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Vagal withdrawal and psychological distress during ventilator weaning and the related outcomes

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ABSTRACT

Objective: This study investigated the associations between changes in autonomic nervous system (ANS) function, psychological status during the mechanical ventilation (MV) weaning process, and weaning outcomes.
Methods: In this prospective study, we recruited 67 patients receiving MV for > 24 h at a medical center in northern Taiwan. Patients' ANS function, represented by heart rate variability (HRV), the rapid shallow breathing index (RSBI), anxiety, fear, and dyspnea, was repeatedly measured 10 min before and 30 min after undergoing a weaning trial. Forty-nine patients capable of sustaining a 2-h weaning trial were successfully weaned.
Results: Compared with the failed group, the success group showed significantly smaller decreases in high-frequency HRV (HRV-HF) and smaller increases in RSBI (per 10 breaths/min/L), fear, dyspnea, and anxiety in response to the weaning trial (odds ratio [OR] = 2.19, 0.81, 0.69, 0.66, and 0.77, respectively; $p < 0.05$). Multivariate analyses revealed that low-frequency HRV before weaning (OR = 2.32; 95% confidence interval [CI] = 1.13–4.78, $p = 0.02$), changes in HRV-HF (OR = 3.33; 95% CI = 1.18–9.44, $p = 0.02$), and psychological fear during the weaning process (OR = 0.50; 95% CI = 0.27–0.92, $p = 0.03$) were three independent factors associated with 2-h T-piece weaning success.
Conclusions: ANS responses and psychological distress during weaning were associated with T-piece weaning outcomes and may reflect the need for future studies to utilize these factors to guide weaning processes and examine their impact on outcomes.

1. Introduction

Mechanical ventilation (MV) is typically used to support the respiratory function of critically ill patients [1–3]. After resolving the underlying problems necessitating MV, most patients can be readily weaned from MV. Prolonged MV is associated with high morbidity and mortality, as well as poor quality of life [4,5]. Accordingly, previous studies have explored the physiological predictors for facilitating successful MV weaning; however, a 20%–30% variance in weaning failure remains unexplained [6,7]. The most recently published guidelines have provided evidence-based recommendations that assist clinicians in safely and effectively weaning critically ill patients from MV [8–10]. Of these, one strong recommendation is using noninvasive mechanical ventilation to prevent extubation failure for high-risk patients [9,10]. There are also five conditional (weak) recommendations: conducting spontaneous breathing trials with inspiratory pressure augmentation, using protocols to minimize sedation, using protocolized rehabilitation directed toward early mobilization, using ventilator liberation protocols, performing a cuff leak test (CLT) for extubation criteria, and administering systemic steroids at least 4 h prior to extubation for patients who failed a CLT [8–10]. However, it is unclear whether these guidelines considered all individual contexts, especially psychological factors, which also critically affect ventilator weaning outcomes [11]. Nevertheless, clinicians have become more aware that successful

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weaning can be hindered not only by physiological dysfunction but also by psychological distress [4,7].

During the MV weaning process, patients can experience the following psychological distress: fear [4], anxiety [12], and dyspnea [13]. In addition, patients on MV have reported experiencing high degrees of uncertainty, discomfort, and fatigue [12,14], as well as feelings of being "out of control" or "tortured by helplessness" [15]. These psychological factors may exert a compromising effect on patients' physiological performance (e.g., respiratory functions) during weaning trials, contributing to weaning failure [4]. Simultaneously considering both psychological and physiological variables has a greater predictive effect regarding weaning success than does solely considering physiological variables [4,16].

Ventilator weaning with a spontaneous breathing trial changes the intrathoracic pressure and thoracic blood volume and flow, which can lead to compensatory autonomic tone alterations that occur to maintain adequate cardiac output and oxygen delivery [17,18]. Autonomic nervous dysfunction is a key factor that renders MV weaning difficult; although no significant changes in cardiac output were noted, one study did observe a significant increase in the catecholamine levels in response to a weaning trial [18]. Heart rate variability (HRV), measured as the variation in sequential inter-beat or R-R intervals on an electrocardiogram (ECG), is a valid noninvasive measure of autonomic nervous system (ANS) function [19]. HRV has also been assessed as a physiological variable related to weaning outcomes [20,21]. Specifically, patients with significantly lower baseline HRVs when receiving MV and a greater reduction in HRVs during a weaning trial or weaning ventilation mode transitions have been found to be at a higher risk for MV weaning failure [18,20].

HRV not only directly links the heart to the central ANS [19], but may also be influenced by patients' emotional responses [22–24]. Indeed, HRV has been considered an indicator derived from psychological and physiological interactions when treating medical and psychological conditions [22,23]. For example, some patients experience psychological distress such as anxiety during the weaning process, which may lead to the downregulation of β-adrenergic receptors, presenting a blunted ability to respond to further elevation in catecholamines and contributing to the reduction in HRV [18]. A high rapid shallow breathing index (RSBI), which is measured as the ratio of respiratory frequency f to tidal volume VT (f/VT) [25], is believed to represent a respiratory center response to both respiratory loading and anxiety during weaning trials [5,26]. According to previous studies, the decrease in the high-frequency component of HRV (HRV-HF), indicating vagal withdrawal, is associated with a higher RSBI in patients who fail to wean from MV [20,21].

Clinical evidence has indicated that even some patients who meet the weaning criteria still fail to pass the weaning trial, which suggests that they had encountered a decline in physiological and psychological status during the weaning process. Therefore, simultaneously exploring changes in ANS function and psychological status during the MV weaning process, and testing the association of those changes with weaning outcomes, are crucial but absent research pursuit. Accordingly, this study was conducted to identify whether the changes in HRV, RSBI, and psychological distress (i.e., self-rated anxiety, fear, and dyspnea) in response to weaning trials were associated with MV weaning outcomes. Our multivariate logistic regression findings confirmed a significant association.

2. Methods

2.1. Study design and population

In this prospective study, we recruited a convenience sample of patients on MV from a 22-bed medical intensive care unit and 21-bed respiratory care center at a medical center in northern Taiwan. Patients were included if they (a) had received MV support for > 24 h; (b) were ready for T-piece weaning; (c) were hemodynamically stable (i.e., systolic blood pressure [SBP] > 90 mm Hg and requiring no or low-dose vasopressors [e.g., dopamine or dobutamine < 5 g/kg/min]); (d) did not require vasoactive agents; (e) had no hyperthermia (≤ 38 °C), (f) had hemoglobin ≥ 10 g/dL (to exclude subjects with inadequate oxygen delivery and respiratory muscle overload [27,28]); (g) were not on a high-carbohydrate diet (to avoid aggravating respiratory distress or acidosis prior to the weaning process [29]); and (h) were alert, cooperative, and able to understand, read, or write Mandarin.

Readiness for weaning was determined by the weaning criteria used in the target medical center, namely: (a) O_2 partial pressure in arterial blood/fraction of inspired oxygen (PaO_2/FiO_2) > 200; (b) positive end-expiratory pressure ≤ 5 cm H_2O; (c) adequate cough; (d) RSBI < 105 breaths/min/L; and (e) not be placed on continuous intravenous infusion of sedatives, analgesics (particularly narcotics), or vasoactive agents [30]. Patients were excluded if they exhibited uncontrolled pain or arrhythmia or if they were ventilator dependent prior to hospital admission. Among the 103 patients approached for this study, 67 agreed to participate. The remaining patients did not participate for the following reasons: lack of interest (n = 23), had self-extubated (n = 3), had received tracheostomy before weaning trials (n = 3), and had used continuous positive airway pressure as the weaning mode (n = 7).

2.2. Data collection

Data on HRV, psychological status (fear, dyspnea, and anxiety), and RSBI were collected 10 min before and 30 min after undergoing a T-piece weaning trial in the morning, and were described as pre- and post-test data, respectively. Notably, HRV was recorded before the measurements of psychological status and RSBI to prevent any influence on the HRV recording. Demographic (age and sex) and clinical (diagnosis on hospital admission, Acute Physiology and Chronic Health Evaluation [APACHE] II score, etiology for MV, duration of MV before the current weaning trial, and prescribed medications) data were collected from the patients' medical charts.

2.3. HRV

The patients' HRVs were measured from heart beat-to-beat signals (sample rate = 256 Hz) by using a three-way ECG recording device (Mind Media BV-NeXus-10, Netherlands). The signals were recorded for a total of 6 min, and HRV analyses were conducted on the most stable 5 min. The signals were then categorized into time- and frequency-domain results using Kubios HRV analysis software (Biosignal Analysis and Medical Imaging Group, Kuopio, Finland) [31]. All artifacts and ectopic beats were removed by using the "smooth priors" Kubios software. The HRV time-domain analysis used the standard deviation of normal-to-normal R-R intervals (SDNN) and the root mean square of successive heartbeat interval differences (rMSSD), whereas the HRV frequency-domain analysis was performed using a fast Fourier transformation of the R-R interval time-series data, with indices of very low frequency (VLF; < 0.04 Hz), low frequency (LF; 0.04–0.15 Hz), and high frequency (HF; 0.15–0.4 Hz). The absolute powers of VLF, LF, and HF were then summed to calculate the total power (TP). Finally, due to the skewedness of the HRV data (1.37–2.35), the SDNN, rMSSD, HF, LF, and TP were converted into natural logarithms (i.e., ln SDNN, ln rMSSD, ln HF, ln LF, and ln TP, respectively) for further inferential statistics.

2.4. Rapid shallow breathing index

The patients' RSBIs were calculated as the f/VT ratio, which was obtained using a variable-orifice pneumotachograph connected to a pulmonary mechanics monitoring system (Ventrak 1550; Novametrix Medical Systems, USA). Immediately after HRV and psychological