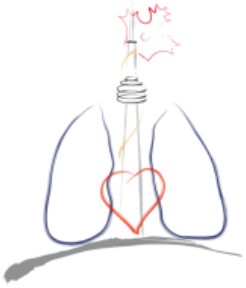
UNIVERSITY OF TORONTO | Interdepartmental Division of Critical Care Medicine



VIRTUAL
ART SLUTSKY RESEARCH DAY

Interdepartmental Division of Critical Care Medicine
University of Toronto

Tuesday June 16, 2020
ZOOM!

Virtual Art Slutsky Day Part I- Honoring our Pediatric and Adult CCM Graduates!

2:00 PM– 3:00 PM

2:00 PM - 2:45PM **Welcome/ Introduction-** David Hall/Dominique Piquette/Briseida Mema

Presentation of Certificates of Training Completion
Presentation of Site Teaching Awards
Presentation of The John Granton and Simon Abrahamson Teaching Awards
Video Montage- Trainee reflections on their training

2:45 PM- 2:55 PM **Presentation: Wellness and Connectedness during COVID-19:**
Drs. Maria Jogova and Melany Gaetani

2:55 PM- 3:00 PM **IDCCM Interprofessional Award/IDCCM Special Achievement Awards**
Dr. Laurent Brochard

3:00 PM- 3:30 PM. **Midafternoon Break**

Virtual Art Slutsky Day Part II

3:30 PM -5:00 PM

3:30-4:00 pm **Welcome –** Dr. Margaret Herridge
Oral Presentations I: Mix of all abstract types (6)
Each Abstract presentation is 5 min/3 slides
All abstracts published in the online Abstract booklet
Session Chairs: Drs. Gail Annich and Mike Detsky

1. Tanya Barretto
“Umbilical cord derived msc-administration modulates the angiogenic response after tbi and rescues vascular dysfunction”

2. Martin Urner
“Time-varying intensity of mechanical ventilation and mortality in patients with acute respiratory failure”

3. Riddhi Kundu
“The utility of nutritional risk index in predicting out comes across hematological malignancy patients with acute respiratory failure”

4. Luca Bastia
“Role of Peep and regional Transpulmonary pressure in Asymmetrical lung injury”

5. Annemijn Jonkman
“An ultra-light, gas-powered, patient-responsive automated Ventilator for use in respiratory failure”

6. Maha Al Mandari
“Efficacy and safety of a bag-valve-mask-based high-acuity, limited operability Ventilator for emergency use”

4:00 – 4:20 pm **Featured Speaker: Dr. Arthur Slutsky**
Topic: Controversies in COVID-19

4:20 – 4:50 pm **Oral Presentations II: Mix of all abstract types (6)**
Each Abstract presentation is 5 min/3 slides
Session Chairs: Dr. Chris Parshuram and Claudia Dos Santos

7. Hiroko Aoyama
"Effect of therapeutic interventions on long term mortality of patients with ards: a systematic review and network meta-analysis"

8. Christopher Yarnell
"Comparing bayesian and frequentist analyses of critical care Studies"

9. Bhushan Katira
"Different effects of positive end-expiratory pressure during pronation and supination. A porcine model of ards"

10. Ayah Nayfeh
"The association between patient ethnicity and family satisfaction with the quality and provision of end-of-life care"

11. Felipe Damiani
"Reverse triggering dyssynchrony during protective lung ventilation affects diaphragm function according to the magnitude of effort"

12. Aditi Jain
"Let 'em breathe! A multidisciplinary approach to improving rates of spontaneous breathing trial (sbt) at Mount Sinai hospital intensive care unit (msh-icu) – a quality improvement project."

4:50 – 4:55 pm **Rest Break**

4:55 – 5:00 pm **Transitions- Tribute to Transitioning Faculty**
SickKids- Dr. Peter Laussen /Dr. Afrothite Kotsakis (Dr. Steven Schwartz**)**

5:00 – 5:05 pm **Presentation of Abstract winners**
Drs. Margaret Herridge and Hannah Wunsch

5:05 pm **Closing Remarks**
Dr. Laurent Brochard

Art Slutsky Day 2019

Thank you!

Have another great year of research and see you (in person!!) next year!

Virtual Art Slutsky Research Day 2020
IDCCM Chair: Dr. Laurent Brochard
IDCCM Director of Research: Dr. Margaret Herridge
IDCCM Associate Director of Research: Dr. Hannah Wunsch

GUEST SPEAKERS

Dr. Arthur Slutsky

Drs. Maria Jogova and Melany Gaetani

ABSTRACT JUDGES

Basic Science Category	Dr. Haibo Zhang Dr. John Marshall Dr. Laurent Brochard
Clinical Research/HSR Category	Dr. Matteo Parotto Dr. Bruno Ferreyro Dr. Margaret Herridge
Physiology Category	Dr. Laurent Brochard Dr. Darlene Reid Dr. Margaret Herridge Mr. Thomas Piraino
Quality Category	Dr. Alberto Goffi Dr. Patricia Murphy Dr. Margaret Herridge
SR/Education Category	Dr. Laveena Munshi Dr. Briseida Mema Dr. Dominique Piquette

And the IDCCM Research Executive
Dr. Laurent Brochard
Dr. Margaret Herridge
Dr. Hannah Wunsch
with Dr. Arthur Slutsky

ORAL PRESENTATION 1

UMBILICAL CORD DERIVED MSC-ADMINISTRATION MODULATES THE ANGIOGENIC RESPONSE AFTER TBI AND RESCUES VASCULAR DYSFUNCTION

TA Barretto[1,2], E Park[1], T Telliyan[1], E Liu[1], D Gallagher[3], C Librach[3], AJ Baker[1,2,4,5]

[1] St. Michael's Hospital, Toronto
[2] Institute of Medical Science, University of Toronto
[3] Create Fertility Centre, Toronto
[4] Critical Care, University of Toronto
[5] Anesthesia, University of Toronto

Introduction: Primary traumatic brain injury (TBI) is followed by ongoing secondary molecular events that adversely affect functional outcome. Blood brain barrier (BBB) permeability and neurovascular unit (NVU) dysfunction are important contributors to poor outcome as blood supply to brain structures is altered, adversely affecting neuronal health. Pericytes of the NVU secrete angiopoetin-1 (ang-1) that binds to the receptor tie-2 on endothelial cells promoting barrier stability. Angiopoetin-2 (ang-2) is an antagonist of tie-2 and promotes vascular sprouting. Loss of pericytes after TBI reduces stability of the BBB. Promoting pericyte-endothelial interaction after TBI may reduce vascular dysfunction and improve outcome by maintaining BBB impermeability. We hypothesize that the perivascular properties of human umbilical cord derived perivascular cells (HUCPVCs) can protect the neurovascular unit translating to white matter protection after TBI.

Methods: Rats were subjected to a moderate fluid percussion injury (FPI), systemically infused with 1.5 x 10^6 cells at 1.5h post-injury and sacrificed at acute time points for analysis.

Results: Vascular leakage as assessed by an Evan's blue assay at 24h and 48h. Values were 6.4 □g and 15.5 □g in FPI rats at 24 and 48h, respectively vs. 1.7 □g in sham rats. HUCPVC treated rats Evan's blue extravasation values were 5.5 □g and 3.3 □g at 24 and 48 hours, respectively. Immunofluorescence area expression of RECA-1 at 24h and 48h, was reduced by 40% in injured animals relative to sham and cell-treated animals. A loss of pericytes, identified using PDGFR□ was observed at 24hours post-injury, 24% (±5, $p<0.05$) reduction relative to sham. HUCPVC treatment was associated with preservation of PDGFRb expression. Increased gene expression of ang-2 was observed after FPI. HUCPVC treatment reduced the increase in ang-2 expression. FPI increased anxiety-related behaviour and impaired long-term memory formation as assessed by the light/dark box test novel object recognition test, respectively. HUCPVCS were associated with a reduction in anxious behaviour.

Conclusion: HUCPVC-administration preserved pericytes and was associated with reduced vascular dysfunction and less anxious behaviour suggesting an important role of pericytes in maintaining NVU function.

ORAL PRESENTATION 2

TIME-VARYING INTENSITY OF MECHANICAL VENTILATION AND MORTALITY IN PATIENTS WITH ACUTE RESPIRATORY FAILURE

M Urner[1,2,6], P Jüni[6,7], B Hansen[6], MS Wettstein[6], ND Ferguson[1,2,3,4,5,6], E Fan[1,2,4,5,6]

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7 *Li Ka Shing Knowledge Institute at St. Michael's Hospital, Toronto, Canada*

Introduction & Objective: Mortality in acute respiratory failure remains high despite the use of lung-protective ventilation. Recent studies have demonstrated an association between baseline ventilation parameters (driving pressure (ΔP) or mechanical power) and outcomes for patients with acute respiratory distress syndrome. Strategies focused on limiting these parameters have been proposed to further improve outcomes. However, it remains unknown if ΔP and mechanical power should be limited over the entire duration of ventilation and in all patients with acute respiratory failure. Therefore, the objective of this study was to estimate the association between exposure to different intensities of mechanical ventilation over time and ICU mortality in patients with acute respiratory failure.

Methods: In this population-based cohort study, we examined if time-varying exposure to either dynamic ΔP or mechanical power was associated with higher mortality in the Intensive Care Unit (ICU). We estimated the strength of associations with Bayesian joint models using data from all adult patients undergoing mechanical ventilation between April 2014 and June 2019 in seven academic ICUs in Toronto.

Results: Of 13408 ventilated patients, 2409 (18%) died in the ICU. Adjusted for baseline characteristics, including age and severity of illness, every daily increment in ΔP (cmH_2O) or mechanical power (Joule/min) was associated with a significant increase in the hazard of death (hazard ratio 1.064; 95% credible interval 1.057 to 1.071 and hazard ratio 1.060; 95% credible interval 1.053 to 1.066, respectively). These associations persisted over the duration of mechanical ventilation.

Conclusion: Cumulative exposure to higher intensities of mechanical ventilation was harmful, even for short durations. Limiting exposure to ΔP or mechanical power should be evaluated in further studies as promising ventilation strategies to reduce mortality in patients with acute respiratory failure.

Supported by: Canadian Institutes of Health Research

ORAL PRESENTATION 3

THE UTILITY OF NUTRITIONAL RISK INDEX IN PREDICTING OUTCOMES ACROSS HEMATOLOGICAL MALIGNANCY PATIENTS WITH ACUTE RESPIRATORY FAILURE

Authors and Affiliations:

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4. Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Canada

Introduction and Objective: Acute respiratory failure (ARF) requiring intensive care unit (ICU) admission is common across patients with hematologic malignancies (HM) and hematopoietic cell transplant (HCT). Nutritional risk index (NRI) is a scoring system derived from albumin and weight, and reflects protein-energy malnutrition and is associated with frailty. NRI has been associated with worse outcomes across a series of populations including acute decompensated heart failure, and chronic kidney disease. Its reliability in the ICU setting in cancer patients has not be evaluated. We wish to evaluate the association between NRI at ICU admission and all-cause ICU mortality in HM/HCT patients with ARF.

Methods: We conducted a retrospective cohort study of HM/HCT patients with ARF requiring mechanical ventilation at Mount Sinai Hospital between 2014-2018. We calculated NRI for all patients using their ICU-admission albumin and weight. NRI = (1.489 × serum albumin, g/L) + {41.7 × weight (kg)/ideal body weight(kg)}). Nutritional risk has been previously categorized as no risk (NRI >100), mild risk (97.5-100), moderate risk (83.5-97.5) and severe risk (<83.5). Our primary outcome was ICU all-cause mortality.

Results: Two-hundred and eighty patients were admitted for ARF requiring mechanical ventilation of which the median age was 62 (IQR 51-68). The most common type of HM was acute leukemia (54%) and 40% of the cohort underwent HCT prior to admission to ICU. Median time between hospital and ICU admission was 15 days (IQR 7-26). Median BMI and albumin at the time of ICU admission was 25 (23-30) and 26 g/L (22-30) respectively. Median ICU admission sequential organ failure assessment (SOFA) score was 11 (9-14), 52% were neutropenic on admission to ICU and 34% were receiving corticosteroids. ICU mortality rate was 51% with a median duration of mechanical ventilation of 4 days (IQR 2-7). Median NRI across the cohort was 87 (79-99) at ICU and 89 (53-93) 7 days prior to ICU (median difference 0.87 (-8.91- 9.59)). Mortality across those at severe risk of malnutrition (NRI <83.5) was 59% (65/111) compared to 46% (76/164) across those

with moderate-no risk (p=0.047). On multivariable analysis, severe NRI on ICU admission (OR 2.34 ,CI 1.04-5.27,p = 0.04) and SOFA score (OR 1.38 ,CI 1.24-1.55, p=<0.001) were significant predictors of ICU mortality

Conclusions: Our exploratory analysis suggests an association between severe NRI risk score and ICU mortality across HM and HCT patients admitted with. respiratory failure. Further research is ongoing to evaluate its role as a prognostic marker adjusting for important confounders.

ORAL PRESENTATION 4

ROLE OF PEEP AND REGIONAL TRANSPULMONARY PRESSURE IN ASYMMETRICAL LUNG INJURY.

Luca Bastia[1 2], Doreen Engelberts[1], Kohei Osada[1], Bhushan H. Katira[1 3 7 11], L. Felipe Damiani[1 4], Takeshi Yoshida[5], Lu Chen[6 7], Niall D. Ferguson[7 8], Marcelo B. P. Amato[9], Martin Post[1 11], Laurent Brochard*[6 7], Brian P. Kavanagh*[1 7 10 11].

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Rationale: Asymmetrical lung injury is a frequent clinical presentation and the effects of PEEP remain unclear. It is widely believed that increasing PEEP to recruit the non-injured lung result in risk of hyperinflation of the less-injured lung. Hence the current suggested setting in this scenario is a low PEEP approach. The validity of esophageal pressure (P_{es}) in this context is also unknown.

Objectives: To compare P_{es} with directly measured pleural pressure (P_{pl}) and investigate how PEEP impacts on ventilation distribution and regional driving transpulmonary pressure (DP_L) during asymmetrical lung injury.

Methods: In 14 mechanically ventilated pigs, lung injury was induced selectively in one of the two lungs. To achieve asymmetrical injury, one lung was blocked while the contralateral one underwent surfactant lavage followed by injurious ventilation. Airway pressure (P_{aw}), dorsal and ventral P_{pl} in the two lungs and P_{es} were measured. Distribution of ventilation was assessed by Electrical Impedance Tomography (EIT). A decremental PEEP trial from PEEP 20 to 0 cmH_2O was perform after a recruitment manoeuvre in normal lungs first and after asymmetrical injury secondly. Pressure-volume curve (P-V curve) of single lung and whole lung were obtained before and after injury.

Results: Asymmetrical lung injury was obtained as shown in Figure 1. Surprisingly ventral P_{pl} and dorsal P_{pl} remained similar in the injured and the non-injured lung across PEEP levels, equalizing inside the respiratory system. P_{es} reflects the dorsal P_{pl} of both sides very similarly compared to ARDS model (Figure 2). V_T distribution between the two lungs was homogenized by increasing PEEP: V_T became equally distributed for PEEP 17 cm H2O and higher (Figure 3). The regional changes in DP_L were similar in the two lungs across PEEP levels and reflect mainly regional V_T redistribution (Figure 4).

Conclusions: In asymmetrical lung injury, P_{pl} equalizes between injured and non-injured lungs, hence esophageal pressure constitute a reliable estimate of dorsal P_{pl}. Equalization of P_{pl} renders regional DP_L similar for both lungs. PEEP homogenizes the distribution of V_T between the injured and the non-injured lung and can be titrate to achieve lowest DP_L.

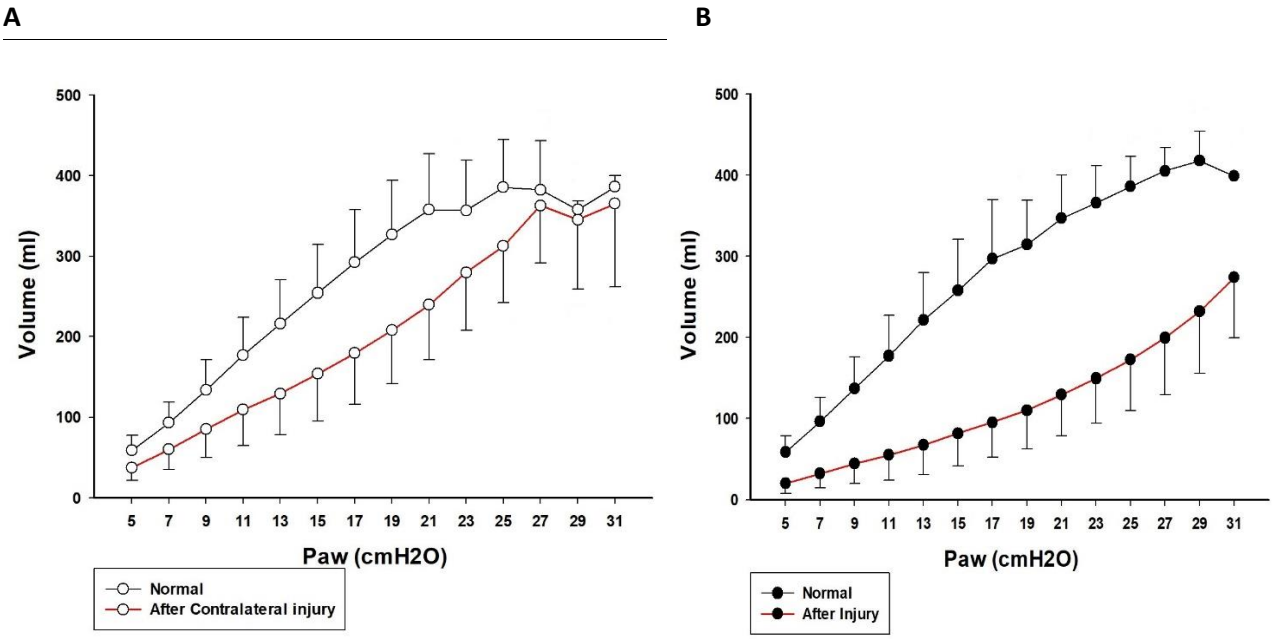

Figure 1: P-V curve before and after asymmetrical lung injury. A) P-V curve before and after contralateral injury. B) P-V curve before and after injury. The two lungs baseline (black lines) is very similar, after injury we can observe a non-injured lung (A) that has a mild injury while the injured lung (B) that has a severe reduction in compliance.

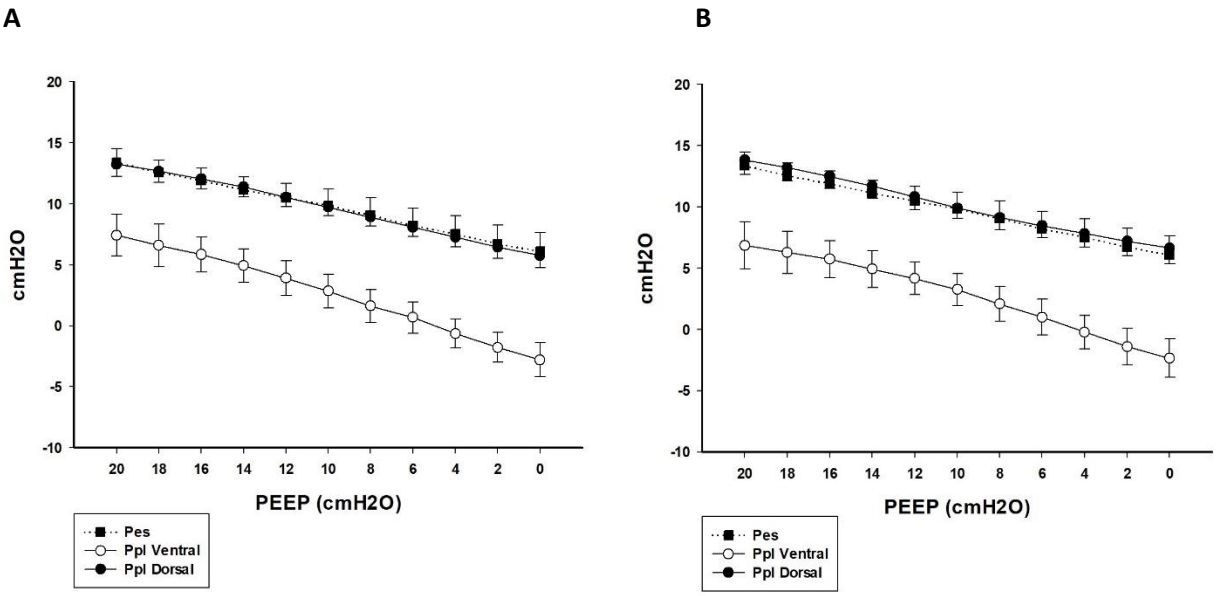

Figure 2. Relationship between P_{pl} recorded ventrally and dorsally in the left and right lung and P_{es} at End-Expiration across PEEP. A) Non-injured Lung. B) Injured Lung. The dorsal P_{pl} is overlapping the P_{es} value across all PEEP levels. Between Injured and Non-Injured Lung minimal change is occurring in both ventral and dorsal Ppl.

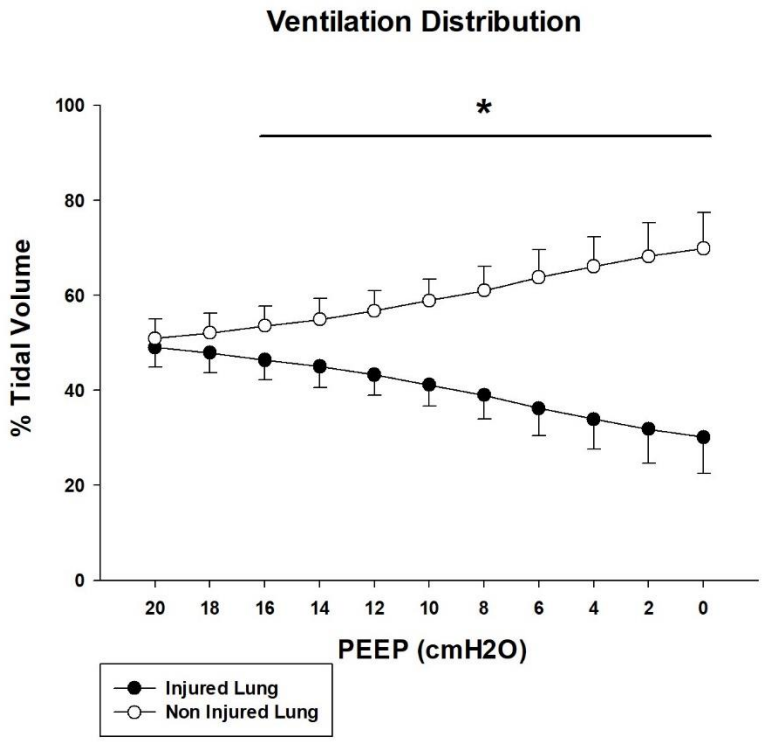

Figure 3. Tidal Volume (V_T) distribution express as a percentage of total V_T in the injured and non-injured lung across PEEP. V_T distribution has been recorded with EIT device. High PEEP homogenizes the system with an even distribution of V_T. * P<0.05.

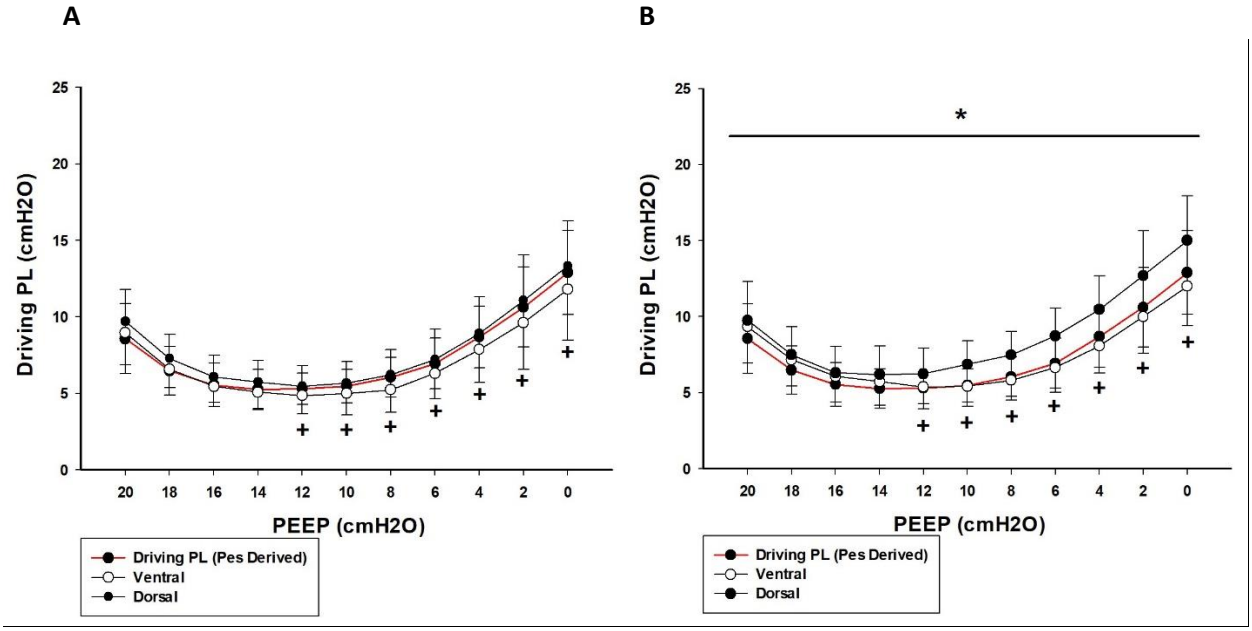

Fig 4. Relationship between Regional Driving Transpulmonary Pressure (Regional DP_L) calculated using Ppl catheters and Driving Transpulmonary Pressure (DP_L) calculated using Pes. A) Non-Injured Lung. B) Injured Lung. DP_L is a good estimation of any Regional DP_L. The regional DP_L absolute values between Injured Lung and Non Injured Lung are similar suggesting similar tidal stress in the two lungs. * P<0.05 Dorsal DP_L compared to DP_L from P_{es}. + P<0.05 Dorsal DP_L compared to Ventral DP_L.

ORAL PRESENTATION 5

AN ULTRA-LIGHT, GAS-POWERED, PATIENT-RESPONSIVE AUTOMATED VENTILATOR FOR USE IN RESPIRATORY FAILURE

AH Jonkman[1,2,3], BH Katira[4,5], A Schreiber[1,2], C Lu[1,2], D Engelberts[4], F Vieira[1,2], A Marquez[6], AS Slutsky[1,2], P Dorian[1,7]*, L Brochard[1,2]*
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Introduction & Objective
In an era of the COVID-19 pandemic, there is a need for innovative, inexpensive, and easily applicable ventilator devices for mass use. The Oxylator is an FDA approved, fist-size, ultra-light, portable ventilation device developed for out-of-hospital emergency ventilation. It delivers automated, pressure-limited, patient-responsive ventilation, therefore requiring minimal operator adjustments. However, it has never been tested in conditions of severe lung injury such as seen in COVID-19 related acute respiratory distress syndrome (ARDS).

Methods
Functioning of the Oxylator with added PEEP valve was extensively tested on a bench (Michigan test lung, ASL 2000, FluxMed), simulating adult patients with various respiratory mechanics, spontaneous breathing, and prolonged unstable conditions where mechanics or breathing effort was changed at every breath. The Oxylator was further tested on a porcine model (n=3) with normal lungs and after inducing lung injury, and compared with pressure control and volume control modes of ventilation.

Results
The Oxylator is very stable and predictable: it delivers the same constant flow (30 L/min) and switches automatically at the inspiratory pressure set (minimum of 20 cmH_2O) above auto-PEEP (Fig.1A). Any change in respiratory mechanics will thus manifest as a change in timing (Fig.1B) and respiratory rate. Simulating a patient with ARDS induces relatively protective ventilation (tidal volumes of 330 mL with compliance of 20 mL/cmH_2O, resulting in a respiratory rate of 30/min). In the porcine model, arterial oxygenation, CO_2 and pH were comparable to classical modes of ventilation.

Conclusion
In case of severe lung injury (low compliance), the Oxylator is a very simple device that can deliver a relatively 'protective' tidal volume at a relatively high respiratory rate. The predictable working mechanism of the Oxylator allows users to estimate tidal volumes from inspiratory time (precisely), or from RR (reasonably well, given variations in I:E ratio). The Oxylator can be an efficient, low-cost practical solution for short-term ventilatory needs in patients with non-compliant lungs, such as seen during the current coronavirus pandemic.

Supported in part by Toronto COVID-19 Action Fund, and CIHR (FDN143285 and OV3-170344). The Oxylator devices were provided free of charge by CPR Medical Devices; the company played no role in the design and conduct of the study.

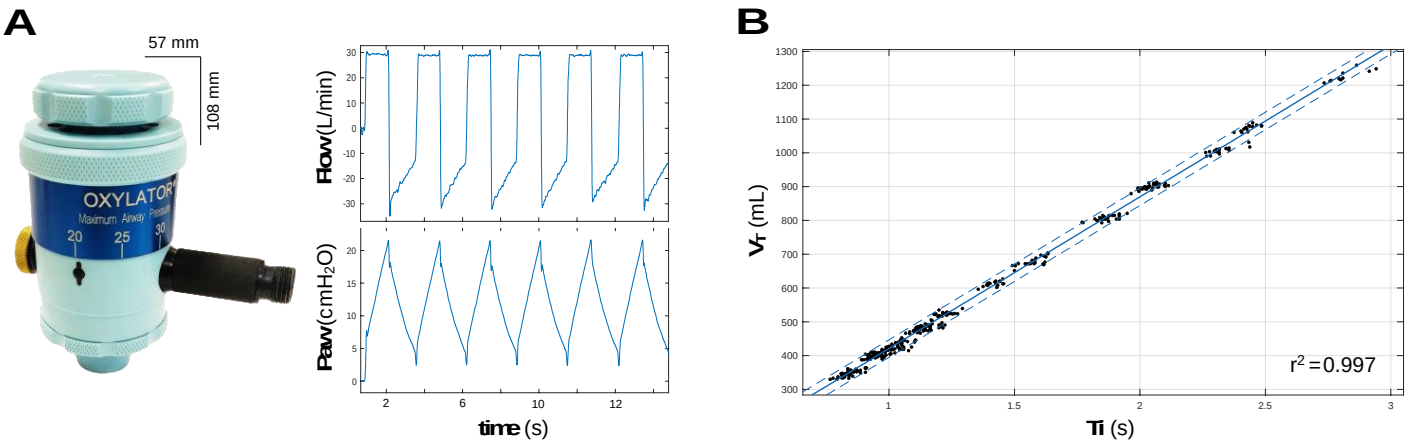

Figure 1. Functioning of the device. **A.** Photo of the Oxylator device (model: EMX, fist-size, 0.25 kg) and resulting flow and airway pressure (Paw) waveforms when no PEEP valve is attached. Inspiration occurs at a constant flow of 30 L/min until Paw reaches the set pressure (in this example 20 cmH2O) above auto-PEEP of the device, which is followed by passive expiration. **B.** Linear relationship between inspiratory time (Ti) and tidal volume (VT) delivered with the device in a bench simulation with varied compliance and resistance. Dashed lines represent the 95% confidence boundaries.

ORAL PRESENTATION 6

EFFICACY AND SAFETY OF A BAG-VALVE-MASK-BASED HIGH-ACUITY, LIMITED-OPERABILITY VENTILATOR FOR EMERGENCY USE

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ABSTRACT

Introduction COVID-19 has demonstrated the need for innovative approaches to the rapid production of ventilators in response to severe shortages. First conceived in the wake of the SARS epidemic in 2003, high-acuity, limited-operability (HALO) ventilators are created with purposeful limitation of functionality to allow for low-cost, high-reliability, limited-footprint, and easy to manufacture and store designs. Numerous designs and development projects are currently underway by various academic and industry groups. The BVM-HALO ventilator is one such device developed through an open-source public-private partnership. This device combines a simple control interface with easily manufacturable and off-the-shelf components to allow for volume-controlled ventilation using any commonly available Bag-Mask-Ventilation (BVM).

Objective To assess device performance and safety in the delivery of standard and lung-safe mechanical ventilation in a mechanical as well as a pig-model and to demonstrate its ability to maintain normal (species adjusted) acid-base parameters while maintaining pressures and tidal volumes within safe limits.

Methods The design passed appropriate bench testing and human factors evaluations as per the Canadian Federal Government's parameters for scaled-down emergency ventilators, except for built-in pressure-based alarm functionality. It achieved a consistently delivered VT up to 1000mls and a maximum PEEP 30cmH2O. The ventilator then underwent animal testing in 1 Yorkshire Pig 80 Kg in weight ventilated for 3 hours, targeting species-adjusted normal physiological parameters of a pH 7.3-7.4, PaO2 > 100 mm Hg, PaCO2 30-55 mmHg, VT 4-10 ml/kg, peak ventilatory plateau pressures <= 25 cm H2O and a PEEP 5-10 (Variable). Vital signs were continuously monitored. Arterial Blood Gas (ABG) analysis was performed every 15 minutes. Ventilator performance data including VT, Pressure and Flow parameters and waveforms were recorded. Ventilation settings were titrated based on acid-base parameters indicated above. The only independent variable was the PEEP, which was set at 0 for the first 30 minutes, increased to 5mm Hg at 30 minutes, then to 10mmHg at 1 hour. PEEP was then maintained at 10mmHg as long as acid-base parameters and safe ventilation pressure, and volume limits were maintained.

Total IV anesthesia and non-depolarizing muscle relaxant were used and titrated to avoid ventilator desynchrony. A standard single-limb ventilator circuit with an adjustable PEEP and Pop-off valve was used.

Results The findings demonstrated the ability to adjust the HALO device to safely calibrate and titrate percent compression to achieve a VT 4-10mls/kg. Delivered VT, RR and PEEP were safely achieved at each titration stage throughout testing. The peak ventilatory plateau pressure was maintained at less than or equal to 25 cmH2O. A baseline

ABG was measured on a standard anesthesia ventilator before initiation. The recorded values pH7.44-7.57, PaO2>400, PaCO2 36-60, HCO3 31-42. The variation in PaCO2 and HCO3 was attributed to the Pig's rapid ability to buffer any changes in PaCO2 and HCO3. Vital signs were monitored throughout with no hemodynamic changes recorded from baseline. The limitation to the device includes the lack of alternative ventilation modes, the lack of traditional, audible ventilator alarms. However, pressure-sensing and pressure-based alarms will be included in the next iteration of the device.

Conclusions The HALO ventilator design can be used to deliver short periods of safe mechanical ventilation. The model could be used to rapidly increase the ventilator capacities of healthcare facilities in emergency settings.

Device design, prototyping and manufacturing was done in collaboration with Promation inc. and was supported by unrestricted in-kind contributions by Promation.

ORAL PRESENTATION 7

EFFECT OF THERAPEUTIC INTERVENTIONS ON LONG TERM MORTALITY OF PATIENTS WITH ARDS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

H Aoyama[1,2], K Uchida[2], K Aoyama[3,4], A Yang[4], P Pechlivanoglou[4,5], M Englesakis[6], Y Yamada[2], E Fan[1,5]

1: *Interdepartmental Division of Critical Care Medicine, University of Toronto*
2: *Department of Anesthesiology, Graduate School of Medicine, University of Tokyo*
3: *Department of Anesthesia and Pain Medicine, The Hospital for Sick Children*
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5: *Institute for Health Policy, Management and Evaluation, University of Toronto*
6: *Library & Information Services, University Health Network*

Introduction:
Most clinical trials of interventions in patients with acute respiratory distress syndrome (ARDS) have focused on improvements in short-term mortality through a reduction in ventilator-induced lung injury (VILI). However, little is known about the impact of these interventions on longer term survival.

Objective:
We performed a network meta-analysis to explore the comparative efficacy of commonly used interventions on 180-day mortality by synthesizing the available evidence among patients with ARDS.

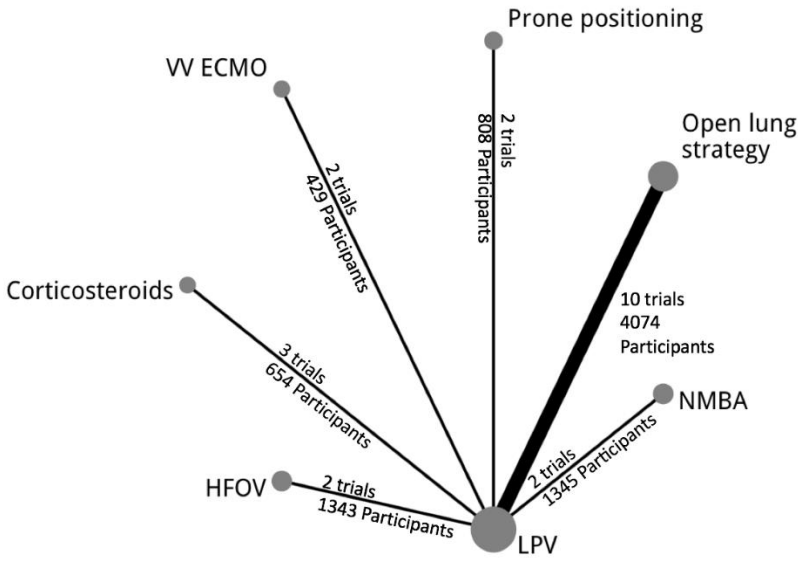
Methods:
Data sources: An electronic search of MEDLINE, MEDLINE In-Process/ePubs Ahead of Print, Embase, Cochrane Controlled Clinical Trial Register (Central), PubMed, and CINAHL was conducted, from database inception to March 6th, 2019.
Study selection: Randomized clinical trials comparing prespecified interventions for adult ARDS patients with lung protective ventilation (LPV). No language restrictions were applied.
Data extraction and synthesis: Data were independently extracted by 2 reviewers and synthesized with Bayesian random-effects network meta-analyses of fractional polynomials model.
Main outcomes and measures: The primary outcome was 180-day mortality.

Results:
Mortality data were extracted for 8653 participants from identified 21 eligible studies that assessed 6 different interventions (venovenous extracorporeal membrane oxygenation [VV ECMO], high-frequency oscillatory ventilation, open lung strategies, prone positioning, neuromuscular blockade, and corticosteroids) and lung protective ventilation (LPV). Survival probability of LPV at 180-days was 0.59 (95% credible interval [CrI] 0.42 – 0.72). Interventions with higher or equal survival probability than LPV at 180-days were prone (0.63, 95% CrI 0.49 – 0.73), corticosteroids (0.62, 95% CrI 0.48 – 0.72), and VV ECMO (0.59, 0.42 – 0.72). Pooled hazard ratios (HRs) for 180-day mortality for individual intervention compared with LPV derived from the primary network meta-analysis showed an advantage for prone positioning and corticosteroids (HR 0.51, 95% CrI 0.24 – 1.10 and HR 0.54, 95% CrI 0.23 – 1.41); however, these were not statistically significant. Indirect comparisons among those 6 interventions showed no statistical significance. In post-hoc sensitivity analyses, there was no difference in results by limiting to trials that included only patients with PaO_2/FiO_2 ratio less than 150 mmHg and no evidence of effect modification based on PaO_2/FiO_2 ratio using network meta-regression.

Conclusion:

This network meta-analysis found that none of 6 prespecified interventions were associated with improved 180-day mortality in patients with ARDS. Strategies to improve longer term outcomes in patients with ARDS will need to employ interventions that are not focused on VILI.

Figure 1. Network geometry of randomized clinical trials with 180-day mortality as an outcome



ORAL PRESENTATION 8

COMPARING BAYESIAN AND FREQUENTIST ANALYSES OF CRITICAL CARE STUDIES

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Introduction and Objective:

Bayesian analysis sometimes leads to re-interpretation of trials analyzed with conventional frequentist methods. The extent to which systematic application of Bayesian analysis would alter interpretation of trials in critical care medicine is unknown.

Methods:

Bayesian methods were used to reanalyze all critical care randomized trials with mortality as primary outcome published in five journals (JAMA, NEJM, the Lancet, the Lancet Respiratory Medicine, AJRCCM) between 2008 and 2018. A minimum clinically important difference (MCID) was estimated for each trial. Priors encompassed skeptical, uninformative, and enthusiastic perspectives. Bayesian analysis suggested "potential benefit" if the probability of exceeding the MCID was greater than 50% and "improbable benefit" otherwise.

Results:

Among 78 interventions deemed negative or indeterminate by frequentist criteria, Bayesian analysis suggested potential benefit in 7 (9%, skeptical prior) to 20 (26%, enthusiastic prior). Fewer interventions suggested potential benefit if the threshold required higher posterior probability of exceeding the MCID and more interventions suggested potential benefit if the threshold used any benefit (ARR > 0) instead of the MCID. All 4 interventions deemed positive by frequentist criteria had 90% probability of any benefit (ARR > 0) by Bayesian analysis but only 2 (50%) showed potential benefit with respect to the MCID. In 13 interventions (17%) the Bayesian interpretation changed from improbable to potential benefit when changing the prior from skeptical to enthusiastic.

Conclusion and Relevance:

Frequentist and Bayesian analyses of randomized clinical trials in critical care generally yielded the same interpretation. However, Bayesian analysis identified interventions where benefit was probable despite the absence of statistical significance, where interpretation depended substantially on choice of prior distribution, and where benefit was improbable despite statistical significance. Incorporating Bayesian analyses into analysis plans can incrementally inform scientific and clinical decisions.

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ORAL PRESENTATION 9

DIFFERENT EFFECTS OF POSITIVE END-EXPIRATORY PRESSURE DURING PRONATION AND SUPINATION. A PORCINE MODEL OF ARDS

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Introduction: Prone position improves oxygenation and mortality in ARDS. Several mechanisms of benefit from pronation have been postulated including the improvement of lung homogeneity. We hypothesized that pronation improves homogeneity of ventilation and stress by reducing the vertical gradient of pleural pressure.

Methods: Series I - 12 pigs (weight 36.1 ± 1.9 Kg), anesthetized, mechanical ventilated and instrumented to received ventral and dorsal pleural catheters, PA catheter, an esophageal balloon and an EIT belt. Lung injury was established via a two-hit model (saline lavages followed by high-stress ventilation). Animal was ventilated on VC (Vt 6ml.kg^{-1}, RR 30/m, FiO2 100%). After a recruitment maneuver (RM) each animal underwent a decremental PEEP protocol (PEEP 20, 15, 10, 5 cmH_2O). Plateau pressure, total PEEP, Pes, dependent and nondependent pleural pressure, EIT, Cardiac output and oxygenation were recorded at each PEEP level. Series II – 9 pigs underwent a crossover study of gradual decrements in PEEP and measurements were taken at each level from 20 cmH_2O to 3 cmH_2O. Vertical gradient of Ppl (Dependent Ppl – nondependent Ppl), distribution of ventilation, regional and total compliance were calculated. Series III – Two pigs underwent CT scan in supine and prone position at PEEP levels similar to Series I. Tidal recruitment, distribution of tidal recruitment and end-inspiratory hyperinflation were calculated; and compared between the two positions. Series IV – General observations were confirmed in human cadavers

Results: Pronation improved oxygenation at low PEEP (167 ± 57 vs 70 ± 5) and did not significantly reduce cardiac output. Pronation increases the regional Ppl (at PEEP 5 cmH_2O, Supine vs Prone ND Ppl 1.5 ± 1.4 vs 3.9 ± 2.2, Supine vs Prone D Ppl 7.9 ± 1.1 vs 8.1 ± 2.2) and maintains the Ppl gradient uniformly across all levels of PEEP, whereas it increases at low levels PEEP during supination (Fig 1). Lower PEEP distributes V_T toward non-dependent regions; in supination (80%) more than pronation (60%) (Fig.2). During pronation, the regional delta P_L (stress) and tidal recruitment is uniformly distributed at all levels of PEEP whereas the dependent stress and tidal recruitment (Fig 3) increases in supination at low levels of PEEP. Level of PEEP required to achieve the best regional lung compliance (C_L) in dependent and non-dependent lung was congruent during pronation (13 and 12 cmH_2O respectively) compared to supination (15 and 9 cmH_2O respectively) (Fig.4). The cephalon-caudal dimension was higher during pronation compared to supination and antero-posterior was higher in supination. Regional uniformization was observed in a single human cadaver.

Conclusions: The vertical P_{pl} gradient, regional ventilation and regional stress are uniform during pronation. This reflects more homogenous lung inflation and ventilation. Potentially this is explained by change in lung shape and dimension during pronation. Setting PEEP is much safer during pronation compared to supination. We believe these changes potentially contribute to improved survival during pronation.

Supported by CIHR (BPK), Restracomp (BHK)

Figure 1 - Vertical Pleural Pressure Gradient at End-Expiration during Supine and Prone Positions

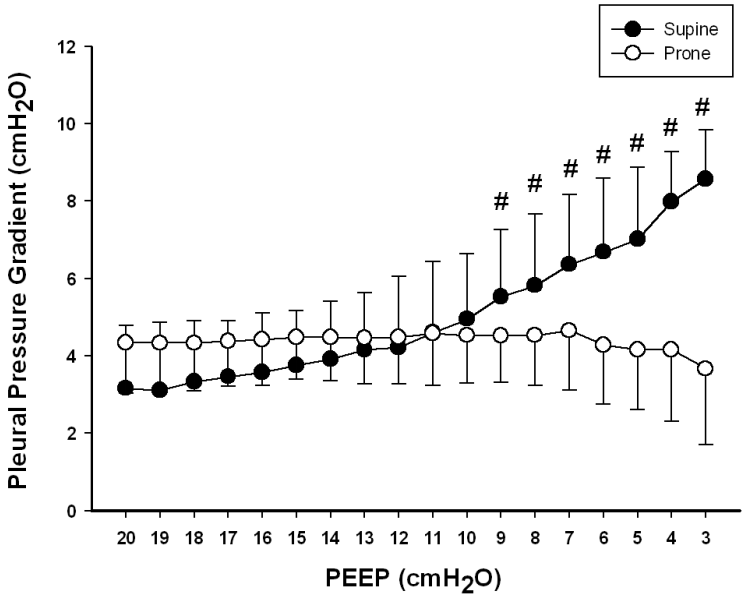


Figure 2 - Regional Distribution of Ventilation during Supination and Pronation.

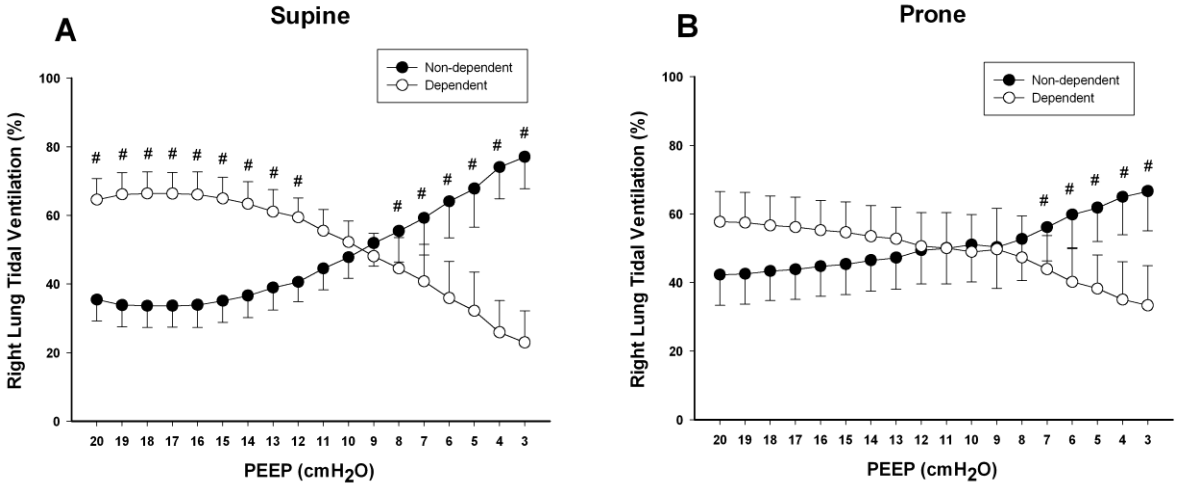


Figure 3 - Total and Regional Tidal Recruitment Distribution on CT

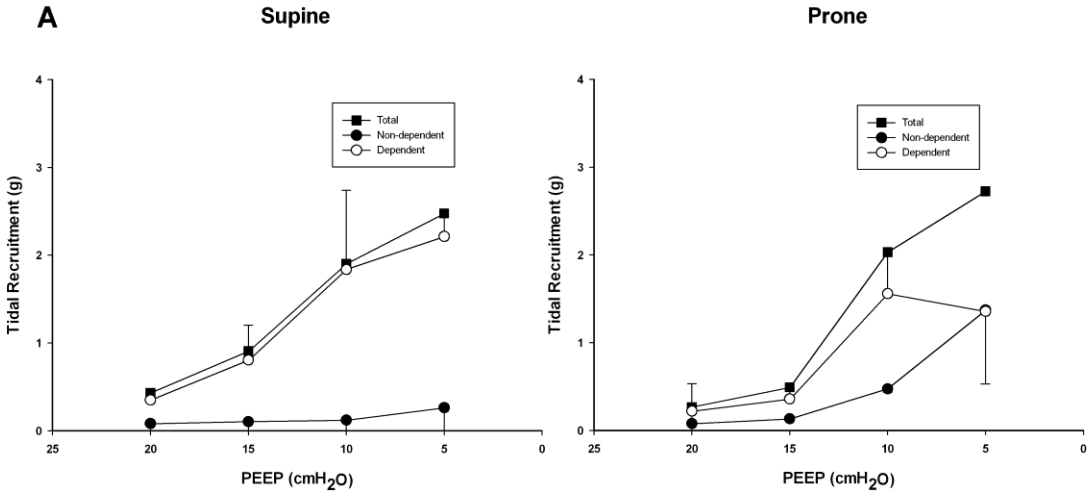
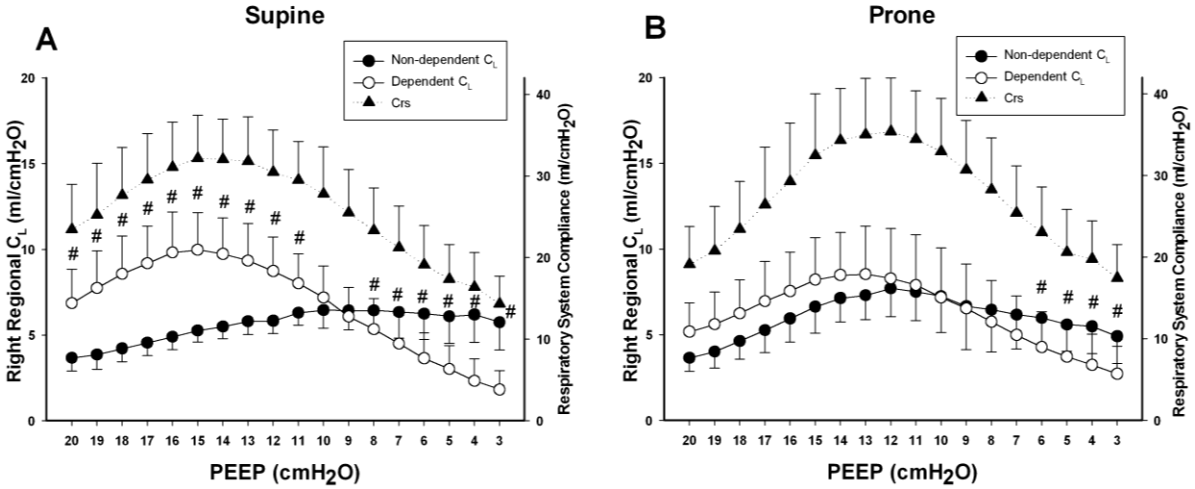


Figure 4 - Regional Lung and Total Respiratory System Compliance during Supine and Prone Postions;



ORAL PRESENTATION 10

THE ASSOCIATION BETWEEN PATIENT ETHNICITY AND FAMILY SATISFACTION WITH THE QUALITY AND PROVISION OF END-OF-LIFE CARE

Authors: A Nayfeh[1] (presenter), B Hales[2], C Dale[2,3], L Gotlib Conn[1,2], T Das Gupta[2], A Chakraborty[2], R Taggar[2], R Fowler[1,2,4,5]

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1. Introduction & Objectives:

Quality care at the end of life (EOL) is an espoused right of every Canadian. Among decedents in Ontario, recently immigrated and ethnic minority patients are more likely to die in intensive care units (ICU) and receive more aggressive life-prolonging treatment in the last six months of life in comparison to other Canadians. It is not clear whether differences are attributable to diverse cultural and ethnic preferences for EOL care, or whether they are a result of specific disparities in the quality of care that occur along the EOL trajectory.

This observational survey-based analysis seeks to evaluate the quality and provision of EOL care for patients of diverse ethnocultural backgrounds, with specific objectives to:

1) Identify the association between patient ethnicity and family satisfaction with the quality of EOL care;
2) Identify the association between family satisfaction with the quality of EOL care and other patient demographic and care delivery characteristics (patient religion, level of religiosity, primary language, language/communication barriers, perceived respect for patient preferences and location of death);
3) Identify high-priority areas for improving the quality of EOL care for patients from diverse ethnocultural backgrounds.

2. Methods:

The End of Life survey (a validated 52-item tool) is routinely administered to next-of-kin of all decedents at Sunnybrook Hospital to measure satisfaction with inpatient EOL care. The primary outcome is the global measure of satisfaction, which asks: *On a scale of 0 to 10 (where 0 means the worst care possible and 10 means the best care possible), what number would you give the overall care that your family member received in the time leading up to their death?* The primary predictor is patient ethnicity (as reported by next-of-kin/family members). We performed a stratified analysis using univariate Poisson regression to identify specific patient ethnic groups with important gaps/differences in family satisfaction with the quality of EOL care. The Mann-Whitney U test was used to examine associations between levels of satisfaction and specific patient characteristics.

Secondary predictors of family satisfaction included the following patient demographic and care delivery characteristics: 1) patient religion, 2) level of religiosity, 3) primary language, 4) language/communication barriers, and 5) care perceived to be consistent with patient wishes and 6) location of death. Univariate Poisson regression was applied to each predictor

variable to determine preliminary associations (at $p<0.2$) for inclusion in the final adjusted model. Descriptive statistics included counts and proportions for categorical variables and means (standard deviations) and medians (interquartile ranges) for continuous variables with a significance threshold level of $\alpha < 0.05$. Statistical analysis was conducted using SPSS software.

3. Results:

Among 1384 surveys (March 2012 to May 2019), 21.4% (n=295) of patients identified as non-Caucasian. Overall, 76.2% of Caucasian and 71.9% of non-Caucasian respondents were "very/completely satisfied" with the overall quality of EOL care. There were no significant differences in ratings of satisfaction between Caucasian vs. non-Caucasians (p=0.133). Family members of patients who died in ICU more likely to be *"very/completely satisfied"* in comparison to patients who died in other units (p=0.007). There were no differences in rates of dying in ICU among patient ethnic groups.

Examining specific ethnicities, family members of Muslim patients and those of Middle Eastern descent were less likely to be satisfied in comparison to other patients (OR 0.81 95%CI 0.60-1.09, p=0.158; OR 0.73 95%CI 0.52-1.03, p=0.073, respectively). The relationship between patient religion (Muslim vs. non-Muslim) and family satisfaction was not influenced by level of patient religiosity (OR 0.76 CI 95% 0.49-1.14, p=0.185).

After adjusting for patient demographic and care delivery characteristics in the multivariable Poisson regression, we found that family members of patients of Middle Eastern descent had lower satisfaction with the quality of EOL care (B=-0.678, SE=0.327, p=0.038). Ratings of satisfaction decreased by 49.2% for family members of Middle Eastern patients in comparison to all other patient ethnic groups. Care consistent with patient wishes (B=1.07, SE=0.167, p<0.001) and language/communication barriers (B=-0.502, SE=0.207, p=0.015) were also significant predictors of family satisfaction in the adjusted model. Family ratings of satisfaction increased by 2.9x for patients whose care was consistent with their wishes, and decreased by 39.5% for those who experienced language/communication barriers. The association of patient religion (Muslim vs. not Muslim) with family satisfaction was B=0.014, SE=0.164, p=0.934. This relationship was not moderated by level of patient religiosity (B=0.021, SE=0.189, p=0.910). Location of death (ICU vs. other) was also a non-significant predictor of family satisfaction (B=0.055, SE=0.033, p=0.087).

4. Conclusions:

Our findings suggest that family members of patients who died in ICU were most commonly very/completely satisfied with the quality and provision of EOL, regardless of patient ethnicity or religious background. Dying in ICU setting with more intensive care may therefore not be an appropriate indicator for measuring quality of EOL care for patients and families. Family members of patients from certain ethnic and cultural backgrounds may experience less satisfaction with quality of care at the EOL. This might be explained, in part, by care delivery characteristics such as respect for patient preferences and language/communication barriers. More research is needed to validate and understand the quality and experience of EOL care that is provided to patients and families from diverse ethnocultural backgrounds.

Support:

This study is supported by: the Department of Critical Care Medicine at Sunnybrook Health Sciences Centre; the Sunnybrook AFP Association through the Innovation Fund of the Alternative Funding Plan from the Academic Health Sciences Centres of Ontario, and the Division of Palliative Medicine, Department of Medicine, University of Toronto; the Dalla Lana School of Public Health, University of Toronto; and the Global Institute of Psychosocial, Palliative and End-of-Life Care (GIPPEC).

ORAL PRESENTATION 11

REVERSE TRIGGERING DYSSYNCHRONY DURING PROTECTIVE LUNG VENTILATION AFFECTS DIAPHRAGM FUNCTION ACCORDING TO THE MAGNITUDE OF EFFORT

L. Felipe Damiani, Doreen Engelberts, Luca Bastia, Kohei Osada, Bhushan Katira, Gail Otulakowski, Ewan Goligher, W. Darlene Reid, Alejandro Bruhn, Laurent Brochard, Brian Kavanagh.

Introduction: In clinical practice, current protective ventilation strategy for patients with acute lung injury often includes less tidal volume, higher frequencies and no deep sedation. Whether this approach promotes the occurrence of reverse triggering dyssynchrony (RT) [1] and if its presence affects diaphragm function according to the level of breathing effort is unknown.

Objectives: To establish an animal model with lung injury using lung protective ventilation to assess whether RT dyssynchrony occurred and what was the impact of RT on the function of the diaphragm

Methods: Twenty-six pigs (35±5kg) were anesthetized, mechanically ventilated, and monitored. Lung injury was induced by surfactant depletion and high-stress ventilation to reach PaO_2 <150 mmHg and 10% decrease in respiratory system compliance. Level of sedation was set based on BIS index targeting 40-60 corresponding with general anaesthesia. Pigs were allocated to receive either non- protective ventilation (n=8; VCV; VT: 10ml/kg; RR: 35 bpm), or protective ventilation (n=18; VCV; VT: ~ 7 ml/kg comparable to LUNG SAFE [2]; RR ~ 42 bpm), for 3 hours. We compared the incidence and entrainment pattern of RT between pro-tective and non protective ventilation. Based on PTP, animals with RT were divided in low, middle, and high level of breathing effort to assess the impact of RT on diaphragm function by measuring twitch transdiaphragmatic pressure normalized to baseline value (PdiTw ratio).

Results: The protective group had significantly lower VT (average 7.2 vs 10 ml/kg; *p*=0.001), higher RR (43 vs 33 bpm; *p*=0.001), and slightly higher PEEP level (9.3 vs 8.3 cmH2O; *p*=0.004) as compared with non-protective group. The level of sedation was similar (BIS: 53 vs 55; *p*=0.131). RT was observed in all animals with protective ventilation (18/18) under different entrainment patterns (Fig 1). Within protective ventilation group, 1:1 RT entrainment was the most frequent pattern, occurring in 83% of animals. Pattern 1:2 was observed in 10 animals (56%) whereas other infrequent patterns such as 1:3, 1:4, 3:1 and 2:1 were also observed in 4 out of 18 animals. Animals from RT high effort group presented a larger decrease in force (34%) as compared with animals with RT middle and low effort which presented a decrease in force of 7% (p-value=0.034), and increase in force of 10% (p-value<0.001), respectively.

Conclusion: Protective mechanical ventilation strategy used in clinical practice (low tidal volume, high respiratory rate) results in reverse triggering dyssynchrony with variable entrainment patterns. RT dyssynchrony with high breathing effort affects diaphragm function whereas RT with low breathing effort seems to protect the diaphragm.

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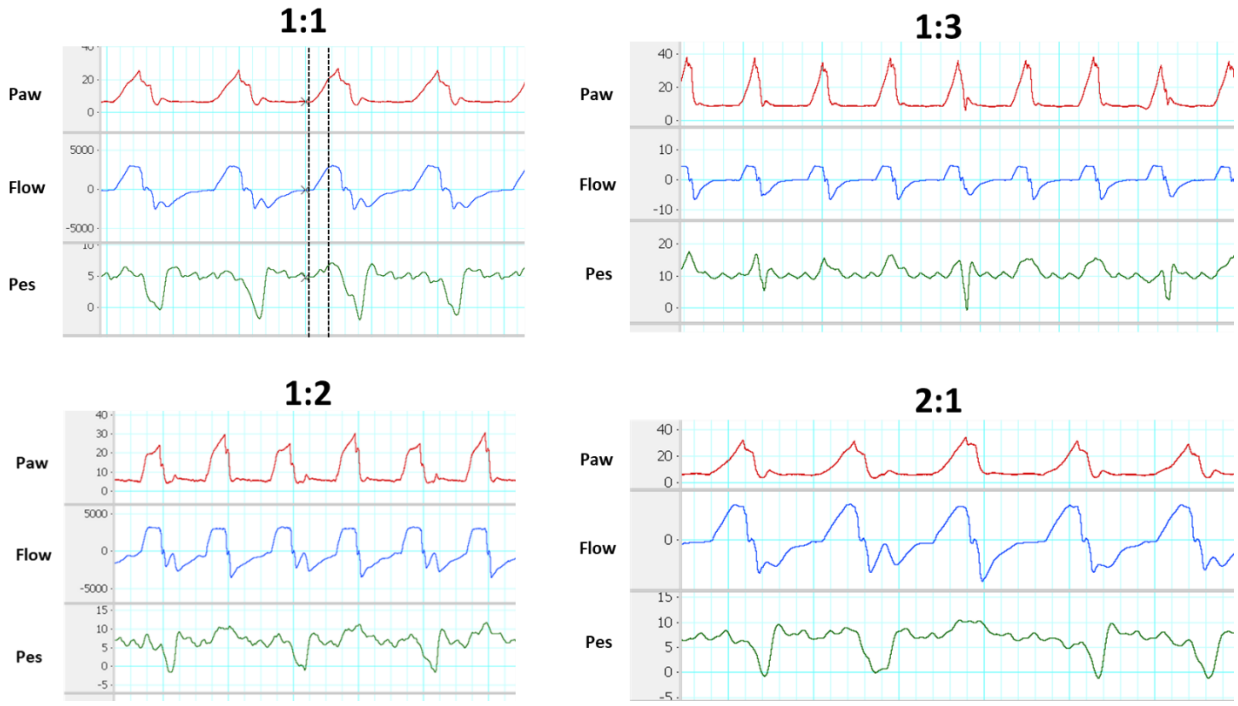
Grant acknowledgment: FD acknowledges partial support from CONICYT-PFCHA/Doctorado Nacional/2017-folio 21171551

Fig 1.



ORAL PRESENTATION 12

LET 'EM BREATHE!

A MULTIDISCIPLINARY APPROACH TO IMPROVING RATES OF SPONTANEOUS BREATHING TRIAL (SBT) AT MOUNT SINAI HOSPITAL INTENSIVE CARE UNIT (MSH-ICU) – A QUALITY IMPROVEMENT PROJECT.

Authors

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Introduction & Objective

Spontaneous Breathing Trial (SBT) assesses patient's ability to breathe while receiving minimal or no ventilator support. Rates of spontaneous breathing trials are an important quality indicator as it helps separate patients that can be liberated from the ventilator immediately versus those that require weaning. Delays in liberation from mechanical ventilation are linked to increased rates of ventilator associated pneumonia, increased ICU and hospital length of stay and higher morbidity and mortality rates. Use of SBT is associated with a 26% reduction in total duration of mechanical ventilation and 70% reduction in weaning time. Low SBT rates are associated with poor outcomes.

A city-wide SBT initiative is in place to measure the rate at which eligible ICU patients undergo SBT. Mount Sinai Hospital (Toronto) ICU places approximately 51% of all eligible patients through an SBT. Our ***primary aim*** was to improve the number of eligible patients put on SBT (to assess readiness for liberation from mechanical ventilation) in our 16 bedded medical-surgical ICU at Mount Sinai Hospital. We set out to improve the SBT rates from the current average of 51% to 70% (arbitrarily chosen value) in a period from September 2018 to June 2019. Our ***secondary aim*** was to understand the reasons behind low SBT rates and thence adopt a multidisciplinary approach for mitigating potential barriers to it.

Methods

This *Quality improvement project* was carried out in a 16 bedded tertiary care medical, surgical ICU at Mount Sinai Hospital, Toronto between September 2018 - June 2019.

Outcome Measures of the project were: Increasing SBT rates on eligible patients as recorded in the iCore data bank, understanding reasons for low SBT and correcting them, engagement of multi-disciplinary team in the ICU SBT process. 7 *stakeholder groups* were identified using email communication - Patients and family, Respiratory therapists (RT), Registered Nurses (RN), Physicians (MD), Data Collectors, ICU Team leaders and Hospital Leadership. *Process Measure:* ICU huddles and bedside discussions helped determine areas of need. Protocol for SBT was studied. Chart reviews and meetings with the iCore team elucidated data collection processes. Shadowing various stakeholders helped understand steps in the process of SBT. Baseline data used was iCore data. *Balancing measures:* We did not identify any unintended consequences as a result of increasing the SBT rate within our ICU.

Fishbone templates (figure 1) were strategically placed in areas of the ICU where stakeholders were encouraged to write their thoughts on why SBTs were not being done.

Figure 1: *Ishikawa Diagram showing barriers to SBT performance*

SBT *process* was *mapped* to shed light on potential barriers (figure 2).

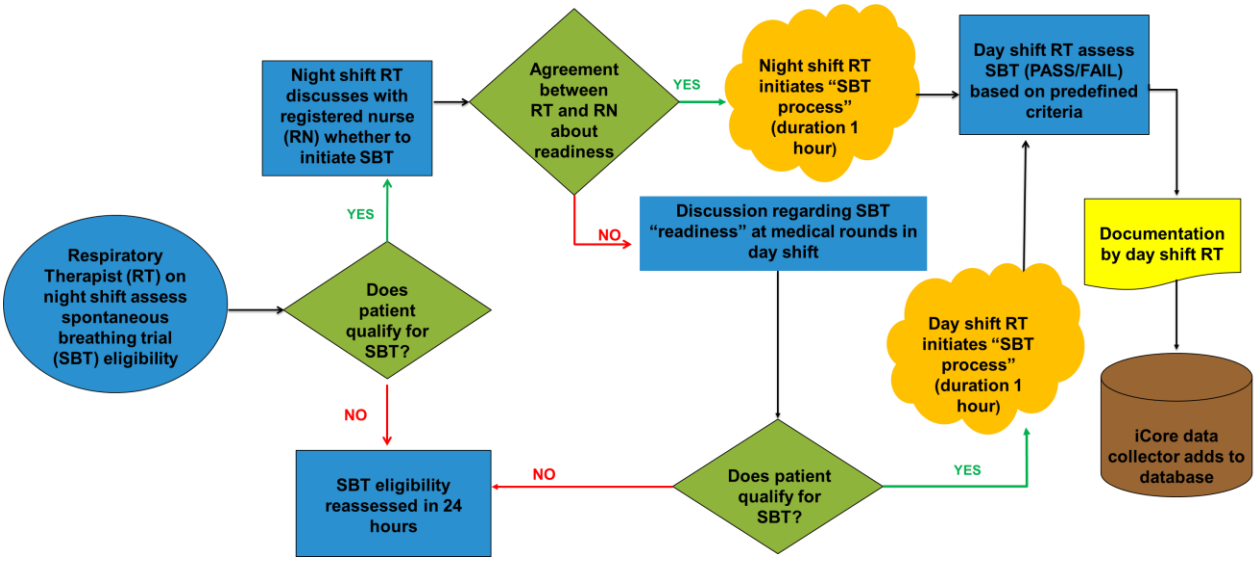

Figure 2: Process Map

We carried out the following *PDSA cycles*:

Cycle	Plan	Do	Study	Act	Time Required
1	Lack of education surrounding SBT literature reduces the rates of SBT being performed	Interviewed RN/RT with patient case examples during huddles	General consensus that SBT is not an interdisciplinary responsibility and RT's were primarily responsible. RN's felt disengaged from this process	Developed short presentations centered around SBT literature and delivered to an interdisciplinary group (RN, RT, MD). We created a short information sheet to be added to all patient care binders at the bedside readily available to all stakeholders	1 month
2	SBT timing with patient care routines (end of night shift) would reduce the initiation and completion of SBT's	Interviewed stakeholders (RT, RN) about SBT timing (changing bath/back care timing…) Proposed idea at physician meeting and discussed feasibility and indications to change SBT timing and duration.	RN felt that patients were too tired to be placed on an SBT following bath and back care. This resulted in a delayed SBT start time and the completion of the SBT was assessed by a different RT, decreasing the likelihood of the SBT being assessed fairly Consensus amongst physicians regarding above changes.	SBT timing moved earlier such that the RT that starts the SBT must be able to observe to completion. We also discussed with RN team about moving bath care to evenings rather than middle of the night	10 days
3	SBT duration of 60 minutes affected RT workload and workflow, reducing SBT initiation	a. Reviewed hospital SBT policy b. reviewed literature on best practice	a. Confirmed that SBT duration can be between 30-120 min b. literature supports this c. doing SBT for 60 min reduced the number of patients placed on SBT at night shift	Changed SBT duration from 60 minutes to 30 minutes	10 days
4	There is inadequate documentation surrounding SBT screening and initiation	Review of data collection process, chart review, and shadowing of stakeholders	Chart review showed some discrepancies: #1: 2 consecutive failed SBT, 3rd one omitted #2: patient was trached #3: patient waiting for surgical airway #4: discrepancy in documentation. Difficult to find SBT documentation within RT and RN charting	Developed daily SBT stickers to be placed in a visible location on both RT and RN charting with clear details around number of attempts, SBT screening, timing, and pass rate.	1 month

We developed surveys to obtain feedback on the above changes. Team leads performed mini-audits bi-monthly to assess adherence and improvement to documentation. SBT rates were tracked monthly following the intervention and audits were performed if SBT rates fell below 70%. Based on the audits, new issues were identified and addressed in follow-up.

Results

We identified 5 main barriers to SBT performance: 1) health professionals' perceptions of patients' readiness for extubation; 2) inconsistencies with bedside clinical documentation hindering data collection; 3) lack of interprofessional engagement surrounding the importance of SBT; 4) educational gaps regarding SBT literature on patient outcomes; 5) SBT process and duration limiting SBT rates.

Both a change in SBT timing from mid-morning to early morning and reducing the duration from 60 to 30 minutes increased the number of SBTs performed during the day. We also encouraged stake-holder involvement by improving education and knowledge surrounding SBT via mini-presentations during safety huddles in the ICU. Information sheets explaining SBT criteria and its importance were placed in each patient chart at the bedside. We also developed stickers for both RT and RN documentation to improve data collection around SBT screening and performance.

Following the interventions, our SBT rates increased from 53% to 71%. Routine audits and amendments have shown sustained change for 6 months.

Conclusion

Several barriers to performance of SBTs were identified including gaps in knowledge and bedside documentation. Through a multidisciplinary approach, we engaged stakeholders and modified the local SBT process resulting in a sustained increase in our SBT rates. We recognize that maintaining this in the long term will require ongoing work and further organizational and system engagement within the hospital.