VIRTUAL ART SLUTSKY RESEARCH DAY
Interdepartmental Division of Critical Care Medicine
University of Toronto

ABSTRACT BOOKLET
VIRTUAL ART SLUTSKY RESEARCH DAY

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Basic Science Abstracts
**Umbilical cord derived MSC-administration modulates the angiogenic response after TBI and rescues vascular dysfunction**

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**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 angiopoietin-1 (ang-1) that binds to the receptor tie-2 on endothelial cells promoting barrier stability. Angiopoietin-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 10⁶ 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 μg and 15.5 μg in FPI rats at 24 and 48h, respectively vs. 1.7 μg in sham rats. HUCPVC treated rats Evan’s blue extravasation values were 5.5 μg and 3.3 μg 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 PDGFRβ was observed at 24 hours post-injury, 24% (±5, p<0.05) reduction relative to sham. HUCPVC treatment was associated with preservation of PDGFRβ 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.
miR-187 mimic targets inflammatory pathways in cardiomyocytes treated with bacterial endotoxin

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Background: Multiple microRNAs (miRs) are dysregulated during myocardial sepsis. Systemic administration of mesenchymal stromal/stem cells (MSCs) mitigates sepsis induced myocardial dysfunction and alters the expression of both miRs and their target mRNAs in the septic heart. In an experimental model, we have identified miR-187 as a putative host-derived MSC-regulated miRNA. Here we investigate the broader pathways and genes which get targeted by miR-187 and if these pathways play a critical role in the pathogenesis and therapeutics of sepsis-induced myocardial dysfunction.

Methods: Primary cardiomyocytes were harvested from 1-2 days old CD1 neonates then transfected with miR-187 mimic and inhibitor (25nM/ml) for 24 hours followed by 24 hours of exposure to bacterial endotoxin lipopolysaccharide (1 µg/mL). Subsequently RNA was isolated from the cells, mRNA profile was obtained using affymatrix Mouse Gene 2.0 ST platform. Using Gene Set Enrichment Analysis (GSEA) the pathways enriched in each experimental groups (miR-187 knock out, miR-187 knock in) with and without lipopolysaccharide exposure were identified.

Results: The expression of key inflammatory cytokines (TNF-α, IL-1β, IL-6) are decreased in cardiomyocytes treated with miR-187 mimic. Other important markers of proinflammation genes (Fasl, S100A4 and S100A9) are also decreased after miR-187 mimic transfection.

Conclusion: Transfecting neonatal cardiomyocytes treated with miR-187 mimic in presence of the LPS decreases pathways involved in inflammation.

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CASPASE-8 HOMO- AND HETERODIMERS DIFFERENTIALLY ACTIVATE PI3-K SIGNALING TO INHIBIT NEUTROPHIL APOPTOSIS

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Introduction: Sepsis – life-threatening organ dysfunction caused by a dysregulated host response to infection – is globally diagnosed in 49 million cases each year, 11 million of which result in death. Neutrophils (PMN) are the cardinal cellular effectors of the innate immune response and play a fundamental role in directing inflammation in septic patients. We have shown that tyrosine phosphorylation of caspase-8 dynamically regulates PMN survival in sepsis, promotes activation of c-Src kinase, and induces PI3-K activation and pro-survival gene transcription. Caspase-8 activation requires its dimerization. Multiple caspase-8 isoforms exist, hence we hypothesized that differential caspase-8 dimerization controls the kinetics of apoptosis and inflammatory signaling by altering the assembly of anti-apoptotic signaling complexes in PMNs.

Methodology: Septic patient and healthy control PMN were isolated by density centrifugation. Control PMN were incubated with LPS (1 µg/ml). Caspase-8A/B isoforms were detected by Western blot and apoptosis was quantified by flow cytometry (ANN V/PI+ staining). Caspase-8 was genetically silenced using siRNA and IAP and NAIP mRNA synthesis was quantified using RT-qPCR. Caspase-8 phospho-mimetic (Y380E) and deficient (Y380F) constructs were generated by mutating a conserved YXXM tyrosine phosphorylation domain in the C-terminus of both caspase-8A and B. Equimolar amounts of caspase-8A/B mutants were co-transfected into human leukemia (HL-60) cells and binding to PI3-K p85 and p110 subunits and phospho-tyrosine (pY) was assessed by immunoprecipitation. Caspase-8 A/B expression in septic patient PMNs was correlated to multiple organ dysfunction score (MODS) and white blood cell (WBC) count. 3 new caspase-8 isoforms were identified in control PMNs by overlaying pre-existing amino acid sequences on NCBI.

Results: Significantly lower rates of apoptosis were observed in LPS stimulated control PMN co-expressing both caspase-8A and B isoforms (n=9; p=0.002) in comparison to those expressing caspase-8A alone (n=5). In septic PMN transfected with caspase-8 siRNA versus scramble siRNA, apoptosis rates increased (31.4±4.4% vs 14.3±6.3%; n=3; p<0.05) and transcription of pro-survival IAP (n=4; p=0.03) and NAIP (n=3; p=0.1) decreased. HL-60 cells co-transfected with caspase-8A/B, and subsequently challenged with LPS, demonstrated lower rates of apoptosis (n=4; p<0.05), greater caspase-8 pY, and greater binding to p85 subunit and activation of the p110 subunit of PI3-K in comparison to A/A or B/B transfections. Septic patients expressing both A/B isoforms demonstrated higher MODS and WBC (n=7; MODS=10, WBC=29) versus those expressing A (n=1; MODS=8, WBC=18) or B alone (n=4; MODS=6, WBC=21). Finally, we reveal 3 new, unreported caspase-8 isoforms that we termed N1, N2 and N3.

Conclusion: Variable dimerization and tyrosine phosphorylation of caspase-8 isoforms regulates the degree of PI3-K activation through p110 release to differentially inhibit neutrophil apoptosis. Since caspase-8 clinical variants can be experimentally determined, they emerge as potential stratification markers for studying heterogeneity in the neutrophil response and apoptosis during infection in patients with sepsis.
NOVEL METRICS IDENTIFY A TRANSCRIPTOMIC SIGNATURE OF IMMUNE FUNCTION IN EARLY SEPSIS AFTER EX VIVO STIMULATION

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Introduction & Objective: How immune dysfunction in sepsis leads to organ failure and ARDS is unclear. Ex vivo endotoxin challenge is a surrogate of immune function which we demonstrated causes in vitro lung endothelial permeability that stratifies septic patients into response categories (AJP:Lung, 2018). There are no physiologically derived transcriptional signatures of endotoxin tolerance in early sepsis. Our objective was to use endothelial permeability and two other metrics to study blood endotoxin responses and compare unstimulated relative to endotoxin stimulated conditions to develop a transcriptomic signature of immune function in early sepsis.

Methods: Blood from 40 septic patients was divided into two fractions and incubated with media (unstimulated) or endotoxin. Supernatants and cells were isolated and responses measured using: (1) supernatant cytokines, (2) lung endothelial permeability after supernatant exposure, and (3) cell RNA expression. Differential gene expression models were fit using continuous outcomes including the three metrics to generate a transcriptomic signature of immune function.

Results: All response metrics demonstrated interpatient variability in stimulated, but not in unstimulated samples. When each metric was tested for differential gene expression, >1,000 genes were differentially expressed in endotoxin-stimulated samples and none in unstimulated samples.

Conclusions: This study establishes that endotoxin tolerance, and thereby immune suppression, is present very early in a substantial proportion of sepsis patients. While prior studies reported a gene signature for endotoxin tolerance from whole blood, this is the first study to test the derivation of this phenotype using ex vivo physiologic and protein data. The ability to generate an endotoxin tolerance signature in stimulated but not unstimulated cells suggests that unstimulated whole blood transcriptomic analysis may be inadequate to draw conclusions about ex vivo immune function in early sepsis.

Figure: Robust gene expression clustering in ex vivo endotoxin stimulated cells (left). Clustering in unstimulated cells (right) was poor and none of the genes were significantly differentially expressed at a false discovery rate of 0.1.
Introduction & Objective: Given our ignorance of the pathogenesis of COVID19, we decided to perform a longitudinal, multi-omic study of biomarkers among COVID19 patients with lung injury. This represents a discovery cohort aiming to find biomarkers that characterize COVID19. These biomarkers would provide biological, mechanistic insights into COVID19’s pathogenesis as well as inform clinical, diagnostic and therapeutic approaches for COVID19, such as the development of prognostic models and identification of phenotypic subgroups.

Methods: We are recruiting patients aged 18 and older admitted to the ICU with respiratory symptoms suspected to be COVID19. The patients found to be positive are the COVID19+ cohort, while the negatives become the COVID19-, control cohort – these are our primary cohorts. There are no other inclusion constrains. We are also recruiting COVID19+ patients on the ward, and COVID19+ patients in the ICU with other presentations. Outcomes: The primary outcome is a composite outcome of death or ECMO up to 3 months from the index ICU admission. Secondary outcomes include (up to 3 months after ICU admission): ICU death of ECMO; ICU length of stay; use of non-invasive respiratory support beyond nasal prongs or face mask in the ICU; length of mechanical ventilation; increase of 2 points in the non-respiratory SOFA score components from the best known baseline. Exploratory outcomes include the use of specific biomarkers as predictive surrogates of disease severity. Our target recruitment is 155 COVID19+ patients from the primary cohort. Standard is not be affected or changed in any way. The sampling times for blood and clinical data collection are days 0 (t0, admission) to day 13 daily, or up to ICU discharge, then once every 2 weeks for up to 5 times. If a blood sample cannot be obtained at t0 or t1, the patient is excluded. We are collecting detailed clinical data, as well as blood samples for: cytokines, blood biomarkers, COVID19 and immune serology, metabolomics, transcriptomics and epigenetics, as well as fixed, frozen blood cells for deep immunophenotyping. Processing is performed in the ICU using an on-site centrifuge and freezer, followed by transport to -80 C within 48 hrs for permanent storage until analysis. We are also performing post-mortem lung and heart, ultrasound guided core biopsies.

Results: We present here a preliminary analysis of our pilot cohort consisting of 26 patients. These were 16 COVID19+ and 10 COVID19- as classified clinically using PCR of nasopharyngeal swabs and endotracheal aspirates from 3 laboratories: SMH, MSH and PHL. Longitudinal serology (see figure) shows that 7 out of 10 COVID19- patients were actually positive for COVID19. Some patients developed the positive serology beyond the 1st admission day. The cytokine analysis also showed evidence of subgroups, with one subgroup of patients showing similar responses of IFNg, IL12 and IL13, while a second set of patients showed similar patterns of response of IL10, IL1RA and CXCL1. Importantly, the 2nd subgroup included both COVID19 positive and negative patients (as assessed by the serological results)

Conclusion: The longitudinal samples suggest that serology plays an important role in the identification of COVID19 patients beyond PCR tests, and that testing over time is important given that some patients became positive later into the admission. It is not known which of these patients is infective and which of these responses are protective and/or neutralizing. Nonetheless, from a clinical and scientific perspective, our results suggest that we suffer from a significant misclassification problem. The cytokine results also highlight the necessity of longitudinal sampling since the patterns of response over time do not synchronize to clinically derived timings. The clinical timings (i.e. day of admission) are arbitrary and do not reflect accurate biological timelines, especially given the heterogeneity of the presentation of COVID19 over time, in severity and clinical phenotype. The preliminary results suggest that clustering by patterns of cytokine responses may help elucidate pathogenic processes directly related to COVID19 vs those incidental to it, but larger patient sample sizes are needed to confirm these conclusions as well as define the cytokine patterns involved in different processes.
The Trojan-like nature of microRNA-193b-5p in Virus-Induced ARDS


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Rationale: ARDS is the leading cause of mortality from seasonal and pandemic H1N1,1,2 Emerging evidence suggests host-derived cellular microRNAs (miRs) play a critical role in alveolar-capillary membrane integrity, and host responses to viral infections.3-6 We hypothesized that increased levels of miR193b-5p during H1N1 results in decreased tight-junction protein occludin expression, associated with increased inflammation and injury. Accordingly, miR-193b-5p inhibition is expected to mitigate lung injury and enhance anti-viral responses in a murine model of H1N1 and in miR-193b deficient mice.

Methods: Mir-193b null mice and litter mates were randomized to H1N1 virus (A/PR/8/34) vs mock infection. Wild type mice (C57Bl/6J, 10 -14 weeks) were randomized to PR8 infection with treated a miR193b-5p inhibitor (INH) versus negative control delivered on day 4 post-infection. Researchers were blinded to group assignments and animals were sacrificed 8 days post viral administration to assess lung injury severity by: histology, bronchoalveolar lavage fluid cell counts and differential, membrane permeability, and viral load. Luciferase assays was performed to examine miR-193b-5p binding to the 3’UTR of occludin. In vitro, Beas2b cells were infected with H1N1 and treated with or without miR-193b-5p inhibitor (INH) or mimic. Beas2b were transfected with the siRNA against occludin or scrambled control. The expression of miR-193b and putative targets was evaluated by qRT-PCR. miR193b-5p expression in response to Interferon β (IFNβ) was determined by qRT-PCR and digital droplet (dd) PCR.

Results: Intranasal H1N1 infection in C57Bl/6J animals resulted in increased pulmonary inflammation, lung edema, increased levels of miR193b-5p (20-fold) and decreased expression of occludin (>50%) that peak at day 5 days post-infection. Reporter construct demonstrates miR-193b-5p binds specifically to the 3’UTR of occludin. In vitro, silencing of occludin results in increased viral load and dysregulation of the host antiviral response. miR193b null mice infected with PR8 show reduced lung injury with significant differences in survival outcomes compared to litter mates. miR193b-5p is IFNb responsive confirmed by qRT-PCR and ddPCR. Inhibition of miR193b-5p mitigates H1N1-induced lung injury, edema formation, viral load, and anti-viral IFNβ and Interferon Regulated Genes expression.

Conclusion: Endogenous miR-193b-5p plays a critical role in regulation of occludin, tight junction function and virus induced lung injury. miR193b null mice exhibit significant survival advantage compared to wild type mice; with reduced lung injury, miR193b-5p is IFNb responsive, a natural host anti-viral response, which is upregulated during infection. Inhibition of miR-193b-5p results in decreased lung injury, inflammation, and viral load.

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References


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

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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\textsubscript{2}O) 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\textsubscript{2}O, resulting in a respiratory rate of 30/min). In the porcine model, arterial oxygenation, CO\textsubscript{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.
DURATION OF DIAPHRAGMATIC INACTIVITY AFTER ENDOTRACHEAL INTUBATION OF CRITICALLY ILL PATIENTS

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Introduction and Objective

At time of intubation for mechanical ventilation, patients are sedated, and diaphragm activity markedly reduced or suppressed. The duration of abnormally low activity is unknown. We sought to determine the time to recovery of diaphragm electrical activity and the factors associated with the duration to recovery.

Methods

Critically ill patients admitted to a 24 bed Medical-Surgical Intensive Care Unit (ICU) and who required intubation had diaphragm electrical activity (EAdi) peak values continuously collected from intubation with a special feeding tube equipped with esophageal sensors. Resumption of a minimal level of spontaneous breathing activity was considered as the beginning of the first 24 h period with a median EAdi value > 5uV. Recordings were collected until recovery of spontaneous breathing, extubation, death or 120h (5 days). A one-hour recording of ventilator and EAdi waveforms was collected daily.

Results

Seventy-five patients were enrolled and 70 were included in the analysis (mean ± standard deviation age 63±16 years old). Main reasons for mechanical ventilation were respiratory (54%), hemodynamic (18%) and neurologic (21%) failure. ICU mortality was 24%. Unanticipated catheter disconnection occurred in 7 patients. The mean time for resumption of EAdi was 34 hours (standard error 5 hours) and median time 20 hours; 54% of patients started to resume activity within 24 hours and 10% still had no recovery after 5 days. A one-hour daily recording showed that 20% of patients exhibited reverse triggering as their first spontaneous activity. When comparing patients recovering before 24 hours vs. later, the factors associated with late recovery were the infusion of paralysis, at least one sedative agent during the first 6 hours after intubation and use of controlled modes of ventilation. Severity of illness indices, reason for intubation and sedation score were not associated with delay of recovery.

Conclusion

More than 40% of patients do not recover any diaphragmatic activity within the first 24 hours after intubation. Sedatives seem to be the main factor explaining a delayed recovery.
MAGNITUDE OF BREATHING EFFORT DURING REVERSE-TRIGGERING COMPARED TO SYNCHRONIZED EFFORTS UNDER PRESSURE SUPPORT VENTILATION

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Abstract:
RATIONALE
Reverse triggering (RT) consists of breathing efforts entrained by mandatory breaths. It can potentially lead to lung injury by increasing lung stress and strain, or to myotrauma by excess diaphragmatic loading and eccentric contractions. Risk of injury likely depends on the magnitude and timing of RT. Little is known about the magnitude of breathing effort during RT. The aim of this study is to describe the magnitude of inspiratory efforts during reverse triggering under assist-control ventilation and compare it to synchronized efforts under pressure support ventilation (PS).

METHODS
Ancillary analysis of the BEARDS study (NCT03447288) that aims at studying the incidence and consequences of RT within the first week of mechanical ventilation for acute hypoxemic respiratory failure (PaO₂/FiO < 200 mmHg). Respiratory tracings (airway pressure, flow and esophageal pressure-Pes) were recorded for 20 minutes, 3 times a day. After a semiquantitative assessment, 16 recordings (one per patient) were randomly selected including 4 with high, medium and low incidence of RT, and 4 under PS. Muscular pressure (Pmus) was computed for each breathing effort as the difference between the chest wall recoil pressure and Pes. Effort load was calculated as the product of the median Pmus and frequency of effort per minute for each tracing. Generalized estimating equations were used to compare Pmus under various circumstances to account for repeated measures.

RESULTS
Patients were predominantly male (75%), aged 69.3 (±11.0) with APACHE III score of 79.9 (±22.9). Sedation score was lower in patients under assist-control with RT compared to PS (SAS median [IQR] 1.0[1.0;2.2 ] vs 3.5 [3.0;4.0] p=0.0003).
A total of 1807 efforts were analyzed (1079 RT and 728 during PS). Frequency of RT ranged from 3 to 26 per minute. Median [IQR] Pmus during RT was 8.7 [5.6;11.9] cmH2O (range 1.3 36.8 cmH2O). Coefficient of variability varied largely between patients (5-106%). Pmus during RT was not different than Pmus during PS (9.5[6.2,12.8] cmH2O, p=0.99). Effort load with high and intermediate frequency of RT was similar to that measured during PS. Magnitude of effort was inversely correlated with the SpO₂/FiO2 (R² 0.21, p=0.05). RT-induced breath-stacking occurred in 19% of reversed-triggered efforts (0.1-4.5 per minute) and Pmus was 9.3[CI95% 2.0 16.6] cmH2O higher than in RT without breath-stacking.

CONCLUSION
Magnitude of breathing effort during RT is highly variable between and within patients but is, on average, comparable to that occurring under PS. RT might lead to variable consequences in susceptible patients according to the magnitude of breathing effort.

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Figure 1. Distribution of the magnitude of inspiratory effort for each patient
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 cmH₂O). 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 cmH₂O to 3 cmH₂O. 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 cmH₂O, 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 cmH₂O respectively) compared to supination (15 and 9 cmH₂O 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 Ppl 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.
Figure 2. Comparison of the magnitude of inspiratory effort according to the type of effort

Figure Legend: Amplitude of Pmus generated during RT with breath-stacking (RT with BS), without breath-stacking during efforts triggering the ventilator in pressure support ventilation (synchronous) and during ineffective expiratory efforts (IEE).

List of abbreviations: RT = Reverse triggering with breath-stacking, BS = breath-stacking, IEE = ineffective efforts during expiration, ACV = assist-controlled ventilation, PSV = pressure-support ventilation, Pmus = muscular pressure per breath
during pronation. Setting PEEP is much safer during pronation compared to supination. We believe these changes potentially contribute to improved survival during pronation.

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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 Positions:
PERSONALIZED VENTILATION TO MULTIPLE PATIENTS USING A SINGLE VENTILATOR: PROOF OF PRINCIPLE

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Intro and objectives
The recent COVID-19 pandemic has led to global demand for ventilators that has outstripped the supply in many parts of the world. To address this deficiency, many ventilator sharing solutions have been proposed and publicized. Unfortunately, many proposals are predicated on uncontrolled pressure mode ventilation. Distribution of the shared tidal volume in these systems is determined by the relative lung compliances of the two patients which may be highly variable and impossible to reliably predict in a clinical setting. This can lead to dangerous over or under-ventilation of the patients and ventilator associated lung injury. In this work, we propose an alternative ventilator splitting solution that can provide individualized volume control ventilation with personalized FiO₂ and PEEP that is independent of the co-ventilated patient.

Methods
Following a previously described design, we used components readily available in our hospital to assemble two “bag-in-a-box” breathing circuits. Each patient circuit consisted of a flexible bag in a rigid container connected via one-way valve to a test lung, along with an inline positive end-expiratory pressure valve, connected to the patient’s expiratory limb. Independent fresh gas flow is connected to each inspiratory limb, filling the patient’s bag with desired tidal volume during “patient” exhalation. During inspiration, gas from the ventilator, in pressure control mode, enters the containers and displaces tidal volume from the bags to the test. To test the pressure independence of the two secondary circuits connected to the test lungs, we varied tidal volume, “respiratory system” compliance, and positive end-expiratory pressure in one lung while measuring the effect on the tidal volume and PEEP of the co-ventilated lung.

Results
We were able to reliably control different tidal volumes and positive end-expiratory pressures in the two lungs under widely different compliances in both lungs. Complete obstruction, or disconnection at the circuit connection to one test lung, had minimal effect (< 5% on average) on the ventilation to the co-ventilated lung.

Conclusion
A secondary circuit “bag-in-the-box” system enables individualized ventilation of two lungs overcoming many of the concerns of ventilating more than one patient with a single ventilator.

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HIGH FLOW NASAL CANNULA: IMPACT of FLOW RATE and MOUTH OPENING

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Introduction: High flow nasal cannula oxygen therapy (HFNC) is a promising treatment for adults with respiratory failure. It provides washout of anatomic dead space and generates positive pressure in the nasopharynx and the alveoli as suggested by increased end-expiratory lung volume. Whether the effects of HFNC are similar to continuous positive airway pressure (CPAP) is unclear and changes in respiratory rate are not well explained.

Objective: Bench study: relationship between flow, nasopharyngeal pressure and inspired volume. Healthy volunteers: comparison of the effects (nasopharyngeal pressure, esophageal pressure, Electrical Impedance Tomography, EIT) of three flow rates (20, 40, 60 L/min), mouth closed (MC) versus open (MO) and CPAP 4cmH2O compared to the maximal flow.

Methods: 1) Bench study using a manikin’s head (MC) and lungs connected to a breathing simulator (ASL 5000) generating steady inspiratory efforts with set lung compliance and airway resistance. Nasopharyngeal pressure was measured with a dedicated catheter and tidal volume was obtained from the simulator under different conditions with HFNC from 0 to 60L/min (Fisher Paykel). 2) Physiological cross-over study in 10 healthy volunteers breathing MC and MO under HFNC at 20, 40 and 60L/min and under CPAP 4cmH2O. Nasopharyngeal pressure was measured using a dedicated 12 French catheter, as well as esophageal pressure (Cooper catheter) was used to compute respiratory effort or pressure-time-product (PTP). Tidal volume and flow were estimated using calibrated electrical impedance tomography (Pulmovista, Draeger). We also computed inspiratory and expiratory resistance. Statistics: comparison between HFNC 60L/min and CPAP by Friedman test and Nemenyi post hoc test; HFNC-MC vs MO at the 3 flow steps by Anova two-way and Bonferroni post hoc test.

Results: The bench data showed that pressure increased with flow up to 4 cm H2O; a progressive reduction in tidal volume with increasing flow was observed. The human study showed that nasopharyngeal pressure at 60L/min with MC reached almost 7 cmH2O, higher than CPAP. There was a huge effects of mouth opening: flow-dependent pressure was increased with MC and inspiratory and expiratory resistances were progressively increased during MC at increasing flows. This was associated with a lengthening of expiratory time and a reduction in respiratory rate. The imposed PTP was increased by MC as well as patient effort (PTP) expressed per Liter of ventilation. Because of a decrease in rate PTP/min did not increase.

Conclusions: Closing the mouth during HFNC- MC increases the resistance to breathing both in a bench and in a healthy volunteer study. In healthy volunteers, HFNC at a flow of 40L/min with MC delivers end-expiratory pressures comparable to CPAP 4cmH2O, whereas HFNC-MC at 60L/min delivers pressure around 7 cmH2O. Closing the mouth increases inspiratory and expiratory resistance, which might explain the decrease in respiratory rate and the prolonged expiration.
ASSOCIATION OF NEUROMUSCULAR BLOCKADE WITH MORTALITY DIFFERS ACCORDING TO BASELINE DIAPHRAGM THICKNESS

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Introduction & Objective: Spontaneous breathing during mechanical ventilation can lead to worsening lung injury in patients with acute respiratory distress syndrome (ARDS), a phenomenon recently recognized as patient self-inflicted lung injury (P-SILI). Neuromuscular blocking agents (NMBAs) are administered to prevent P-SILI, but a recent large randomized trial found no benefit when compared to a standard sedation strategy. The intensity of the inspiratory effort will depend—at least in part—on the force-generating capacity of the diaphragm. If the risk of P-SILI varies according to diaphragm muscle mass and strength, then the influence of NMBAs on clinical outcome may also vary according to diaphragm characteristics. We set out to establish whether the association between use of NMBAs and mortality in patients with acute hypoxemic respiratory failure (AHRF) differs according to baseline diaphragm thickness (Tdi).

Methods: Secondary analysis of a previously published prospective cohort study of critically ill patients receiving mechanical ventilation. For this analysis, the study cohort was a priori restricted to patients with baseline PaO$_2$/FiO$_2$ $\leq$200, as these patients are hypothetically at higher risk of P-SILI. A Bayesian Cox proportional hazards regression model using minimally informative priors was constructed to quantify the association between administration of NMBA by continuous infusion at any time in the first 48 hours of mechanical ventilation and 90-day mortality (censored at hospital discharge), adjusting for a priori defined confounders measured at baseline. To determine whether the association between NMBA and mortality varied according to baseline Tdi, the model included an interaction term for baseline Tdi dichotomized at the median value ($\leq$2.3 mm vs >2.3 mm).

Results: Of 193 patients in the original study cohort, 132 had baseline PaO$_2$/FiO$_2$ $\leq$200 and were included in the analysis. Overall, NMBAs were not associated with 90-day mortality (median adjusted hazard ratio (aHR) for death 0.81, 90% CrI 0.39 to 1.69). However, the association between NMBA and mortality varied substantially according
to baseline Tdi (aHR for interaction 0.20, 90% CrI 0.05 to 0.8, Bayes factor 33.78, posterior probability of interaction 97%). In patients with baseline Tdi ≤2.3 mm, NMBAs were associated with higher mortality (aHR 2.61, 90% CrI 0.76 to 8.67, Bayes factor 8.76, posterior probability of HR>1 90%) whereas in patients with baseline Tdi >2.3 mm, NMBAs were associated with lower mortality (aHR 0.38, 90% CrI 0.12 to 1.18, Bayes factor 12.03, posterior probability of HR<1 92%).

**Conclusion:** In this secondary analysis of a previously published prospective cohort study, the association between use of NMBAs and mortality in patients with acute hypoxemic respiratory failure differed according to baseline diaphragm thickness.

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ABDOMINAL MUSCLE FUNCTION DURING SPONTANEOUS BREATHING TRIALS TO PREDICT EXTUBATION FAILURE

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Introduction and Objective: Extubation failure occurs in up to 20% of patients who pass a spontaneous breathing trial (SBT) and is associated with extremely poor outcomes, including high mortality. Strategies for identifying patients at high risk of extubation failure are needed to improve the management of weaning. Ultrasound measurements of abdominal muscle thickening fraction (TF) may be useful to monitor abdominal muscle activity and function, however, their accuracy have not yet been established in mechanically ventilated patients.

Accordingly, our objectives were: 1) to assess the reproducibility of abdominal muscle ultrasound measurements in mechanically ventilated patients; 2) to quantify TF of the abdominal muscles during an SBT in response to increased load on the respiratory system; and 3) to determine whether abdominal muscle TF during coughing predicts extubation success.

Methods: In 57 mechanically ventilated patients, TF of right external oblique (EO), internal oblique (IO), transversus abdominis (TrA) and rectus abdominis (RA) was measured before and during SBT and during coughing. Reproducibility of TF was assessed using a random effects model. Discriminative validity to predict reintubation was assessed using ROC curve analysis.

Results: Interobserver reproducibility was satisfactory given their observed distributions for TFIO and TFRA (mean ± SD 14.7±14.8% and 8±6.7%, reproducibility coefficients 6.26% and 5.33% respectively), moderately acceptable for all the other muscles.

Changes in TF during the SBT varied widely between patients. At 5 minutes into the SBT, TF was significantly higher in patients who failed the SBT compared to patients who passed for TFIO (difference 7.2%, 95% CI 2.2 – 13.2), TFTrA (difference 13.2%, 95% CI 0.9 – 24.8), but not for TFEO or TFRA.

To assess abdominal muscle function, we computed the sum of TFRA, TFTrA and TFIO during coughing (coughTFab). Among patients extubated (n=30), coughTFab was substantially lower in patients who required reintubation within 72 hours (n= 7) (49% vs 147%, p= 0.007). A threshold of 70% for coughTFab could predict need for reintubation with acceptable accuracy (Se= 83%, Sp= 89%, AUROC= 86% [95%CI 58 – 100]).

Conclusions: Internal oblique and rectus abdominis TF showed the highest reproducibility. Internal oblique and transversus abdominis TF were significantly higher in patients failing an SBT compared to patients passing, consistent with elevated expiratory muscle effort in response to increased load. Abdominal muscle thickening during coughing may identify patients at high risk for reintubation.
Reverse Triggering Dyssynchrony during Protective Lung Ventilation affects diaphragm function according to the magnitude of effort

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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 PaO₂ <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 protective 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.
References:


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Fig 1.
Role of PEEP and Regional Transpulmonary Pressure in Asymmetrical Lung Injury.

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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 (D_{pl}) 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_{2}O 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 H_{2}O and higher (Figure 3). The
regional changes in $\Delta P_L$ 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 $\Delta P_L$ 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 $\Delta P_L$.

**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 $P_{pl}$.

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 $V_T$. * $P<0.05$.

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

Clinical/HSR Abstracts
POTENTIAL MAGNITUDE OF COVID-19-INDUCED HOSPITAL RESOURCE DEPLETION IN ONTARIO, CANADA

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**ABSTRACT**

**Introduction and Objective:** The global spread of coronavirus disease 2019 (COVID-19) continues in several jurisdictions, causing significant strain to healthcare systems. The purpose of our study is to predict the impact of the COVID-19 pandemic on patient outcomes and hospital resource utilization in Ontario, Canada.

**Methods:** We developed an individual-level simulation to model the flow of COVID-19 patients through the Ontario hospital system. We simulated different combined scenarios of epidemic trajectory and hospital healthcare capacity. Outcomes include numbers of patients needing admission to the ward, Intensive Care Unit (ICU), and requiring ventilation; days to resource depletion; and numbers of patients awaiting resources and deaths associated with limited access to resources.

**Results:** We demonstrate that with effective early public health measures, hospital system resources need not be depleted. For scenarios considering late or ineffective implementation of physical
distancing, hospital system resources would be depleted within 14-26 days. Resource depletion was also avoided or delayed with aggressive measures to rapidly increase ICU, ventilator, and acute care hospital capacity.

**Conclusion:** We found that without aggressive physical distancing measures the Ontario hospital system would have been inadequately equipped to manage the expected number of patients with COVID-19, despite the rapid capacity increase. This lack of hospital resources would have led to an increase in mortality. By slowing the spread of the disease via ongoing public health measures and having increased hospital capacity, Ontario may have avoided catastrophic stresses to its health care system.
FUROSEMIDE USE IN PEDIATRIC INTENSIVE CARE: PRACTICE PATTERNS

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Introduction & Objective: Furosemide is one of the most commonly used medications in intensive care. Indications are broad and definitions of therapeutic success are poorly defined. Clinical practice pattern variation is observed when the same intervention is operationalized in different ways. Examples of this include intravenous verses enteral use of medications such as antibiotics or acetaminophen or documented variation in surgical frequency, type, clinical outcome and surgical planning of similar disease processes. Extrapolation of this concept questioning variation and practice patterns that potentially exist within medical practices may help identify clinically important associations.

The objectives of this study were to describe the volume, dose and frequency of furosemide use in critically ill children and to describe patterns of furosemide administration over time and within selected patient subgroups.

Methods: A retrospective cohort study was performed at a single, free standing, paediatric, quaternary center. Eligible patients were admitted to either the paediatric or cardiac ICU during the period 31 July 2006 to 30 July 2015 for a duration of 6 hours or more and had one or more documented administrations of intravenous furosemide during their ICU admission. The primary study outcomes were the number of furosemide administrations, type, frequency and length of stay per patient. Secondary outcomes were the frequency and type of furosemide administrations by patient subgroup and over time by provider.

Results: 17,199 eligible admissions were admitted to the ICU. Of the 1,954,171 total administrations furosemide administrations accounted for a total 118,438 (6%). There was a total of 113,951 (96%) intermittent doses of furosemide and 4,487 (4%) infusions that ran for a total of 55,679,276 hours. There was a total of 3,617 (33%) patients admitted to the pediatric intensive care unit (PICU) and 4,830 (76%) patients admitted to the cardiac intensive care unit (CICU) who received one or more doses of furosemide. Of the total 8,447 (49%) patients receiving furosemide there was a median (IQR) 6 (2-14) intermittent doses of furosemide throughout their ICU stay. Of the patients who received furosemide infusions the median (IQR) length of infusion in was 128 (39-1085) hours.

Conclusions: The variation observed with furosemide in both administration type and patient population could represent an area of clinical uncertainty with opportunity for ongoing exploration. Further investigation such as prospective randomized control trial evaluating high versus low dose furosemide therapy or intermittent vs infusion furosemide with focus on starting doses and end points could provide a better understanding of the need for indications, endpoints and clinical impact of furosemide.
REPETITIVE BLOOD DRAWS AND BLOOD WASTE IN THE INTENSIVE CARE UNIT: A RETROSPECTIVE COHORT STUDY

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Introduction & Objectives: Frequent laboratory testing in the intensive care unit (ICU) facilitates patient monitoring and titration of invasive therapies. However, excessive phlebotomy may harm critically ill patients and represent a target for stewardship initiatives. Our objectives were to 1) Quantify daily phlebotomy volume for ICU patients including blood wasted during vascular access, and 2) explore the impact of daily phlebotomy volume on ICU acquired anemia (nadir hemoglobin < 80 g/L) or the need for red blood cell transfusion.

Methods: This was a retrospective cohort study at an academic tertiary care center in Toronto, Ontario. Index Medical Surgical ICU admissions between September 2014 and August 2015 of 72 hours or longer were included. Total average daily phlebotomy volume was calculated using blood received in the lab for diagnostic testing and blood discarded as waste at the bedside during vascular access. Bedside waste per blood draw was determined through prospective audit in March 2018. Multivariable logistic regression assessed total average daily phlebotomy volume as a predictor of 1) new ICU acquired nadir hemoglobin (< 80 g/L), 2) the need for red blood cell transfusion, and 3) hospital mortality. Patients with a major bleeding events (hemoglobin drop ≥ 30 g/L in 24 hours) were excluded. Control variables included sex, age, ICU length of stay, day 1 hemoglobin, and day 1 Sequential Organ Failure Assessment (SOFA) score.

Results: There were 428 index ICU admissions. Median patient age was 63.8 yr, 41% female, 51% invasively mechanically ventilated at admission, with mean SOFA score 5.9 +/- 3.3. Forty-four patients (10%) had major bleeding events. Mean bedside waste during the 2018 prospective phlebotomy audit (144 draws) varied: 3.9 mL for arterial, 5.5 mL for central venous, and 6.25 mL for peripherally inserted central venous catheters. Mean phlebotomy volume per patient day was 49.6 +/- 24.8 mL, which includes 33.2 +/- 15.6 mL received by the lab and 16.4 mL +/- 9.2 mL discarded at the bedside as waste. There was a mean of 3.8 vascular access events per day. Total average daily phlebotomy volume (mL) was predictive of new nadir hemoglobin < 80 g/L (parametric estimate 0.052, p<0.001) the need for red blood cell transfusion (0.051, p<0.001) and inpatient mortality (0.03, p<0.005). For every 5 mL increase in average daily phlebotomy, the odds ratio (OR) for developing a new hemoglobin < 80 g/L in the ICU was 1.30 (95% CI 1.10 - 1.52) and requiring a blood transfusion during ICU admission was 1.29 (95% CI 1.16 - 1.47).

Conclusion: Laboratory testing for ICU patients requires a substantial volume of blood, especially when considering blood discarded as waste during vascular access. Total average ICU phlebotomy volume is associated with new nadir hemoglobin < 80 g/L and the need for red cell transfusion in multivariable regression with severity of illness estimated by day 1 SOFA score. ICU acquired anemia and red cell transfusion may be appropriate outcome measures for future phlebotomy stewardship programs.

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SINGLE-CENTRE EVALUATION OF DIFFERENTIAL LEUKOCYTE RATIOS AS BIOMARKERS OF MORTALITY IN PATIENTS WITH ACUTE-ON-CHRONIC LIVER FAILURE ADMITTED TO THE INTENSIVE CARE UNIT

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Introduction and Objectives:
Acute-on-chronic liver failure (ACLF) is characterized by rapid deterioration of hepatic function along with multorgan failures following an acute insult in patients with cirrhosis and often necessitates intensive care unit (ICU) admission. ACLF is associated with significant morbidity and mortality. In recent years, differential leukocyte ratios including neutrophil-to-lymphocyte ratio (NLR) and monocyte-to-lymphocyte ratio (MLR) have been evaluated in different ICU populations as predictors of mortality. Our aim is to assess NLR and MLR in ACLF patients admitted to the ICU as biomarkers of mortality.

Methods:
Retrospective cohort study of 599 cirrhotic patients admitted to the Liver Intensive Therapy Unit at King’s College Hospital from 2009 until 2016. Grade of ACLF was determined at the time of ICU admission. Hematological data including neutrophil count, lymphocyte count, and monocyte count was obtained at the time of ICU admission. Primary outcome was in-hospital mortality. NLR and MLR were correlated with the primary outcome. Subgroups of patients including those with alcohol liver disease and sepsis were also evaluated regarding NLR and MLR and in-hospital mortality.

Results:
Overall 599 cirrhotic patients were evaluated with 375 (62.6%) being male and median age of 52 years (15-78). 181 (30.2%) patients had ACLF grade 0, 67 (11.2%) had ACLF grade 1, 127 (21.2%) had ACLF grade 2, and 224 (37.4%) had ACLF grade 3. Alcohol was the etiology of chronic liver disease in 296 (49.4%) of patients. Sepsis was present in 277 (46.2%) of patients. In-hospital mortality occurred in 249 (41.6%) patients. Both NLR and MLR were higher in patients with ACLF grades 2 and 3 compared with no ACLF (p<0.0001 for both). Both NLR and MLR were higher in patients with in-hospital mortality (p<0.0001 for both). NLR predicted outcome with an area under the receiver operating characteristic (AUROC) of 0.684 (95%CI 0.641-0.727, p<0.0001) and MLR predicted outcome with AUROC of 0.630 (0.590-0.669, not significant). In the alcohol liver disease group, NLR and MLR both were higher in patients with in-hospital mortality (not significant and p<0.0001 respectively). NLR predicted outcome in this group with AUROC of 0.685 (0.62-0.72, p<0.0001) while MLR predicted outcome with AUROC of 0.635 (0.570-0.700, p<0.0001). In the sepsis group, both NLR and MLR were higher in patients with in-hospital mortality (p<0.01 for both). NLR predicted outcome in this group with AUROC of 0.662 (0.598-0.726, p<0.0001) and MLR predicted outcome with AUROC of 0.614 (0.546-0.681, p=0.001).

Conclusions:
ACLF is associated with high neutrophil and monocyte counts along with low lymphocyte counts. NLR and MLR are associated with higher grades of ACLF and in-hospital mortality. However, NLR and MLR were not highly accurate predictors of in-hospital mortality even in subgroups of alcohol liver disease and patients with sepsis suggesting this is a pan-ACLF phenomenon unrelated to etiology or bacterial infection.
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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Introduction & Objective: Every day, Critical Care Clinicians bear witness to human experiences that are, at once, universal and exceptional. As they attend to individual patients, they actively participate in the cycles of grief, joy, sickness, and recovery that all of us encounter between the boundary points of life and death. Critical Care Clinicians occupy privileged positions in the lives of others, and as such develop a unique understanding of the complex factors informing how the paths of their patients and fellow practitioners unfold. The objectives of this endeavor were integrate art and the humanities within intensive care. Through various creative writing styles we aimed to allow the broader group to share important life experiences and emotions related to life as an intensive care physician.

Methods: A self-nominated multidisciplinary group of professionals who work in the intensive care unit gathered to share evolve ideas. These were then written in various creative writing styles by the authors to express the humanity throughout the profession. Guided discussion, feedback and learning around various creative writing styles was done throughout by a hired specialist.

Results: The final group consisted of nurses, fellows and staff within intensive care. We were able to compile 14 various writing pieces expressing a wide spectrum of emotion and experience in intensive care. The various styles included poems, reflections, letters, short stories and anecdotal comparisons. Satisfaction among members on a personal and professional level was reported as high.

Conclusions: Ultimately, the writers all demonstrate how professional fulfilment can be a potent antidote to burnout and a meaningful answer to why medical professionals continue to work in such a strenuous field. We chose to use writing as means to reflect on experiences. We were reminded of how we started, how far we have come; the stakes we deal with each day and the emotionally and physically demanding aspects of our jobs. Most importantly however these works remind us that our challenges and successes are shared - with the lives we impact and each other.
SEVERE ILLNESS GETTING NOTICED SOONER: VALIDATION OF A PAEDIATRIC ILLNESS RECOGNITION TOOL FOR CAREGIVERS

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Introduction and Objective
Timely identification of severe illness provides opportunity to prevent clinical deterioration and reduce morbidity and mortality. An expert panel consisting of parents and multidisciplinary providers created the Severe Illness Getting Noticed Sooner (SIGNS)-for-Kids as a public health tool to help caregivers identify and articulate the manifestations of severe illness in children. The tool was created during a consensus development workshop to incorporate expert opinion and previously published symptom checklists of severe illness. The SIGNS tool consists of five domains (Behavior, Breathing, Skin, Fluids and Response to usually effective treatment). The objective of this study was to review the sensitivity of the tool in a cohort of children with fatal illnesses as an initial validation step.

Methods
A retrospective review of pediatric deaths between January 2013 and December 2018 was performed using records from the coroner’s office. Eligible patients had an index event described and were <18 years and >36 weeks gestational age at the time of event, had observations/reports for > 6 hours prior to the index event, and were not in an intensive care unit (ICU) or under anaesthetist supervision. The index events were defined as cardiac arrest, respiratory arrest, intubation, transfer to ICU, interfacility transfer, or urgent surgical procedure. Traumatic events and infants with sudden unexplained death were excluded from analysis. The main outcome was the presence of SIGNS items. Secondary measures were the time before index events that each of the SIGNS were present, and the time to death from the index event. Analyses were descriptive.

Results
Two hundred records were screened. After exclusion of 145 cases with incomplete records or traumatic deaths and 5 infants with sudden unexplained death, the records of 50 children met inclusion criteria. One or more SIGNS criteria were present before index event in 48 (96%). Breathing abnormality (n=26, 52%) was the most frequently observed item with a mean (SD) duration of 47 (51) hours prior to index event. Over half (n=28, 56%) had SIGNS documented for ≥24 hours before initial escalation and 42 (84%) died within 48 hours after index event.

Conclusions
48 of 50 children had SIGNS criteria present before index event, and half had SIGNS present >24 hours. These data provide initial evidence of the sensitivity of the SIGNS criteria as markers of severe illness and suggest that the tool may help caregivers identify symptoms early enough to permit intervention. Future studies will focus on establishing specificity and construct validity as well as caregiver usability prior to implementation of the screening tool.
ASSOCIATION OF ENTERAL FEEDING PRACTICES AND FREQUENCY OF NECROTIZING ENTEROCOLITIS IN CRITICALLY ILL NEONATES WITH CONGENITAL HEART DISEASE

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Introduction and Objective
Enteral nutrition (EN) is often withheld from neonates with congenital heart disease due to concerns of necrotizing enterocolitis (NEC), despite limited evidence showing no association between the two in this population. This study sought to confirm the association between EN and NEC and determine if this relationship was influenced by feeding practices.

Methods
This single-center retrospective study included all neonates with congenital heart disease admitted to the Cardiac Critical Care Unit (CCCU) at the Hospital for Sick Children, Toronto between July 1st, 2016 and May 30th, 2018. Subjects were identified from a comprehensive nutrition database of all CCCU admissions; those meeting inclusion for whom EN was initiated and subsequently held for at least 48 hours were reviewed for NEC. Those who were born prematurely (less than 37 weeks gestational age), had a previous history of NEC, or diagnosed with gastrointestinal tract anomalies were excluded. NEC severity was graded retrospectively according to Bell’s criteria. Surgical complexity was measured by cardiopulmonary bypass times and categorized using the Society of Thoracic Surgeons – European Association for Cardio-Thoracic Surgery Congenital Heart Surgery Mortality Categories. Subjects meeting NEC diagnosis were compared to the remainder. Continuous data were analyzed as median with interquartile range and frequency with proportions were used for categorical variables. Univariable logistic regression was utilized to evaluate the direction and strength of association between NEC and subject demographics, cardiac physiology, surgical complexity, and enteral feeding practices. Multivariable models included predictors with possible associations but were limited due to a low frequency of NEC in the cohort.

Results
A total of 241 neonates were admitted and initiated on EN in the CCCU. The overall prevalence of NEC in this cohort was 5.4% (13/241). Subjects diagnosed with NEC had similar birthweight, gestational age, CCCU admission weight, prostaglandin dependence and surgical complexity as those without. Patients with NEC had longer duration of mechanical ventilation (23 vs 5 days, p=0.001), were slower to return to birthweight (25 vs 8 days, p=0.003), and had longer CCCU (59 vs 8 days, p=0.001) and hospital length of stay (91 vs 8 days, p=0.001). Both groups had similar timing of EN initiation, EN advancement, and maximum EN volume, but NEC was associated with higher EN caloric density (0.80 vs 0.67 kcal/mL, p=0.002) and older age at which maximum EN volume was obtained (26 vs 12 days, p=0.001). In logistic regression models, NEC was also associated with single ventricle physiology (p=0.006) and presence of diastolic flow reversal (p=0.009). Multivariable analysis demonstrated that single ventricle physiology was no longer associated with NEC after controlling for caloric density (p=0.70).

Conclusion
Delivery of higher caloric density EN was the only feeding practice associated with NEC in neonates with congenital heart disease. Although NEC was associated with single ventricle physiology and diastolic flow reversal, the association with single ventricle physiology was lost when controlling for caloric density.
THE UTILITY OF NUTRITIONAL RISK INDEX IN PREDICTING OUTCOMES ACROSS HEMATOLOGICAL MALIGNANCY PATIENTS WITH ACUTE RESPIRATORY FAILURE

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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.
THE ICU AND HOSPITAL ENVIRONMENT: PERSPECTIVES OF VISITORS TO THE ICU

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INTRODUCTION & OBJECTIVE

Family members of critically ill patients spend prolonged periods of time in the ICU and environs. It is important to know what amenities and comforts are of value to them during this stressful time, and what they perceive is necessary to the patient. Using formal survey methodology, this study aims to identify priorities for ICU visitors in the hospital, inside the ICU waiting room, and within the ICU itself, as well as to highlight any differences in needs amongst various visitor populations.

METHODS

With input from patients, family members, and the ICU inter-disciplinary healthcare team, and using formal survey methodology, we designed a questionnaire to evaluate what is important for visitors to the ICU. The paper survey included questions relating to the environment of the patient rooms, the waiting room, hospital facilities, and respondent demographics. Respondents were provided categorical response options (“Not at all important” to “Extremely important”), and an opportunity to enter textual responses. In 4 Ontario University-affiliated ICUs, visitors (family members and friends) to the ICU were invited by a research assistant to complete the anonymous questionnaire. Results are summarized as Ns and percentages.

RESULTS

To date we have 200 respondents, 60.5% female, age range <20 to 90+ years, 79% report English as their first language. 41% are children of a patient, 25% are a spouse/partner, and 11% are a sibling. The 5 most important factors in the hospital environment (in descending order, based on % of respondents rating the factor as “Very Important” or “Extremely Important”), include directive signage to the ICU (83%), parking near the hospital (80%), healthy and affordable food available for purchase (80%), discounted parking (78%), and sleeping facilities provided near the ICU (59%). The 5 most important factors in the ICU waiting room and environment include 24/7 visitation (94%), restrooms situated nearby (86%), a water dispenser (86%), free WIFI (82%), and comfortable furniture for visitors (79%). The 5 most important factors in the patient’s ICU room include seating for visitors (94%), access to natural light (78%), access to fresh air (74%), low noise levels (73%), and the dimming of lights at night (73%).

CONCLUSION
Results from this multi-center study highlight factors important to ICU visitors across multiple hospital sites, providing valuable insight to healthcare teams on how to improve the hospital and ICU environment for patients and their families.
THE ASSOCIATION BETWEEN PATIENT ETHNICITY AND FAMILY SATISFACTION WITH THE QUALITY AND PROVISION OF END-OF-LIFE CARE

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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 α < 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 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.

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LUNG ULTRASOUND INTEGRATED ASSESSMENT FOR THE DIAGNOSIS OF SARS-COV-2 PNEUMONIA IN THE EMERGENCY DEPARTMENT

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Introduction & Objective. Accurate diagnostic testing for identification of SARS-CoV-2 infection is critical. Currently, the most used test is the reverse transcription polymerase chain reaction (RT-PCR). Although highly specific, it has shown to be affected by a non-insignificant proportion of false negative results. We aimed to explore whether the integration of lung ultrasound (LUS) with clinical evaluation could improve the identification of false negative SARS-CoV-2 RT-PCR results.

Methods. This was a prospective cohort study enrolling consecutive adult patients presenting with symptoms potentially related to SARS-CoV-2 infection to the emergency department (ED) of an Italian tertiary academic hospital between April 1st and April 28th, 2020. In all patients, immediately after the initial clinical assessment, a LUS evaluation was performed and the likelihood SARS-CoV-2 infection, based on both clinical and LUS findings (“integrated” assessment), was recorded. RT-PCR SARS-CoV-2 detection was performed at first on nasopharyngeal swab samples. All RT-PCR positive cases were considered true positive. In patients with negative RT-PCR result, when clinical, sonographic, laboratory, or imaging evaluations were suspicious of infection, further testing was performed, including repeated RT-PCR. Patients were re-classified as infected if the second RT-PCR test (performed within 72 hours) resulted positive. If all molecular tests were concordantly negative, the patient was classified as a true negative case.

Results. We enrolled 228 patients; 107 had SARS-CoV-2 infection. Among the 142 patients who initially had negative RT-PCR, 21 resulted positive at a subsequent molecular test. All these cases were correctly identified by the integrated assessment. Conversely, the integrated approach wrongly classified as infected six patients and non-infected other six patients. Sensitivity and negative predictive value of the clinical-LUS integrated assessment were higher than first RT-PCR (94.4% vs 80.4%, p<0.01; 95% vs 85.2%, p<0.01).

Conclusion. This study suggests that, in patients presenting to the ED with symptoms commonly associated with SARS-CoV-2 infection, the integration of LUS with clinical evaluation may help to identify false negative results occurring with nasopharyngeal specimens, analyzed with RT-PCR.
Title: MORTALITY ASSOCIATED TO SEVERITY OF AKI USING pRIFLE CRITERIA AT INITIATION OF RRT (IN CRITICALLY ILL CHILDREN)

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Introduction: The high mortality and morbidity in critically ill children treated with renal replacement therapy (RRT) have multifactorial components.

Objectives: To evaluate the association between the severity of acute kidney injury (AKI) at RRT initiation using the pediatric RIFLE criteria (pRIFLE) and the patient outcomes.

Method: Retrospective, observational study in a single Swiss center pediatric intensive care unit (PICU). Data extraction was performed for the first episode of RRT in children admitted to the PICU between 2008 and 2018.

Results: Ninety-four patients required RRT during the study period. Of these, 86.2% presented with AKI according to the pRIFLE criteria at RRT initiation (stage “R” (risk) 8.6%, stage “I” (injury) 13.6%, and stage “F” (failure) 77.8%). When assessing the duration in stage “F” before RRT initiation, we found that 27% of children spent less than 24h, 21.3% between 28-48h, 8.5% between 48-72h, and 9.5% more than 72h.

Overall mortality was 45.7% with 3 children (3%) requiring chronic RRT. The distribution of patients according to the pRIFLE criteria was similar among survivors and non-survivors with a majority of children in the stage “F” (69% in the non-survivor and 64% in survivors groups). Time spent in stage “F”, had no effect on mortality; 57% in children with more than 24h and 50% in children with less than 24h in stage “F”. There was also no difference in PICU lengths of stay, duration of mechanical ventilation, and duration of RRT according to the pRIFLE criteria at RRT initiation. In multivariable logistic regression analysis, non-surgical cardiac disease (odds ratio, 16.73; 95%CI 1.6-174.387), an elevated PELOD score at RRT initiation (odds ratio, 1.076; 95%CI 1.031-1.124) and elevated fluid balance at RRT initiation (odds ratio, 1.006; 95%CI 1.001-1.012) were associated with an increase odds of mortality.

Conclusion: In this cohort of PICU pediatric patients requiring RRT, the majority presented with stage “F” of the pRIFLE criteria. The severity of AKI according to the pRIFLE or the duration at “F” stage before RRT initiation didn’t predict mortality or morbidity. An elevated PELOD score, a diagnosis of a non-surgical cardiac disease or an elevated fluid balance were associated with increased mortality.
Abstract

HOSPITAL DISCHARGE KIDNEY DYSFUNCTION AND TREATMENT WITH ANTI-HYPERTENSION MEDICATION AFTER PEDIATRIC EXTRACORPOREAL MEMBRANE OXYGENATION

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Introduction: Acute kidney injury (AKI) is frequent in children treated with extracorporeal membrane oxygenation (ECMO) and associated with mortality and morbidity. AKI may incur risk for long-term chronic kidney disease (CKD). Recovery from AKI may be associated with long-term CKD risk.

Objectives: In children treated with ECMO, determine a) prevalence of hospital discharge kidney dysfunction (DischKidDysf: discharge serum creatinine [SCr] ≥1.5X pre-ECMO baseline) and need for anti-hypertensive medication (DischHTNmeds); b) associations between AKI on ECMO, and other factors (e.g. ECMO duration, ECMO indication, age, oxygenation index) with DischKidDysf and DischHTNmeds.

Methods: 6-center retrospective cohort study (Kidney Injury During Membrane Oxygenation cohort) of children (<18 yrs old) on ECMO≥24 hrs from 2007-11. Exposure: AKI (SCr criteria of the KDIGO definition) during ECMO, defined as a) any AKI (yes/no) and ≥Stage 2 AKI (yes/no), regardless of renal replacement therapy[RRT]; b) AKI and ≥Stage 2 AKI, including RRT as an AKI criterion. Outcomes: as in objectives. Analyses: Univariable analyses comparing AKI and clinical factors between patients with vs. without outcomes.

Results: N=345 included (median[IQR] age 25 days[2-457]; 61.2%(216/354) VA ECMO; 38.8%(137/354) VV ECMO; ECMO indication pulmonary(62.1%), cardiac(20.9%), ECPR(17%); 197(55.6%) AKI and 126(35.6%) ≥Stage 2 AKI, disregarding RRT; 234(66.1%) AKI and 189(53.4%) ≥Stage 2 AKI, including RRT as an AKI criterion. N=43(12.1%) had DischKidDysf; 115(33.3%) had DischHTNmeds. Patients with DischKidDysf were significantly more likely to have AKI on ECMO (any AKI: 95.4% vs. 50.2, p<0.0001), regardless of AKI definition. Similarly, patients with DischHTNmeds were more likely to have AKI on ECMO (any AKI: 72.2% vs. 48.1%, p<0.0001). Older age, oxygenation index, non-renal complications, ECMO indication, and center were all associated with DischKidDysf and with DischHTNmeds (all p≤0.05). Fewer ECMO hours was associated with DischKidDysf (p=0.03); VA ECMO mode was more common in patients with DischHTNmeds (80.9% vs. 52.2%, p=0.001).

Conclusion: DischKidDysf and DischHTNmeds are common after pediatric ECMO, suggesting that kidney health follow-up should be considered in ECMO survivors. Discharge kidney outcomes are associated with AKI on ECMO and patient/treatment/illness severity factors. Future work will determine if the relation of AKI with discharge kidney outcomes is independent of these factors.
Art Slutsky Research Day Abstract

Title: LONG-TERM SUSTAINABILITY AND ACCEPTANCE OF ANTIMICROBIAL STEWARDSHIP IN INTENSIVE CARE: A RETROSPECTIVE COHORT STUDY

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Introductions & Objective

The implementation of antimicrobial stewardship programs (ASP) in intensive care units (ICUs) has increased in response to rising rates of antimicrobial resistance but data regarding their sustainability is lacking. This study aimed to evaluate long-term uptake of an ASP audit-and-feedback program along with potential predictors of stewardship suggestions and acceptance across a diverse ICU population.

Methods

We conducted a retrospective cohort study at Sunnybrook Hospital in Toronto, Canada evaluating ICU patients who received an ASP assessment between April 2010 and September 2019. We examined trends in suggestion and acceptance rates and identified patient-, infection-, and treatment-related characteristics associated with receiving an ASP suggestion and suggestion acceptance using multivariate logistic regression.

Results
The ASP provided 7749 antibiotic assessments over the study period, and made a suggestion to alter therapy in 2826 (36%). Factors associated with a higher likelihood of receiving a suggestion to alter therapy included longer hospital length of stay (OR 1.15 per day; 95% CI 1.00-1.32), admission to cardiovascular (1.37; 1.06-1.76) or burn surgery (1.88; 1.50-2.36) vs. general medicine, and preceding duration of antibiotic use >5 days (1.33; 1.10-1.60). Assessment of aminoglycosides (2.91; 1.85-4.89), carbapenems (1.93; 1.54-2.41), and vancomycin (2.71; 2.19-3.36) versus ceftriaxone were more likely to result in suggestions to alter therapy. The suggestion acceptance rate was 67% (1895/2826), which was stable throughout the study period. Admission to a level 3 ICU was associated with higher likelihood of acceptance of suggestions (1.50; 1.14-1.97). Factors associated with lower acceptance rates were admission to burn surgery (0.64; 0.45-0.91), treatment of pneumonia (0.64; 0.42-0.97 for community-acquired and 0.65; 0.44-0.94 for ventilator-acquired), unknown source of infection (0.66; 0.48-0.92), and suggestion types of “narrow spectrum” (0.65; 0.45-0.94), “change formulation (oral to intravenous or vice versa) of antibiotic” (0.42; 0.27-0.64), or “change agent of therapy” (0.63; 0.40-0.97) versus “change of dose”.

Conclusion
An ASP implemented over a decade resulted in sustained suggestion and acceptance rates. These findings support the need for a persistent presence of audit-and-feedback over time with more frequent suggestions to alter potentially nephrotoxic agents, increased efforts towards specialized care units, and further work approaching infectious sources that are typically treated without pathogen confirmation and identification.

Supported by
N/A
TIME-VARYING INTENSITY OF MECHANICAL VENTILATION AND MORTALITY IN PATIENTS WITH ACUTE RESPIRATORY FAILURE

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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 (∆P) 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 ∆P 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 ∆P 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 ∆P (cmH₂O) 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 ∆P 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
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.

Supported by: CIHR CGS-M award (CJ Yarnell), National Institutes of Health (K23-HL133489, R21-HL145506, PI Beitler, an Early Career Investigator award from the Canadian Institutes of Health Research AR7-162822 (EC Goligher), National Institute on Aging Beeson Career Development Award K08AG051184 (M Hua).
CLASSIFICATION OF COVID-19 VERSUS SEASONAL FLU AND COMMON COLD BY SYMPTOMS-BASED MACHINE LEARNING MODELS: A TOOL FOR COMMUNITY AND HEALTHCARE PROVIDERS
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Introduction and Objective: The COVID-19 shares many symptoms with seasonal flu and common cold making it difficult to differentiate from each other, which may result in unnecessary fear or/and cross-infection leading to cluster outbreak. We hypothesized that despite these similarities, COVID-19 presents a unique combination of symptoms that can be used to distinguish patients with COVID-19 from those with seasonal flu or common cold.

Methods: We retrospectively analyzed the medical records of 599 patients with confirmed COVID-19 and 832 patients with seasonal flu or common cold in Jiangsu Province, China. We used machine learning (XGboost) to train, test, and validate computational models based on demographics, body temperature, and 19 self-reported symptoms from each of these two cohorts.

Results: We established up to 500 training and testing models and found that the algorithm of 100 models is sufficient since there was no difference in the levels of sensitivity and specificity to classify the two cohorts of patients between 100 models and 500 models. Furthermore, the excellent classification performance of the 100 models was examined and supported by a repeated validation approach using a set of patients whose data were never seen in the training and testing models.

Conclusion: Our computational models, with unique combinatory patterns of symptoms, can be used to differentiate patients with COVID-19 infection from those with seasonal flu or common cold. These artificial intelligence (AI) models can form the basis for the development of a convenient screening tool online or on mobile devices for use by patients, healthcare providers, and policymakers for timely and effective decision-making.

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VIRTUAL
ART SLUTSKY
RESEARCH DAY

Interdepartmental Division of Critical Care Medicine
University of Toronto

Quality Improvement Abstracts
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.*
INTERVENTIONS TO IMPROVE INTERPROFESSIONAL BEDSIDE ROUNDS IN A PAEDIATRIC CRITICAL CARE UNIT
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Introduction & Objective
Communication errors are the leading root cause of preventable adverse events (AEs) in hospitals in the United States (1). Further, AEs occur in critical care units (CCUs) at nearly double the rate of general care. Patient care rounds are regularly scheduled meetings attended by the patient care team. They provide health care providers (HCPs) with the opportunity to review and discuss patient data, develop a shared mental model of the patient and make decisions regarding the care plan (2).

Rounds are the most important opportunity for interprofessional communication but are also complex. Several challenges impede effective communication during rounds such as frequent interruptions (3), misrepresentations of data (4) and misalignment in HCPs goals and objectives for attending rounds (5). While several CCU rounding best practices have been identified (2) to address barriers such as these, implementations of best practices have produced mixed results. Contextual factors must be taken into consideration before implementing best practices and interventions that have been successful elsewhere. By elucidating HCPs needs, and aligning intervention design to those needs, effective interventions can improve communication within CCUs. The overarching goal of this study was to elucidate HCPs rounding needs and to transform those needs into intervention(s) within a paediatric CCU.

Methods
To elucidate user needs, interview and survey data were collected from attending physicians, medical trainees (i.e., fellows and residents), nurse practitioners (NPs), registered nurses (RNs), respiratory therapists (RTs) and other interprofessional staff. An online intervention survey was also distributed to HCPs to collect rounding intervention ideas and to further implicitly elucidate needs. With a thorough understanding of stakeholders rounding needs, a participatory design approach (i.e., an approach that seeks to include both designers and users as active participants in the design process) (6) was taken to design interventions for improving morning rounds. A design team was created that included Human Factors specialists and representatives from all professions who attend rounds (i.e., attending physicians, medical trainees, NPs, RNs, RTs, dietitians, and pharmacists). A design training session and a series of three workshops were conducted with the design team to generate potential intervention ideas, and to select and prototype an intervention bundle for evaluation in future work.

Results
Collective and specific needs were elucidated from interview and survey data and grouped into themes. The main needs identified led to specific changes such as (1) to address the need for clear and appropriate content communicated at morning rounds, we redesigned the process such that within-discipline physician handover is conducted prior to and separate from morning rounds (currently physician handover is embedded into rounds) which enables the day medical trainee to present on rounds (instead of the overnight medical trainee who is the most sleep deprived person), (2) to address the need for more interprofessional team engagement, our redesign focuses on ensuring each team member is called upon to provide their patient specific input.

Conclusions
Results from study demonstrate that a participatory design approach can be taken to redesign rounds which is a complex process that involves multiple stakeholders with varying and sometimes conflicting viewpoints (5). Critical to the success of the participatory design approach, was a thorough understanding of user needs, which was enabled by the collection of interview and survey data. Future work will focus on simulation testing of the intervention bundle to evaluate its efficacy at addressing identified user needs prior to implementation into the CCU.
References


INTRODUCING A DELIRIUM SCREENING AND MANAGEMENT PROGRAM IN PAEDIATRIC CRITICAL CARE

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Introduction & Objectives

Paediatric delirium occurs in 17-25% of patients in the critical care unit, however, standardized routine delirium detection and management strategies were inconsistently applied in our PICU/CCCU. In order to align with best practice, our team implemented delirium screening with associated delirium management pathways for our paediatric and cardiac critical care patients (PICU/CCCU).

Methods

The SickKids Paediatric Delirium (SKPD) program is an education grounded, clinical focused intervention that is led by a cross-departmental, multidisciplinary working group. The initial 6 month program was conducted in a 41-bed quaternary care PICU/CCCU in a large, urban paediatric hospital. Over 330 nurses, physicians, and interdisciplinary team members participated. Clinician education involved in-class learning, interactive case studies, a self-directed e-learning module, and on-unit practice support. Post-education, nursing staff were surveyed to explore their experience of preparation to apply the components of the SKPD program.

Results

Seventy-five completed surveys had been returned at the time of this submission. Results show that 81.3% of nurses felt prepared to use the delirium pathways in their practice, 72% felt supported in their use of the pathways, 60% felt it is a practical/efficient strategy to manage delirium in the CCU, and 54.67% felt it is an effective strategy.

Conclusions

The SKPD was effective in preparing frontline clinicians to apply the delirium screening tools and management intervention. Ongoing awareness and training are needed to ensure staff continue to feel supported and prepared to use the pathways and see the clinical outcomes that illustrate that it is an effective strategy to detect and manage paediatric delirium.
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.

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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](image-url)
SBT process was mapped to shed light on potential barriers (figure 2).

Figure 2: Process Map

We carried out the following PDSA cycles:

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Plan</th>
<th>Do</th>
<th>Study</th>
<th>Act</th>
<th>Time Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lack of education surrounding SBT literature reduces the rates of SBT being performed</td>
<td>Interviewed RN/RT with patient case examples during huddles</td>
<td>General consensus that SBT is not an interdisciplinary responsibility and RT's were primarily responsible. RN's felt disengaged from this process</td>
<td>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</td>
<td>1 month</td>
</tr>
<tr>
<td>2</td>
<td>SBT timing with patient care routines (end of night shift) would reduce the initiation and completion of SBT's</td>
<td>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.</td>
<td>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.</td>
<td>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</td>
<td>10 days</td>
</tr>
<tr>
<td>3</td>
<td>SBT duration of 60 minutes affected RT workload and workflow, reducing SBT initiation</td>
<td>a. Reviewed hospital SBT policy b. reviewed literature on best practice</td>
<td>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</td>
<td>Changed SBT duration from 60 minutes to 30 minutes</td>
<td>10 days</td>
</tr>
<tr>
<td>4</td>
<td>There is inadequate documentation surrounding SBT screening and initiation</td>
<td>Review of data collection process, chart review, and shadowing of stakeholders</td>
<td>Chart review showed some discrepancies: #1 2 consecutive failed SBT, 3rd one omitted #2 patient was tracked #3 patient waiting for surgical airway #4 discrepancy in documentation. Difficult to find SBT documentation within RT and RN charting</td>
<td>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.</td>
<td>1 month</td>
</tr>
</tbody>
</table>
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.
**PREPARED: PEDIATRIC CRITICAL CARE EMERGENCY PREPARDNESS APPLICATION FOR REAL-TIME CAPACITY ASSESSMENT AND DEPLOYMENT DURING COVID-19 IN THE PROVINCE OF ONTARIO**

AR Lehr, AH Shevell, M Vargas-Gutierrez, A McCormick, G Annich

*Department of Critical Care Medicine, Hospital of Sick Children, University of Toronto*

**Introduction and objectives:** In the Province of Ontario there are currently 85 paediatric critical care beds which represents 2.4 beds per 100,000 children. From the perspective of efficiency, Critical Care Information System (CCIS) has become a key component of Ontario’s Critical Care Strategy for data collection, analysis and reporting. Furthermore, for communication purposes between hospital across the province, nurses and doctors continue to depend on telephone, email and various messaging services. Therefore, the current system in place does not allow for prompt communication and real-time assessment of bed capacity, human and material resources and transport capability which limits efficient allocation of scarce resources. With the SickKids expertise in web-based application development and collaboration from all pediatric hospitals in the province, our objectives are 1) to develop PREPARED with customization and integration into hospital systems; 2) to evaluate PREPARED; 3) to refine PREPARED.

**Methods:** This 3-year project will be divided in three phases. Phase I will consist of planning using an adequate sample of stakeholders needs assessment and development while testing its integrative capacity by measuring the accuracy between data source and data extracted. Phase 2 will consist of training participants with measures of participation rate and post-test performance, the validation with observational data on usability and the launching at SickKids. Similarly, phase 3 will consist of training, validation and launch in the four other collaborating hospitals. Health system performance will be assessed using real life and simulations database analysis and cost-effectiveness analysis balancing timeliness of care outcomes vs resource utilization, cost of PREPARED and cost of care. Finally, semi-structure interviews, focus groups and redcap survey will assess global user satisfaction.

**Expected Results:** PREPARED will integrate real-time information from various data sources such as hospital dashboard and CCIS to generate available resources in terms of personal protective equipment, invasive and non-invasive ventilator and ED, OR, PICU and WARD beds and ultimately will be able to suggest recommendations to optimize transfers. PREPARED will also allow sharing of resources and policies among hospitals. Furthermore, it will also compile historical data for ongoing performance analysis.

**Conclusion:** PREPARED, an emergency preparedness application, will offer real-time updates about surge capacity and resource availability which should optimize the response system in pandemic and mass casualty events among all five provincial paediatric critical care systems.
AN EVALUATION OF DIFFERENCES ACROSS COVID-19 PRE-PRINT RESEARCH STUDIES AND THEIR FINAL PUBLISHED FORMAT DURING THE COVID-19 PANDEMIC

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2- University Health Network/Sinai Health System International Fellowship Program
3- Division of Critical Care Medicine, Department of Medicine, Queens University

INTRODUCTION: The COVID-19 pandemic has emerged as one of the greatest challenges faced by the health care system. We have witnessed a rapid dissemination of data over the last 6 months. This data has been shared on various platforms including pre-prints. A pre-print is a completed research paper which has not yet undergone peer review but has been shared publicly. Benefits of pre-prints allow for timely release of results, credit for uncovering a finding first and feedback from the public. Sharing of COVID-19 data in the form of pre-print has allowed earlier access of potentially useful diagnostic, therapeutic and preventive strategies for COVID-19. It remains unclear the degree to which pre-prints may change from their original format to the final peer-reviewed publication in journals. Peer review of pre-prints may lead to minor modifications to major changes including re-analysis, reframing of study, or reporting on outcomes/ adverse events not previously available in the first draft.

OBJECTIVES: We wish to evaluate the degree to which pre-prints may be modified from their preliminary format posted to the final versions published.

METHODS: We are evaluating COVID-19 pre-prints published between January1, 2020-April 30, 2020. The pre-print platform of interest is Medrxiv (https://connect.medrxiv.org/relate/content/181). At the time of this study, a pre-print repository of COVID-19 studies was created by Medrxiv. We searched the pre-defined subspecialty categories of Respiratory Medicine, Intensive Care and Critical Care Medicine and Emergency Medicine. We included any COVID-19 pre-print observational or randomized studies of humans posted on the preprint website during the above time period. We then searched PubMed using the pre-print first author and keywords from the manuscript to identify if it was published in a medical journal (search planned up until June 30, 2020).

Our primary outcome of interest is change in the named primary or secondary outcomes of the study. Our secondary outcomes are any modification in the results of the primary or secondary outcomes, or change to the conclusions (graded as minor or major). We further categorize whether the totality of these changes lead to no, minor, moderate or significant implications to the interpretation of the study (definitions in Table 1). This study represents work in progress and our PubMed search up until May 31, 2020.

RESULTS: One-thousand, seven-hundred and fifty-eight COVID-19 pre-prints were posted between January 2020-April 30, 2020. A total of 115 were limited to the subspecialty areas of Critical Care (55), Respiratory (44) and Emergency Medicine (16). Forty-seven preprints fulfilled our inclusion criteria of human studies of COVID-19 within these subspecialty areas. Ten pre-prints were published at the time of our search. Median time to publication was 50 days (IQR 30-66). The mean impact factor of the journals was 17 (SD 5). Publications originated from China, US, Netherlands and Canada. All 10 pre-prints were observational studies. Eight of 10 pre-prints (80%) had a modification in their named primary outcome, results of the primary or secondary outcomes, or wording of the conclusions (Table 1) (1/10 study - named primary outcome modification, 3/10 studies - change in results of the primary or secondary outcomes, 6/10 studies- change to conclusions). Two studies demonstrated major changes to the conclusion (1 study removal of multivariable logistic regression result, 1 study removal of a recommendation of treatment). The implications of the changes were felt to be significant in 1 study (a recommendation for a treatment that the results did not support was removed). The implications of the changes were felt to be moderate for 2/10 studies.

CONCLUSIONS: Eighty percent of pre-prints published between pre-print posting and manuscript publication underwent modifications. Most of the changes were minor; however, the implications of these modifications were felt to be moderate or significant in 30% of the studies. This represents work in progress and the final PubMed search will be conducted on June 30, 2020. The sample of publications in this review likely represents a higher quality of pre-prints given the rapid time to publication
<table>
<thead>
<tr>
<th>STUDY</th>
<th>DESIGN</th>
<th>JOURNAL</th>
<th>NUMBER OF PATIENTS</th>
<th>NAMED OUTCOMES MODIFIED</th>
<th>PRIMARY OUTCOME RESULTS MODIFIED</th>
<th>SECONDARY OUTCOME RESULTS MODIFIED</th>
<th>CONCLUSIONS</th>
<th>IMPLICATIONS of CHANGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor associated with hospital admission and critical illness among 5,279 people with coronavirus disease 2019 in New York City: Prospective cohort study</td>
<td></td>
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<tr>
<td>Petrelli et al.</td>
<td>Prospective cohort study</td>
<td>BMJ</td>
<td>PP 4,103 Pub 5,279</td>
<td>Yes (Primary)</td>
<td>Yes (*attributable to greater sample size)</td>
<td>Yes (factors associated with mortality changed on MV analysis)</td>
<td>Minor modifications</td>
<td>Moderate*</td>
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<td>COVID-19 patients exhibit less pronounced immune suppression compared with bacterial septic shock patients</td>
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<td>Kox et al.</td>
<td>Prospective cohort study</td>
<td>Critical Care</td>
<td>PP 24 Pub 24</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No modifications</td>
<td>None</td>
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<tr>
<td>ICU and ventilator mortality amongst critically ill adults with coronavirus disease 2019</td>
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<tr>
<td>Auld et al.</td>
<td>Prospective cohort study</td>
<td>Critical Care Medicine</td>
<td>PP 217 Pub 217</td>
<td>No</td>
<td>Yes (*attributable longer follow up time period)</td>
<td>No</td>
<td>Minor modifications</td>
<td>Minor</td>
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<tr>
<td>Clinical characteristics of coronavirus disease 2019 in China</td>
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<td>Guan et al.</td>
<td>Retrospective cohort study</td>
<td>NEJM</td>
<td>PP – 1,099 Pub – 1,099</td>
<td>No</td>
<td>No (*not modified but articulated better)</td>
<td>No</td>
<td>Major modifications</td>
<td>Moderate**</td>
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<tr>
<td>Comorbidity and its impact on 1,590 patients with COVID-19 in China: A Nationwide Analysis</td>
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<tr>
<td>Guan et al.</td>
<td>Retrospective cohort study</td>
<td>European Journal of Respirology</td>
<td>PP – 1,590 Pub – 1,590</td>
<td>Yes (Secondary)</td>
<td>No</td>
<td>Yes</td>
<td>Minor modifications</td>
<td>None</td>
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<td>Clinical features and short-term outcomes of 221 patients with COVID-19 in Wuhan, China</td>
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<tr>
<td>Zhang et al.</td>
<td>Retrospective cohort study</td>
<td>Journal of Clinical Virology</td>
<td>PP – 221 Pub – 221</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Minor modifications</td>
<td>None</td>
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<tr>
<td>ACE-2 Expression in the Small Airway Epithelia of Smokers and COPD Patients: Implications for COVID-19</td>
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<td>Leung et al.</td>
<td>Prospective cohort study</td>
<td>European Respiratory Journal</td>
<td>PP .42 Pub – 42</td>
<td>No</td>
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<td>Minor modifications</td>
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<td>Study Title</td>
<td>Study Type</td>
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<td>Publication</td>
<td>Modifications</td>
<td>Implications</td>
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<td>Association of diabetes mellitus with disease severity and prognosis in COVID-19: A retrospective cohort study</td>
<td>Zhang et al.</td>
<td>Retrospective cohort study</td>
<td>Diabetes Research and Clinical Practice PP – 258 Pub – 258 No</td>
<td>No</td>
<td>Minor modifications</td>
<td></td>
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<tr>
<td>Adjuvant Corticosteroid Therapy for Critically Ill Patients With COVID-19</td>
<td>Lu et al.</td>
<td>Retrospective cohort study</td>
<td>Critical Care PP - 244 Pub - 244 No</td>
<td>No</td>
<td>Major modifications Significant***</td>
<td></td>
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<td>Emergency Medical Services resource capacity and competency amid COVID-19 in the United States: Preliminary findings from a national survey</td>
<td>Gibson et al.</td>
<td>Prospective survey study</td>
<td>Heliyon PP Not provided Pub Not provided N/A</td>
<td>N/A</td>
<td>No modifications</td>
<td></td>
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</table>

*higher mechanical ventilation mortality rates, different factors associated with mortality on multivariable logistic regression analysis
**removal of multivariable logistic regression analysis demonstrating factors associated with worse outcomes
***preprint suggested consideration of corticosteroid use despite analysis suggesting no benefit and potential harm with longer exposures, this was removed in published version

Minor modifications of conclusions: minor changes to wording
Major modification of conclusions: results omitted or added

Implications: Minor (differences minor and likely not results in major practice changes ), Moderate (differences potentially practice changes ie. update in statistics, change in risk factors associated with outcome), Significant (differences would have resulted in major practice changing behaviour)

BMJ British Medical Journal; NEJM New England Journal of Medicine; N/A – not available; PP – pre-print; Pub – PubMed;
EFFECT OF THERAPEUTIC INTERVENTIONS ON LONG TERM MORTALITY OF PATIENTS WITH ARDS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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2: Department of Anesthesiology, Graduate School of Medicine, University of Tokyo
3: Department of Anesthesia and Pain Medicine, The Hospital for Sick Children
4: The Hospital for Sick Children Research Institute, Peter Gilgan Centre for Research and Learning
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 PaO2/FiO2 ratio less than 150 mmHg and no evidence of effect modification based on PaO2/FiO2 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
PAEDIATRIC NURSE BURNOUT: A REVIEW OF THE LITERATURE

L. Buckley¹, W. Berta², K. Cleverley³, C. Medeiros⁴, K. Widger⁵
¹The Hospital for Sick Children, Department of Critical Care Medicine, Toronto, ON, Canada, ²University of Toronto, IHPME, Toronto, ON, Canada, ³University of Toronto, Lawrence S. Bloomberg Faculty of Nursing, Toronto, Canada, ⁴University of Toronto, Nursing, Toronto, Canada, ⁵University of Toronto, Lawrence S. Bloomberg Faculty of Nursing, Toronto, Canada

Introduction & Objectives

Burnout in paediatric nurses may be unique from adult care nurses because of the specialized nature of providing care to children who are typically seen as a vulnerable population, the high potential for empathetic engagement, and the inherent complexities in the relationships with families. The aim of this study was to investigate, among paediatric nurses: i) the prevalence and/or degree of burnout ii) the factors related to burnout iii) the outcomes of burnout and iv) interventions to prevent and/or mitigate burnout.

Methods

A scoping review was performed according to PRISMA-ScR guidelines. CINAHL, EMBASE, MEDLINE, PsycINFO, ASSIA, and The Cochrane Library were searched to identify relevant quantitative, qualitative and mixed-method studies on paediatric nurse burnout.

Results

Our search resulted in seventy-eight studies that were analyzed. We found burnout is prevalent in paediatric nurses, with mean reported raw subscale scores: Emotional Exhaustion=22.45 (SD=6.54) (moderate), Depersonalization=6.95 (SD=3.38) (moderate), Personal Accomplishment=29.15 (SD=11.48) (high). Directed content analysis indicated a number of factors impacting burnout including: nurse demographics; work environment; and work attitudes. Similarly a number of outcomes of burnout were identified including: nurse retention; nurse wellbeing; patient safety; and patient-family satisfaction. There was little evidence of effective interventions to address paediatric nurse burnout.

Conclusions

Paediatric nurse burnout is prevalent; there are attitudinal and environmental factors that may be addressed through interventions by nursing schools, nursing management, healthcare organizations, and professional associations.
LONG-TERM RISK OF CARDIOVASCULAR EVENTS FOLLOWING HOSPITALIZATION FOR SEPSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES INCLUDING 1,695,975 INDIVIDUALS

Authors: LB Kosyakovsky1*, F Angriman2*, E Katz3, NKJ Adhkari2, LC Godoy4,5, DT Ko6, DS Lee6,7, RS Rosenson8, ME Farkouh4,5,7, ME Detsky9, L Bibas10, and PR Lawler4,5,7.

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*These authors contributed equally.

Introduction: Sepsis results in persistent dysregulated inflammation, coagulation, and metabolism, which may contribute to increased cardiovascular disease (CVD) risk. There is an incomplete understanding of whether sepsis is associated with higher long-term risk of CVD. We conducted a systematic review and meta-analysis to determine the association between hospitalization for sepsis and subsequent long-term CVD events.

Methods: MEDLINE, Embase, Cochrane Controlled Trials Register, and Cochrane Database of Systematic Reviews were searched from inception to May 2020 to identify observational studies of adult sepsis survivors (defined by ICD codes or consensus definitions) measuring long-term CV outcomes. The primary outcome was a composite of myocardial infarction (MI), CV death, and stroke. Random-effects models estimated the pooled cumulative incidence of CV events and adjusted hazard ratios of CV events relative to hospital or population controls. Where reported, odds ratios were included as risk ratios under the assumption of <10% incidence in non-septic controls, and risk ratios were taken as hazard ratios under the assumption of no censoring. Outcomes were analyzed at maximum follow-up (primary analysis) and stratified by time (<1 year, 1-2 years, and >2 years) since sepsis.

Results: Of 14,927 records screened, 25 studies (22 cohort studies, 2 case-crossover studies, and 1 case-control) involving 1,695,975 individuals were included. The pooled cumulative incidence of CVD events was 9% (95% CI; 5-14%). Sepsis was associated with an increased risk (adjusted HR 1.51, 95% CI 1.28-1.78) of CVD events at maximum follow-up; between-study heterogeneity was substantial (I²=97.6%). There was no significant difference in the degree of increased risk when comparing studies utilizing population-based and hospital-based controls. Significantly elevated risk was observed up to 5 years following sepsis.

Conclusions: Sepsis survivors experience an approximately 50% increase in risk of late CVD events, which may persist for years following the initial episode. These results highlight a potential unmet need for early cardiac risk stratification and optimization in sepsis survivors.
RESIDENT EPA ASSESSMENT – IS SIMULATION A VALID TOOL FOR ASSESSING RESIDENT ENTRUSTABILITY IN ACUTE CARE SCENARIOS?

Principle Investigators: A Leal Barceló, CAM Anderson, B Mema, H Christian

Affiliations: Department of Critical Care Medicine, The Hospital for Sick Children, University of Toronto

Introduction and Objective: Entrustable Professional Activities (EPAs) are objective assessments of the competence and abilities of Paediatric Residents (PR). There are five EPAs mapped to PICU (table 1).

According to a recent paper by Schumacher et. al in JAMA, the EPA’s mapped to PICU (Resuscitation and Stabilization) are amongst those that require the most supervision to reach an entrustable level (1). However, clinical exposure to these emergency events are low (2,3,4). The most frequent and reliable exposure PR get to these type of scenarios is in simulation.

Currently, many institutions use simulation as a mechanism to expose PR to critically ill patients and assess them (5). Although the role of simulation in training seems to be clearly beneficial in many fields (6,7), there is limited validity evidence about the use of simulation to assess acute care skills. The purpose of our study is to collect validity evidence for use of simulation to assess the Resident’s ability to resuscitate critically ill patients and conduct critical conversations as outlined in their Core of Discipline EPA: EPA COD2&7. If simulation is a valid assessment tool, then it may be used as a formal part of the critical care rotation to supplement the infrequent opportunity for PR to take the lead in real-life acute care scenarios.

Methods:
- **Study Design:** Validity Study.
- **Participants:** PR rotating through the PICU during Academic year 2020-2021.
- **2 simulations each PR. Scenarios will be developed by the principle investigators and reviewed with senior faculty to ensure accuracy. Varied monthly.**
- **Data Collection/Resident Assessment:** PR rotating through PICU will have 2 simulations/block. Each simulation will be assessed using the EPA milestones on a 5-point scale: 1 (requires intervention) to 5 (excellent), Minimum Passing Score of 4 indicates that the PR is autonomous at the clinical activity
- **Data Analysis:** Kane’s framework for Assessing Validity (Figure 1)
  - **Proposed Decision:** Simulation may be used to assess the entrustability of PR to autonomously resuscitate a paediatric patient or effectively communicate life altering news
  - **Hypothesis:** Simulation provides a valid assessment of PR performance in acute situations
  - **Testing Assumptions:**
    - **Scoring:** (from observation to a score) 2 simulation scenarios/PR assessed by EPA/milestone framework. Raters will be trained
    - **Generalization:** (from one score to the universe of scores) Assessment of inter-rater variability using Generalizability theory for reliability and creation of decision studies
    - **Extrapolation:** (from test score to real life score) Correlation of Simulation scores with ITER and EPA’s completed from observed clinical events in real-life,
    - **Implications:** Assuming Simulation is accurate and representative, it could be used as a tool to determine the abilities of Residents to act autonomously in situations requiring acute management/resuscitation. This could be determined with long-term follow up of PR study participants.

Results: Project is currently in the development phase and awaiting REB approval. As such, results are unavailable.

Conclusions: The strength of the validity evidence we are able to collect will depend on the results of the correlation between ITER, real clinical EPA scores, and the simulation EPA scores from our study. If there is enough validity evidence to conclude that simulation provides a valid assessment of critical care EPAs then it may be useful to incorporate simulation into core residency rotations in order to provide an adequate opportunity for assessment.
Table 1

<table>
<thead>
<tr>
<th>EPA COD-2</th>
<th>Resuscitating and stabilizing critically ill neonates/infants, children, and adolescents</th>
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<tbody>
<tr>
<td>EPA COD-3</td>
<td>Managing acute illness in neonates/infants, children and adolescent</td>
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<tr>
<td>EPA COD-4</td>
<td>Managing episodic longitudinal care of infants/children/adolescents with increased complexity</td>
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<tr>
<td>EPA COD-6</td>
<td>Discharging, handing over, and transferring the care of complex patients</td>
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<tr>
<td>EPA COD-7</td>
<td>Communicating with patients and families in complicated/complex situations</td>
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</table>

Figure 1
REFERENCES:


PREPAREDNESS THROUGH SIMULATION: TEACHING PEDIATRIC PROTECTED CODE BLUE DURING COVID-19 PANDEMIC

AH Shevell¹, AR Lehr¹, M Vargas-Gutierrez¹, S Dunbar², G Annich¹

¹Department of Critical Care Medicine, University of Toronto
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Introduction & Objective: In January 2020, the World Health Organization (WHO) declared the outbreak of the novel coronavirus (COVID-19) a public health emergency of international concern. The resuscitation of a patient under investigation (PUI), called a “Protected Code Blue,” requires healthcare providers to adopt practices and precautions to ensure they are meeting the highest standard of care, while minimizing risk of exposure to providers. We aimed to use high-fidelity in-hospital interdisciplinary simulation to train healthcare providers and assess and improve our current response system to the emergency management of COVID-19 pediatric patients.

Methods: In a single quaternary pediatric hospital, simulations of Protected Code Blue involving multidisciplinary participants were conducted by a simulation and resuscitation educator and content experts, including intensive care physicians, chief residents and an occupational health nurse. Clinical practice guidelines were developed using a two-step method: first, using the current evidence in the literature and second, by identifying barriers and solutions from simulation debrief sessions.

Results: We conducted five simulations from March 4, 2020 to March 13, 2020, involving seventy-six participants. Themes of barriers and solutions within the current response system were grouped in four main categories: communication and team organization, material organization, physical space organization and knowledge gaps. The following teaching tools were developed and disseminated to healthcare providers: Just-in-Time Training document, poster and video highlighting Protected Code Blue practice guidelines within the critical care unit and hospital-wide.

Conclusion: Simulation served as a valuable approach to assess and optimize our institution’s readiness for the COVID-19 pandemic. We strongly recommend implementing similar in-hospital training exercises in other institutions to better prepare for infectious pandemic or other health crises.
Electroencephalography in the Acute Care Environment: A Systematic Review of Educational Initiatives for Non-Experts

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Introduction and Objectives: Formal interpretation of electroencephalography (EEG) in acute-care units is often performed by trained experts, including neurophysiologists and epileptologists. Owing to the rapid expansion of EEG, delays in formal interpretation are often encountered, with possible implications for patient management. Numerous studies have investigated the role of educational programs to enable non-experts (e.g. nurses and residents) to recognize EEG patterns at the bedside. However, the overall content, structure, duration, and efficacy of these EEG training programs remains unknown. We therefore conducted a systematic review of EEG educational programs for non-experts in adult and pediatric/neonatal acute-care settings (emergency departments (ED) and intensive care units (ICU)). Our primary outcome was to describe important similarities, differences, and overarching themes among training programs.

Methods: We searched for studies published on MEDLINE, Embase, Cochrane central, CINAHL, and Web of science. To be considered for inclusion, studies were required to present sufficient details of their educational program, including (to the extent possible) content covered, program structure and duration, assessment methods, and trainee experience. Randomized control trials, cohort studies, and descriptive studies were all considered for inclusion. Data was presented in a qualitative manner and organized by theme.

Results: Our search yielded a total of 7,034 studies, of which 5,626 were screened. Twenty-six full-length studies met our predefined inclusion criteria. Studies were all published in English and included 23 cohort studies, two descriptive studies, and one RCT. The majority of studies were single center in design and originated in the USA. One study was performed in the ED, 15 in adult ICUs, four in pediatric ICUs, and six in neonatal ICUs. The majority of EEG training programs were geared towards ICU nurses (16 studies), followed by ICU physicians, and ICU fellows. Most training programs focused on quantitative or processed forms of EEG rather than short/intermittent EEG. By far the most common training program was for amplitude-integrated EEG (14 studies) followed by color density spectral array (6 studies). EEG education programs involved a mix of large group didactic lectures, small group sessions, and self-learning or one-on-one review with EEG experts. In 16 studies, the overall length of the training program was one day or shorter. Trainee response was positive in the subset of studies reporting this variable.

Conclusion: The majority of EEG training programs involve ICU nurses, quantitative EEG, and are relatively short in duration. Such data could inform future EEG curriculum design for non-experts in acute-care settings.