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Automated respiratory therapy system based on the ARDSNet protocol with systemic perfusion control

Abstract: A medical expert system of automatic artificial ventilation is set up in a star topology with additional closed-loop hemodynamic control. Arterial blood pressure (MAP) is controlled by noradrenaline (NA) as a controlling variable. The overall patient-in-the-loop expert system can intensively and intelligently perform a long-term treatment based on the Acute Respiratory Distress Syndrome Network (ARDSNet) protocol. Three main goals are actively carried out, namely the stabilization and regulation of oxygenation, plateau pressure and blood pH value. The developed system shows a distinctive experimental result based on a 31.5-kg pig, in order to fulfill the ventilatory goals and to ensure proper systemic perfusion. Hence, this system has enormous potentials to realize a commercial system for individual patient with ARDS.

Keywords: Closed-loop ventilation; automatic ventilation therapy; ARDS; ARDSNet protocol

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1 Introduction

Acute respiratory distress syndrome (ARDS) is a rapidly evolving and life-threatening respiratory disorder, caused by inflammation of the lung parenchyma leading to impaired gas exchange. Progressive hypoxia and multiple organ failure are usually onset. Common patterns of ARDS can be observed by shortness of breathing, appearance of bluish skin, loss of active aerated lung volume [1] due to the formation of noncardiogenic pulmonary edema, elevated airway and tissue resistance and evidence on radiograph for a certain degree of infiltration. Recent definition of ARDS was defined by the “Berlin definition” [2], which categorized the severity of the syndrome, namely severe ARDS, moderate ARDS and mild ARDS based on the ratio of arterial oxygen tension and fraction of inspired oxygen (PaO₂/FiO₂) [3].

The mortality rate of ARDS is approximately 43% [4], which remained unchanged for decades. Hence, it is a great challenge to reduce this rate in critical and intensive cares. To treat the patients with ARDS, mechanical ventilation is the primary therapeutic approach. Various ventilation strategies can be applied to rescue the patients, for example low tidal volume ventilation, high frequency oscillation, or the open lung management [5, 6].

In this article, an automatic respiratory therapy system is set up based on the well-known ARDSNet protocol [7], which showed a significant reduction of mortality for 8.8% (31% vs. 39.8%) compared to the conventional ventilation therapy of a higher tidal volume. In addition, a control of hemodynamics in terms of mean arterial blood pressure (MAP) is carried out to ensure appropriate systemic perfusion. Our aim is therefore to set up a medical expert system for the automatic respiratory therapy with hemodynamic control to treat patients with ARDS using the ARDSNet protocol. Subsequently, the automatic system is validated for 5-hour ventilation therapy using a 31.4-kg pig with induced severe ARDS as a case study.

2 Methods

2.1 System configuration

The designed closed-loop ventilation system is characterized by a star topology, shown in Fig. 1, where a centralized panel PC (PPC-154T, Advantech Co., Ltd, Taipei, Taiwan) connects directly to all medical devices. The two actuators are composed of a mechanical ventilator (Servo 300, Maquet Critical Care AB, Solna, Sweden) and an infusion pump (Perfusor compact S, B. Braun, Melsungen, Germany). Other measuring devices include an electrical impedance tomography (EIT) system (Goe MF II, Dräger AG, Lübeck, Germany), a pulse oximeter (CeVOX; Pul-
sion Medical Systems SE, Feldkirchen, Germany), a capnograph (CO₂ SMO+, Philips Respironics, Best, The Netherlands) and a patient monitor (Sirecust 960, Siemens AG, Munich, Germany). All data communication protocols except for the EIT connection are based on an asynchronous RS-232 interface with a sampling time of 100 ms. The EIT system is used in our system for a real-time reference monitoring of ventilation at bedside. At the mechanical ventilator, airway pressure and airway flow are converted by a 12 bit analog-to-digital (A/D) converter (KPCMCIA-12AI-C, Keithley Instruments Inc., Cleveland, OH, USA).

The computed commands of ventilatory variables are transmitted from the panel PC in order to control the mechanical ventilator by a 12 bit digital-to-analog (D/A) converter (PCMDA12B, SuperLogics Inc., Waltham, MA, USA). The knowledge-based ventilation and hemodynamic control protocols were coded by graphical programming with LabVIEW 7.1 software (National Instruments, Austin, TX, USA) and fuzzyTECH 5.54 software (INFORM GmbH, Aachen, Germany). The automatic adjustment of ventilatory settings and hemodynamics can be realized by this configuration.

2.2 Algorithm implementation

The ARDSNet protocol is classified as a protective ventilation strategy. A key aspect is to implement a low tidal volume (VT) of 6 ml/kg of the predicted body weight (PBW). Based on the protocol [7, 9], the following goals must be implemented.

2.2.1 Oxygenation goal: PaO₂ for 55-80 mmHg or SpO₂ for 88-95%

A piecewise linear combination of PEEP and FiO₂ was applied to control oxygenation, as shown in Table 1.

<table>
<thead>
<tr>
<th>PEEP [mbar]</th>
<th>5</th>
<th>5</th>
<th>8</th>
<th>8</th>
<th>10</th>
<th>10</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>FiO₂</td>
<td>0.3</td>
<td>0.4</td>
<td>0.4</td>
<td>0.5</td>
<td>0.5</td>
<td>0.6</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Table 1: PEEP and FiO₂ combination (Lower PEEP/Higher FiO₂ table).

Note that PEEP refers to positive end-expiratory pressure and is applied to prevent lung collapse. PEEP and FiO₂ should be simultaneously adjusted in order to stabilize and control PaO₂ or SpO₂ in an appropriate range.

2.2.2 Plateau pressure goal: Pplat ≤ 30 mbar

Based on the ARDSNet protocol, Pplat must be checked at least every 4 hours and after change of PEEP or VT. In the experiments, Pplat will be automatically checked by the panel PC every 10 mins. An inspiratory pause was set to 0.5 s for 5 consecutive breaths, and the average of Pplat from these breaths was used to compute the measured Pplat. According to the protocol, the following rules apply for VT adjustment.

1. If Pplat > 30 mbar, tidal volume per weight (VT_PW) may be decreased by 1 ml/kg with the minimum value of 4 ml/kg.
2. If Pplat < 25 mbar and VT_PW < 6 ml/kg, VT_PW may be increased by 1 ml/kg until Pplat > 25 mbar or VT_PW = 6 ml/kg.
3. If Pplat < 30 mbar and breath stacking or dyssynchrony is detected during the ventilation therapy, VT_PW is allowed to be 7 or 8 ml/kg.
2.2.3 pH goal: 7.30-7.45

In our experiment, arterial pH values were measured by arterial blood gas analysis (ABL 5, Radiometer Copenhagen, Copenhagen, Denmark) every 30 mins; this value was manually entered into the panel PC for further evaluation of the pH goal. The initial respiratory rate ($RR_{\text{initial}}$) is set to approximate baseline minute ventilation ($MV_{\text{baseline}}$), but limited by the maximum value of 35 bpm. The initial setting of RR is computed by eq. (1), where $V_{TPW}$ has a unit in ml/kg.

$$RR_{\text{initial}} = \frac{MV_{\text{baseline}}}{V_{TPW} \times BW}$$ (1)

Further adjustment of RR is based on the measured pH value by the resulting acidosis or alkalosis. The procedures for blood pH management are provided below.

Rules for acidosis management (pH < 7.30)

1. If pH = 7.15-7.30, increase RR until pH > 7.30 or PaCO$_2$ < 25 mmHg with maximum RR = 35 bpm.
2. If pH < 7.15, RR must be set to 35 bpm.
3. If pH remains < 7.15, $V_{TPW}$ may be increased in 1 ml/kg steps until pH > 7.15 with maximum $V_{TPW} = 8$ ml/kg.

Rule for alkalosis management (pH > 7.45)

If pH > 7.45, RR should be decreased.

2.3 Hemodynamic control

To ensure oxygen transport from the lung to tissues, the control of hemodynamics is implemented in order to achieve normotension by automatic infusion of noradrenaline (NA). Hence, sufficient systemic perfusion for vital organs is guaranteed during the course of respiratory therapy. The increase in NA from the sympathetic nervous system enhances the rate of heart contractions, ultimately resulting in an increase of mean arterial blood pressure (MAP). With this pharmacological infusion, we can then formulate another feedback control loop for the control of MAP based on NA using a knowledge-based controller [6] and the goal is to ensure that MAP is in between 85 and 105 mmHg, in order to prevent not only hypotension but also possible hypertension.

2.4 Animal preparation

With the approval from the local animal ethical committee, one 31.5-kg pig was premedicated, anesthesized and intubated. A spectrophotometry catheter was placed for the continuous monitoring of SaO$_2$ at the carotid artery, which was used to monitor oxygenation. Severe ARDS condition was induced by repetitive lavage with warmed saline [10] until PaO$_2$/FiO$_2$ < 100 mmHg for at least 20 mins. The automatic respiratory therapy with hemodynamic control was then performed to validate our system.

3 Results

The automatic respiratory therapy was implemented for five hours using the 31.5-kg male pig and the experimental results are given in Fig. 2. The animal was lavaged and exposed to a severe ARDS condition for 30 mins before the activation of automatic ventilation. After the lavage, PaO$_2$/FiO$_2$ was 54.9 mmHg and PaCO$_2$ was 69.6 mmHg. This reflects an extreme condition of impaired gas exchange with hypoxia and hypercapnia, confirming the suitability of this animal model of induced ARDS [10]. Based on the functional electrical impedance tomography (fEIT) shown in Fig. 2, we can see that ventilation was slightly lost from both lungs after the lavage as a consequence of surfactant wash-out and of some remaining saline solution in the lungs. The fEIT images also showed an improvement of ventilation in the course of our automated therapy with no complications.

During ventilation therapy, all goals were simultaneously carried out for five hours. The oxygenation was significantly improved. Based on SaO$_2$ measurement after lavage at the critical state, SaO$_2$ was 82% and the system can control SaO$_2$ between 88% and 95% by manipulating FiO$_2$ and PEEP, based on Table 1. The severe hypoxia was recovered by 5 mins after the automatic ventilation therapy. The system can distinctively stabilize and control oxygenation throughout the course of therapy.

Secondly, the plateau pressure was kept between 25 and 30 mbar to minimize potential ventilator-induced lung injury (VILI), which is a protective measure by adjusting $V_{TPW}$ between 4 and 6 ml/kg. In our experiment, we used the actual weight for the setting of tidal volume, instead of the predicted body weight (PBW). To fulfill the goal of plateau pressure, the system automatically adjust tidal volume to keep plateau pressure in a range according to the instruction of the ARDSNet protocol.

Due to a current limitation of continuous measurement of blood pH, the samplings were taken with an interval of approximately 30 mins. The measured blood pH was 7.26 after the lavage, suggesting a respiratory acidosis. It was clear that the system increased respiratory rate...
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(RR) to get rid of excessive CO₂ [11]. Therefore, blood pH can eventually be in control between 7.30 and 7.45.

Finally, the hemodynamic response of mean arterial blood pressure (MAP) corresponding to the automatic NA infusion was also shown in Fig. 2. Neither hypotension nor hypertension occurred during the course of automatic ventilation therapy. This control objective was achieved by the implementation of the knowledge based controller [6]. However, at the beginning of automatic ventilation therapy, a manual intervention was necessary for initializing the proper amount of NA.

4 Conclusion

The automatic respiratory system with hemodynamic control can strictly perform multi-objective ventilation therapy of the ARDSNet protocol for patients with ARDS. The stabilization and control of oxygenation, plateau pressure, blood pH control and system perfusion are vital for improving an impaired gas exchange and protecting possible lung injury, caused by the ventilator. Based on this pioneering work and concept, the developed algorithms have great potentials for being integrated into a commercial system, which should benefit to the medical doctor, the patients with ARDS and the whole community in terms of workload reduction, continuous protocol-driven care, and reduction of healthcare cost.

Author’s Statement

Conflict of interest: Authors state no conflict of interest. Material and Methods: Informed consent has been obtained from all individuals included in this study. Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors’ institutional review board or equivalent committee.

References