Comparison of Mainstream End Tidal Carbon Dioxide on Y-Piece Side Versus Patient Side of Heat and Moisture Exchanger Filters in Critically Ill Adult Patients: a prospective observational study

Satoshi Tamashiro
Department of Clinical Engineering, Okinawa Prefectural Nanbu Medical Center and Children's Medical Center
Izumi Nakayama
Department of Health Data Science, Graduate School of Data Science, Yokohama City University
Koichiro Gibo
Department of Emergency Medicine, Okinawa Prefectural Chubu Hospital
Junichi Izawa (izawa.junichi.87r@st.kyoto-u.ac.jp)
Department of Intensive Care Unit, Department of Internal Medicine, Okinawa Prefectural Chubu Hospital

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Research Article

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Abstract

Introduction: Whether HMEF impairs the accuracy of mainstream $EtCO_2$ measured on the Y-piece (filtered) side of HMEF compared to that on the patient (unfiltered) side is unclear.

Methods: We conducted a prospective observational method comparison study in a teaching hospital in Japan between July 2019 and December 2019. Critically ill adult subjects receiving mechanical ventilation with HMEF were included. We performed a noninferiority comparison of the accuracy of $EtCO_2$ measurements on the two sides of HMEF. The accuracy was measured by the absolute difference between $PaCO_2$ and $EtCO_2$. We set the non-inferiority margin at +1 mmHg in accuracy difference between the Y-piece side and the patient side of HMEF. We also assessed the agreement between $PaCO_2$ and $EtCO_2$ using Bland-Altman analysis.

Results: Among thirty-seven subjects, the accuracy difference was -0.14 mmHg (95% CI, -0.58–0.29), and the upper 95% CI limit did not exceed the predefined margin of + 1 mmHg, establishing non-inferiority of $EtCO_2$ on the Y-piece side of HMEF (*P* for non-inferiority <0.001). In the Bland-Altman analyses, 95% limits of agreement between $PaCO_2$ and $EtCO_2$ were similar in both sides of HMEF (Y-piece side, -8.67–+10.65 mmHg; patient side, -8.93–+10.67 mmHg).

Conclusions: The accuracy of mainstream $EtCO_2$ measurements on the Y-piece side of HMEF was noninferior to that on the patient side in critically ill adult subjects. Mechanically ventilated adult subjects could be accurately monitored with mainstream $EtCO_2$ on the Y-piece side of the HMEF unless their tidal volume was extremely low.

Introduction

End-tidal carbon dioxide ($EtCO_2$) monitoring is a non-invasive, continuous measurement of exhaled carbon dioxide (CO_2) that offers real-time information about patients' ventilation, perfusion, and metabolism [1–4]. In ICU, $EtCO_2$ monitoring ensures the integrity of the ventilator circuit and assists the titration of mechanical ventilation [5]. Furthermore, a detailed assessment of $EtCO_2$ provides valuable insights into pathological respiratory physiology, such as increased physiologic dead space in critically ill patients [5]. The importance of $EtCO_2$ monitoring for patient safety has been increasingly recognized, and many professional societies have adopted its use as a standard of practice [3].

Heat and moisture exchanger filters (HMEFs) are widely used humidifier devices, especially during the current coronavirus disease 2019 pandemic for their filtering function. In ventilator circuits with HMEF, an $EtCO_2$ sensor is placed either on the patient side or the Y-piece side of HMEF. On the patient side, exhaled gas reaches an $EtCO_2$ sensor before being filtered by HMEF, thereby coughed up secretions from patients can contaminate the sensor and interrupt continuous monitoring. On the Y-piece side, in contrast, the exhaled gas is measured after being filtered by the HMEF, reducing the risk of sensor contamination.

Current anesthesia guidance during the coronavirus disease 2019 pandemic recommends using an HMEF and sampling gas from the Y-piece (filtered) side of the HMEF [6]. However, HMEF alters the components of exhaled gas during filtering, and thus affects $EtCO_2$ values and waveforms [7]. Previous studies reported that $EtCO_2$ measured with the sidestream method on the Y-piece side of HMEF showed lower values than that on the patient side [8, 9]. Inaccurately low $EtCO_2$ values could lead to misrecognition of CO_2 retention and threaten patient safety [10].

In the ICU, the mainstream $EtCO_2$ measurement is preferred because it has a faster response time than the sidestream method [5]. Yet, the accuracy of mainstream $EtCO_2$ on the Y-piece side of HMEF has not been evaluated [5]. This study aimed to investigate whether the accuracy of mainstream $EtCO_2$ measurement on the Y-piece side of the HMEF was noninferior to that on the patient side in critically ill adult patients receiving mechanical ventilation. This non-inferiority design is based on the benefits conferred by HMEF when measuring on the Y-piece side.

Methods

Study Design and Setting:

This study was approved by the institutional review board (2019-No.17). The requirement for written informed consent was waived by the institutional review board. The protocol was registered *a priori* in the UMIN-CTR (UMIN-CTR ID: 000037317).

This was a single-center prospective observational method comparison study in a tertiary care teaching hospital in Japan, which had 550 beds with 12 general ICU beds, conducted between July 2019 and December 2019.

Selection of the Patients

We prospectively screened all patients of mechanical ventilation in the ICU between July 16, 2019, and December 9, 2019. Patients were eligible when they were adults (≥ 20 years) receiving invasive mechanical ventilation, HMEF was used in the ventilator circuit, and an arterial line was placed. Patients were excluded when they were pregnant, previously enrolled in this study, patients or next of kin refused study participation, or they met any of the following safety criteria. The safety criteria were: PEEP ≥ 10 cmH_2O, fraction of inspired oxygen ≥ 0.6, heart rate < 40 bpm or 130 ≥ bpm, mean blood pressure < 60 mmHg or ≥ 110 mmHg, saturation of percutaneous oxygen < 90%, respiratory rate ≥ 40 breaths/min, or temperature < 36 or ≥ 38.5°C. These criteria followed the Japanese guidelines for early mobilization of mechanically ventilated patients [11, 12]. We also excluded patients when treating physicians judged the patient as inappropriate for study participation.

Measurement of $EtCO_2$

For eligible patients, we measured $EtCO_2$ on the two sides of the HMEF and $PaCO_2$ during the daytime (8:00–17:00) on weekdays. The timing of the measurements was based on the clinical indication of arterial blood gas analysis. We measured the first $EtCO_2$ on either the Y-piece side or the patient side of the HMEF, where the $EtCO_2$ sensor was placed (Fig. 1). Then, we switched the $EtCO_2$ sensor to the opposite side of the HMEF and measured the second $EtCO_2$. On each side, we averaged $EtCO_2$ from three consecutive breaths. CO_2 sensor zeroing was performed when we switched the position of the sensor, or the baseline flow did not return to zero in the capnography. Clinical engineers in the study team measured $EtCO_2$, simultaneously collected arterial blood, and submitted it for blood gas analysis to measure $PaCO_2$. Each $EtCO_2$ reading was performed before the results of blood gas analysis returned; thus, readers of $EtCO_2$ were unaware of the $PaCO_2$ value. The $EtCO_2$ sensor was Capnostat5 (Respironics), HMEF was Hygrobag S (Medtronic), and the blood gas analyzer was ABL800 (RADIOMETER).

We recorded patient demographics and clinical characteristics, including acute physiology and chronic health evaluation II (APACHE II) scores [13], vital signs, and ventilatory parameters, as shown in Tables 1 and 2. All patients were followed up until hospital discharge, and hospital outcomes were recorded.

Table 1
Patients Demographics, Characteristics at EtCO2 measurements and Outcomes.

Variables	N = 37
Demographics	
Age (median [IQR])	70 [60–79]
Male (%)	21 (57%)
BMI (median [IQR])	21.8 [19.6–25.3]
Current or former smoker (%)	17 (46%)
Location prior to ICU admission (%)	
Operating room	20 (54%)
Emergency room	11 (30%)
Ward	6 (16%)
ICU admission diagnosis (%)	
Cardiovascular	7 (19%)
Respiratory	4 (11%)
Gastrointestinal	10 (27%)
Neurological	8 (22%)
Metabolic	2 (5%)
Genitourinary	1 (3%)
Obstetrics and gynecology	2 (5%)
Musculoskeletal	1 (3%)
Trauma	2 (5%)
APACHE II score (median [IQR])	19 [16–25]
Characteristics at $EtCO_2$ measurements	
Time from intubation (median [IQR]), hour	21 [14–24]
Days form ICU admission (median [IQR]), day	2 [2–2]

$EtCO_2$, end-tidal carbon dioxide; IQR, interquartile range; BMI, body mass index; ICU, Intensive Care Unit; APACHE, acute physiology and chronic health evaluation; $PaCO_2$, partial pressure of arterial carbon dioxide; PaO_2, partial pressure of arterial oxygen; P/F ratio, the ratio of arterial oxygen partial pressure to fraction of inspired oxygen; FiO_2, fraction of inspired oxygen; PEEP, positive end expiratory pressure.

Variables	N = 37
Vital signs during measurement (median [IQR])	
Systolic blood pressure, mm Hg	129 [109–144]
Diastolic blood pressure, mm Hg	63 [56–72]
Mean arterial pressure, mm Hg	88 [77–101]
Heart rate, /min	82 [72–95]
Body temperature, Celsius	36.9 [36.6–37.4]
Percutaneous oxygen saturation (%)	98 [97–99]
Arterial blood gas analysis and ventilator settings (median [IQR])	
$PaCO_2$, mm Hg	38.2 [34.9–41.6]
PaO_2, mm Hg	93.0 [83.8–124.0]
pH	7.43 [7.42–7.45]
Bicarbonate, mmol/L	25.3 [22.5–27.1]
P/F ratio	364 [317–410]
FiO_2	0.25 [0.21–0.35]
PEEP, cm H_2O	5 [5–5]
Patient outcomes	
ICU stay (median [IQR]), day	4 [2–7]
Survival discharge	20 (54%)
Transfer	11 (30%)
Death	6 (16%)

$EtCO_2$, end-tidal carbon dioxide; IQR, interquartile range; BMI, body mass index; ICU, Intensive Care Unit; APACHE, acute physiology and chronic health evaluation; $PaCO_2$, partial pressure of arterial carbon dioxide; PaO_2, partial pressure of arterial oxygen; P/F ratio, the ratio of arterial oxygen partial pressure to fraction of inspired oxygen; FiO_2, fraction of inspired oxygen; PEEP, positive end expiratory pressure.

Table 2
Paired Observations on Y-piece side and patient side of HMEF.

	Y-piece side N = 37	Patient side N = 37	Difference * (Y-piece side - Patient side)	*P* value†
$EtCO_2$, (mean [SD]), mm Hg	37.4 (5.5)	37.5 (6.1)	-0.1 (1.6)	0.65
Absolute difference between $PaCO_2$ and $EtCO_2$, (mean [SD]), mm Hg	3.6 (3.4)	3.8 (3.3)	-0.1 (1.5)	0.58
Ventilator monitoring values during measurement, (mean [SD])				
Tidal volume, mL	418 (137)	431 (154)	-3.1 (40.7)	0.64
Minute volume, L	6.2 (1.7)	6.3 (1.7)	-0.2 (0.6)	0.10
Respiratory rate, /min	17 (4.7)	17 (4.9)	-0.1 (1.2)	0.79
Peak pressure, cm H_2O	14.1 (5.0)	14.2 (4.8)	-0.1 (0.7)	0.53
HMEF, heat and moisture exchanger filter; $EtCO_2$, end-tidal carbon dioxide; SD, standard deviation.				
* Differences between paired observations.				
† Two-tailed *P* values of the paired samples t-test.				

Statistical analysis

We labeled $EtCO_2$ measured on the Y-piece side of HMEF as “the index measurement,” $EtCO_2$ measured on the patient side as “the alternative measurement,” and $PaCO_2$ as “the reference standard [14].” We assessed the accuracy of $EtCO_2$ measurements by the absolute difference between $PaCO_2$ and $EtCO_2$ [15]. We defined Δ*Y-piece side* as the absolute difference between $PaCO_2$ and $EtCO_2$ measured on the Y-piece side of HMEF, and Δ*patient side* as the absolute difference between $PaCO_2$ and $EtCO_2$ measured on the patient side. We compared the accuracy of the two $EtCO_2$ measurements by *the accuracy difference* defined as Δ*Y-piece side* - Δ*patient side*. We calculated *the accuracy difference* in each patient and estimated the mean and 95% CI.

In the non-inferiority comparison of accuracies of the two $EtCO_2$ measurements, we set *a priori* the non-inferiority margin of + 1 mmHg in *accuracy difference*. The size of the margin was determined from a clinical standpoint and previous reports [8, 9, 16]. We declared non-inferiority of the Y-piece side if the upper limit of the CI for *accuracy difference* did not exceed the predefined margin of + 1 mmHg. This means that we accepted the Y-piece side if the absolute difference between $PaCO_2$ and $EtCO_2$ on the Y-piece side was not more than + 1 mmHg compared to the absolute difference between $PaCO_2$ and $EtCO_2$ on the patient side. We calculated *the P*-value for non-inferiority using two one-sided paired-sample t-tests. From the pilot observation, SD of *the accuracy difference* between the Y-piece side and the patient side was estimated at 1.5 mmHg. The calculated sample size for the non-inferiority test was 35 paired observations with a 5% one-sided significance level and 90% power.

In addition, on each side of the HMEF, we assessed the agreement between $PaCO_2$ and $EtCO_2$ using Bland-Altman analysis [17]. We graphically presented the variation of differences between $PaCO_2$ and $EtCO_2$ against their average (Bland-Altman plot). As a measure of lack of agreement, we estimated the mean difference and 95% limits of agreement [17]. We performed Bland-Altman analysis for $EtCO_2$ on the Y-piece side and $EtCO_2$ on the patient side separately, then compared the graphics and statistics of the two analyses. According to the reporting standards for Bland-Altman analysis, to ensure that the limits of agreement were meaningful summary statistics of the differences, we checked the following assumptions: repeatability, normality, and constant variation. Repeatability represents within-patient variation in repeated measurements of $EtCO_2$ in the same patient [18]. We recorded three $EtCO_2$ measurements per position per patient and assessed the repeatability of $EtCO_2$. We graphically checked whether the differences were normally distributed and whether variations in the differences were constant across the range of measurements.

Previous studies reported that differences between $EtCO_2$ on the Y-piece side and $EtCO_2$ on the patient side of HMEF were greater when the tidal volume was small [8, 9]. Therefore, we evaluated the relationship between the differences and tidal volume using Pearson's correlation coefficient and linear regression.

We presented patient characteristics as medians with interquartile ranges (IQR) for continuous variables and as proportions for categorical variables. We presented paired observations of $EtCO_2$ values, absolute differences, and ventilator monitoring values on the two sides of the HMEF as means with SDs. The means of differences between paired observations were compared with paired samples t-test, and two-sided *P*-values were reported. All statistical analyses were performed using R (The R Foundation for Statistical Computing, ver.3.5.2) and EZR (Saitama Medical Center, Jichi Medical University, ver.1.40), which is a graphical user interface for R [19]. Figure 3,4 and Supplemental Fig. 1 (Supplementary Information 1) were created using JMP (ver.16.1.0).

Results

Between July 16, 2019, and December 9, 2019, there were 167 patients on mechanical ventilation in the ICU, and screening for full eligibility criteria was completed in 132 of them (Fig. 2). Among the 52 eligible patients, we excluded 15 that met the exclusion criteria, leaving 37 patients in the study. In all 37 patients, two $EtCO_2$ measurements and $PaCO_2$ were collected. The median age was 70 years (IQR, 60–79), 57% (21/37) were male, 76% (28/37) were emergency ICU admissions, and the median acute physiology and chronic health evaluation II score was 19 (IQR, 16–25) (Table 1). The major diagnoses were cardiovascular (19% [7/37]), respiratory (11% [4/37]), gastrointestinal (27% [10/37]), and neurological diseases (22% [8/37]).

At the time of $EtCO_2$ measurements, the median number of days from ICU admission was 2 days (IQR, 2–2), and the median time from intubation was 21 hours (IQR, 14–24). Most of the patients had stable vital signs; the median systolic blood pressure was 129 mmHg (IQR, 109–144), body temperature was 36.9°C (IQR, 36.6–37.4), and respiratory rate was 16 breaths per minute (IQR, 14–19). The median partial pressure of arterial oxygen was 93.0 mmHg (IQR, 83.8–124.0), $PaCO_2$ was 38.2 mmHg (IQR, 34.9–41.6), and the ratio of partial pressure arterial oxygen to fraction of inspired oxygen was 364 (IQR, 317–410). The ventilator mode was continuous spontaneous ventilation in 46% (17/37) of the patients. The median fraction of inspired oxygen was 0.25 (IQR, 0.21–0.35) and PEEP was 5 cmH_2O (IQR, 5–5). The median ICU stay was 4 days (IQR, 2–7), and the hospital mortality rate was 16% (6/37).

The paired observations on the Y-piece side and the patient side of the HMEF are presented in Table 2. The means of $EtCO_2$ were 37.4 mmHg (SD, 5.5) and 37.5 mmHg (SD, 6.1) on the Y-piece side and the patient side, respectively. The mean difference in $EtCO_2$ (Y-piece side – patient side) was − 0.1 (SD, 1.6). The estimated *accuracy difference* (Δ*Y-piece side* - Δ*patient side*) was − 0.14 mmHg (95% CI, -0.58–0.29). The upper limit of the CI for *accuracy difference* did not exceed the predefined margin of + 1 mmHg, establishing non-inferiority (*P* for non-inferiority < 0.001) (Fig. 3).

In the Bland-Altman analyses, the mean difference between $PaCO_2$ and $EtCO_2$ on the Y-piece side was 0.99 mmHg (95% CI, -0.66–2.63), and 95% limits of agreement was − 8.67 mmHg (95% CI, -11.51– -5.84) to 10.65 mmHg (95% CI, 7.82–13.49). The mean difference between $PaCO_2$ and $EtCO_2$ on the patient side was 0.87 mmHg (95% CI, -0.80–2.54), and 95% limits of agreement was − 8.93 mmHg (95% CI, -11.81– -6.06) to 10.67 mmHg (95% CI, 7.80–13.55) (Supplementary Information 1: Supplemental Table 1). The estimated 95% limits of agreement were almost identical, indicating that the degree of agreement between $PaCO_2$ and $EtCO_2$ was similar on the Y-piece side and the patient side (Fig. 4). The square root of within-patient variance of $EtCO_2$ was 0.65 mmHg on the Y-piece side and 1.01 mmHg on the patient side, suggesting that the repeatability of the two $EtCO_2$ were sufficient. Histograms of differences between $PaCO_2$ and each of the two $EtCO_2$ measurements showed roughly normal distributions. Graphical inspection revealed that the variations in the differences were constant across the range of measurements (Fig. 4).

The relationship between tidal volume and difference in Y-piece side $EtCO_2$ and patient-side $EtCO_2$ are assessed in Supplemental Fig. 1 (Supplementary Information 1). There was no significant linear relationship (regression coefficient, -0.001 [95% CI, -0.005–0.003], correlation coefficient, -0.096).

Discussion

In this prospective method comparison study, we found that the accuracy of mainstream $EtCO_2$ measurement on the Y-piece side of HMEF was noninferior to that on the patient side. In adult ventilated patients using HMEF, our results support measuring $EtCO_2$ with the mainstream method on the Y-piece side of HMEF.

Relation to previous studies

Our observation contrasted with previous studies, which showed that sidestream $EtCO_2$ measurement on the Y-piece side of HMEF was lower than that on the patient side [8, 9, 20]. A study investigating 30 adult patients under general anesthesia reported that sidestream $EtCO_2$ on the Y-piece side of the breathing filter was lower than that on the patient side by -8.85 mmHg (95% CI, -19.58– -1.95) [8]. Similar results were reported in healthy children and critically ill adult patients [9, 20]. Several mechanisms were proposed as the reason for the lower $EtCO_2$ values on the Y-piece side of HMEF. First, the internal volume of the HMEF serves as an additional dead space in the ventilator circuit. While exhaled gas passes through the HMEF, the dead space from the HMEF is added to the exhaled gas. This addition dilutes exhaled CO_2 and thus lowers the Y-piece side of $EtCO_2$ [7]. The impact of dilution is particularly large in patients with low tidal volumes, such as pediatric patients [7]. Second, the sidestream capnometer aspirates a large volume of gas (150–200 ml/min) from the ventilator circuit during sampling [21]. The sampled gas tends to entrain fresh gas from the ventilator circuit, resulting in dilution of exhaled CO_2 [21]. The dilution of $EtCO_2$ with fresh gas entrainment is pronounced as the sampling site becomes closer to the ventilator, that is on the Y-piece side of HMEF [22]. These dilution effects explain the lower $EtCO_2$ values on the Y-piece side of HMEF.

In contrast, using the mainstream method, we found that the absolute difference between $PaCO_2$ and $EtCO_2$ was similar on both sides of the HMEF. The mainstream method of $EtCO_2$ measurement avoids mixing with fresh gas and does not dilute exhaled CO_2 during sampling. In adult patients undergoing brain surgery, mainstream $EtCO_2$ showed better agreement with $PaCO_2$ than sidestream $EtCO_2$ [21]. Considering these findings, we suspected that the sidestream method with large sampling volume was a major source of error in the Y-piece side $EtCO_2$ in previous studies [8, 9, 20]. Our study results also suggested that the dilution effect of dead space from HMEF was clinically small in adult patients with tidal volume within the observed range in this study (5–95 percentile range, 254–576 ml) [20]. Indeed, we could not find a significant relationship between tidal volume and difference in Y-piece side $EtCO_2$ and patient side $EtCO_2$ (Supplementary Information 1: Supplemental Fig. 1). In summary, we thought that the mainstream method and sufficient tidal volume were the main factors that maintained the accuracy of $EtCO_2$ on the Y-piece side of the HMEF in our study.

Implications for clinicians

Placing the $EtCO_2$ sensor on the Y-piece side of the HMEF has several advantages. HMEF prevents patients' secretions from interfering with the $EtCO_2$ sensors. Further, this position reduced the risk of health care workers' exposure to unfiltered exhaled gases, during circuit disconnection or zeroing $EtCO_2$ sensor [23]. HMEF is a cost-effective choice for humidification in situations including prolonged mechanical ventilation with less active diseases, recovering patients after elective surgery, patients without thick secretions, and cases of over-humidification with a heated humidifier [24]. Our study results suggested that patients in these situations could be safely monitored with mainstream EtCO2 on the Y-piece side of HMEF. The results of our study provide supporting evidence for current guidance on HMEF use during the coronavirus disease 2019 pandemic. (COVID 19 Anesthesia Machines and Equipment Maintenance. Anesthesia Patient Safety Foundation [6].

Of note, in small pediatric patients, it was reported that the dead space applied by HMEF induced CO_2 retention and $EtCO_2$ monitoring on the Y-piece side of HMEF failed to detect elevated CO_2 [10, 25]. Our study results should not be applied to pediatric patients.

Strengths and weaknesses of this study

We prospectively investigated the accuracy of mainstream $EtCO_2$ measurements. The readers of $EtCO_2$ were unaware of $PaCO_2$, which was the reference standard in this study. Our declaration of non-inferiority was based on an *a priori* defined non-inferiority margin. Our conclusion was based on the assessment of both mean difference and limits of agreement, following the reporting standards for method comparison study [18]. These features contributed to the quality of accuracy comparison in this study.

This study had several limitations. First, the included patients were selected as appropriate cases for HMEF; thus, they had relatively stable respiratory status. Our results were not directly applicable to patients under more severe conditions, such as extreme hypercapnia or very low tidal volume. We believe that such a severe patient is not a good candidate for the HMEF circuit. Second, the median time from HMEF placement to $EtCO_2$ measurement was 16 hours (IQR, 11–19). We could not refer to the accuracy of $EtCO_2$ under conditions with prolonged use of HMEF, although a study showed that 120-hour use of HMEFs did not increase their resistance [26]. Third, the choice of the non-inferiority margin was based on clinical judgment. However, we set a stricter margin (1 mmHg) for non-inferiority compared to a previous study (5 mmHg) [16]. Also, the non-inferiority test was conducted according to the prespecified analysis plan including sample size calculation and the pre-defined non-inferiority margin [27]. Fourth, despite prospective screening, 35 of 167 patients on mechanical ventilation could not undergo screening for the eligibility criteria. These patients required mechanical ventilation for a short period and were extubated before screening. Thus, their characteristics were considered to be similar to those of the study patients. We believe that excluding them from the analysis did not materially affect the study results. Fourth, despite prospective screening, 35 of 167 patients on mechanical ventilation could not undergo screening for the eligibility criteria. These patients required mechanical ventilation for a short period and were extubated before screening. Thus, their characteristics were considered to be similar to those of the study patients. We believe that excluding them from the analysis did not materially affect the study results. Fifth, we examined only one HMEF device (Hygrobag S, Medtronic), which had 45 ml of dead space. It might not be appropriate that we directly apply the study results to other HMEF devices, particularly those with larger dead space [28].

Conclusions

The accuracy of mainstream $EtCO_2$ measurements on the Y-piece side of HMEF was noninferior to that on the patient side in critically ill adult patients. Mechanically ventilated adult patients humidified with HMEF could be safely monitored with mainstream $EtCO_2$ on the Y-piece side of the HMEF unless their tidal volume was extremely low. This method of $EtCO_2$ measurement reduces sensor malfunctions and the risk of health care workers' exposure to unfiltered gas while maintaining accuracy.

Abbreviations

CI
confidence interval
CO_2
carbon dioxide
$EtCO_2$
End-tidal carbon dioxide
HMEF
heat and moisture exchanger filter
ICU
intensive care unit
IQR
interquartile range
$PaCO_2$
partial pressure of arterial carbon dioxide
PEEP
positive end expiratory pressure
SD
standard deviation.

Declarations

Ethics approval and consent to participate

This study was approved by the Research ethics committee of Okinawa Chubu Prefectural Hospital (2019-No.17). The requirement for written informed consent was waived by the institutional review board.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

All the authors declare that they have no conflicts of interest.

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Not applicable.

Authors' contributions

ST, IN and JI designed the study, conceptualized the data acquisition, acquired the data, and interpreted the data. ST, IN, and KG contributed to the data analysis. JI supervised the study. IN and ST wrote the first draft of the manuscript, and all authors commented on the previous version of the manuscript. All authors read and approved the final manuscript.

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Authors' information (optional)

Satoshi Tamashiro and Izumi Nakayama have contributed equally to this work and share first authorship.

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Figures

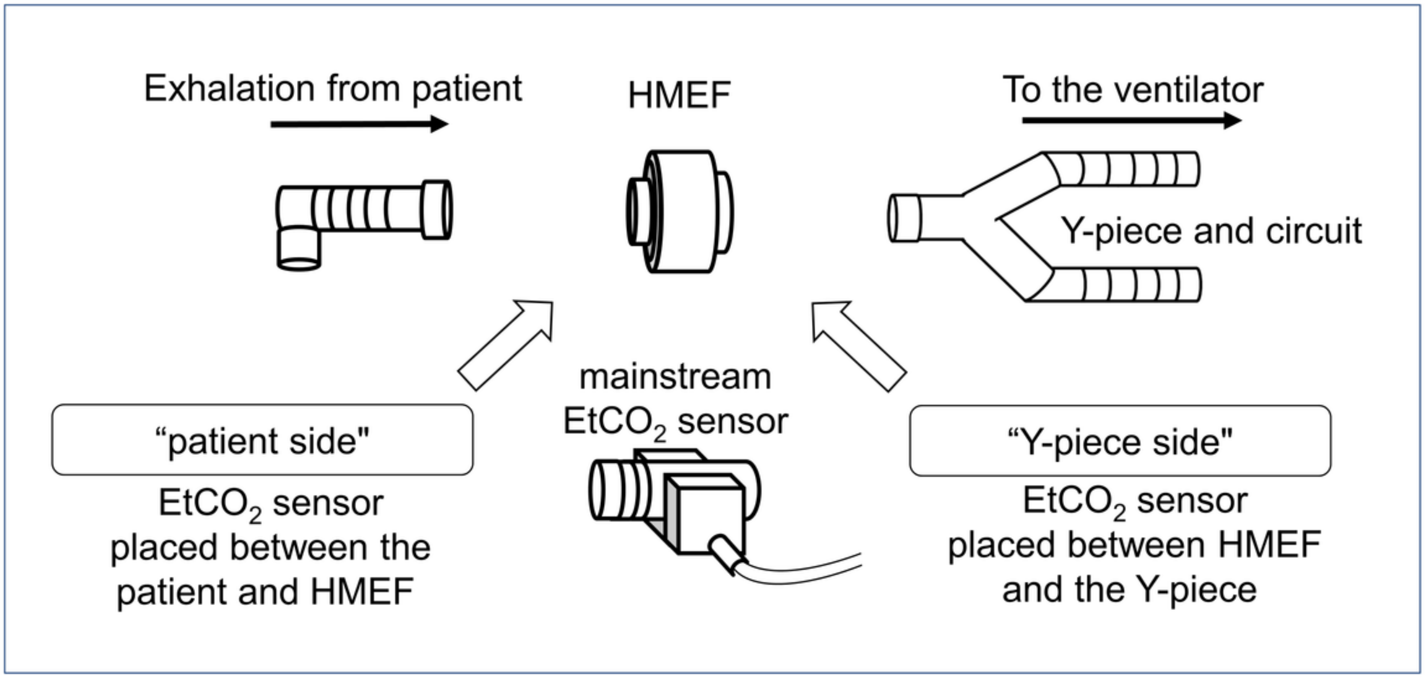

Figure 1

Relative positions of $EtCO_2$ sensor and HMEF in the ventilator circuit. $EtCO_2$, end-tidal carbon dioxide; HMEF, heat and moisture exchanger.

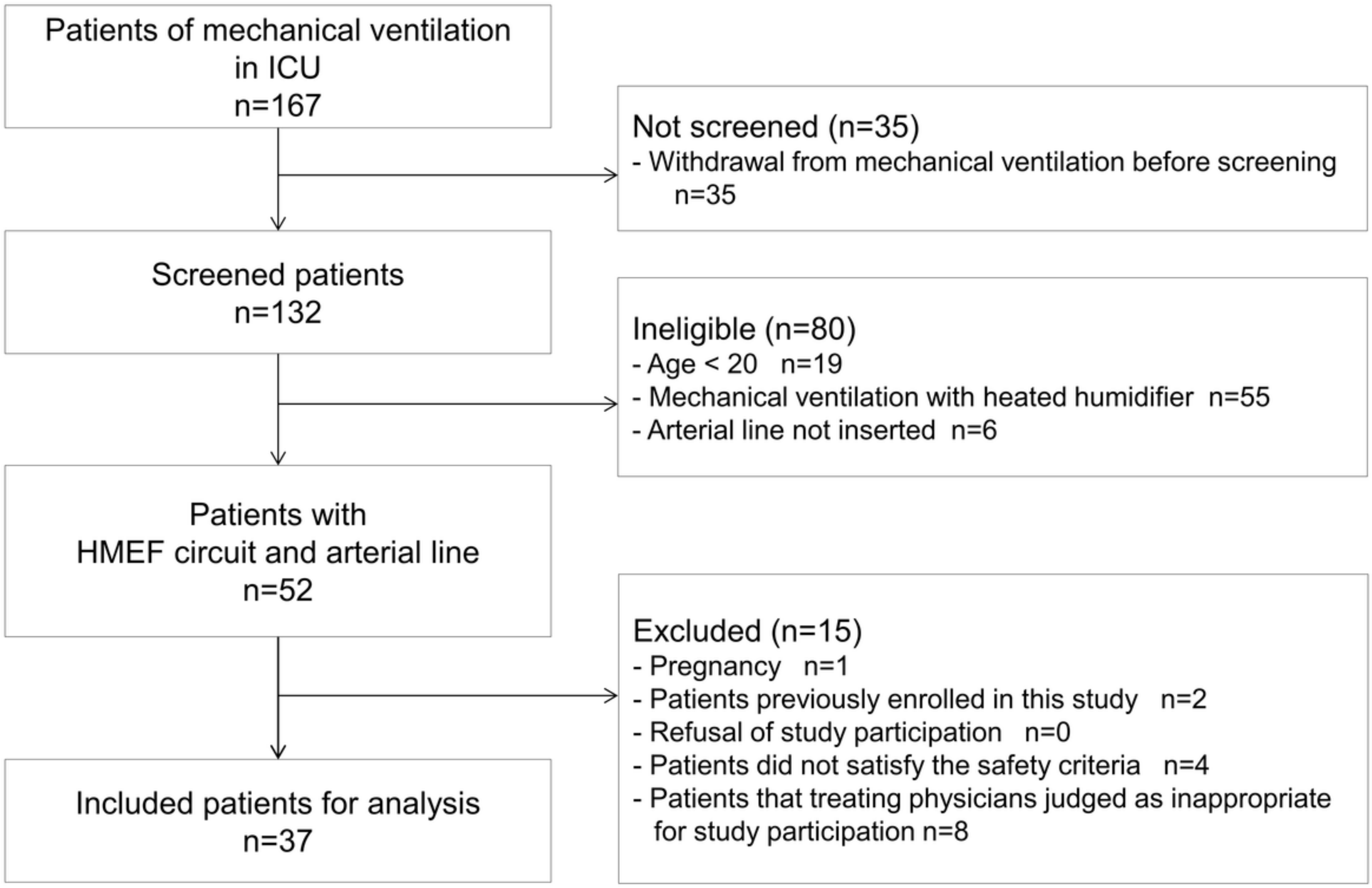

Figure 2

Flow of patients of mechanical ventilation. HMEF, heat and moisture exchanger filter.

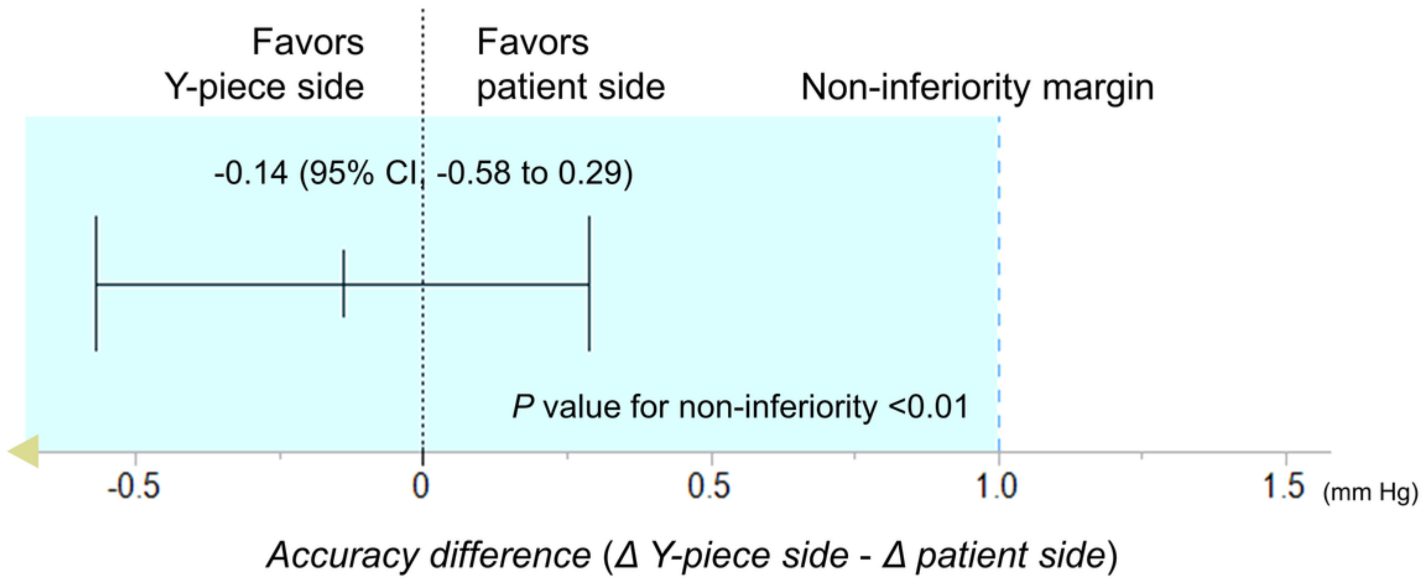

Figure 3

Estimated accuracy difference and the non-inferiority margin. The estimated accuracy difference with 95% CI was compared to the pre-defined non-inferiority margin of +1 mm Hg. The blue-tinted region indicated that mainstream $EtCO_2$ on the Y-piece side of HMEF is noninferior to that on the patient side. We defined Δ Y-piece side as the absolute difference between $PaCO_2$ and $EtCO_2$ on the Y-piece side of HMEF, and Δ patient side as the absolute difference between $PaCO_2$ and $EtCO_2$ on the patient side. Accuracy difference was defined as Δ Y-piece side - Δ patient side. $EtCO_2$, end-tidal carbon dioxide; HMEF, heat and moisture exchanger filter.

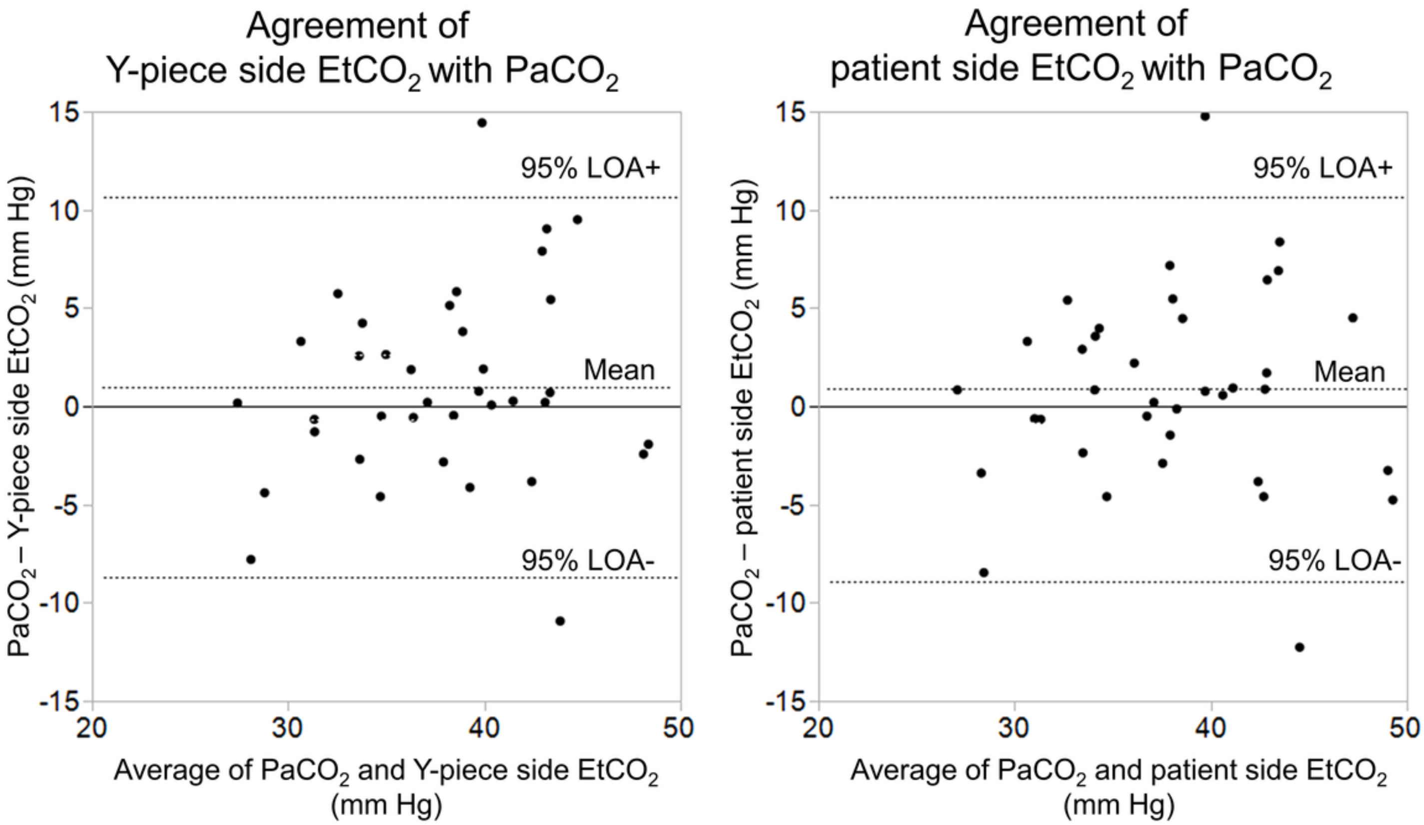

Figure 4

Bland-Altman plots showing the variation of differences between $PaCO_2$ and $EtCO_2$. $EtCO_2$, end-tidal carbon dioxide; LOA, limit of agreement.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- EtCO2SupplementaryInformationMay022022.docx