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REGISTERED REPORTS

Effects of three endotracheal tube cuff pressure control measures on microaspiration of gastric content: Study protocol for randomised controlled trial

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Abstract

Aim: To analyse the effect of endotracheal tube cuff pressure control measures on the microaspiration of the stomach contents by measuring at the level of pepsin in deep tracheal aspiration.

Design: A single-blind, randomised controlled trial.

Methods: This trial protocol was reported using the SPIRIT checklist. Endotracheal tube cuff pressure control will be provided with pilot balloon finger palpation, intermittent and continuous. The pepsin level will be measured during deep tracheal secretions in order to assess the effect of different endotracheal tube cuff pressure control measures on the microaspiration of the stomach contents. The samples will be examined within the first 4 h, between the 5th and 24th hours, and between the 25th and 48th hours after intubation. The level of pepsin will be considered positive according to the cut-off value. In addition, the effect of different endotracheal tube cuff pressure controls on the incidence of ventilator-associated pneumonia will be examined. In study group 1, study group 2 and the control group, the number of patients is planned to be 56.

Trial registration: ClinicalTrials.gov Identifier, Number NCT04061083. Registered in 2019.

Discussion: The findings will show the effect of different endotracheal tube cuff pressure control methods on microaspiration of stomach content and the possible changes in pepsin level in deep tracheal aspirates.

Conclusion: This study will shed light on future studies regarding pepsin level as a biomarker in treatment and follow-up patients receiving mechanical ventilator support using an ETT and emphasise the importance of multidisciplinary studies.

Relevance to clinical practice: As a result of the findings to be obtained from this study, the effect of endotracheal tube cuff pressure control on gastric content microaspiration and ventilator-associated pneumonia will be determined and the most appropriate endotracheal tube cuff pressure control method will be identified to prevent it. Nurses' awareness of endotracheal tube cuff pressure measurement methods will be increased. The frequency and methods of endotracheal tube cuff pressure

control will provide strong evidence that can be included in the ventilator-associated pneumonia prevention care bundle.

KEYWORDS
aspiration, endotracheal tube cuff pressure, mechanical ventilation complication, respiratory, smart cuff manager, ventilator-associated pneumonia

1 | INTRODUCTION

The first intervention to do for critically respiration depressed patients at different levels is to secure their airways in the shortest time and support their respiration (Lapinsky, 2015; Gümüş et al., 2014; Gündoğan et al., 2011; Olgun et al., 2011). Maintaining endotracheal tube (ETT) cuff pressure is considered an important factor during invasive mechanical ventilation and in patient care. (Chenelle et al., 2015; Farré et al., 2002; Nseir et al., 2015). Preservation of normal pressure of the ETT cuff is a key factor for preventing microaspiration of gastric content during mechanical ventilation (Farré et al., 2002; Nseir et al., 2015). Normal ETT cuff pressure should be around 20–30 cm H_2O (Kapucu & Özden, 2014; Lizy et al., 2011; Lorente et al., 2007). Sufficient ETT cuff pressure allows effective positive pressure ventilation, prevents microaspiration of gastric content and subglottic secretions to the lower respiratory tract, and thus, potentially prevents ventilator-associated pneumonia (VAP) (Lizy et al., 2011).

ETT cuff pressure is affected by environmental circumstances/factors and therapeutic interventions/factors (Khalil et al., 2019). These factors are body positions (Lizy et al., 2011; Athiraman et al., 2015), peak inspiratory pressure (PIP) (Chenelle et al., 2015), core body temperature (Lizy et al., 2011; Erolçay et al., 2002), blood pressure, the opening of the sternum and pleura (Erolçay et al., 2002), nitrous oxide use (Shin et al., 2015), ventilator pressures, tracheal aspiration (Lizy et al., 2011) and agitation (Sole et al., 2009). These factors cause a decrease or increase in the cuff volume, resulting in a deviation from its normal value. There appears to be variation in ETT cuff pressure with altitude (e.g. during helicopter transport) and time (Khalil et al., 2019). It is known that there is a significant decrease in ETT cuff pressures in case of supine position (Athiraman et al., 2015), body temperature decrease, opening the sternum and pericardium (Erolçay et al., 2002), tracheal aspiration (Lizy et al., 2011) and sedation (Sole et al., 2009). The risk of microaspiration potentially increases with decreased ETT cuff pressure (Sole et al., 2009). When the ETT cuff pressure decreases, microaspiration occurs as a result of small volumes of oropharyngeal secretions or gastric contents (acid or non-acid) passing into the airways (Johannson et al., 2017; Lee et al., 2010).

Serious complications may arise where normal ETT cuff pressure cannot be ensured. High ETT cuff pressure (>30 cm H_2O) causes complications such as nerve paralysis, tracheoesophageal fistula, tracheal wall damage, subglottic scarring, tracheal stenosis, hoarseness (Sole et al., 2009; Coffin et al., 2008), mucosal ischemia (Kapucu & Özden, 2014; Gaszyńska et al., 2014), in particular post-operative cough, sore throat, haemoptysis expectorating (Muallem & El-Khatib, 2011) and serious morbidity due to tracheal damage (Lizy et al., 2011). Low ETT cuff pressure (<20 cm H_2O) causes progress of secretion piling in the subglottic area to lower respiratory tract and VAP development (Kapucu & Özden, 2014; Nseir et al., 2015; Farré et al., 2002). ETT cuff pressure should be monitored and controlled continuously to minimise these complications (Muallem & El-Khatib, 2011).

What does this paper contribute to the wider global clinical community?

- Microaspiration is the most important physiopathological mechanism in the development of ventilator-associated pneumonia.
- The endotracheal tube cuff pressure control method is an effective intervention in preventing microaspiration.
- Methodological example for the studies to be done in determining microaspiration.

Three different methods are used to control the ETT cuff pressure. These are pilot balloon finger palpation (Hardcastle et al., 2016; Liu et al., 2010), intermittent and continuous (Rouzé & Nseir, 2013) ETT cuff pressure control. Finger palpation of the pilot balloon is one of the methods used to determine whether ETT cuff pressure is sufficient (Liu et al., 2010). Health care professionals usually predict ETT cuff pressure on pilot balloons through finger palpation (Sole et al., 2008). The pilot balloon finger palpation method is used as the endotracheal tube cuff pressure control method in the intensive care units where the study will be conducted. Using a manometer, intermittent ETT cuff control is widely used to prevent ICU infection or complications about ETT cuff overpressure (Rouzé & Nseir, 2013). To maintain ETT cuff pressure, continuous automatic ETT cuff pressure control devices were developed. These devices keep the ETT cuff pressure within the predetermined limits (Lizy et al., 2011).

The VAP in patients who receive respiration support in the intensive care unit (ICU) is the most frequent infection of lung parenchyma tissue in health care (Kapucu & Özden, 2014; Rouzé & Nseir, 2013). The incidence of VAP in intensive care patients who receive mechanical ventilator support through ETT for at least

2 days varies from 10% to 20% (Blot et al., 2016). Microaspiration of gastric content is the most important pathogenic mechanism of VAP development (Blot et al., 2016; Jaillette et al., 2015; Nseir et al., 2015; Blot et al., 2014; Dewavrin et al., 2014; Baskan, 2010; Farré et al., 2002) and microaspiration of gastric content is reported in 50%–75% of the ICU patients (Schallom et al., 2013). Most of the symptoms of microaspiration are clinically asymptomatic except for temporary impairment such as airway contraction and pressure increase (Gaszyńska et al., 2014). Risk factors for microaspiration are non-closure of vocal cords, longitudinal folds in ETT cuffs and ETT cuff pressure lower than 20 cm H_2O, zero positive end-expiratory pressure, low peak inspiratory pressure, tracheal aspiration, gastroesophageal reflux, loss of anatomical integrity of inferior oesophageal sphincter, gastric distension, patients in a supine position, the viscosity of secretions on ETT cuff, pressure on ETT cuff, tracheal diameter, coma, sedation and hyperglycaemia (Rouzé & Nseir, 2013; Nseir et al., 2011).

2 | BACKGROUND

Preventive strategies for VAP have been determined and used among VAP prevention bundles. With the advance of such care, there has been a significant reduction in VAP speed and prevention of VAP has become possible (Okgün Alcan & Demir Korkmaz, 2015). The manuals for preventing VAP suggest that the minimum value of ETT cuff pressure should be 20 cm H_2O irrespective of the type and frequency of control. The control of ETT cuff pressure is not mentioned as an important factor in the VAP prevention bundle (Rouzé & Nseir, 2013). Continuous control of ETT cuff pressure is necessary for reducing VAP (Branson & Hess, 2015; Jaillette & Nseir, 2015); however, ETT pressure control systems should be reviewed before they are included in the VAP prevention bundle (Jaillette & Nseir, 2015; Zolfaghari & Wyncoll, 2011). The continuous control of ETT cuff pressure is an issue that has not been resolved regarding the prevention of VAP (Lizy et al., 2011).

Kamrani et al. (2017) compared the finger palpation of the pilot balloon and the intermittent control with a manometer. Controlling the ETT cuff pressure intermittently using a manometer (70.0%) reduced the risk when compared to the method of finger palpation of the pilot balloon (80.0%) and the pepsin analysis made on tracheal secretions was statistically significant (30.72 ± 43 ng/mL for 20.24 ± 35.7 ng/mL, $p = .042$) (Kamrani et al., 2017). Rouzé et al. (2017) compared the intermittent control with a manometer and the continuous control with an electronic device. The positive pepsin incidence in tracheal secretions was 67% in the group where continuous ETT cuff control was made using an electronic device and 71% in the group where intermittent control with a manometer was made. No statistically significant difference was found between the groups ($p = .83$) (Rouzé et al., 2017). Nseir et al. (2011) compared the intermittent control with a manometer and the continuous control with a pneumatic device. The microaspiration development was 18% in the continuous control group and 46% in the intermittent control group and the difference between the groups was significant ($p = .002$). The pepsin concentration in the tracheal secretion was 195 ng/mL in the continuous control group and 251 ng/mL in the intermittent control group and the difference was significant ($p = .043$) (Nseir et al., 2011). In this regard, it was aimed to determine the effect of three different ETT cuff pressure control measures on microaspiration of gastric contents and VAP development.

3 | THE STUDY

3.1 | Aim

The aim of this randomised controlled trial was to determine the effect of three different ETT cuff pressure control measures on microaspiration of gastric content and on VAP development. The study will also investigate the relationship of socio-demographic characteristics and clinical features such as age, gender, height, weight, body mass index, medical diagnosis, chronic diseases, consciousness, presence of nasogastric (NG) tube, position, the reason for intubation, type of nutrition, drugs used (antibiotics, stress ulcer prophylaxis and sedative agents), Ramsay Sedation Score (RSS), transport and transfusion status, ventilator, respiration and hemodynamic values on microaspiration of gastric content.

3.2 | Methodology

This trial protocol was reported using the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist (Chan et al., 2013) (Supplementary File S1).

3.2.1 | Study design

This is a single-blind randomised controlled trial that compares finger palpation of the pilot balloon, intermittent and continuous ETT cuff pressure methods used to prevent microaspiration of gastric content for ICU patients. A manometer (VBM™, Medizintechnik GmbH,) will be used to ensure intermittent ETT cuff pressure in study group 1 (intermittent group). A smart cuff manager (Reference 730: TROCOE medical GmbH,) will be used to ensure continuous ETT cuff pressure in study group 2 (continuous group). The pilot balloon finger palpation method will be used to monitor ETT cuff pressure in the control group.

3.2.2 | Time frame

The study is planned to be conducted for 12 months. The proposed time frame for the execution of the study can be seen in Figure 1.

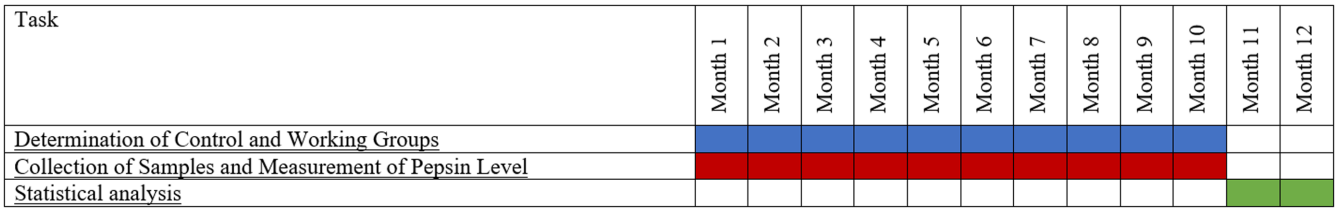

FIGURE 1 Gantt chart depicting the expected time frame for the development of the review

TABLE 1 Follow-up periods for all study endpoints

Endpoint	Follow-up start time	Follow-up finish time
Primary Microaspiration		
Pepsin I	Randomization	4 h after intubation
Pepsin II	5 h after intubation	24 h after intubation
Pepsin III	25 h after intubation	Extubation/death/transfer-discharge from ICU† or 48 h after intubation
Secondary *Microbiologically confirmed VAP‡	Randomization	48 h after intubation

†Intensive Care Unit, ‡Ventilator-Associated Pneumonia.

*Fibroscopy or protected specimen brushing at 103 cfu/mL, Broncho-alveolar lavage method at 104 cfu/mL and endotracheal secretion aspiration at 106 cfu/mL.

3.2.3 | Study population

The population of the study consists of the patients hospitalised in the Internal Medicine, Neurology, Neurosurgery, General Surgery, Anaesthesia, Isolation and Diseases ICU of a University Hospital. The Hospital meets the medical care needs of patients with a capacity of 1000 beds. The ICUs where the study will be conducted are third-level ICUs. According to the memorandum of the ICU standards of the Ministry of Health, the third-level ICUs have the highest level of medical care and treatment units, which can be used to serve all complicated patients who need to be monitored due to underlying illnesses (highly risky), respiratory insufficiency and/or multiple organ dysfunction. They also can be used for supportive treatments such as respiratory support, renal replacement therapy and plasmapheresis (Sağlık Bakanlığı, 2017; Gündoğan et al., 2011).

Inclusion criteria for the sampling of the study are as follows: being 18 years and above, voluntariness of the patients or their relatives and having a need of mechanical ventilator support with an ETT for 48 h. The criteria of exclusion from the sample are as follows: having contraindication of semi-sitting position, having a contraindication to enteral nutrition, patients who have spent more than 48 h on a mechanical ventilator at the initial assessment, having tracheostomy, gastroesophageal reflux disease (GERD), aspiration pneumonia or any suspicion of it and nasal ETT intubation. It has been stated that risk factors for microaspiration of gastric contents occur in the first 48 h. Accordingly, the study is planned during this period, since infections over 48 h may be associated with chronic exposure to mechanical ventilation and the development of the underlying disease rather than microaspiration of gastric contents. In addition, it is stated in the study that a 48 h period may reflect routine care provided during the entire mechanical ventilation period (Nseir et al., 2011). Therefore, the study will be performed for 48 h of mechanical ventilation to determine microaspiration.

3.2.4 | Study endpoints

Three different pepsin levels will be investigated in the evaluation of microaspiration of gastric content, which is a primary result. Pepsin I level will be evaluated with the first deep tracheal aspirate obtained within 4 h after the patients are intubated. Pepsin II level will be evaluated with tracheal aspirates obtained within the period from the fifth hour to the 24th hour after intubation. Pepsin III level will be evaluated with deep tracheal aspirate obtained between the 25th hour and the 48th hour after the patients are intubated. The quantitative pepsin in the samples will be measured using the enzyme-linked immunosorbent assay (ELISA). The cut-off value will be found after the measurement values. The test with the values below the cut-off will be deemed negative and the test with the values above the cut-off will be deemed positive in determining microaspiration.

Microbiological examination results of the samples requested by the physician and taken within the first 48 h will be monitored in the evaluation of the secondary result VAP. There will be no routine culture sampling. According to the description by the American Thoracic Society (ATS), the presence of bacteria will be deemed positive in the samples taken using respiratory tract fibroscopy or

protected specimen brushing at 10^3cfu/ml, in the samples taken using Broncho-alveolar lavage method at 10^4cfu/mL and in the samples taken using endotracheal secretion aspiration at 10^6cfu/ml (Marjanovic et al., 2017) (Table 1).

3.2.5 | Sample size

Power analysis was done to determine the number of patients to be distributed to Group 1, Group 2 and the control group. The power analysis was done using GPower 3.1.9.2 software. Thus, the significance level was $\alpha = 0.05$ (%5), the effect size was $d = 0.5$, and the number of patients in each group was 51 for the power at 1-$\beta = 0.80$. Missing, bad or lost data (in case patients were exitus) were considered and the number of patients was designed to be 56 for each group.

3.2.6 | Randomization procedure

A simple randomization method will be used by a third party to determine the groups by lottery in sealed envelopes without the knowledge of the researchers. The participants will be separated into study group 1 (intermittent ETT cuff pressure control), study group 2 (continuous ETT cuff pressure control) and control group (finger palpation of the pilot balloon). No bedding or blockage will be used in the randomization procedure.

3.2.7 | Intervention and assessment

The appropriateness of patients who have received mechanical ventilator support using an ETT in the ICUs will be evaluated based on the inclusion and exclusion criteria. The patients who have been included in the study will be evaluated in terms of age, gender, height, weight, body mass index, medical diagnosis, chronic diseases, consciousness, presence of nasogastric (NG) tube, position, the reason for intubation, type of nutrition, drugs used (antibiotics, stress ulcer prophylaxis and sedative agents), Ramsay Sedation Score (RSS), transport and transfusion status, ventilator, respiration and hemodynamic values.

The cuff pressure of the patients in all groups will be controlled every 8 h. Smart cuff manager will be attached to the patients in study group 2. The Smart Cuff Manager adjusts the ETT cuff pressure and prevents the balloon pressure from falling or overpressure. It regulates the internal pressure of the ETT cuff. It can keep the pressure between 20–30-cm H_2O continuously. The smart cuff manager has an elastic pad in a transparent, spherical slot. After the air is injected into the balloon, it maintains the pressure at an optimal value and compensates for pressure variations in the cuff. (TRACOE smart Cuff Manager; https://assets.website-files.com/5e43a61af75ce2f5073778f6/5ef5efa969a197cde89bb3af_REF_730-5_EN.pdf). In study group 1, ETT cuff pressure control will be provided with a manometer, measured every 8 h and set to 25-cm H_2O. In study group 2, ETT cuff pressure control will be provided with a smart cuff manager and will maintain 25-cm H_2O pressure continuously. ETT cuff pressure control will be done with a manometer every 8 h in the continuous group. Each patient's ETT cuff pressure will be recorded every 8 h for 48 h after intubation. Control values of ETT cuff pressure for study groups 1 and 2 will be evaluated as 25-cm H_2O based on study results (Nseir et al., 2015; Nseir et al., 2011; Valencia et al., 2007). If the pressure deviates to 25-cm H2O in study group 1, it will be saved and reset to 25-cm H2O. In study group 2, the ETT cuff pressure is maintained as a constant 25-cm H_2O due to the feature of the smart cuff manager. The Smart Cuff device provides continuous control due to its working principle. In the continuous control group, pressure measurement will be made every 8 h as a precaution against situations that may disrupt this working principle.

Samples will be taken from the patients through open aspiration. The first deep tracheal secretion sample to be used to determine pepsin I level will be taken 4 h after intubation. Tracheal secretion samples will be collected between the 5th and 24th hours after intubation for pepsin II level determination, and between 25th and 48th hours or until death and discharge for pepsin III level determination.

Although no routine VAP sampling will be done, the culture samples from the patients under suspicion will be monitored by the physicians for 48 h.

All ETT cuff pressure measurements, collection and analysis of samples will be done by the researchers. Against any problem, the nurses will be given training in advance (Soyer et al., 2020).

Figure 2 shows the flow chart of the study procedures. Table 2 presents registrations, interventions and evaluations.

3.2.8 | Data management

The study data will be recorded in data collection forms and computers. Furthermore, the digital data will be backed up in the mail address of the researcher. The nurse observation forms will be used during patients' care and other records will be kept in the relevant clinic until the patient dies or is discharged. After the exitus or discharge of patients, it will be sent to the archive. The data will be kept for 15 years after the study is completed. The original documents will be kept for a minimum of 5 years.

Information of all the participating patients will be kept confidential. Names or identifiers of the patients will not be disclosed in any database. Information that may identify the patients in scientific publications, project reports and declarations will not be published.

3.2.9 | Statistical analysis

The data will be analysed using Statistical Package for the Social Sciences (SPSS) for Windows 21.0 (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) Software.

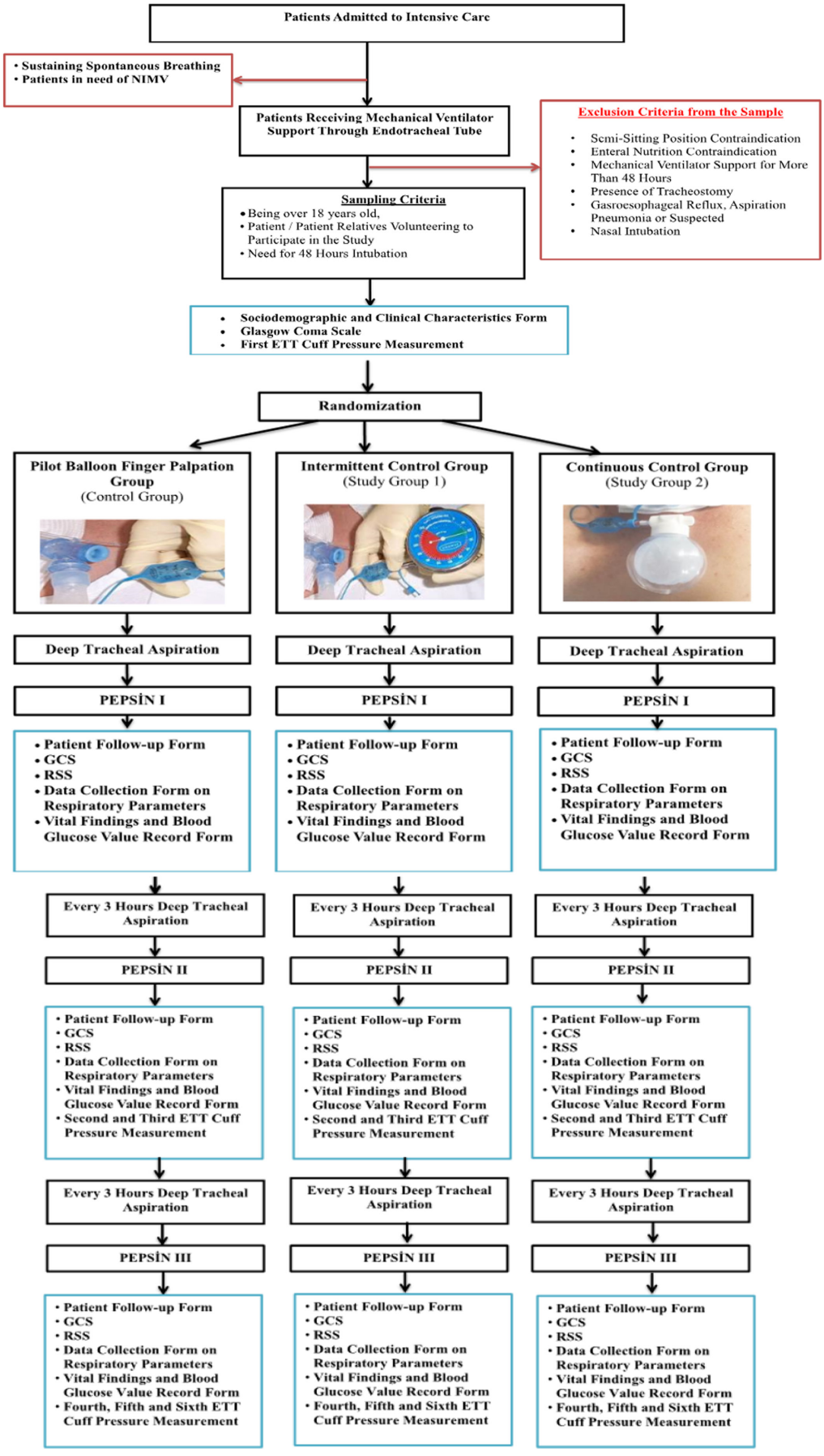

FIGURE 2 Research design

TABLE 2 Schedule of enrolment, interventions and assessments

	STUDY PERIOD																							
	ENROLMENT	ALLOCATION	POST-ALLOCATION																					CLOSE OUT
ORAL INTUBATION HOURS			4	6	8	9	12	15	16	18	21	24	27	30	32	33	36	39	40	42	45	48	
ENROLMENT																							
Eligibility Screen	✓																						
Informed Consent	✓																						
Randomization		✓																					
INTERVENTIONS																							
Continuous		✓																					
Intermittent		✓																					
Finger palpation		✓																					
PRESSURE MEASUREMENT																							
Continuous		✓			✓			✓			✓			✓				✓					
Intermittent		✓			✓			✓			✓			✓				✓					
Finger palpation		✓			✓			✓			✓			✓				✓					
SAMPLE COLLECTION																							
DTA† for Pepsin I		✓																					
Analysis Pepsin I		✓																					
DTA† for Pepsin II				✓		✓	✓	✓		✓	✓	✓											
Analysis Pepsin II							✓																
DTA† for Pepsin III													✓	✓		✓	✓	✓		✓	✓	✓	
Analysis Pepsin III																✓							
ASSESSMENT																							
Sociodemographic Characteristics	✓																						
Clinical Feature																							
Medical Diagnosis	✓																						
Chronic Diseases	✓																						
Consciousness (Glasgow Coma Scale)	✓	✓										✓											✓
Presence of NG Tube	✓																						
Position	✓																						
Reason for Intubation	✓																						
Type of Nutrition		✓										✓											✓
Use of drugs (antibiotics, stress ulcer prophylaxis and sedative agents)		✓										✓											✓
Ramsay Sedation Score		✓										✓											✓
Transport status		✓										✓											✓
Transfusion status		✓										✓											✓
ETT‡ diameter and level		✓										✓											✓
Ventilation Mode		✓										✓											✓
FiO_2§		✓										✓											✓
Tidal Volume		✓										✓											✓
PEEP¶		✓										✓											✓
Respiratory rate		✓										✓											✓
Frequency of aspiration		✓										✓											✓
Arterial pH		✓										✓											✓
PaO_2††		✓										✓											✓
$PaCO_2$‡‡		✓										✓											✓
HCO_3§§		✓										✓											✓
BE¶¶		✓										✓											✓
Hemodinamic monitoring		✓										✓											✓
Tracheal culture result		✓										✓											✓

†Deep Tracheal Aspiration. ‡Endotracheal Tube, § Fraction of Inspired Oxygen, ¶ Positive End Expiratory Pressure, ††Partial Pressure of Oxygen, ‡‡ Partial Pressure of Carbon Dioxide, §§ Bicarbonate, ¶¶Base Curve

- Patients' socio-demographic and clinical attributes will be reported using frequencies, percentage distribution, mean and standard deviation.
- Chi-Square Test or Fisher's Exact Test will be conducted to assess the differences in socio-demographic characteristics and clinical features and to determine homogeneity between the control, intermittent and continuous ETT cuff pressure control groups.
- Kolmogorov–Smirnov Test will be used to check the appropriateness of data to normal distribution.
- Independent two-sample *t*-test, one-way analysis of variance will be used for the relationships between the variables that fit the normal distribution, and the Mann–Whitney *U*-test will be used for the variables that do not fit the normal distribution.
- Pearson Chi-square significance test and Fisher Exact will be applied in the analysis of categorical data.
- Socio-demographic and clinical features that affect the microaspiration values will be determined by the logistic regression model. Odds ratios (ORs) and their associated 95% confidence intervals (95% CIs) will be presented in the logistic regression model.
- All *p* values lower than 0.05 will be taken as significant in all results ($p < .05$).

3.2.10 | Trial status

This study has now ended. The recruitment started in May 2019 and ended in December 2019. Information about the important protocol changes that emerged during the study was conveyed to the relevant institutions by the researchers. ClinicalTrials.gov Identifier, Number NCT04061083. Registered on August 19, 2019.

3.3 | Ethical consideration

The suggested project was examined by the Ege University Faculty of Medicine Noninvasive Clinical Studies Ethics Committee and deemed appropriate with the committee's decree number 17–7.1/15 dated August 18, 2017. Also, the Afyonkarahisar Health Sciences University Hospital chief physician gave approval to conduct the study in the institution with article number E.24854 dated May 30, 2017. Furthermore, the verbal and informed consent forms will be taken from the patients or their relatives after they are told about the aim and scope of the study before it is conducted.

3.3.1 | Reporting of adverse events and monitoring

Many undesired events may occur in intubated patients who are getting mechanical ventilator support in ICUs. Undesired events specific to ETT cuff pressure control methods that will be applied in accordance with the aim of the study will be reported. The events reported to the ethical committee will be reintubation rates of the patients due to pressure changes in study group 1 and optimal pressure in study group 2. In particular, air leakage may occur in the incomplete closure of the airway of the 25-cm H2O pressure and during ventilation in patients with continuous ETT pressure due to the wide trachea or intubation tubes not suitable for the width of the trachea. These events will also be reported.

3.3.2 | Validity and reliability

The research team has the expertise to carry out all stages of the research. The cuff pressure of the patients will be controlled by an intensive care specialist, nurse and researcher, and the ETT cuff pressure method in the group will be observed together. Devices with ETT cuff pressure will be calibrated in line with the manufacturer's recommendation. Tracheal aspirate samples of patients will be taken and stored by the researcher. The temperature of the stored cabinets will be checked twice every day. Kits and samples will be stored at −20 degrees. Verification will be provided by analysing all samples in duplicate. The sensitivity of the kits to be used is 0.26 ng/mL. In the analysis of the samples and in the statistical analysis, the information revealing the patient's group will be hidden. In addition, a pilot study will be conducted with two patients in each group.

4 | DISCUSSION

The aim of this project was to analyse the effect of ETT cuff pressure control on the microaspiration of gastric content based on the pepsin level in deep tracheal aspiration. One of the objectives is to determine the most effective method in preventing microaspiration by providing continuous ETT cuff pressure through finger palpation of the pilot balloon in the control group, intermittently using a manometer every 8 h in study group 1 and continuously a smart cuff manager in the study group 2. The finger palpation of the pilot balloon, which has been examined in terms of frequent intermittent and continuous microaspiration in other studies and is widely used will also be evaluated. This is the first randomised controlled trial to investigate the effect of three ETT cuff pressure control on the microaspiration of gastric content. It will also help determine the most effective method for preventing microaspiration and thus, will contribute to the related literature.

The pepsin values of the patients at three different times for 48 h will be determined. Thus, the pepsin level and its change over time in deep tracheal aspirates will be determined to evaluate the effect of ETT cuff pressure control on the microaspiration of gastric content. Besides that, it will be possible to make comparisons according to clinical conditions that may affect the microaspiration like patients' socio-demographic characteristics and clinical features such as age, gender, height, weight, body mass index,

medical diagnosis, chronic diseases, consciousness, presence of NG tube, position, the reason for intubation, type of nutrition, drugs used, RSS, transport and transfusion status, ventilator, respiration and hemodynamic values.

Although no routine VAP sampling will be done, the culture samples from the patients under suspicion will be monitored by the physicians for 48 h. Also, the correlation between VAP and microaspiration of gastric content that is known as the most important pathogenic mechanism of VAP development will be estimated.

4.1 | Limitations

The manometer used to measure the ETT cuff pressure can measure pressure up to 120 cmH_2O; therefore, ETT cuff pressure values higher than this will not be detected. Some DTA samples taken for analysis cannot be used because the patient's secretion volume will be insufficient. The dilution of the DTA samples taken from the patients is required to be dark and sticky. It is thought that even if dilution is performed, analysis difficulties will be experienced in some samples or the analysis cannot be performed. Since tracheal culture samples are not routinely taken from patients, it will not be possible to determine whether VAP develops in patients without symptoms. Due to the restoration processes in some ICUs, patients will not be included during this process.

5 | CONCLUSION

The multidisciplinary study is important in nursing studies. However, there are few studies on biochemical tests in nursing in the related literature. This study will shed light on future studies regarding pepsin level as a biomarker in treatment and follow-up of patients receiving mechanical ventilator support using an ETT and emphasise the importance of multidisciplinary studies.

Furthermore, it is aimed to raise and maintain awareness of the nurses working in the intensive care units about the intermittent and continuous endotracheal tube cuff pressure control methods, apart from the cuff pressure control method that they routinely apply with the pilot balloon finger palpation method. This will also be an important step towards the prevention of gastric content microaspiration and patient safety practices.

6 | RELEVANCE TO CLINICAL PRACTICE

As a result of the findings to be obtained from this study, the effect of endotracheal tube cuff pressure control on gastric content microaspiration and ventilator-associated pneumonia will be determined and the most appropriate endotracheal tube cuff pressure control method will be reached to prevent it. The frequency and methods of endotracheal tube cuff pressure control will provide strong evidence that can be included in the ventilator-associated pneumonia prevention care bundle. Furthermore, nurses will gain knowledge about endotracheal tube cuff pressure control methods and they will recognise the devices used during the control. Nurses will provide important steps in the selection of the most appropriate endotracheal tube cuff pressure, diagnosis of microaspiration, preparation of samples and progress of the study. Clearly explaining the stages in the diagnosis of microaspiration will shed light on future studies.

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CONFLICT OF INTEREST

No conflict of interest has been declared by the author(s).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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