Study of APRV and ICP in Patients with Severe Traumatic Brain Injury

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Introduction

Management of patients with Traumatic Brain Injury (TBI) emphasizes on prevention of secondary insults such as hypotension and hypoxemia which negatively impact outcomes [1]. Both hypotension [2-4] and hypoxemia [5,6] are not only independent risk factors for increased mortality in patients with TBI, but also lead to increased intracranial pressure (ICP), which is also another independent risk factor for high mortality [4,7-10].

All patients with severe TBI (Glasgow Coma Scale ≤8) require sedation and mechanical ventilation for airway protection, oxygenation and minimization of obnoxious stimuli which may elevate ICP [11]. Mechanical ventilation, however, carries risks of increasing intrathoracic pressure, airway pressure (Paw) and may lead to increased ICP [12,13].

Airway pressure release ventilation (APRV) is a mode of mechanical ventilation that switches between high (P_{High}) and low (P_{Low}) continuous positive airway pressure while allowing spontaneous breathing at both phases. Alveolar recruitment and oxygenation occur during P_{High} whereas ventilation occurs during brief releases to P_{Low} [14,15]. APRV has been used successfully in patients with multisystem trauma [16-19]. However literature about APRV and patients with severe TBI has been scant as concern that APRV with high positive airway pressure could result in elevated ICP still exists.

Dart et al [16] showed that APRV could be used to improve oxygenation among multisystem trauma patients with ARDS or acute lung injuries, without affecting airway pressure (Paw). The authors informally mentioned that several patients with TBI in their studies tolerated APRV well without increasing ICP. Nemer et al reported that pressure-controlled recruitment maneuver with peak pressure up to 50 cm H_2O for 2 minutes did not increase ICP in patients with subarachnoid hemorrhage [20]. A single case report published successful oxygenation of a hypoxemic patient with subarachnoid hemorrhage using APRV without increase of patient's ICP [21]. In addition to improving oxygenation, APRV was also shown to improve cerebral blood flow and spinal blood flow in animals undergoing APRV with spontaneous breathing [22].

Hypothesis

Therefore, we hypothesize that APRV could be safely used in patients with severe TBI as it does not increase their ICP and compromising their Cerebral Perfusion Pressure (CPP), while preventing hypoxemia and hypercapnia in these patients.

Project Primary Goal

This pilot study, to the best of our knowledge, is the first study that specifically investigates the efficacy of APRV among patients with severe TBI. We aim to investigate whether APRV can safely oxygenate patients without compromising their ICP and CPP.

Study Personnel

Principal Investigator: Dr. Debora Stein

Co-investigator: Ms. Claire Rosen (point of contact)

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Study Methodology

Methods:

We will conduct an observational crossover study. We aim to recruit 50 patients with severe TBI requiring intracranial pressure monitoring during their stay at the Neuro Trauma ICU at the R Adams Cowley Shock Trauma Center. Each patient at admission will initially receive a primary mode of mechanical ventilation as determined by the attending trauma intensivists.

12-18 hours after recruitment, continuous monitoring of patients' ICP and hemodynamic status (ICP, HR, RR, SpO_2, $EtCO_2$, MAP, CPP, SpO2, and EtCO2) will commence to collect patients' baseline data for 30 minutes. Patients will then undergo low tidal volume mechanical ventilation (LOTV), serving as a control mode of ventilation, for 2 hours prior to switching back to the primary mode of ventilation for 30 minutes. Next, patients will be placed on APRV for 2 hours. While receiving APRV, patients' ICP and hemodynamic status will be continuously monitored and recorded for comparison and analysis. After 2 hours of APRV, patients will be switched back to their previous mode of ventilation and more data are collected for another 30 minutes. This sequence of ventilation is illustrated in figure 1.

Intracranial pressure will be measured every 15 minutes during the study period. While undergoing low tidal volume ventilation and APRV, patient's volume statuses and cardiac functions will also be assessed using a non-invasive, non-radioactive modality such as Transthoracic Echocardiography.

Figure 1. Sequence of mechanical ventilation and data collection.

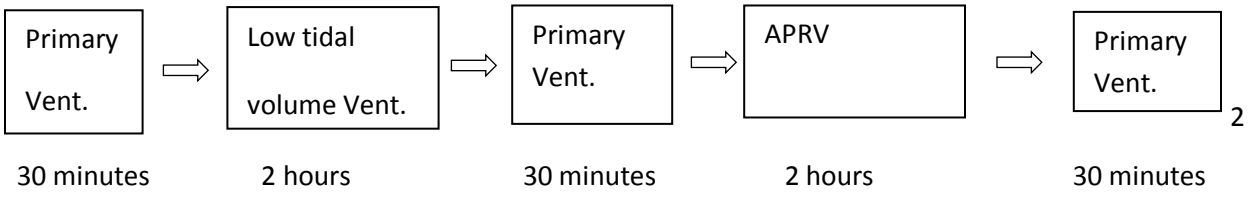


Figure 2. Flow chart of APRV Protocol:

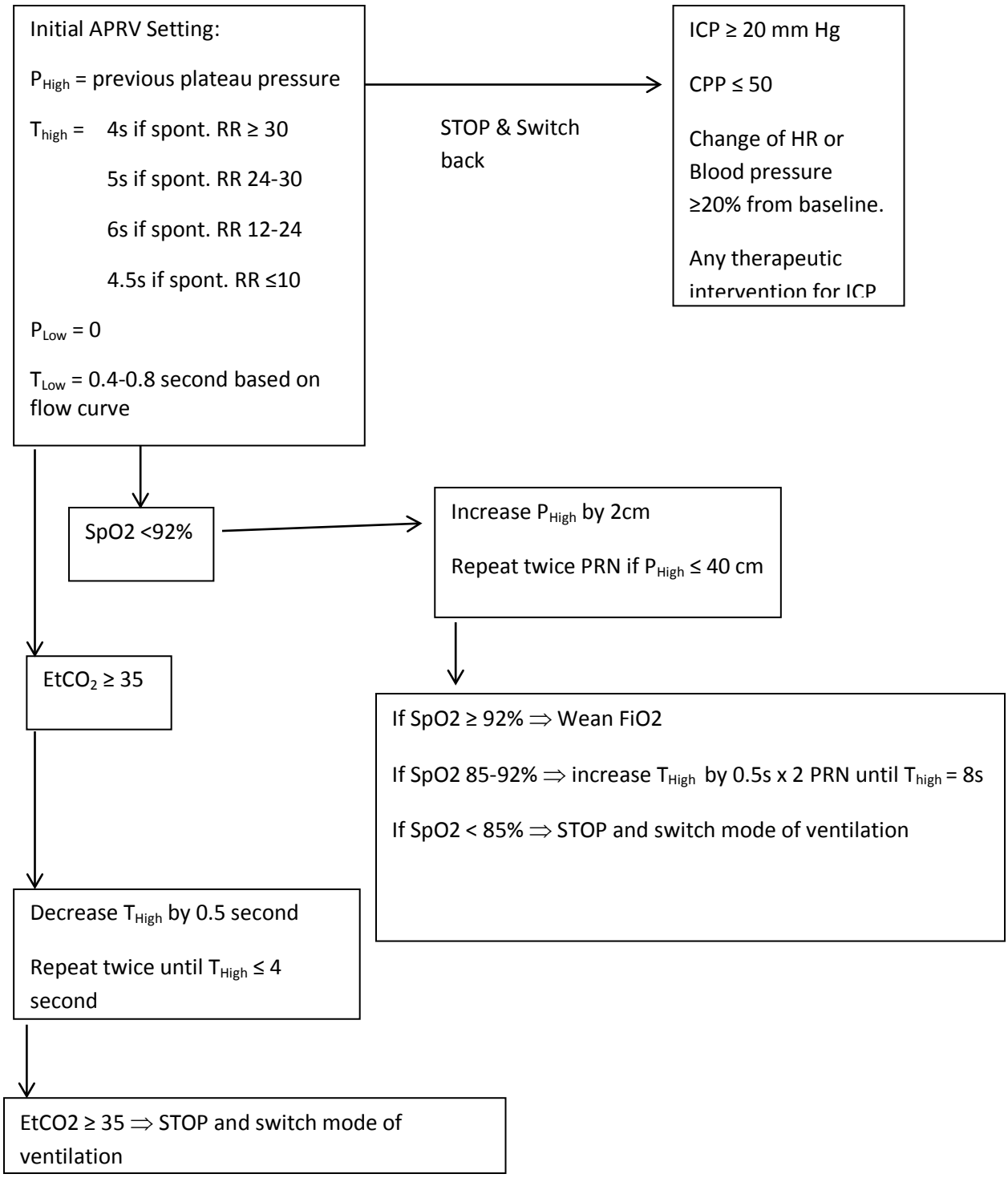
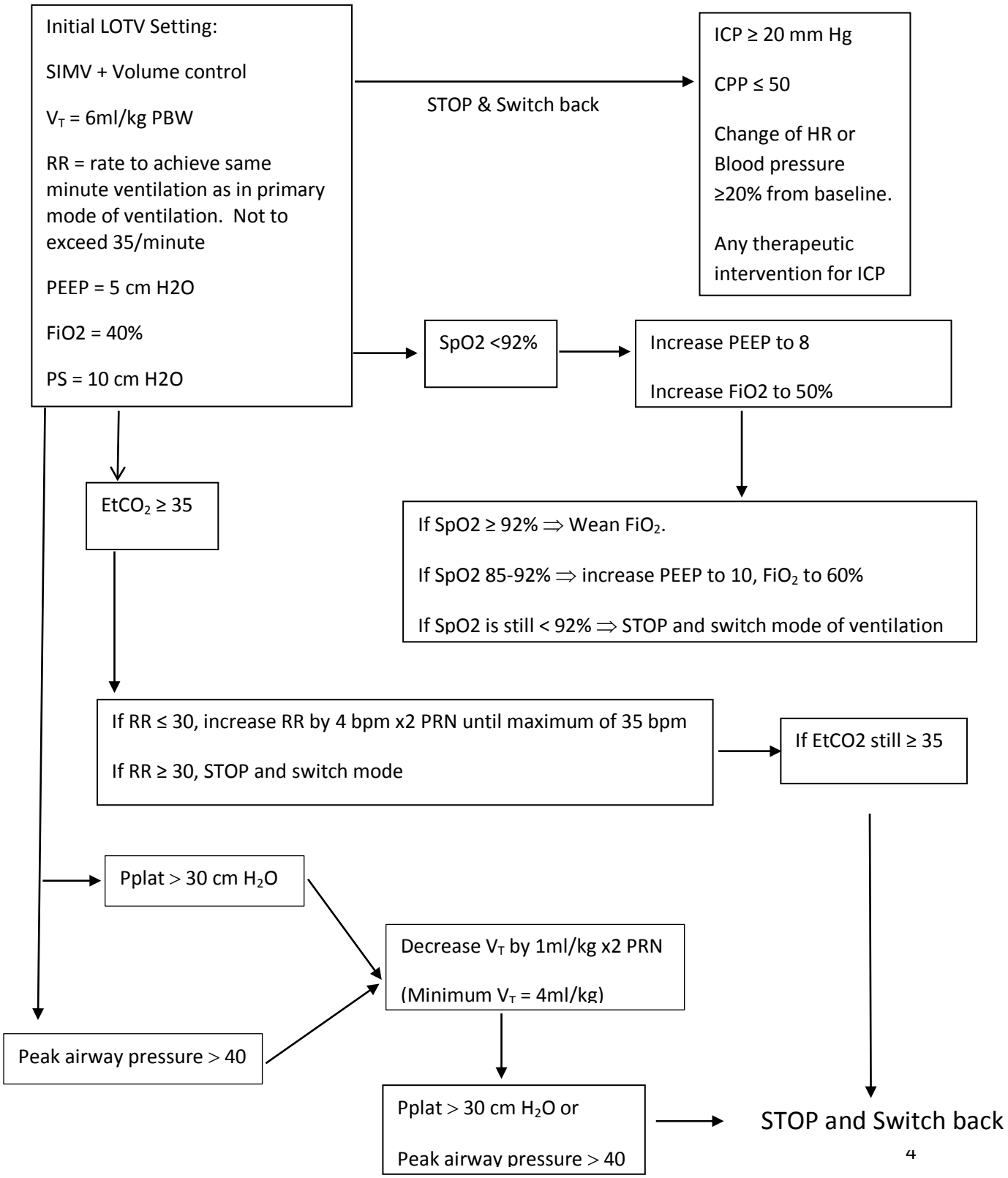


Figure 3. Flow Chart for LOTV protocol



Inclusion Criteria

- Intracranial pressure monitoring
- Mechanically ventilated

Exclusion Criteria

- Age < 18
- Pregnant women
- Prisoners
- Initial mode of ventilation = APRV
- Providers' judgments

Consent:

The patients will not be able to consent for themselves, due the severity of their conditions. We will seek consent from legally authorized representative if available or patients' next-of-kin.

Outcomes

- Primary outcome: ICP
- Secondary outcomes: MAP, CPP, SpO2, $EtCO_2$, any interventions for ICP or for hemodynamic instability.

Analysis Plan

Data Security:

Patient's data will be recorded on a standardized Microsoft Excel spreadsheet. This spreadsheet will first be password-protected, then encrypted by commercial 128-bit encryption software (www.boxcryptor.com). The encrypted spreadsheet then will be stored in a secure, password-protected online storage with extra security designed for corporation (OneDrive for Business by Microsoft Corporation, Redmond WA; https://onedrive.live.com/about/en-nz/business/).

These measures of security allow maximal collaborations between investigators while enhancing safety for patients' protected health information.

Data Analysis:

We aim to report our findings as following:

Table 1. Patient Demographics
Number of patients
Age (years)
Gender
BMI
Mechanism of injury Motor vehicle collision, n (%) Gunshot wound, n (%) Fall, n (%)
GCS score
ISS
Primary mode of mechanical ventilation
PaO2/FiO2 ratio
ICU length of stay (days)
Hospital length of stay (days)
Mortality

Table 2. Outcome Measurements						
Dependent Measure (Mean, Interquartile)	**Baseline**	**LOTV**	**APRV**	**Conventional MV**		***p*-value**
				Pre-APRV	**Post-APRV**	
ICP						
MAP						
CPP						
CVP						
Heart Rate						
Respiratory Rate						
SpO_P						
$EtCO_2$						
Volume status by TTE						
Therapeutic interventions for ICP, blood pressure						

Table 3. Adverse Events	
Patients not tolerating APRV N, (%)	

Causes N, (%)	Elevated ICP
	CPP < 50
	Hypoxemia
	Hypercapnia
	Tachycardia

All continuous variables will be reported as mean with interquartile values (IQR).

Estimated Study Length

There were 1259 patients with isolated blunt TBI (Abbreviated Injury Scale of brain was ≥ 2 while AIS for other body region was ≤ 2) admitted to the R Adams Cowley Shock Trauma Center in 2013. Therefore, we estimate that we will be able to recruit 2-3 patients per week.

Our pilot study is expected to finish recruitment within 6-8 months.

Target Conferences

The American Association for the Surgery of Trauma: Sept. 09-12, 2015

The Society of Critical Care Medicine 44th Congress: January 17-21, 2015

Budget:

None

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