$ and $ETCO_2$. *Results*. The a-$ETCO_2$ was 3.0 ± 2.1 mmHg for patients aged 16 to <65 years and 4.1 ± 3.1 mmHg for patients ≥65 years. The a-$ETCO_2$ was 2.4 ± 3.1 mmHg for patients aged 16 to 25 years, 3.1 ± 2.2 mmHg for patients aged 26 to 35 years, 3.0 ± 2.2 mmHg for patients aged 36 to 45 years, 3.4 ± 2.0 mmHg for patients aged 46 to 55 years, 3.2 ± 2.0 mmHg for patients aged 56 to 64 years, 4.3 ± 3.2 mmHg for patients aged 65 to 74 years, and 3.7 ± 2.8 mmHg for patients aged 75 to 84 years. *Conclusion*. The arterial to end-tidal partial pressure gradient of carbon dioxide tended to increase with increasing age.

1. Introduction

End-tidal carbon dioxide ($ETCO_2$) is clinically used as a positive indicator of endotracheal intubation, an alert in the event of disconnection, and an estimation of arterial CO_2 tension ($PaCO_2$). $ETCO_2$ refers to the partial pressure of CO_2 at the end of expiration and reflects $PaCO_2$ [1]. $ETCO_2$ can be used to guide minute ventilation during general anesthesia. If a higher arterial to end-tidal partial pressure gradient of CO_2 (P[a-ET]CO_2) is expected, anesthetists may make incorrect judgments and provide the wrong ventilation setting.

Generally, $PaCO_2$ is considered to exceed $ETCO_2$ [2, 3]. This is because CO_2 diffuses according to its partial gradient from a comparatively higher partial pressure in the pulmonary capillary to a lower concentration in the alveolus in several conditions, such as increases in the anatomical dead space, increases in the physiologic dead space, and the presence of pulmonary embolism. The P(a-ET)CO_2 is approximately 3.6 to 4.6 mmHg in healthy awake patients [2, 3]. Anatomical and physiologic dead space increase with increasing age; thus, increasing age may influence P(a-ET)CO_2 values. However, the influences of increasing age on P(a-ET)CO_2 are not well known.

Therefore, the aim of this study was to evaluate P(a-ET)CO_2 according to age in the supine position during general anesthesia and determine the effects of a wide range of ages on P(a-ET)CO_2.

2. Patients and Methods

This retrospective study was approved by the Committee on Clinical Investigation for Human Research at Iwate Medical University.

We evaluated 596 patients aged ≥16 years who underwent general anesthesia in the supine position from January 2001 to December 2013. The anesthetic charts of these 596 patients, all classified as American Society of Anesthesiologists physical status I or II (with the exception of patients with conditions such as asthma, respiratory disease, obesity (body mass index of ≥25 kg/m^2), and smoking), were retrospectively reviewed to investigate age, height, weight, % forced vital capacity (%FVC), % forced expiratory volume in 1 second ($FEV_{1.0}$%), and P(a-ET)CO_2.

First, the patients were divided into two groups by age: Group I (adult; aged 16 to <65 years) and Group II (older individuals; aged 65 to 84 years). Second, patients aged 16 to 84 years were classified into seven groups by age, with each group covering one decade: Group A (aged 16–25 years), Group B (26–35 years), Group C (36–45 years), Group D (46–55 years), Group E (56–64 years), Group F (65–74 years), and Group G (75–84 years). Anesthesia was induced with intravenous propofol (1-2 mg/kg of ideal body weight) or thiopental sodium (3–5 mg/kg of ideal body weight). Muscle relaxation was provided with vecuronium bromide (0.1 mg/kg of ideal body weight) or rocuronium bromide (0.8 mg/kg of ideal body weight). After tracheal intubation, anesthesia was maintained in almost all patients with sevoflurane (1%-2%) and nitrous oxide gas if necessary, and all patients were mechanically ventilated. We usually used RAE cuffed tracheal tubes (Cuffed Murphy Eye; Covidien, Mallinckrodt, Ireland) for oral intubation and Parker Flex-Tip PFHV tubes (Parker Medical, Highlands Ranch) for nasal intubation. The ventilator settings were as follows: tidal volume, 8 to 10 mL/kg of ideal body weight; respiratory rate, 10 to 12 breaths/minute; peak airway pressure, <20 cmH_2O; PEEP, 0 cmH_2O; and inspiratory oxygen concentration, 33% or 40%. At 30 to 60 min after adjustment of the mechanical ventilator settings, a blood sample was drawn from the radial artery or dorsalis pedis artery. At the same time, $ETCO_2$ was measured at the proximal end of the tracheal tube. The $PaCO_2$ was measured from the arterial blood sample using a blood gas analyzer (RAPIDLab 1265; Siemens, Dublin, Ireland), and each rectal temperature was entered into the analyzer. The $ETCO_2$ sampling line was connected to a sidestream capnometer (Capnomac Ultima; Datex-Engstrom, Helsinki, Finland). The maximum terminal value was taken from the expiration curve of the capnograph.

The $ETCO_2$ value was usually written on both the anesthesia record and blood gas analysis form when the arterial blood sample was obtained. The rectal temperature is usually measured in all patients undergoing general anesthesia in our institution. The authors checked the $PaCO_2$ and $ETCO_2$ on both the anesthesia record and blood gas analysis form, and the P(a-ET)CO_2 was calculated with each arterial blood gas and $ETCO_2$ reading.

Values are presented as mean ± standard deviation. Statistical analysis was performed using SPSS, version 11.0 (SPSS, Inc., Chicago, IL, USA). Statistical analysis employed Student's unpaired t-test for comparisons between two groups and one-way analysis of variance followed by multiple-comparison testing using the Scheffe test for comparisons among groups. The relationship between P(a-ET)CO_2 and age was investigated by Pearson's correlation coefficient test. Correlation coefficients were obtained using simple regression analysis (Excel software, 2003; Microsoft, Redmond, WA, USA). Differences were considered statistically significant at a P value of <0.05.

3. Results

Patients' characteristics and laboratory data are presented in Table 1.

When we compared Groups I and II, we found significant differences in age, height, weight, %FVC, $FEV_{1.0}$%, and P(a-ET)CO_2 (Table 1(a) and Figure 1(a)). The P(a-ET)CO_2 was 3.0 ± 2.1 mmHg for patients aged 16 to <65 years and 4.1 ± 3.1 mmHg for patients aged 65 to 84 years.

Significant differences in age and body mass index were observed among Groups A to G. Patients in Group G had lower body weights than patients in Groups A, B, C, D, and E; patients in Group F had lower body weights than patients in Groups A, B, and C; patients in Group E had lower body weights than patients in Groups A and B; and patients in Group D had lower body weights than patients in Group B. Patients in Group G had lower body heights than patients in Groups A, B, C, D, E, and F and patients in Group E had lower body heights than patients in Groups A and C. Patients in Group G had lower body surface areas than patients in Groups A, B, C, D, E, and F and patients in Group F had lower body mass indices than patients in Groups A and B. Patients in Group G had a lower %FVC than patients in Groups A and D and patients in Group E had a lower %FVC than patients in Group A. Patients in Group G had a lower $FEV_{1.0}$% than patients in Groups B and E; patients in Group F had a lower $FEV_{1.0}$% than patients in Groups A, B, and C; patients in Group E had a lower $FEV_{1.0}$% than patients in Groups A and B; patients in Group D had a lower $FEV_{1.0}$% than patients in Groups A and B; and patients in Group C had a lower $FEV_{1.0}$% than patients in Group A.

Patients in Group A had a lower P(a-ET)CO_2 than patients in Groups F and G. The P(a-ET)CO_2 was 2.4 ± 3.1 mmHg in patients aged 16 to 25 years, 3.1 ± 2.2 mmHg in patients aged 26 to 35 years, 3.0 ± 2.2 mmHg in patients aged 36 to 45 years, 3.4 ± 2.0 mmHg in patients aged 46 to 55 years, 3.2±2.0 mmHg in patients aged 56 to 64 years, 4.3±3.2 mmHg in patients aged 65 to 74 years, and 3.7 ± 2.8 mmHg in patients aged 75 to 84 years (Table 1(b) and Figure 1(b)). P(a-ET)CO_2 tended to increase with increasing age. Figure 2 showed the correlation between age and P(a-ET)CO_2; P(a-ET)CO_2 linearly increased with increasing age (P[a-ET]CO_2 = 1.9524 + 0.0265 × age; r = 0.23; P < 0.05) and there was a slight correlation between the two.

4. Discussion

In this study, we found that the mean P(a-ET)CO_2 was 2.4 to 4.3 mmHg and that the P(a-ET)CO_2 tended to increase with increasing age in patients anesthetized in the supine position.

Table 1: Patient profiles and laboratory data by age.

(a) Comparison of patients aged 16 to less than 65 years (Group I) and those aged 65 to less than 84 years (Group II)

Group	I (age from 16 to less than 65 years)	II (age more than 65 years)
Number	425	171
Age (yrs)	36.3 ± 15.4	73.8 ± 5.6*
Height (cm)	164.2 ± 8.9	155.1 ± 9.0*
Weight (kg)	58.1 ± 9.7	51.8 ± 8.5*
Body mass index	21.3 ± 2.2	21.4 ± 2.1
Body surface area (m^2)	1.61 ± 0.15	1.49 ± 0.14
%FVC (%)	111.7 ± 16.3	107.8 ± 19.5*
$\%FEV_{1.0}$ (%)	84.7 ± 8.2	78.8 ± 8.3*
a-$ETCO_2$ (mmHg)	3.0 ± 2.1	4.1 ± 3.1*

* $P < 0.05$ versus Group A.

(b) Comparison among groups according to patient age (from 16 to 84 years in one decade increments)

Group	A (16–25 years)	B (26–35 years)	C (36–45 years)	D (46–55 years)	E (56–64 years)	F (65–74 years)	G (75–84 years)
Number	148	91	49	70	67	97	74
Age (years)	20.8 ± 4.7	29.8 ± 2.9*	40.8 ± 2.8*,#	51.4 ± 2.7*,#,§	60.5 ± 2.2*,#,§,†	69.8 ± 3.2*,#,§,†,‡	80.2 ± 2.7*,#,§,†,‡,**
Height (cm)	165.7 ± 8.9	166.2 ± 8.6	165.1 ± 8.3	161.5 ± 8.8#	160.0 ± 7.7#,§	157.3 ± 9.0*,#,§	150.4 ± 14.4*,#,§,†,‡,**
Weight (kg)	58.2 ± 9.8	58.5 ± 9.7	60.3 ± 10.7	58.5 ± 9.3	55.2 ± 8.8*,§	53.5 ± 8.4	49.4 ± 11.1*,#,§,†,‡
Body mass index	20.8 ± 2.1	21.1 ± 2.3	21.5 ± 2.3	21.9 ± 2.1	21.4 ± 2.4	21.5 ± 1.9	21.3 ± 2.3
Body surface area (m^2)	1.64 ± 0.15	1.64 ± 0.15	1.61 ± 0.13	1.63 ± 0.15	1.55 ± 0.14	1.52 ± 0.14*,#	1.45 ± 0.13*,#,§,†,‡,**
%FVC (%)	106.5 ± 16.3	114.4 ± 14.8	112.8 ± 18.1	113.4 ± 15.3	116.7 ± 15.0*	110.5 ± 20.1	103.9 ± 21.0#,†
$\%FEV_{1.0}$ (%)	89.5 ± 9.9	86.9 ± 7.0	83.7 ± 6.2*	81.1 ± 5.7*,#	80.5 ± 6.0*,#	78.1 ± 4.7*,#,§	79.0 ± 8.3*,#
a-$ETCO_2$ (mmHg)	2.4 ± 3.1	3.1 ± 2.2	3.0 ± 2.2	3.4 ± 2.0	3.2 ± 2.0	4.3 ± 3.2*	3.7 ± 2.8*

* $P < 0.05$ versus Group A, # $P < 0.05$ versus Group B, and § $P < 0.05$ versus Group C.
† $P < 0.05$ versus Group D, ‡ $P < 0.05$ versus Group E, and ** $P < 0.05$ versus Group F.

We obtained P(a-ET)CO_2 values of 2.4 to 4.3 mmHg, similar to the gradient of values previously reported for other clinical situations. Several prior studies have focused on the type of surgery or operating position, but age has not been previously considered in anesthetized patients. The typical P(a-ET)CO_2 is approximately 2.0 to 5.0 mmHg in healthy adults [1]. The following P(a-ET)CO_2 values have been found in anesthetized neurosurgical patients. In mechanically ventilated neurosurgical patients undergoing craniotomies in various studies, the average P(a-ET)CO_2 was 7.2 ± 3.3 mmHg in 35 patients [3], 3.6 mmHg in 24 stable patients [2], 4.24 ± 4.42 mmHg [4], and 4.6 ± 2.5 mmHg [5]. Another study assessed the accuracy of $ETCO_2$ in estimating $PaCO_2$ during neurosurgical procedures according to surgical position; the average P(a-ET)CO_2 was 6 ± 3 mmHg for patients in the supine position, 7 ± 3 mmHg in the lateral position, 5 ± 5 mmHg in the prone position, and 5 ± 5 mmHg in the sitting position [6]. The main differential in the present study is the wide range of ages assessed, not the type of surgery or position. Because of the high number of patients investigated, our results have great potential to be used as reliable basic data regarding P(a-ET)CO_2 during general anesthesia.

P(a-ET)CO_2 tended to increase with increasing age. In the two main categories of age, the P(a-ET)CO_2 for patients aged 16 to <65 years was higher than that for patients aged 65 to 84 years. In the seven subcategories of age, with each group covering one decade, the P(a-ET)CO_2 was higher with increasing age. The P(a-ET)CO_2 can be explained by the theories of dead space, shunting, and ventilation-perfusion mismatch (V/Q mismatch) [7, 8]. Increased intrapulmonary shunting and decreased functional residual capacity with ventilation-perfusion inhomogeneity have been recognized as part of the associated pathophysiology [9, 10]. It is recognized that V/Q mismatch can occur in patients given general anesthesia or in those with lung disease [11]. Herr et al. [12] reported that an increased F_IO_2 was associated with increases in venous admixture and might result in slightly increased P(a-ET)CO_2. However, Russell and Graybeal [3] and Russell et al. [13] found no significant influence of F_IO_2, cardiac output, systemic vascular resistance, pulmonary vascular resistance, or infusions of dopamine, nitroglycerine, and nitroprusside on the P(a-ET)CO_2. In the present study, anesthesia was performed at O_2 concentrations of 33% or 40%, and whether F_IO_2 influenced P(a-ET)CO_2 was unclear.

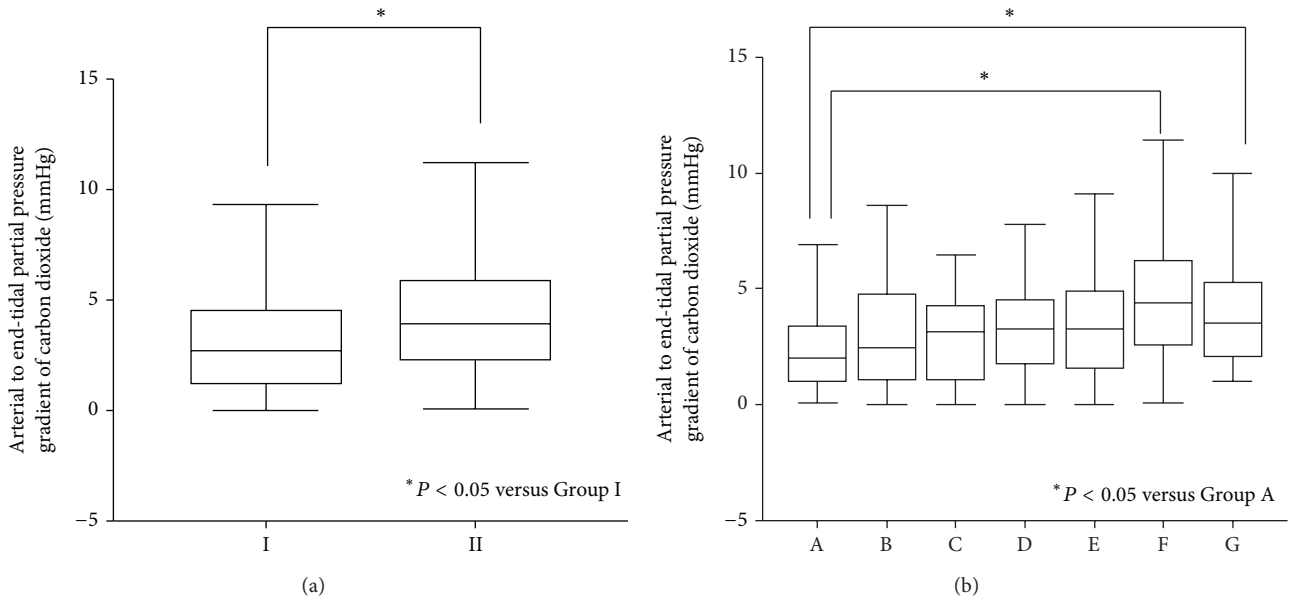

Figure 1: Comparison of arterial to end-tidal partial pressure gradient of carbon dioxide among groups according to age. (a) Comparison of patients aged 16 to <65 years (Group I) and patients aged ≥65 years (Group II). There is a significant difference between the two groups. (b) Comparison of arterial to end-tidal partial pressure gradient of carbon dioxide among groups according to patient age (16–84 years in one-decade increments). The arterial to end-tidal partial pressure gradient of carbon dioxide tends to increase with increasing age, and there is a significant difference between Group A and Groups F and G.

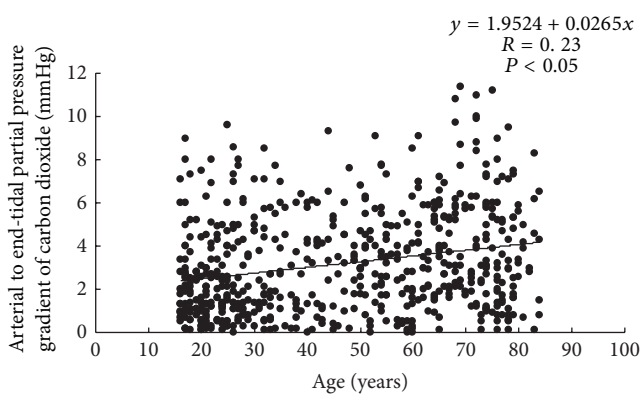

Figure 2: Relationship between arterial to end-tidal partial pressure gradient of carbon dioxide and age. A poor positive correlation is found between the arterial to end-tidal partial pressure gradient of carbon dioxide and age ($r = 0.23$, $P < 0.05$).

Based on the above findings, physiological changes are likely attributed to the increased P(a-ET)CO_2 because the anatomical and physiological dead spaces increase with increasing age.

In this study, there was a slight correlation between P(a-ET)CO_2 and age. However, the correlation between P(a-ET)CO_2 and age was lower ($r = 0.23$) than that reported previously in other clinical situations. In a study of elective craniotomies, Russell and Graybeal [3] reported a correlation coefficient (r) of 0.632 in the supine position and an r^2 of 0.61 in the supine position, 0.62 in the lateral position, 0.55 in the prone position, and 0.46 in the sitting position [6]. The $ETCO_2$ did not provide a stable reflection of PaO_2 in this study.

In conclusion, P(a-ET)CO_2 tended to increase with increasing age and there was a slight correlation between P(a-ET)CO_2 and age. We must be aware that greater differences in P(a-ET)CO_2 are expected with increasing age and ensure that $ETCO_2$ is used to guide minute ventilation during general anesthesia.

Abbreviations

$ETCO_2$:	End-tidal carbon dioxide
$PaCO_2$:	Partial pressure of carbon dioxide in arterial blood
P(a-ET)CO_2:	Arterial to end-tidal partial pressure gradient of carbon dioxide
F_IO_2:	Fraction of inspiratory oxygen.

Conflict of Interests

The authors declare that they received no financial support and have no conflict of interests.

Disclosure

The authors do not have a financial relationship with the organization that sponsored the research.

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