

Capnography and Pulse Oximetry Improve Fast Track Extubation in Patients Undergoing Coronary Artery Bypass Graft Surgery: A Randomized Clinical Trial

Seyed Tayeb Moradian

Baqiyatallah University of Medical Sciences

Fatemah Beitollahi

Baqiyatallah University of Medical Sciences

Mohammad Saeid Ghiasi

Baqiyatallah University of Medical Sciences

Amir vahedian-azimi (✉ Amirvahedian63@gmail.com)

Trauma Research Center, Nursing Faculty Baqiyatallah University of Medical Sciences, Tehran, Iran

<https://orcid.org/0000-0002-1678-7608>

Research

Keywords: Airway extubation, Coronary artery bypass, Capnography, Blood gas analysis, pulse oximetry

Posted Date: May 7th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-496561/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background

Use of capnography as a non-invasive method during the weaning process for fast track extubation (FTE) is controversial. We conducted the present study to determine whether pulse oximetry and capnography could be utilized as alternatives to arterial blood gas (ABG) measurements in patients under mechanical ventilation (MV) following coronary artery bypass graft (CABG) surgery.

Methods

In this randomized clinical trial, 70 patients, who were candidates for CABG surgery, were randomly assigned into two equal groups ($n = 35$); the intervention group and the control group. In the intervention group, the ventilator management and weaning from MV was done using Etco_2 from capnography and SpO_2 from pulse oximetry. Meanwhile, in the control group, weaning was done based on ABG analysis. The length of intensive care unit (ICU) stay, time to extubation, number of manual ventilator setting changes, and alarms were compared between the groups.

Results

The end-tidal carbon dioxide (ETCO_2) levels in the intervention group were completely similar to the partial pressure of carbon dioxide (PaCo_2) in the control group (39.5 ± 3.1 vs. 39.4 ± 4.32 , $P > 0.05$). The mean extubation times were significantly shorter in the intervention group compared to those in the control patients (212.2 ± 80.6 vs. 342.7 ± 110.7 , $P < 0.001$). Moreover, the number of changes in the manual ventilator setting and the number of alarms were lower in the intervention group ($P < 0.05$). However, the differences in the length of stay in ICU between the two groups were not significant ($P = 0.219$).

Conclusion

According to our results, the use of non-invasive monitors, including capnography and pulse oximetry, is emphasized in order to utilize FTE after CABG surgery. Furthermore, it is a safe and valuable monitor that could be a good alternative for ABG in this population. Nevertheless, further studies with larger sample sizes and on different disease states and populations are required to assess the accuracy of our findings.

Trial registration:

IRCT, IRCT201701016778N6, Registered 3 March 2017, <https://www.irct.ir/trial/7192>

Background

Fast track extubation (FTE) is an accepted method for weaning patients from mechanical ventilation (MV) after coronary artery bypass graft (CABG) surgery. The duration of MV in patients undergoing cardiac surgery is usually between 1–6 hours. Long-term MV might trigger certain complications, such as infection, atelectasis, and increased mortality (Badhwar et al. 2014, Cheng et al. 1996). With a proper management and early withdrawal of the endotracheal tube, the complications and costs would reduce (García-Delgado et al. 2014, Badhwar et al. 2014). FTE can decrease health care costs following CABG surgery up to 50% (Reis et al. 2002). Utilizing a proper anesthesia technique during surgery and post-surgery management, FTE can be applied in patients undergoing CABG surgery without any specific complications (Akhtar and Hamid 2009).

The readiness of patients for weaning is usually assessed by arterial blood gas (ABG) sampling. ABG is the gold standard for the monitoring of oxygenation and ventilation during the postoperative MV (Gerdung et al. 2016). Arterial line cannulation is employed in the operating room and ICU settings to provide easy access for continuous and real-time systemic blood pressure measurements, blood gas analysis, and other laboratory measurements. However, based on evidence, this process is not without risk factors (Lakhal and Robert-Edan 2017). The process of inserting arterial line (over 48 or 72 hours) is an invasive procedure with several complications, for instance infection, local hematoma, vascular injury, thrombosis, disseminated intravascular coagulation, and reduced cardiac output (Sood et al. 2010, Long et al. 2017, Taghizadieh et al. 2016). On the other hand, Iran, as a developing country with sanctions, cannot access advanced medical equipment, such as ABG analyzers. Therefore, in order to minimize these complications and having easier access, finding an alternative non-invasive method seems to be reasonable.

The use of pulse oximetry as a valid non-invasive tool for oxygenation monitoring has been agreed upon by the public for many years (Nitzan et al. 2014). In several cases, the pulse oximetry is used as the only criterion to check oxygenation and to make oxygenation-associated changes in MV. The utilization of a capnography is also recommended under different clinical conditions (Cambra Lasaosa and Pons Odena 2003). Capnography is a method in which the infrared radiation is employed to measure the carbon dioxide (CO₂) in exhaled air. This method includes the non-invasive measurement of CO₂, providing information on ventilation (effectiveness of CO₂ elimination), perfusion (CO₂ transportation in vasculature), and metabolism (production of CO₂ via cellular metabolism) in intubated and spontaneously breathing patients (Nassar and Schmidt 2016, Kugelman et al. 2008). Capnography in certain conditions, for instance confirmation of the correct place of the endotracheal tube, is recommended as the standard of care (Cumming and McFadzean 2005). Yet in some other circumstances, such as cardiopulmonary resuscitation and changing the MV settings, there are numerous differences between the existing data and there are no similar recommendations (Turle et al. 2015, Pantazopoulos et al. 2015, Rasera et al. 2015). Certain studies have mentioned the lack of correlation between these variables and have considered the difference between them high (Warner et al. 2009). On

the other hand, some other studies have reported an equal role for these two parameters in monitoring the level of CO₂ (Kugelman et al. 2008, Kerr et al. 1996).

The substantial debate is that whether capnography and pulse oximetry could be efficient alternatives for ABG analysis during the process of weaning from mechanical ventilation (MV). Therefore, capnography and pulse oximetry are used in this study for monitoring during the MV and management of the ventilator setting. The current study aimed to assess the feasibility and safety of non-invasive monitoring techniques during the weaning process in patients undergoing the CABG surgery.

Methods

Study design and Participants

This study was a randomized controlled clinical trial conducted between February and March 2018 with Trial Registration Number (IRCT201701016778N6) in Iranian Registry of Clinical Trials (IRCT). We conducted this research on 70 patients, who underwent CABG surgery at Jamaran Heart Hospital in Tehran, Iran. The patients who met the inclusion criteria were selected through convenient sampling and randomly assigned into two equal groups (n = 35); the intervention group and the control group. Due to the nature of this clinical trial study, which compared two different methods, there was no possibility of blinding. Randomization sequence was created with Excel 2007 (Microsoft, Redmond, WA, USA) with a 1:1 allocation, using random block sizes of 2 and 4 by an investigator with no clinical involvement in the trial. The study protocol was reviewed and approved by the Ethics Committee of Baqiyatallah University of Medical Sciences, Tehran, Iran, under code IR.BMSU.REC.1395.141. In addition, one day ahead of the operation, we explained the objectives of this study to the participants and obtained the informed consent.

Inclusion and exclusion criteria

The eligible participants in this study were those with a negative history of stroke or other severe neurologic disorders, chronic obstructive pulmonary disease, and ejection fraction (EF) less than 30%. On the other hand, patients below the age of 18 or over 80, with chest tube drainage > 400 mL/h at the first 4 hours after surgery, hemodynamic instability (requiring intra-aortic balloon pump or high dose inotrope), loss of consciousness, and subjects who needed MV more than 24 hours after the surgery were excluded from the study.

Sample size

We calculated the sample size of this study based on the Altman's nomogram for the two sided hypothesis with a power of 90% and $\alpha = 0.05$ and according to similar studies ($P = 0.03$ and the effect size = 1.3). Based on the nature of the clinical trial study and the probability of sample size drop, 10% drop was considered as the attrition rate and the final sample size for each group was considered to be 35 subjects.

Our Center

Our center is a single specialty heart center with a multi-disciplinary team including cardiac surgeon, cardiac anesthesiologist, nurses, internal medicine, echocardiographer, perfusionist, electro-physiologist, interventionist, and cardiac rehabilitation specialist. Patients who are candidate for surgery are assessed by anesthesiologist before surgery. Also, all patients above 60 years old are screened by pulmonologist and based on comorbidities, patients are screened by nephrologist, neurologist, endocrinologist and hematologist. Our ICU is a 10-bed ICU which is designed for cardiac surgical procedures. The ICU and operation room are in the same environment and on two floors. After the surgery, patients are transferred directly to the ICU and managed by experienced nurses. Usually, patients remain in ICU for two days, and the enhanced recovery after surgery protocols, including fast tract extubation, early mobilization, and minimal sedation strategy, are utilized. Sedation infusion and also using from bolus doses of sedatives such as midazolam is discouraged and patients are oriented as soon as possible. Fast tract extubation is the routine procedure during the weaning and extubation.

Procedure and data collection

Anesthesia and surgical protocols were similar in both groups. Anesthesia was induced and maintained using midazolam, fentanyl, and propofol, and paralysis was achieved by atracurium. The patients were intubated after anesthesia induction and ventilated during the surgery. The following setting was applied in the operating room: tidal volume of 8–10 mL/kg, positive end-expiratory pressure (PEEP) of 5 cmH₂O, and respiratory rate (RR) of 12 breaths per minute. During cardiopulmonary bypass, ventilation was stopped and continuous positive airway pressure of 5 cmH₂O was applied. We performed the surgery using the standard procedure through median sternotomy (Aybek et al. 2002). Following the surgery, adaptive support ventilation (ASV) was applied for mechanical ventilation management. A Galileo with software version GBC 01.202 (Hamilton Medical AG, Rhäzüns, Switzerland) was employed for managing the patient during the MV. Although weaning and extubation is a clinical decision made at the bedside, it is based on many factors including wakefulness, comfort, and the patient's ability to cough and secrete. In both groups, the MV weaning criteria were MIN VOL% 60–65%, F control (number of controlled breathes) zero, f Spont > 10 (number of spontaneous breathes), P_{insp} < 8 (the amount of automatically adjusted pressure support). Figure 1 represents standard weaning process algorithms in ASV mode (Fernández et al. 2013).

In both groups, the initial ventilator settings were minute volume 100%, oxygen inspiratory fraction (F_{io₂}) of 100%, positive end-expiratory pressure of 5 cm H₂O, and flow trigger sensitivity of 4 l/min. Following 10 minutes, we performed an ABG analysis. Simultaneously, the ETCO₂ and SPO₂ were measured. The goal for PaCO₂ was 38 to 43 mmHg. Based on our clinical pilot, the Etco₂ was 2–4 mmHg lower than PaCO₂. Therefore, this difference was considered in all the settings and interpretations regarding PaCO₂. If the PaCO₂ was greater than 45 the minute volume increased by 10 to 20%, and if it was lower than 35 the minute volume decreased 10 to 20%. In the intervention group, the trend was monitored with capnography and in the control group, another ABG analysis was performed 10 to 20 minutes after any

changes in the setting. The FIO₂ was changed to target oxygen saturation about 95%. This was measured in the control group with ABG or pulse oximetry and in the intervention group with pulse oximetry. Equal basic settings were employed on both groups and Fast-track extubation was employed for all the patients.

ASV mode

Adaptive Support Ventilation (ASV) is an intelligent advanced closed-loop ventilation mode that maintains constant minimum mandatory ventilation based on preset minute volume% and ideal body weight. Depending on patients' status, this mode provides a range of ventilation support including Pressure Controlled Ventilation (PCV), Synchronized Intermittent Mandatory Ventilation (SIMV), or Pressure Support Ventilation (PSV). Ventilator switches between these forms automatically. ASV adjusts respiratory rate, tidal volume, and inspiratory time continuously and it depends on the mechanism of the lung and the efforts of the patients (Arnal et al. 2008, Moradian et al. 2017). The controlled settings of this mode included the following items: patients' ideal body weight (IBW), the value of minute respiratory volume in percentage (Min volume), positive end expiratory pressure (PEEP), fraction of inspired oxygen (Fio₂), the level of ventilator sensitivity for the breath of the patient (Trigger), and the maximum pressure that must be applied (cmH₂o). The most important settings in ASV are ideal body weight and Minute volume. The ventilator uses the Otis equation for determining the appropriate rate and volume based on measuring patients' respiratory compliance and resistances during the initial five breaths. By improving the patient situation, ventilator switches from controlled breaths to spontaneous breaths. During the spontaneous breathing, gradually by improving the patient situation, the inspiratory pressure support decreases. Ventilator continuously adapts the settings and supports patients' needs.

Training

In spite of published data about capnography, it is not used widely in Iranian clinical practice. For this reason, in order to reduce the staff fear of its accuracy a 4-hour training class was conducted for ICU staff with clinical work in the pilot phase for one month. In those sessions, the data from the capnography and ABG were compared and the results were presented to them. Based on our data, the Etco₂ was usually 2–4 mmHg lower than PaCO₂. Thus, this difference was considered in all the settings and interpretation regarding PaCO₂.

Statistical analysis

Categorical variables were described as frequency rates and percentages, and continuous variables were described using mean \pm standard deviation (SD) values. The comparison of demographic characteristics and baseline measures between the two groups herein were done with independent t-test for continuous variables and Chi-square test or Fisher's exact test (in case of low sample) for categorical variables. The normality of the numeric variables was checked employing Kolmogorov-Smirnov test. The repeated measures analysis of variance (RMANOVA) was used to compare the vital signs and ABG measurements between the groups. Furthermore, we did pairwise comparisons with Sidak post hoc test. The assumption of sphericity was addressed utilizing Mauchly's test of sphericity. Once the assumption was not satisfied

($P < 0.05$), the Greenhouse-Geiser correction of P-value was utilized. To assess the effect of intervention, we used the analysis of covariance (ANCOVA) after controlling for baseline measures and confounders in the main effect model. All the data were analyzed using the Statistical Package for the Social Sciences (SPSS) 21.0 statistical package (Chicago, IL, USA); two-side $P < 0.05$ indicated a statistically significant difference.

Results

A total of 70 patients enrolled in the current study according to the inclusion and exclusion criteria. Three patients were excluded due to hemodynamic instability (1 subject from the intervention group) and bleeding (2 subjects from the control group). Therefore, the analyses were performed in the remaining 67 patients (34 patients in the intervention group and 33 patients in the control group). Figure 2 depicts the patients' flowchart of the study.

The mean \pm SD ages of the participants were 58.1 ± 9.6 and 60.8 ± 9.3 years in the intervention and control, respectively. There were no significant differences between the groups in terms of age ($P = 0.244$). In terms of gender, 19 participants (55.9%) in the intervention group and 22 (66.7%) in the control group were male ($P = 0.365$). Baseline demographic and clinical characteristics of the participants in the two groups are presented in Table 1. Based on our findings, there were no significant differences between the groups regarding the demographic characteristics and baseline ABG measurements ($P > 0.05$). However, in terms of intraoperative parameters, the duration of the surgery (based minutes) in the control group was significantly lower than that in the intervention group (235.7 ± 49.2 min vs. 259 ± 39.8 min, $P = 0.035$).

Table 1
Baseline demographic and clinical characteristics of the participants in two groups of study

Variables	Intervention group (n = 34)	Control group (n = 33)	P-value
Demographic characteristics			
Age (mean ± SD)	58.12 ± 9.66	60.85 ± 9.32	0.244
Gender (male, %)	19 (55.9)	22 (66.7)	0.365
Body mass index (mean ± SD)	27.93 ± 4.38	27.81 ± 4.78	0.908
Smoking (yes, %)	1 (2.9)	6 (18.2)	0.054
Opium history (yes, %)	5 (14.7)	1 (3)	0.197
Comorbidities			
Renal diseases (yes, %)	3 (8.8)	1 (3)	0.614
Diabetes mellitus (yes, %)	15 (44.1)	16 (48.5)	0.808
Hypertension (yes, %)	22 (64.7)	19 (57.6)	0.549
Clinical characteristics			
EF (mean ± SD)	47.21 ± 7.09	48.94 ± 5.41	0.226
Pump time, min (mean ± SD)	63.32 ± 25.69	57.33 ± 27.94	0.364
Intraoperative parameters			
Type of operation (CABG, %)	19 (55.9)	22 (66.7)	0.365
DO, min (mean ± SD)	259 ± 39.87	235.76 ± 49.2	0.035*
Arterial blood gas (ABG) measurements			
Blood PH (mean ± SD)	7.36 ± 0.04	7.36 ± 0.04	0.804
PaCO ₂ , mm Hg (mean ± SD)	37 ± 4.30	36.18 ± 4.48	0.449
PaO ₂ , mm Hg (mean ± SD)	114.41 ± 45.30	103.18 ± 32.91	0.250
SpO ₂ , % (mean ± SD)	97.41 ± 2.13	96.82 ± 2.06	0.252
BE, mm Hg (mean ± SD)	-4.08 ± 2.24	-4.50 ± 2.15	0.436
HCO ₃ , mEq/L (mean ± SD)	21.19 ± 1.99	19.90 ± 4.68	0.147
Abbreviation; EF: Ejection fraction, DO: Duration of operation, PaCO ₂ : partial pressure of carbon dioxide, PaO ₂ : partial pressure of oxygen, SpO ₂ : Oxygen saturation, BE: Base excess HCO ₃ : Bicarbonate * <0.05 was considered statistically significant.			

Comparisons of hemodynamic parameters and vital signs of the patients on different times between the two groups and within group are respectively presented in Tables 2 and 3. There were significant differences between the intervention and control groups concerning tidal volume (VT) $P= 0.016$, inspiratory pressure (Pi) $P= 0.006$, and fraction of inspired oxygen (Fio₂) $P= 0.002$. Nevertheless, the differences of other characteristics between the two groups were not significant ($P > 0.05$).

Table 2

Comparison of ventilator and respiratory in three different times between the intervention and control groups

Parameters	Groups	Baseline	Trigger time	Extubation time	P-value**	P-value***
VT, min	Intervention	100	82.35 ± 4.96	77.21 ± 6.87	< 0.001	0.016
	Control	100.61 ± 2.07	86.97 ± 6.72	78.64 ± 5.89	< 0.001	
	P-value*	0.093	0.002	0.365		
Pi, cmH2O	Intervention	12.62 ± 1.64	10.88 ± 1.75	8.35 ± 1.68	< 0.001	0.006
	Control	12.85 ± 1.50	11.61 ± 1.54	10.03 ± 1.57	< 0.001	
	P-value*	0.603	0.078	< 0.001		
Fio2, %	Intervention	52.94 ± 6.29	40.44 ± 1.89	40	< 0.001	0.002
	Control	58.94 ± 10.05	43.03 ± 5.98	41.67 ± 4.44	< 0.001	
	P-value*	0.005	0.019	0.033		
PEEP, cmH2O	Intervention	4.94 ± 0.34	4.94 ± 0.34	4.91 ± 0.37	0.325	0.679
	Control	5	5	4.88 ± 0.54	0.211	
	P-value*	0.328	0.326	0.774		
Flow total	Intervention	12.32 ± 1.06	13.26 ± 2.72	16.21 ± 2.64	< 0.001	0.785
	Control	12.30 ± 0.84	13.55 ± 2.26	15.64 ± 2.57	< 0.001	
	P-value*	0.931	0.648	0.375		
Flow control	Intervention	12.32 ± 1.06	4.32 ± 3.28	-	< 0.001	0.054
	Control	12.30 ± 0.84	6.18 ± 3.72	-	< 0.001	
	P-value*	0.931	0.034	-		
TVE	Intervention	545.5 ± 122.2	459.7 ± 111.7	487.5 ± 119.15	0.231	0.322
	Control	500.1 ± 91.61	488.2 ± 98.91	482.03 ± 91.8	0.274	

Abbreviation; VT: Tidal volume, Pi: Inspiratory pressure, Fio2: Fraction of inspired oxygen, PEEP: Positive end-expiratory pressure, TVE: Total expiratory volume, $P < 0.05$ was considered statistically significant, *Independent t-test between two groups, ** Time-interaction within group based on RMANOVA, *** Time-interaction between two groups

Parameters	Groups	Baseline	Trigger time	Extubation time	P-value**	P-value***
	P-value*	0.090	0.309	0.833		
Abbreviation; VT: Tidal volume, Pi:Inspiratory pressure, Fio2: Fraction of inspired oxygen, PEEP: Positive end-expiratory pressure, TVE: Total expiratory volume, $P < 0.05$ was considered statistically significant, *Independent t-test between two groups, ** Time-interaction within group based on RMANOVA, *** Time-interaction between two groups						

Table 3

Comparison of vital signs of patients on different times between the intervention and control groups

Parameters	Groups	Baseline	Trigger time	Extubation time	Post extubation	P-value**	P-value***
Heart rate, bpm	Intervention	83 ± 12.31	86.47 ± 11.85	89.47 ± 9.45	88.03 ± 8.49	0.002	0.380
	Control	86.24 ± 12.71	87.48 ± 13.45	91.36 ± 12.43	90.7 ± 12.51	0.019	
	*P-value	0.293	0.744	0.485	0.310		
RR, per/min	Intervention	12.32 ± 1.06	13.06 ± 2.04	16.21 ± 2.64	16.85 ± 2.24	< 0.001	0.755
	Control	12.24 ± 0.83	13.61 ± 2.20	16.03 ± 2.69	16.97 ± 1.81	< 0.001	
	*P-value	0.730	0.296	0.789	0.816		
Systolic BP, mm Hg	Intervention	119.24 ± 15.7	126.06 ± 12.55	126.26 ± 13.61	119.29 ± 11.44	0.010	0.653
	Control	113.03 ± 23.7	127.76 ± 18.17	125.06 ± 12.03	120.33 ± 18.22	0.006	
	*P-value	0.210	0.657	0.703	0.780		
Diastolic BP, mm Hg	Intervention	61.38 ± 10.92	67.88 ± 8.37	67.56 ± 7.89	65.94 ± 9.76	0.004	0.736
	Control	61.79 ± 12.65	68.79 ± 9.76	68.76 ± 9.13	65.70 ± 11.43	0.011	
	*P-value	0.889	0.685	0.567	0.925		
MAP, mm Hg	Intervention	79 ± 12.01	85.74 ± 8.83	85.32 ± 8.09	81.94 ± 9.79	0.011	0.851
	Control	76.09 ± 13.13	85.67 ± 11.34	84.82 ± 10.44	84.09 ± 12.23	0.001	
	*P-value	0.347	0.978	0.825	0.429		
SpO ₂ , %	Intervention	98.2 ± 1.68	97.41 ± 1.32	97.55 ± 1.76	97.29 ± 1.36	0.034	0.169
	Control	98.87 ± 1.51	97.42 ± 1.56	96.87 ± 1.86	96.81 ± 1.94	0.013	
	*P-value	0.407	0.972	0.130	0.249		

Abbreviation; RR: Respiratory rate, BP: Blood pressure, MAP: Mean arterial pressure, SpO₂: Oxygen saturation, * Independent t-test between two groups, ** Time-interaction within group based on RMANOVA, *** Time-interaction between two groups

Figure 2 demonstrates the ETCO₂ level distribution of the patients in the intervention group. The mean of ETCO₂ in the intervention group was compared to the PaCO₂ in the control group at extubation time. The data indicated no statistically significant differences between them (39.5 ± 3.0 vs. 39.4 ± 4.3 , 95% CI: -1.7-1.8, $P=0.935$).

The mean duration of MV was 212.2 ± 80.6 (min) and 342.7 ± 110.7 (min) in the intervention and control groups, respectively ($P < 0.001$). FTE (MV duration < 6 hours) was observed in 33 (97.1%) of the patients in the intervention group and 18 (54.5%) of the patients in the control group. The intervention group was of 4.8 (95%CI: 1.4–15.5; $P=0.008$) times more chance than the control group from FTE perspective. However, the differences in the length of stay in ICU between the two groups was not significant ($P=0.219$). The number of alarms ($P < 0.001$) and manual ventilator setting changes ($P=0.027$) were significantly lower in the intervention group. In addition, no significant differences were observed in compliance between the groups ($P=0.289$). Meanwhile, the differences in the mean of airway resistant between the two groups was significant ($P=0.045$). Comparison of extubation time, length of ICU stay, airway resistance, and compliance are listed in Tables 4 and 5.

Table 4

Comparison of airway resistance and compliance in different times between the intervention and control groups

Parameters	Groups	Baseline	Trigger time	Extubation time	P-value**	P-value***
Resistance (cm H ₂ O/L/sec)	Intervention	8.03 ± 1.99	8.18 ± 1.51	7.38 ± 1.59	0.025	0.049
	Control	8.64 ± 1.93	8.3 ± 1.81	8.76 ± 1.73	0.362	
	P-value*	0.210	0.757	0.001		
Compliance (L/cm H ₂ O)	Intervention	50.62 ± 16.01	49 ± 14.08	49.03 ± 14.77	0.702	0.289
	Control	53.64 ± 16.01	51.39 ± 15.74	53.18 ± 14.19	0.677	
	P-value*	0.435	0.514	0.244		

*Independent t-test between two groups, ** Time-interaction within group based on RMANOVA, *** Time-interaction between two groups, Sidak post hoc tests shows significant differences between resistance in trigger and extubation time ($P=0.005$)

Table 5
Comparison of extubation time and length of ICU stay between the intervention and control groups

Parameters	Intervention (n = 34)	Control (n = 33)	P-value
Alarm (mean ± SD), number	16.38 ± 3.82	19.75 ± 3.45	< 0.001*
Manipulations (mean ± SD), number	6.20 ± 2.08	7.72 ± 3.29	0.027
Time to extubation, min	212.20 ± 80.61	342.72 ± 110.73	< 0.001
Length of ICU stay, day	1.96 ± 0.19	2.10 ± 0.55	0.219
Early extubation (< 6 hours)	33 (97.1%)	18 (54.5%)	< 0.001**
* Independent t-test, ** Fisher's exact test			

Discussion

In this study, the use of non-invasive monitoring including capnography and pulse oximetry accelerated the weaning process and increased the number of FTE in intervention group. According to the results of the present study, in terms of vital signs and the amount of arterial oxygen saturation (SpO₂), there were no significant differences between the intervention and control groups. However, there was a significant difference between the two groups regarding tidal volume (VT), inspiratory pressure (Pi), and fraction of inspired oxygen (Fio₂). In the current study, the number of manual setting changes of ventilator and alarms in the intervention group significantly decreased compared to the control group. The reduction in both alarm and manual setting changes is of great importance. In fact, the increase in the number of alarms may lead to alarm fatigue, which is an important concern for patients' safety (Ruskin and Hueske-Kraus 2015, Sendelbach and Funk 2013, Jones 2014).

In addition, our data revealed no significant differences between the values of PaCO₂ and ETCO₂ at the weaning time; however, we observed a statistically significant linear relationship between them ($P < 0.001$). PaCO₂ and ETCO₂ had a strongly positive correlation ($r = 0.918$), meaning that these variables tend to increase together. In other words, ETCO₂ could be used instead of PaCO₂ for monitoring. In this regard, the results of the present study are consistent with those of the studies conducted by Taghizadeh et al. (Taghizadieh et al. 2016), Aminiahidashti et al. (Aminiahidashti et al. 2018), McSwain et al. (McSwain et al. 2010), Moses et al. (Moses et al. 2009), and Garcia et al. (Garcia et al. 2003). They all reported the same results in terms of the correlation between ETCO₂ and PaCO₂ and suggested that capnography could be employed as a non-invasive method, and it is a surrogate for PaCO₂ which if high, signals a respiratory acidosis or if low, a respiratory alkalosis or when combined with pH and serum bicarbonate, a compensatory mechanism. In contrast to our results, certain studies have reported that the correlation between these variables is not sufficient (Kugelman et al. 2016, García Cantó et al. 1997, Heines et al. 2013). A pilot study by Drew et al. (Drew et al. 1998), in which they used non-invasive methods during the weaning process, exhibited that the hypothesis that capnography would allow more

rapid weaning from MV, and requires fewer ABGs during the process, was not true. Moreover, in a study by Casati et al. (Casati et al. 2000), the role of capnography was reported to be inappropriate in patients with spontaneous breathing. This contradiction may be attributed to the different research methods or different populations. For example, some studies have generally not included a comprehensive statistical analysis accounting for the differences in physiologic dead space ventilation and the resulting gradient between ETCO₂ and PaCO₂. In addition, some other studies have been reviewed in patients with critical conditions.

The results of this work revealed that the use of capnography and pulse oximetry accelerated the weaning process in the patients undergoing CABG surgery. FTE is found to be the best practice for management of cardiac surgery patients, which improves the recovery and reduces the complications (Gutsche et al. 2014). In this study 97.1% of the intervention group and 54.5% of the control group had FTE, which was reported 49.5% FTE in a study by Akhtar et al. (Akhtar and Hamid 2009). Our results showed that the use of capnography could improve the FTE by the identification of hypercapnic episodes during the weaning process. In some centers, due to the fear of hypercapnic episodes, the FTE is delayed. Hence, using ETCO₂ with continuous monitoring can reduce this fear. On the other hand, one of the uses of capnography is the discovery of hypercapnic episodes (Saura et al. 1996).

In some studies, changes in ETCO₂ was observed from breath to breath and from the controlled to the spontaneous breathing (Gerdung et al. 2016). Therefore, the momentary monitoring is not reliable and the ETCO₂ should be monitored continuously during the weaning process. Due to the importance of FTE in cardiac surgery, various changes are made to MV settings in a short time. Due to some restrictions such as limited access to ABG analyzers in developing countries and the fact that ABG method is an invasive method, a non-invasive monitor, which is easily accessible, inexpensive, and accurate, is very useful. The available data showed that both capnography and pulse oximetry have the above-mentioned features.

Despite the availability of capnography in many ICUs, it is not frequently used in the routine practice. One of the reasons might be the medical staff's fear of the risks and the proper linkage between the PaCO₂ and ETCO₂ (Georgiou et al. 2010, Langan et al. 2014). As mentioned in the method section, we had a 4-hour class with a pilot clinical phase for assuring the staff of the accuracy of Etco₂. This increased the trust of ICU staff.

The principal strength of this study is being conducted in a real-world setting. All the patients were screened by a pulmonologist and the medical staffs in our center were trained. The limitation of this study is the sample size which was small; therefore, it was not possible to determine the cutting point for ETCO₂. Accordingly, a larger sample size study is recommended to determine the cutting point.

Conclusion

In this study, patients underwent two different weaning processes, and as the results showed, the rate of change and movement toward extubation was faster in the non-invasive monitoring method. Therefore, the difference observed in these values was quite natural and not unexpected. Clinically, this difference is

significant because it reduces the separation time and the patient moves faster to be released from mechanical ventilation support. Using the non-invasive monitors including capnography and pulse oximetry enhances the rate of FTE in cardiac surgery. It is also a safe and correct monitor and could be a good alternative for ABG in this population. Nevertheless, the fact that in some conditions the relationship between ETCO₂ and PaCO₂ was not well described primarily necessitates the determination of a capnography on which patients could rely. Precautions should be taken and other respiratory parameters, including tidal volume and respiratory rate, should be taken into consideration. In addition, further studies are required with larger sample sizes in different disease status and populations for the assessment of the accuracy of our findings.

Abbreviations

Fast track extubation (FTE), Mechanical ventilation (MV), Artery bypass graft (CABG), Arterial blood gas (ABG), End-tidal carbon dioxide (ETCO₂), Partial pressure of carbon dioxide (PaCO₂), Positive end-expiratory pressure (PEEP), Respiratory rate (RR), Adaptive support ventilation (ASV), Oxygen saturation (SpO₂), Fraction of inspired oxygen (Fio₂), Ideal body weight (IBW).

Declarations

Ethics approval and consent to participate: Not applicable

Consent for Publication: Not applicable

Availability of data and material: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. In addition, this article contains supplementary material, which is available to authorized users.

Competing interests: The authors declare that they have no competing interests.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions: A.V-A developed the study concept. All authors contributed to the study design. Testing and data collection were performed by S-T.M, F.B and A.V-A. The data analysis and interpretation was performed by F.B and M-S.G under the supervision of A.V-A. F.B drafted the manuscript, and S-T.M and A.V-A provided critical revisions. All authors approved the final version of the manuscript for submission.

Acknowledgements: This project was done by Baqiyatallah University of Medical Sciences, Tehran, Iran with a registration code of IRCT201701016778N6 at clinical trial center. Thanks to guidance and advice from the "Clinical Research Development Unit of Baqiyatallah Hospital". Also, we thank Jamaran heart hospital staff for their assistance in this work.

References

- Akhtar, M. I. & Hamid, M. Success and failure of fast track extubation in cardiac surgery patients of tertiary care hospital: one year audit. *J Pak Med Assoc.* 2009;59(3):154-6.
- Aminiahidashti, H., Shafiee, S., Zamani Kiasari, A. & Sazgar, M. Applications of End-Tidal Carbon Dioxide (ETCO₂) Monitoring in Emergency Department; a Narrative Review. *Emerg (Tehran).* 2018;6(1):e5.
- Arnal, J.-M., Wysocki, M., Nafati, C., Donati, S., Granier, I., Corno, G. & Durand-Gasselín, J. Automatic selection of breathing pattern using adaptive support ventilation. *Intensive care medicine.* 2008;34(1):75-81.
- Aybek, T., Dogan, S., Neidhart, G., Kessler, P., Matheis, G., Wimmer-Greinecker, G. & Moritz, A. Coronary artery bypass grafting through complete sternotomy in conscious patients. *Heart Surg Forum.* 2002;5(1):17-20; discussion 20-1.
- Badhwar, V., Esper, S., Brooks, M., Mulukutla, S., Hardison, R., Mallios, D., Chu, D., Wei, L. & Subramaniam, K. Extubating in the operating room after adult cardiac surgery safely improves outcomes and lowers costs. *J Thorac Cardiovasc Surg.* 2014;148(6):3101-9.e1.
- Cambra Lasaosa, F. J. & Pons Odena, M. [Pulse oximetry and capnography]. *An Pediatr (Barc).* 2003;59(3):259-64.
- Casati, A., Gallioli, G., Scandroglio, M., Passaretta, R., Borghi, B. & Torri, G. Accuracy of end-tidal carbon dioxide monitoring using the NBP-75 microstream capnometer. A study in intubated ventilated and spontaneously breathing nonintubated patients. *Eur J Anaesthesiol.* 2000;17(10):622-6.
- Cheng, D. C., Karski, J., Peniston, C., Asokumar, B., Raveendran, G., Carroll, J., Nierenberg, H., Roger, S., Mickle, D., Tong, J., Zelovitsky, J., David, T. & Sandler, A. Morbidity outcome in early versus conventional tracheal extubation after coronary artery bypass grafting: a prospective randomized controlled trial. *J Thorac Cardiovasc Surg.* 1996;112(3):755-64.
- Cumming, C. & Mcfadzean, J. A survey of the use of capnography for the confirmation of correct placement of tracheal tubes in pediatric intensive care units in the UK. *Paediatr Anaesth.* 2005;15(7):591-6.
- Drew, K., Brayton, M., Ambrose, A. & Bernard, G. End-tidal carbon dioxide monitoring for weaning patients: a pilot study. *Dimens Crit Care Nurs.* 1998;17(3):127-34.
- Fernández, J., Miguelena, D., Mulett, H., Godoy, J. & Martínón-Torres, F. Adaptive support ventilation: State of the art review. *Indian J Crit Care Med.* 2013;17(1):16-22.
- García-Delgado, M., Navarrete-Sánchez, I. & Colmenero, M. Preventing and managing perioperative pulmonary complications following cardiac surgery. *Curr Opin Anaesthesiol.* 2014;27(2):146-52.

- García Cantó, E., Gutiérrez Laso, A., Izquierdo Macián, I., Alberola Pérez, A. & Morcillo Sopena, F. [The value of capnography and exhaled CO₂ in neonatal intensive care units]. *An Esp Pediatr.* 1997;47(2):177-80.
- Garcia, E., Abramo, T. J., Okada, P., Guzman, D. D., Reisch, J. S. & Wiebe, R. A. Capnometry for noninvasive continuous monitoring of metabolic status in pediatric diabetic ketoacidosis. *Crit Care Med.* 2003;31(10):2539-43.
- Georgiou, A. P., Gouldson, S. & Amphlett, A. M. The use of capnography and the availability of airway equipment on Intensive Care Units in the UK and the Republic of Ireland. *Anaesthesia.* 2010;65(5):462-7.
- Gerdung, C. A., Adeleye, A. & Kirk, V. G. Noninvasive monitoring of CO₂ during polysomnography: a review of the recent literature. *Curr Opin Pulm Med.* 2016;22(6):527-34.
- Gutsche, J. T., Erickson, L., Ghadimi, K., Augoustides, J. G., Dimartino, J., Szeto, W. Y. & Ochroch, E. A. Advancing extubation time for cardiac surgery patients using lean work design. *J Cardiothorac Vasc Anesth.* 2014;28(6):1490-6.
- Heines, S. J., Strauch, U., Roekaerts, P. M., Winkens, B. & Bergmans, D. C. Accuracy of end-tidal CO₂ capnometers in post-cardiac surgery patients during controlled mechanical ventilation. *J Emerg Med.* 2013;45(1):130-5.
- Jones, K. Alarm fatigue a top patient safety hazard. *Cmaj.* 2014;186(3):178.
- Kerr, M. E., Zempsky, J., Sereika, S., Orndoff, P. & Rudy, E. B. Relationship between arterial carbon dioxide and end-tidal carbon dioxide in mechanically ventilated adults with severe head trauma. *Crit Care Med.* 1996;24(5):785-90.
- Kugelman, A., Bromiker, R., Riskin, A., Shoris, I., Ronen, M., Qumqam, N., Bader, D. & Golan, A. Diagnostic accuracy of capnography during high-frequency ventilation in neonatal intensive care units. *Pediatr Pulmonol.* 2016;51(5):510-6.
- Kugelman, A., Zeiger-Aginsky, D., Bader, D., Shoris, I. & Riskin, A. A novel method of distal end-tidal CO₂ capnography in intubated infants: comparison with arterial CO₂ and with proximal mainstream end-tidal CO₂. *Pediatrics.* 2008;122(6):e1219-24.
- Lakhal, K. & Robert-Edan, V. Invasive monitoring of blood pressure: a radiant future for brachial artery as an alternative to radial artery catheterisation? *J Thorac Dis.* 2017;9(12):4812-4816.
- Langhan, M. L., Kurtz, J. C., Schaeffer, P., Asnes, A. G. & Riera, A. Experiences with capnography in acute care settings: a mixed-methods analysis of clinical staff. *J Crit Care.* 2014;29(6):1035-40.
- Long, B., Koyfman, A. & Vivirito, M. A. Capnography in the Emergency Department: A Review of Uses, Waveforms, and Limitations. *J Emerg Med.* 2017;53(6):829-842.

- Mcswain, S. D., Hamel, D. S., Smith, P. B., Gentile, M. A., Srinivasan, S., Meliones, J. N. & Cheifetz, I. M. End-tidal and arterial carbon dioxide measurements correlate across all levels of physiologic dead space. *Respir Care*. 2010;55(3):288-93.
- Moradian, S. T., Saeid, Y., Ebadi, A., Hemmat, A. & Ghiasi, M. S. Adaptive support ventilation reduces the incidence of atelectasis in patients undergoing coronary artery bypass grafting: a randomized clinical trial. *Anesthesiology and pain medicine*. 2017;7(3).
- Moses, J. M., Alexander, J. L. & Agus, M. S. The correlation and level of agreement between end-tidal and blood gas pCO₂ in children with respiratory distress: a retrospective analysis. *BMC Pediatr*. 2009;9:20.
- Nassar, B. S. & Schmidt, G. A. Capnography During Critical Illness. *Chest*. 2016;149(2):576-585.
- Nitzan, M., Romem, A. & Koppel, R. Pulse oximetry: fundamentals and technology update. *Med Devices (Auckl)*. 2014;7:231-9.
- Pantazopoulos, C., Xanthos, T., Pantazopoulos, I., Papalois, A., Kouskouni, E. & Iacovidou, N. A Review of Carbon Dioxide Monitoring During Adult Cardiopulmonary Resuscitation. *Heart Lung Circ*. 2015;24(11):1053-61.
- Rasera, C. C., Gewehr, P. M. & Domingues, A. M. PET(CO₂) measurement and feature extraction of capnogram signals for extubation outcomes from mechanical ventilation. *Physiol Meas*. 2015;36(2):231-42.
- Reis, J., Mota, J. C., Ponce, P., Costa-Pereira, A. & Guerreiro, M. Early extubation does not increase complication rates after coronary artery bypass graft surgery with cardiopulmonary bypass. *Eur J Cardiothorac Surg*. 2002;21(6):1026-30.
- Ruskin, K. J. & Hueske-Kraus, D. Alarm fatigue: impacts on patient safety. *Curr Opin Anaesthesiol*. 2015;28(6):685-90.
- Saura, P., Blanch, L., Lucangelo, U., Fernández, R., Mestre, J. & Artigas, A. Use of capnography to detect hypercapnic episodes during weaning from mechanical ventilation. *Intensive Care Med*. 1996;22(5):374-81.
- Sendelbach, S. & Funk, M. Alarm fatigue: a patient safety concern. *AACN Adv Crit Care*. 2013;24(4):378-86; quiz 387-8.
- Sood, P., Paul, G. & Puri, S. Interpretation of arterial blood gas. *Indian J Crit Care Med*. 2010;14(2):57-64.
- Taghizadieh, A., Pouraghaei, M., Moharamzadeh, P., Ala, A., Rahmani, F. & Basiri Sofiani, K. Comparison of end-tidal carbon dioxide and arterial blood bicarbonate levels in patients with metabolic acidosis referred to emergency medicine. *J Cardiovasc Thorac Res*. 2016;8(3):98-101.

Turle, S., Sherren, P. B., Nicholson, S., Callaghan, T. & Shepherd, S. J. Availability and use of capnography for in-hospital cardiac arrests in the United Kingdom. Resuscitation. 2015;94:80-4.

Warner, K. J., Cuschieri, J., Garland, B., Carlbom, D., Baker, D., Copass, M. K., Jurkovich, G. J. & Bulger, E. M. The utility of early end-tidal capnography in monitoring ventilation status after severe injury. J Trauma. 2009;66(1):26-31.

Figures

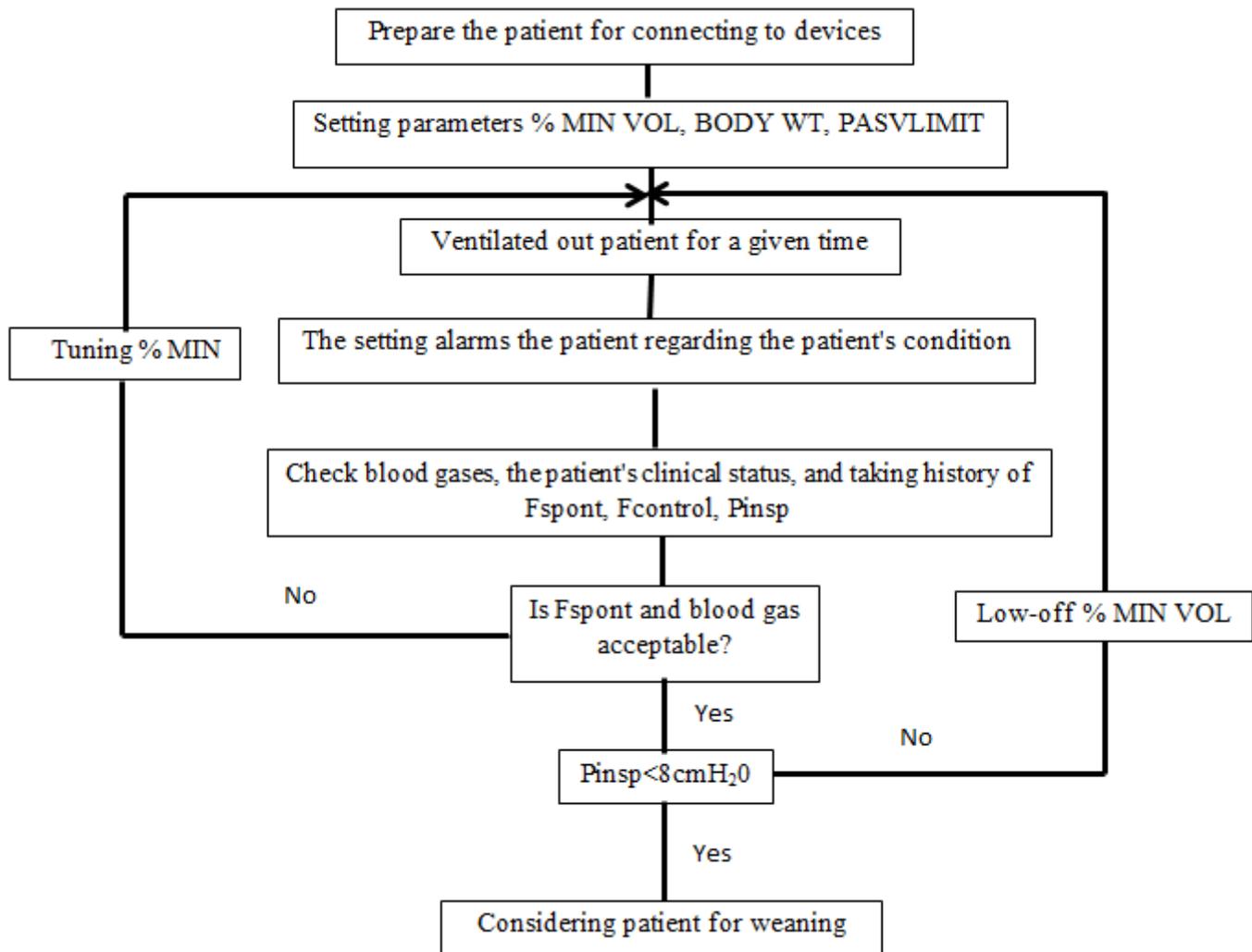


Figure 1

Standard weaning process algorithm in adaptive support ventilation (ASV) mode MIN VOL: minute volume, WT: weight, F spont: frequency of spontaneous breathing, F control: frequency of controlled breathing, P insp: inspiratory pressure

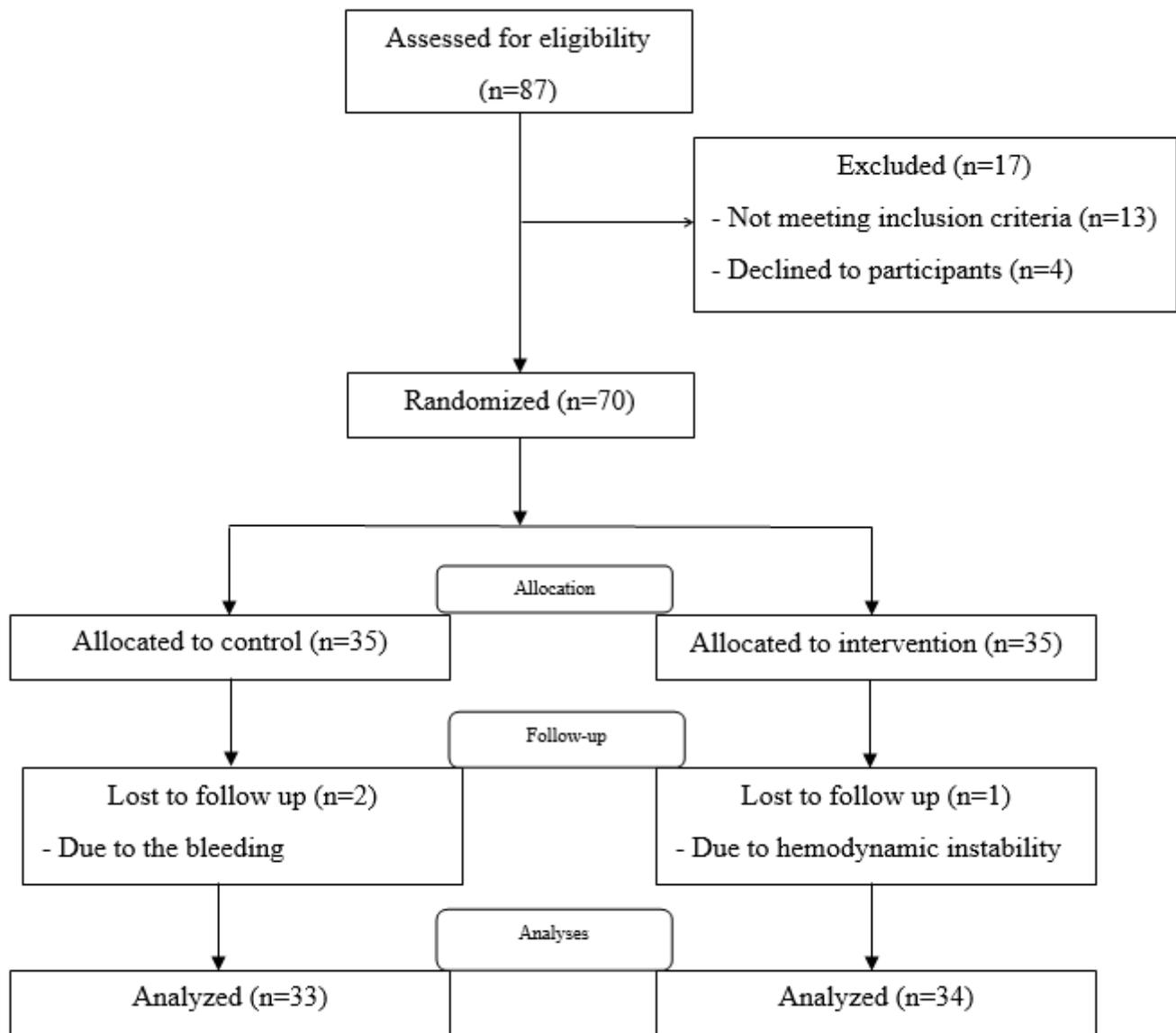


Figure 2

The study flow chart

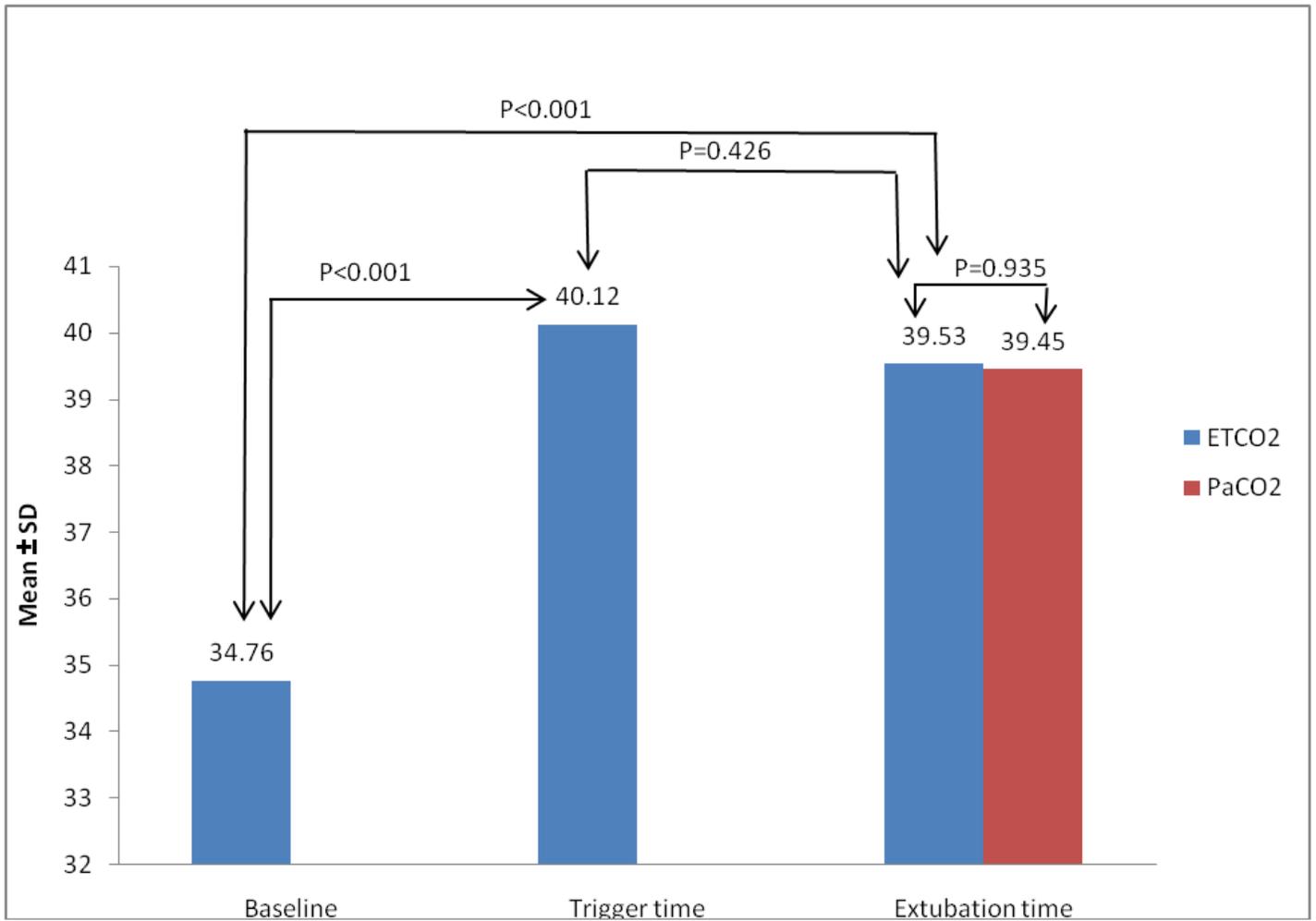


Figure 3

ETCO2 level distribution of patients in intervention group and compare to the PaCO2 in control group at extubation time