# World Journal of
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# Artificial intelligence and computer simulation models in critical illness

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## Abstract

Widespread implementation of electronic health records has led to the increased use of artificial intelligence (AI) and computer modeling in clinical medicine. The early recognition and treatment of critical illness are central to good outcomes but are made difficult by, among other things, the complexity of the environment and the often non-specific nature of the clinical presentation. Increasingly, AI applications are being proposed as decision supports for busy or distracted clinicians, to address this challenge. Data driven "associative" AI models are built from retrospective data registries with missing data and imprecise timing. Associative AI models lack transparency, often ignore causal mechanisms, and, while potentially useful in improved prognostication, have thus far had limited clinical applicability. To be clinically useful, AI tools need to provide bedside clinicians with actionable knowledge. Explicitly addressing causal mechanisms not only increases validity and replicability of the model, but also adds transparency and helps gain trust from the bedside clinicians for real world use of AI models in teaching and patient care.

**Key words:** Artificial intelligence; Digital twin; Critical illness; Predictive enrichment; Causation; Simulation models

**Core tip:** Widespread implementation of electronic health records coupled with increased

computer power has led to the increased use of artificial intelligence and computer modeling in clinical medicine. To be clinically useful, artificial intelligence models need to be built on accurate data, take into consideration causal mechanisms, and provide actionable information at the point of care.

## INTRODUCTION

The complex nature of critical illness calls for an exploration of alternative approaches to assist clinicians in their timely diagnosis and management. Artificial intelligence (AI) applications have transformed various human domains from economics to traffic and have recently been introduced into health care.

## AI IN HEALTH CARE

Widespread implementation of electronic health records (EHRs) has led to the increased use of AI and computer modeling in clinical medicine. The hope is that these techniques will prove superior to traditional epidemiologic and statistical approaches and will unlock insights that lead to the development of new treatment recommendations and prediction models. AI can be defined as the field of computer science that enables computers to perform the human cognitive tasks[1]. The interest in AI and systems science methodologies in the research community has grown rapidly in recent years[2]. Specific AI applications of interest to critical care include machine and deep learning algorithms, "in silico" simulation models, and "digital twins".

### Machine learning

Machine learning (ML) is an application of AI that develops statistical analysis models using computational technologies applied to big data[3]. The following learning techniques could be used: (1) Supervised learning techniques include but are not limited to linear regression, decision trees, and Naive Bayes. The models developed based on these are normally used for anomaly detection with the use of algorithm approximating a known output with a higher accuracy from a labeled data set, for example: Electrocardiogram interpretation by the automated machine or detection of a lung nodule from a chest X ray or a CT scan based on pattern recognition[4,5]. The aim of models developed using this technique is to decipher rules and latent relationships within data. "Support Vector Machine" is an example of supervised ML algorithm which is used for both classification and regression challenges and give a different dimension to the ensemble models. They are crucial in cases which require high predictive power but these algorithms are hard to visualize due to the complexity in formulation; (2) Unsupervised learning: Unsupervised ML models are developed using clustering techniques which includes segmenting data by some shared attributes, detecting anomalies that do not fit to any group and simplifying datasets by aggregating variables with similar attributes. The main goal is to study and determine the intrinsic and often hidden structure of the data. These models use algorithms on unlabeled data with no outputs to predict but are exploratory and intend to find naturally occurring patterns within the data[6]. This technique can be condensed in two major types of problems that unsupervised ML models try to solve, clustering and dimensionality reduction; (3) Semi-supervised learning uses a dataset with unlabeled as well as labeled data to increase the learning precision and appropriate prediction of label function. Further the model is trained and retrained with the estimated labels from the previous step[7]. These semi-supervised ML models are commonly used in medicine such as in voice recognition (medical dictation applications), data mining, and video surveillance (used in e-ICUs)[8,9]; and (4) Reinforcement learning: Reinforcement ML algorithms learn by observing the result of an action taken by the algorithm and applying a similar algorithm where the data are limited or missing[10]. The algorithm iteratively learns from previous response (reward or penalty) and acts with a goal to receive maximum reward in the future.

### Deep learning

Deep learning (DL) refers to the automatic determination and processing of the parameters in a network, on the basis of experience. DL is a ML technique that is designed with multiple layers of neurons, including input and output layers, and so-called "hidden layers"[11]. This idea of hidden layers (neural network) is inherited from a popular engineering and cognitive science topic since the 1980s[12,13]. The input data is passed through the layers, and the complexity of output function increases from layer to layer. In the recent past, the use of DL models in medicine has introduced the idea of data analytic modeling from expert-driven feature to data-driven feature. Large and complex databases (with longitudinal event sequences and continuous data points) have made it possible to train complex DL models. These models developed from large and complex databases with multiple hidden neural layers provide limited transparency to the users and are aptly described as "black box" models. The user of "black box" AI knows inputs and understands outcomes of the model, but how the output value was generated is unknown. These DL models are most commonly utilized in the field of medicine for following categories of analytical tasks: (1) Disease detection or classification, where DL models are used to detect a specific disease(s) with the help of data mining from EHR[14]; (2) Sequential prediction of clinical events, where DL models predict future clinical events learning from the previous event sequences[15]; (3) Concept embedding, where DL models derive feature representation of clinical concepts algorithmically from the EHR data[16]; (4) Data augmentation, where DL models create realistic data elements for the use in clinical research or otherwise based on real EHR data[17]; and (5) EHR data privacy, where DL models derive techniques to protect patient EHR privacy by de-identification[18].

In simpler words, it would be easier to understand the relationship of AI, ML and DL by visualizing them as 3 concentric circles with DL being the innermost circle which is a subset of ML. ML in turn is a part of the greater all-encompassing concept of AI (thus AI fits inside both ML and DL).

### In silico simulation models and digital twins

"In silico" experimentation or simulation involves mathematical and computer based exemplifications to construct models[19]. Computer based experiments can then be carried out to conduct investigations of hypotheses in a virtual environment without actually involving human subjects. The Archimedes model illustrates the use of mathematical techniques to reproduce the complex nature of disease[20]. The core model is a set of ordinary differential equations, which represent the physiologic, clinical, and social pathways that are relevant to diabetes and diabetes-related complications. The use of causal pathways (*i.e.*, Disease Acyclic Graphs) distinguishes Archimedes from conventional, associative AI models[17]. Digital twin is a type of simulation model that combines current data from the object with its simulation model to enhance insight and assist with decision making[21,22]. The digital twin has proven to be effective in industry and transportation, such as gas turbine fleet, rail fleet, and production line. The advantage of this approach is the ability to get the representative operational updates from the real-world object that allows model to give an accurate prediction and to give the feedback to the real-world state directly to make operational changes.

## AI IN CRITICAL CARE

Critical illness offers a number of advantages for the developers of AI models compared to chronic disease, such as the availability of large quantities of qualitative and quantitative data and relatively short trajectory of critical illness to a stable outcome. This results in the possible iterative testing of hypotheses raised by simulation modeling in independent patient cohorts. For example, recently, a group of computer scientists and clinicians from the Imperial College, London, United Kingdom used an AI approach to develop a decision support model aptly named AI Clinician[23]. Using reinforcement learning (RL), AI Clinician is designed to assist with optimal treatment interventions for sepsis in real-time. It was developed and validated in two clinical databases: MIMIC-III and e-ICU research database[24,25]. Similar methodology has recently been applied to the continuous prediction of acute kidney injury (AKI)[26]. Tools that are developed based on the current AI models have low specificity in predicting the intervention points for real life sepsis patients. This is one of the major obstacles faced by AI models for treating the critically ill patients. While most of the currently devised models are based on the retrospective data from the data banks, the accuracy and performance of these algorithms on real-time data

may not achieve the same level. Patient privacy concerns and question of responsibility may preclude rapid integration of AI models into current ICU practice. High heterogeneity of patients and their specific needs could be easily illustrated by managing a patient on mechanical ventilation. "Intelligent" ventilation modes may do more harm than good without thorough supervision by a specialist.

The above examples highlight a new approach to predictive and prognostic analytics in the area of critical care. Although these models yielded clinically plausible results, major shortcomings limit inferences and use in the real world of bedside clinical medicine. First, built exclusively from retrospective EHR data, the models suffer from missing data and imprecise timing (back charting) particularly during the initial, golden hours of critical illness. Not unlike retrospective studies using traditional methods (logistic regression), the output results are only hypothesis raising and require prospective confirmation.

## PROGNOSTIC (ASSOCIATIVE) *VS* PREDICTIVE (ACTIONABLE) AI MODELS

While offering marginal improvements in performance over traditional epidemiological or logistic regression approaches, associative AI models generally underperform in the live clinical setting and struggle to breach the threshold of usefulness for most clinicians[27]. Even accurate prognostic enrichment (classifying patients with high or low likelihood of death or AKI) is of limited value to the bedside clinician. For example, the prediction model of AKI does not provide any predictive enrichment with regards to potential intervention[26]. For example, will my patient benefit from a red cell transfusion, or continuous *vs* intermittent renal replacement?

Predicting the risk *vs* the benefit of a particular treatment (*i.e.*, actionable AI) is more difficult. Differences between associative and inquisitive/actionable AI are highlighted in Table 1. In contrast to "black box" associative AI, actionable AI models should explicitly address causal relationships[28]. Directed acyclic graphs – (DAG) approach has been increasingly used to address causal relationships in different research domains[29]. DAGs facilitate integration of expert knowledge into data driven AI models and are well suited for building advanced AI algorithms and simulation models.

Bayesian networks are DAGs whose nodes represent variables in the Bayesian sense: They may be observable quantities, latent variables, unknown parameters or hypotheses. Edges represent conditional dependencies; nodes that are not connected (no path connects one node to another) represent variables that are conditionally independent of each other. Each node is associated with a probability function that takes, as input, a particular set of values for the node's parent variables, and gives (as output) the probability (or probability distribution, if applicable) of the variable represented by the node. Directed acyclic graphical model is a probabilistic graphical model (a type of statistical model) that represents a set of variables and their conditional dependencies – also known as the Bayesian network Model.

Unidirectional arrows of DAGs are based on known causal effects (and prior knowledge) (Figure 1). DAGs enable clear representation and better understanding of the key concepts of exposure, outcome, causation, confounding, and bias. DAGs are built as simple integers of physiology as a basis to building complex patterns for seamless functionality of a simulation model and AI application. One of the advantages of using multiple basic DAGs to build a complex model is that, the model can be easily disassembled as individual components (DAGs) to ensure that the complex model can be better understood and refined as necessary.

## CONCLUSION

In a complex critical care environment clinicians are challenged with making decisions with a high degree of uncertainty under time constraints. Data driven associative AI models hold promise for better prognostication and to augment the diagnostic process but thus far have not been proven useful for bedside clinicians. Transparency of the model in terms of analytics and algorithms is important for patient safety and to earn the trust of the treating clinician[30]. Actionable AI models are more challenging to build and require explicit consideration of causal mechanisms. Accurate prediction of the response to treatment or intervention without exposing the patients to potential risks is an ultimate AI challenge for the benefit of patient and clinicians alike.

**Table 1 Differences between associative artificial intelligence and actionable artificial intelligence models**

| Models based on associative artificial intelligence | Models based on actionable artificial intelligence |
| --- | --- |
| These applications are built using available historical public or institutional data repositories[26,31,32]. | These applications are built more often on the prospectively collected data points, predicting risk *vs* benefit of a particular treatment or intervention[17,30,33,34]. |
| Almost always based on retrospective data[35,36]. | Developed using the data points that are collected prospectively in real-time[30,34]. |
| Purely data driven associative models often without explicit consideration of causal pathways[37-39]. | These models are developed with an understanding based on the underlying causal pathways, therefore providing greater clinical utility and accuracy[40-42]. |
| *Representative examples:* Development and validation of a data driven tool to predict sepsis based on vital signs by Mao *et al*[43]. Provides no actionable benefit to the bedside clinician. Similarly, a model developed to predict AKI in a patient based on retrospectively collected dataset from electronic health records by Tomasev *et al*[26]. The model was associated with high false positive alerts (2 false positive alerts for each true alert). | *Representative examples*: Improving the safety of ventilator care by avoiding ventilator-induced lung injury. Electronic algorithm based on near real-time data and notification of bedside providers giving actionable information, developed by Herasevich *et al*[33]. Artificial neural network based model developed for forecasting ICP for medical decision support, by Zhang *et al*[42]. This model provided actionable treatment planning for patients based on the predicted future trends of ICP. |

AKI: Acute kidney injury; ICP: Intracranial pressure.



**Figure 1 Directed acyclic graph of acute brain failure.** Orange boxes: Concepts; Orange solid border: Actionable clinical points; Orange interrupted border: Semi-actionable clinical points. GCS: Glasgow coma scale; MAP: Mean arterial pressure; Glu: Serum glucose; Mg: Serum magnesium; Ca: Serum calcium; Meds: Medications; HR: Heart rate; BP: Blood pressure; Focal Def: Focal neurological deficits; ICP: Intracranial pressure; $NH_3$: Ammonia; Na: Serum sodium; Hb: Serum hemoglobin; BUN: Blood urea nitrogen; Osmo: Serum osmolality; TSH: Thyroid stimulating hormone; $CO_2$: Serum carbon dioxide; CPP: Cerebral perfusion pressure; ABI: Acute brain injury; CAM: Confusion assessment method for intensive care unit.

# ACKNOWLEDGEMENTS

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**Retrospective Study**

# Hypotension after intensive care unit drop-off in adult cardiac surgery patients

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## Abstract

**BACKGROUND**
Hypotension is a frequent complication in the intensive care unit (ICU) after adult cardiac surgery.

**AIM**
To describe frequency of hypotension in the ICU following adult cardiac surgery and its relation to the hospital outcomes.

**METHODS**
A retrospective study of post-cardiac adult surgical patients at a tertiary academic medical center in a two-year period. We abstracted baseline demographics, comorbidities, and all pertinent clinical variables. The primary predictor variable was the development of hypotension within the first 30 min upon arrival to the ICU from the operating room (OR). The primary outcome was hospital mortality, and other outcomes included duration of mechanical ventilation (MV) in hours, and ICU and hospital length of stay in days.

**RESULTS**
Of 417 patients, more than half (54%) experienced hypotension within 30 min upon arrival to the ICU. Presence of OR hypotension immediately prior to ICU transfer was significantly associated with ICU hypotension (odds ratio = 1.9; 95% confidence interval: 1.21-2.98; $P < 0.006$). ICU hypotensive patients had longer MV, 5 (interquartile ranges 3, 15) *vs* 4 h (interquartile ranges 3, 6), $P = 0.012$. The patients who received vasopressor boluses ($n = 212$) were more likely to experience ICU drop-off hypotension (odds ratio = 1.45, 95% confidence interval: 0.98-2.13; $P = 0.062$), and they experienced longer MV, ICU and hospital length of stay ($P < 0.001$, for all).

*CONCLUSION*
Hypotension upon anesthesia-to-ICU drop-off is more frequent than previously reported and may be associated with adverse clinical outcomes.

**Key words:** Hypotension; Cardiac surgery; Intensive care; Postoperative care; Care transfer; Drop-off

**Core tip:** Hypotension is a frequent complication in adult cardiac surgery patients upon intensive care unit admission. This complication has been anecdotally called "anesthesia drop-off syndrome" and we decided to study this retrospectively. Our results suggest that this complication is more frequent than previously reported and that it may be associated with adverse outcomes.

## INTRODUCTION

Perioperative hypotension is one of the most common complications after cardiac surgery and this may adversely affect clinical outcomes[1-5]. It is frequently encountered upon intensive care unit (ICU) admission, where patients become hypotensive in the immediate post-operative period, shortly after the arrival from the operating room (OR). This has been anecdotally termed "anesthesia drop-off syndrome". However, data is limited in the literature regarding the actual prevalence of hypotension that develops shortly after the transfer of patients to the ICU after cardiac surgery. One study evaluated the occurrence of hemodynamic instability in the first 2 h post cardiac surgery and the most common complication was found to be hypotension, occurring in 34% of the patients after admission to the ICU[6]. Hypotensive patients usually require administration of vasopressor boluses prior to or during the transfer from the OR to the ICU as a temporizing measure. The hypotension and necessity for use of vasopressors have been previously associated with increased hospital length of stay (LOS) as well as mortality, relative to the patients who maintained hemodynamic stability[7-9].

Given the proposed discrepancy between the clinical occurrence and limited data on rate of hypotension starting shortly after the anesthesia to ICU transfer, we aimed to evaluate its prevalence and also how this may relate to the pertinent clinical outcomes. We hypothesized that the occurrence of initial hypotension in the ICU is more frequent complication among post-cardiac surgery ICU patients than previously reported and that patients who experience this complication will have more adverse clinical outcomes. We also aimed to better assess the association between the occurrence of initial hypotension in the ICU and the use of vasopressor bolus administered immediately prior to or during the transfer from the OR to the ICU.

## MATERIALS AND METHODS

We conducted a retrospective study of adult patients undergoing cardiac surgery at a tertiary academic medical center in the United States in the 2-year period (January 1, 2015 to December 31, 2016). We excluded patients who underwent cardiac transplantation or a combination of other solid organ transplantation and the cardiac surgery. The study protocol was approved by the Mayo Clinic Institutional Review Board as a minimal risk study, therefore the need for informed consent had been waived.

The primary independent variable was the development of hypotension within the first 30 min upon transfer from the OR ("ICU hypotension"). As there is no single, generally accepted, definition of hypotension[10] we used one of the common

definitions used in biomedical research: A systolic blood pressure < 90 mmHg or mean arterial pressure < 65 mmHg per arterial catheter tracing. We abstracted demographic and baseline characteristics, comorbidities, including coronary artery disease (CAD), atrial fibrillation, diabetes mellitus (DM), pulmonary hypertension, liver disease, kidney disease, infective endocarditis, immunosuppression; and all pertinent clinical variables including: Vitals, laboratories, type and urgency of surgery, bypass and cross-clamp time (CCT), medications and blood products delivered during the surgery and immediately prior to transfer to ICU, as well as presence of hypotension in the OR ("OR hypotension"). A vasopressor bolus use was abstracted from the electronic chart documentation by the provider. Although the exact doses of vasopressors given were not abstracted, our anesthesiologists mostly use norepinephrine (100 μg) and/or vasopressin (1 unit), and much less frequently epinephrine (10 μg). The primary outcome was hospital mortality and secondary outcomes were duration of mechanical ventilation (MV) in hours, and ICU and LOS in days. All data were manually extracted from an electronic medical record. The anesthesia notes during the surgery were extracted partially from plotted diagrams and partially from nominal data.

### Statistical analysis

The continuous variables were reported as median values with interquartile ranges (IQR) and the categorical variables were reported as counts and proportions. We used nonparametric statistical tests; Fisher's exact and Wilcoxon Rank-Sum tests, as applicable. The predictor variables in univariate analyses with a $P$ value of less than 0.1 were included in the subsequent multivariate analyses. We used nominal logistic and linear regressions, as appropriate. Statistical significance was considered at $P$ value of < 0.05. As we performed analysis mainly for the exploratory purpose, no corrections for multiple comparisons were done. We used JMP 10 Pro statistical software for analysis from SAS (Cary, NC, United States).

## RESULTS

Out of 1273 cardiothoracic surgeries performed within the study period, 437 patients underwent non-transplant cardiac surgery and were eligible for our study. Twenty patients were excluded subsequently as they lacked detailed blood pressure recordings, leaving 417 patients for the study analyses (Figure 1). The majority of patients were white (85%), males (73%), of median age 67 years (IQR 59, 73), and with median body mass index (BMI) of 28 (IQR 25, 32). The two most commonly performed surgeries were coronary artery bypass grafting (46%) and valvular surgery (29%). The detailed baseline characteristics are listed in Table 1. The median bypass time (BT) was 116 min (IQR 90, 150) and the median CCT was 80 min (IQR 55, 105). While 76% of all surgeries were elective (pre-scheduled), 24% were either emergent (within 24 h of admission) or urgent (24-72 h after hospital admission). The overall postoperative mortality was 3%. The median MV duration was 4 h (IQR 3, 9), and the median ICU and hospital LOS were 2 (IQR 1, 3) and 7 days (IQR 5, 10), respectively.

### ICU hypotension

Total of 227 patients (54%) were found to be hypotensive within 30 min upon transfer to the ICU. Nearly three quarters of the whole cohort did not have OR hypotension immediately prior to transfer to the ICU (Figure 2). Presence of OR hypotension immediately prior to ICU transfer was expectedly associated with ICU hypotension [OR = 1.9; 95% confidence interval (CI): 1.21-2.98; $P$ < 0.006]. About two-thirds of patients with preceding OR hypotension continued with ICU hypotension and half of those without preceding OR hypotension developed ICU hypotension upon ICU transfer. Higher BMI, history of DM and CAD were associated with significantly higher unadjusted risk of developing ICU hypotension (Table 2). ICU hypotension was associated with the longer duration of MV in hours: 5 (IQR 3, 15) *vs* 4 (IQR 3, 6), $P$ = 0.012. Although statistically significant, the clinical significance appeared to be limited only to the patients in the upper quartile (Table 3). Based on the chart documentation, 212 patients received vasopressor boluses around (immediately prior or during) the transfer to the ICU (Figure 3). The patients who received vasopressor bolus on transfer were somewhat more likely to experience ICU drop-off hypotension (OR = 1.45, 95%CI: 0.98-2.13; $P$ = 0.062), although this did not quite reach statistical significance. Of the 212 patients who received bolus, 125 (55%) experienced immediate ICU hypotension. Of these 125 patients with ICU hypotension, 78 did not have preceding OR hypotension and 47 did and continued with ICU hypotension from the OR (OR = 1.78; 95%CI: 0.97-3.26; $P$ = 0.074). Of 12 patients who died, 9 received the bolus during the transfer and 3 did not (OR = 2.99; 95%CI: 0.8-11.2; $P$ =

| Table 1  Basic demographics of the study population, *n* (%) | | |
|---|---|---|
| **Basic demographics** | **Overall** | **ICU hypotension** |
| Total | 417 | 227 |
| Sex | | |
| Male | 305 (73) | 172 (76) |
| Female | 112 (27) | 55 (24) |
| Median age (IQR) | 67 (59, 73) | 67 (58, 74) |
| Race | | |
| Not disclosed | 9 (2) | 5 (2) |
| White | 356 (85) | 197 (87) |
| Other | 52 (13) | 25 (11) |
| Median BMI (IQR) | 28 (25, 32) | 29 (26, 33) |
| Mortality | | |
| Alive | 405 (97) | 217 (96) |
| Dead | 12 (3) | 10 (4) |
| Type of surgery | | |
| Aortic graft | 21 (5) | 11 (5) |
| CABG | 193 (46) | 113 (50) |
| Ventriculomyotomy | 26 (6) | 9 (4) |
| Valve | 122 (29) | 63 (28) |
| Aortic graft + CABG | 3 (0.7) | 1 (0.4) |
| Valve + CABG | 30 (7) | 23 (10) |
| ASD repair | 7 (2) | 4 (2) |
| Aortic graft + valve | 12 (3) | 2 (1) |
| ASD repair + valve | 3 (0.7) | 1 (0.4) |
| Need or surgery | | |
| Elective | 318 (76) | 175 (77) |
| Urgent/emergent | 99 (24) | 52 (23) |
| Comorbidities | | |
| CAD | 278 (67) | 164 (72) |
| Afib | 81 (19) | 42 (19) |
| AICD/PM | 21 (5) | 11 (5) |
| DM | 137 (33) | 89 (39) |
| PHTN | 21 (5) | 13 (6) |
| LD | 27 (7) | 18 (8) |
| KI | 88 (21) | 53 (23) |
| Active IE | 6 (1) | 2 (1) |
| IS | 16 (4) | 10 (4) |

ICU: Intensive care unit; IQR: Interquartile range; BMI: Body mass index; CABG: Coronary artery bypass graft; ASD: Atrial septum defect; CAD: Coronary artery disease; Afib: Atrial fibrillation; AICD/PM: Automatic implantable cardioverter defibrillator/pacemaker; DM: Diabetes mellitus; PHTN: Pulmonary hypertension; LD: Liver disease; KI: Kidney injury; IE: Infective endocarditis; IS: Immunosuppressed.

0.14). Receipt of vasopressor bolus during the transfer was significantly associated with longer MV duration, ICU and hospital LOS ($P < 0.001$, for all). All variables with $\alpha \leq 0.1$ in univariate analysis were included in multivariate analysis. When adjusted in the multivariate analysis, CAD, DM and longer BT were significantly associated with the development of ICU hypotension (Table 4).

### *Mortality and secondary outcomes*

Overall hospital mortality was not significantly associated with ICU hypotension (OR = 4.33; 95%CI: 0.94-20.02; $P = 0.073$); likely given relatively low overall mortality of 3% (Table 5). The female sex was significantly associated with longer ICU and hospital LOS, while longer BT and higher American Society of Anesthesiologists (ASA) physical status score were significantly associated with longer MV, ICU and hospital LOS. When adjusted for multiple covariates, no single variable was significantly

Cardiothoracic ICU patient pool from January 2015 – December 2016 (*n* = 1430)

Device placements excluded (*n* = 73)

Thoracic (non-cardiac) surgeries excluded (*n* = 638)

Transplant heart (*n* = 35) and transplant lung (*n* = 90) excluded

*n* = 437

Patients without proper blood pressure recordings excluded (*n* = 20)

Included patients (*n* = 417)

**Figure 1  Schematic representation of the study population.** ICU: Intensive care unit.

associated with the mortality. In order to avoid overfitting of the model, variables such as CCT (collinear with BT) and pulmonary hypertension (low frequency), were excluded.

## DISCUSSION

In this retrospective study from a single academic center, we have demonstrated that hypotension in the initial 30 min upon ICU admission after cardiac surgery occurs more frequently than previously reported and this may be associated with adverse clinical outcomes. More than half of the patients received vasopressor boluses during the OR to ICU transfer, which has also been associated with adverse outcomes.

The results of our study have important implications for anesthesia and ICU practitioners. The frequency of hypotension in the first 30 min upon ICU arrival in our study was substantially higher (54%), relative to a European study which examined the hemodynamic status of cardiac surgical patients in the initial two-hour post-operative period (34%)[6]. It is likely that the frequency of hypotension could have been even higher in our study had we prolonged the observation period to two-hour period similar to the aforementioned study. Given that the patients with ICU hypotension may experience worse clinical outcomes, it is necessary to address potentially modifiable factors. In our cohort, significant unadjusted predictors for hypotension upon arrival to the ICU were elevated BMI, history of DM and CAD, all well-established risk factors for cardiovascular morbidity. After adjustments in the multivariate regression analysis, DM and longer cardiopulmonary bypass remained significantly associated with the development of ICU hypotension. Presence of DM has been previously associated with the higher cardiovascular morbidity, higher rates of pneumonia and sepsis, which may contribute to increased mortality, relative to non-diabetic patients[11-15]. It is important that both preoperative as well perioperative blood sugar control are maximized in order to reduce the hyperglycemia-related adverse outcomes[16-18]. Despite the fact that the significance of longer BT has been well documented to negatively affect post-operative rate of complications and mortality[19], our analysis (Table 5) does not show any significant difference between longer BT and mortality. It is plausible to expect that the future improvements in operative techniques and avoidance of cardiopulmonary bypass altogether would likely further reduce postoperative complications thus improving morbidity and mortality. During the time period of data collection, off-pump surgery was very infrequently done at our institution and this would not affect the results.

Previously, female sex was reported to be significantly associated with adverse

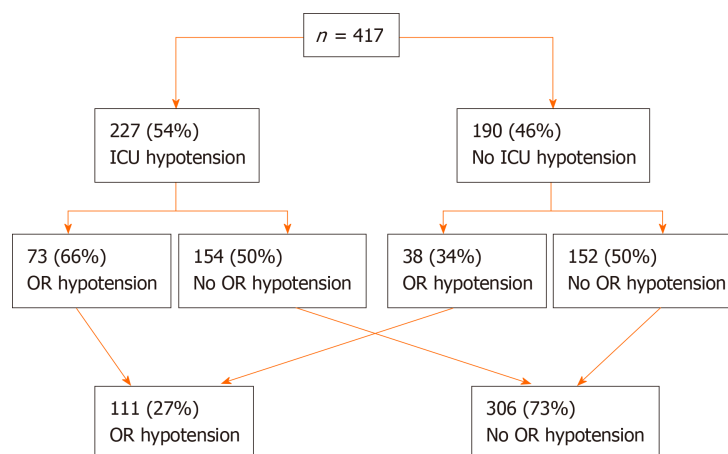**Table 2 Association of baseline characteristics with intensive care unit hypotension and mortality**

| Baseline characteristic | ICU hypotension, *n* = 227 | No ICU hypotension, *n* = 190 | *P* value | Alive, *n* = 405 | Dead, *n* = 12 | *P* value |
| --- | --- | --- | --- | --- | --- | --- |
| Age, median (IQR) | 67 (58, 74) | 68 (59, 73) | 0.73 | 67 (59, 73) | 64 (59, 67) | 0.42 |
| Male sex, *n* (%) | 172 (76) | 133 (70) | 0.22 | 299 (74) | 6 (50) | 0.0935 |
| BMI, median (IQR) | 29 (26, 33) | 27 (25, 31) | 0.01 | 28 (25, 32) | 32 (27, 38) | 0.039 |
| CAD, *n* (%) | 164 (72.2) | 114 (60.0) | 0.009 | 272 (67) | 6 (50) | 0.23 |
| DM, *n* (%) | 89 (39.2) | 48 (25.3) | 0.003 | 133 (33) | 4 (33) | 1.0 |
| Afib, *n* (%) | 42 (19) | 39 (21) | 0.62 | 78 (19) | 3 (25) | 0.71 |
| AICD/PM, *n* (%) | 11 (5) | 10 (5) | 1.00 | 20 (5) | 1 (8) | 0.47 |
| PHTN, *n* (%) | 13 (6) | 8 (4) | 0.51 | 18 (12) | 3 (25) | 0.018 |
| IE, *n* (%) | 2 (1) | 4 (2) | 0.42 | 6 (1) | 0 (0) | 1.0 |
| LD, *n* (%) | 18 (8) | 9 (5) | 0.23 | 27 (7) | 0 (0) | 1.0 |
| KD, *n* (%) | 53 (23) | 35 (18) | 0.23 | 86 (21) | 2 (17) | 0.78 |
| IS, *n* (%) | 10 (4) | 6 (3) | 0.61 | 16 (4) | 0 (0) | 1.0 |
| Elective surgery, *n* (%) | 175 (77) | 143 (75) | 0.73 | 309 (76) | 9 (75) | 1.0 |
| ASA, *n* (%) | | | 0.42 | | | 0.02 |
| 2 | 1 (0.5) | 1 (0.4) | | 2 (0.5) | 0 (0) | |
| 3 | 94 (49) | 94 (41) | | 186 (46) | 2 (17) | |
| 4 | 94 (49) | 130 (57) | | 215 (53) | 9 (75) | |
| 5 | 1 (0.5) | 2 (0.9) | | 2 (0.5) | 1 (8) | |
| EF%, median (IQR) | 60 (51, 64) | 62 (54, 66) | 0.29 | 60 (53, 65) | 62 (53, 67) | 0.62 |
| BT, median (IQR) | 117 (90, 150) | 114 (85, 148) | 0.10 | 115 (89, 148) | 152 (108, 240) | 0.0008 |
| CCT, median (IQR) | 81 (60, 105) | 77 (53, 108) | 0.10 | 80 (55, 105) | 111 (59, 160) | 0.018 |
| Transfusion, n (%) | 138 (61) | 124 (65) | 0.36 | 252 (62) | 10 (83) | 0.22 |
| Pressors, *n* (%) | 178 (78) | 138 (73) | 0.21 | 305 (75) | 11 (92) | 0.31 |
| Bolus given, *n* (%) | 125 (59.0) | 87 (41.0) | 0.06 | 203 (50) | 9 (75) | 0.14 |
| Hb, median (IQR) | 13 (12,14) | 13 (12, 14) | 0.79 | 13 (12, 14) | 13 (10, 14) | 0.48 |
| Hct, median (IQR) | 40 (35, 42) | 40 (36, 42) | 0.86 | 40 (36, 42) | 40 (33, 44) | 0.73 |
| PLT, median (IQR) | 203 (163, 248) | 198 (159, 233) | 0.18 | 201 (161, 243) | 186 (155, 236) | 0.69 |
| Cre, median (IQR) | 1.1 (0.9, 1.4) | 1 (0.9, 1.2) | 0.13 | 1 (0.9, 1.3) | 1.1 (0.9, 1.9) | 0.80 |
| Ca, median (IQR) | 9.3 (8.9, 9.6) | 9.3 (8.9, 9.6) | 0.78 | 9.3 (8.9, 9.6) | 9.2 (8.6, 9.4) | 0.49 |
| Pre-op SBP, median (IQR) | 125 (110, 139) | 126 (110, 139) | 0.69 | 126 (110, 139) | 114 (98, 144) | 0.18 |
| Pre-op MAP, median (IQR) | 84 (73, 94) | 83 (74, 96) | 0.89 | 84 (74, 95) | 80 (49, 91) | 0.066 |

ICU: Intensive care unit; IQR: Interquartile range; *n*: Number of patients; BMI: Body mass index; CAD: Coronary artery disease; DM: Diabetes mellitus; Afib: Arterial fibrillation; AICD/PM: Automatic implantable cardioverter defibrillator/pacemaker; PHTN: Pulmonary hypertension; IE: Infective endocarditis; LD: Liver disease; KD: Kidney disease; IS: Immunosuppressed; ASA: American Society of Anesthesiologists; EF: Ejection fraction; BT: Bypass time; CCT: Cross-clamp time; Hb: Hemoglobin; Hct: Hematocrit; PLT: Platelet; Cre: Creatinine; Ca: Calcium; pre-op: Pre-operation; SBP: Systolic blood pressure; MAP: Mean arterial pressure.

postoperative outcomes[20]. Females with the acute coronary syndrome resulting in cardiogenic shock, those with acute aortic dissection, ruptured abdominal aortic aneurysms, or those undergoing non-cardiac surgery, have been shown to have higher mortality rates compared to men[21-25]. Also, females with cerebral complications after cardiac surgery have shown to have a higher mortality than males[24,26]. In our study, females experienced significantly longer unadjusted ICU and hospital lengths of stay. Although the female sex was previously associated with the use of higher tidal volumes (relative to the height measurement) and more ventilator induced lung injury[27], there was no observed difference in duration of MV relative to the males in our cohort. There is a strong impetus for extubation of patients within 6 h of the cardiac surgery[28]. When adjusted for pertinent clinical variables and compared to men, females in our cohort were not more likely to die during the hospital stay.

The ASA physical status score subjectively assesses the patients' overall health prior to surgery. It has been shown that ASA score is associated with longer ICU and LOS, longer MV, and increased mortality[2,29,30]. In our study, ICU and LOS, as well as MV duration were significantly associated with ASA score, and there was a trend for higher hospital mortality with the rising ASA score, accordingly.

Based on the chart documentation, more than half of patients received boluses of short-acting vasopressors during the transfer from the OR to the ICU. The

**Figure 2 Intensive care unit and operating room hypotension frequency.** ICU: Intensive care unit; OR: Operating room.

anesthesiology transport teams routinely carry syringes of resuscitative medications for any unanticipated needs that may occur during the transfer. It is possible that even more patients had received the bolus dosing without the subsequent chart documentation, although this is speculative. Why this may be important? Frequently, ICU receiving team may not be aware of use of vasopressor boluses during the transfer and the development of hypotension soon after the anesthesia drop-off is not anticipated, which leads to delayed and reactive treatment strategy that may be suboptimal. This is anecdotally termed "anesthesia drop-off syndrome" in the ICU, where soon after the transfer from the OR, the patients tend to develop hypotension that was not present at the arrival of the patient into the ICU and during the actual transfer of care from anesthesia to ICU team. As it has been previously suggested that hypotension is associated with adverse outcomes[11,13,31], it is important that any use of vasopressor bolus on transfer is readily communicated to the receiving ICU team, to enable anticipatory rather than reactive management of hypotension. For the same reasons, it may be more appropriate to up titrate the dose of ongoing vasopressor drip rather than to push additional IV bolus, as such bolus dosing may not be obvious to the receiving team. This is currently subject of qualitative improvement and patient safety initiatives spanning both anesthesiology and ICU providers at our institution, as the current process of care needs to be improved.

We have abstracted a vast amount of clinical information on all patients, including vital signs, complete blood counts, pertinent hemodynamic variables such as preoperative and intraoperative echocardiography (systolic and diastolic function, valvular function), transfusion of blood products and cell saver, administration of crystalloid and colloid solutions, CCT, estimated blood loss and development of other OR complications, among others. It is interesting that none of these variables were significant adjusted risk predictors by itself for developing hypotension upon ICU arrival. This implies that the perioperative management of cardiac surgery patients is complex and of a very dynamic nature where the multitude of factors play pertinent roles.

The main study limitation lies in its retrospective design. We relied on abstraction of data from the electronic medical records and at best our data is as good as the chart documentation itself. Relative to this, there might have been time delays between the exact occurrence of the event and the time it was documented in the chart. While this delay may have not been substantial during the intraoperative period, the retrospective charting of the medications administered during the actual patient transfer to the ICU may have been affected, including possibility for the lack of documentation, altogether. This may possibly in part explain why the substantial number of patients, who were not recorded to be hypotensive in the OR immediately prior to the transfer to the ICU, were documented to have received boluses of short-acting vasopressor medications during the transfer.

The study was done at the single academic medical center and since we excluded the patients who underwent transplantation surgery, these factors limit the generalizability of our findings to the certain extent. There was a relatively low mortality and therefore small number of patients who died predisposed multivariate model to overfitting and may not be completely reliable. At our institution, there are no established or preferred teams of certain surgeons and anesthesiologist. All surgeons work with all anesthesiologists depending only on the scheduling.

| Table 3 Unadjusted association of intensive care unit hypotension with clinical outcomes | | | |
|---|---|---|---|
| Item | ICU hypotension | No ICU hypotension | *P* value |
| Hosp. LOS, median (IQR) | 7 (5, 10) | 7 (5, 9) | 0.49 |
| ICU LOS, median (IQR) | 2 (1, 4) | 2 (1, 3) | 0.21 |
| MV hours, median (IQR) | 5 (3, 15) | 4 (3, 6) | < 0.001 |
| Hosp. mortality, *n* (%) | 10 (4.4) | 2 (1.1) | 0.07 |

ICU: Intensive care unit; Hosp: Hospital; LOS: Length of stay; IQR: Interquartile range; MV: Mechanical ventilation.

Therefore, it is unlikely that individual surgeons or anesthesiologists could affect the results.

Nevertheless, despite the above limitations, the high proportion of patients who were hypotensive immediately upon transfer from the OR to the ICU dictates the need for novel strategies and protocol implementations to assure the safest transition of care between the anesthesiology and ICU teams, which in turn may improve overall patient outcomes.

In summary, we have demonstrated that the occurrence of hypotension in the initial 30 min upon OR to ICU transfer is frequent and substantially more so than previously reported. Our findings have important implications for the anesthesia and ICU care teams as the occurrence of hypotension have been associated with adverse clinical outcomes. Administration of any medications during the actual transfer of the patient from the OR to the ICU should be readily communicated to the receiving ICU team. It is suggested that there is a room for improvement in the OR to ICU hand off process and renewed strategies that assure smooth transition of care and patient's safety are needed.

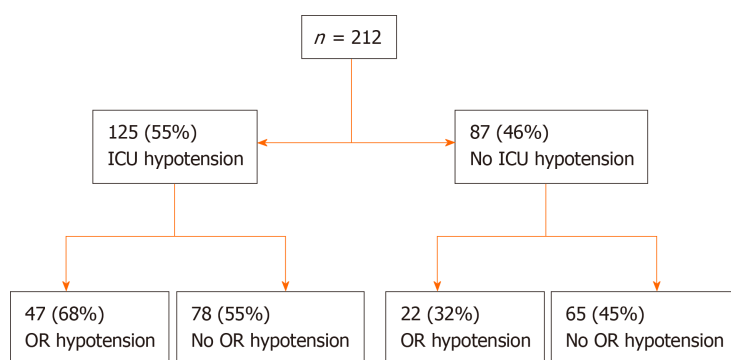**Table 4 Multivariate analysis for intensive care unit hypotension**

| Item | ICU hypotension | |
| --- | --- | --- |
| | **OR; 95%CI** | ***P* value** |
| BMI | 1.02; 0.99-1.07 | 0.13 |
| CAD | 1.69; 1.09-2.62 | 0.018 |
| DM | 1.66; 1.06-2.61 | 0.025 |
| BT | 1.004; 1.0002-1.008 | 0.034 |
| Bolus | 1.2; 0.79-1.82 | 0.38 |

Cross clamp time excluded because of linear correlation with bypass time. ICU: Intensive care unit; OR: Odds ratio; CI: Confidence interval; BMI: Body mass index; CAD: Coronary artery disease; DM: Diabetes mellitus; BT: Bypass time.

**Table 5 Multivariate analysis for mortality**

| Item | Mortality | |
| --- | --- | --- |
| | **OR; 95%CI** | ***P* value** |
| Sex | 0.74; 0.06-7.99 | 0.80 |
| BMI | 0.93; 0.76-1.14 | 0.51 |
| ICU hypotension | 0.27; 0.03-2.74 | 0.27 |
| Lowest MAP (pre-op) | 0.96; 0.89-1.02 | 0.19 |
| BT | 1.01; 0.43-23.8 | 0.33 |
| ASA | 3.19; 0.79-1.82 | 0.26 |

Cross clamp time excluded because of linear correlation with bypass time; Pulmonary hypertension (low frequency) excluded to prevent overfitting). OR: Odds ratio; CI: Confidence interval; BMI: Body mass index; ICU: Intensive care unit; MAP: Mean artery pressure; pre-op: Pre-operative; BT: Bypass time; ASA: American Society of Anesthesiologists.



**Figure 3 Number of patients receiving the vasopressor bolus on transfer.** ICU: Intensive care unit; OR: Operating room.

## ARTICLE HIGHLIGHTS

### Research background

Perioperative hypotension is one of the most common complications after cardiac surgery and this may adversely affect clinical outcomes. However, data is limited in the literature regarding the actual prevalence of hypotension that develops shortly after the transfer of patients to the intensive care unit (ICU) after cardiac surgery. Hypotensive patients usually require administration of vasopressor boluses prior to or during the transfer from the operating room (OR) to the ICU as a temporizing measure. The hypotension and necessity for use of vasopressors have been previously associated with increased hospital length of stay as well as mortality, relative to the patients who maintained hemodynamic stability.

### Research motivation

Given the proposed discrepancy between the clinical occurrence and limited data on rate of hypotension starting shortly after the anesthesia to ICU transfer, we aimed to evaluate its

prevalence and also how this may relate to the pertinent clinical outcomes.

### Research objectives

We hypothesized that the occurrence of initial hypotension in the ICU is more frequent complication among post-cardiac surgery ICU patients than previously reported and that patients who experience this complication would have adverse clinical outcomes. We also aimed to better assess the association between the occurrence of initial hypotension in the ICU and the use of vasopressor bolus administered immediately prior to or during the transfer from the OR to the ICU.

### Research methods

We conducted a retrospective study of adult patients undergoing cardiac surgery in a 2-year period. The primary independent variable was the development of hypotension within the first 30 min upon transfer from the OR ("ICU hypotension"). We abstracted demographic and baseline characteristics, comorbidities, and all pertinent clinical variables, as well as presence of hypotension in the OR ("OR hypotension"). A vasopressor bolus use was abstracted from the electronic chart documentation by the provider. All data were manually extracted from an electronic medical record. The anesthesia notes during the surgery were extracted partially from plotted diagrams and partially from nominal data.

### Research results

We have demonstrated that hypotension in the initial 30 min upon ICU admission after adult cardiac surgery occurs more frequently than previously reported and this may be associated with adverse clinical outcomes. The results of our study have important implications for anesthesia and ICU practitioners. Given that the patients with ICU hypotension may experience worse clinical outcomes, it is necessary to address potentially modifiable factors. More than half of patients received boluses of short-acting vasopressors during the transfer from the OR to the ICU. Why this may be important? Frequently, ICU receiving team may not be aware of use of vasopressor boluses during the transfer and the development of hypotension soon after the anesthesia drop-off is not anticipated, which leads to delayed and reactive treatment strategy that may be suboptimal. This is currently subject of qualitative improvement and patient safety initiatives spanning both anesthesiology and ICU providers at our institution, as the current process of care needs to be improved. The main study limitation lies in its retrospective design. We relied on abstraction of data from the electronic medical records. The study was done at the single academic medical center and since we excluded the patients who underwent transplantation surgery, these factors limit the generalizability of our findings to the certain extent. Nevertheless, despite the above limitations, the high proportion of patients who were hypotensive immediately upon transfer from the OR to the ICU dictates the need for novel strategies and protocol implementations to assure the safest transition of care between the anesthesiology and ICU teams, which in turn may improve overall patient outcomes.

### Research conclusions

We have demonstrated that the occurrence of hypotension in the initial 30 min upon OR to ICU transfer is frequent and substantially more so than previously reported. Our findings have important implications for the anesthesia and ICU care teams as the occurrence of hypotension have been associated with adverse clinical outcomes. Administration of any medications during the actual transfer of the patient from the OR to the ICU should be readily communicated to the receiving ICU team.

### Research perspectives

It is suggested that there is a room for improvement in the OR to ICU hand off process and renewed strategies that assure smooth transition of care and patient's safety are needed.

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**Observational Study**

# Critical care practice in India: Results of the intensive care unit need assessment survey (ININ2018)

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## Abstract

**BACKGROUND**
A diverse country like India may have variable intensive care units (ICUs) practices at state and city levels.

**AIM**
To gain insight into clinical services and processes of care in ICUs in India, this would help plan for potential educational and quality improvement interventions.

**METHODS**
The Indian ICU needs assessment research group of diverse-skilled individuals was formed. A pan- India survey "Indian National ICU Needs" assessment (ININ 2018-I) was designed on google forms and deployed from July 23rd-August 25th, 2018. The survey was sent to select distribution lists of ICU providers from all 29 states and 7 union territories (UTs). In addition to emails and phone calls, social medial applications-WhatsApp™, Facebook™ and LinkedIn™ were used to remind and motivate providers. By completing and submitting the survey, providers gave their consent for research purposes. This study was deemed eligible for category-2 Institutional Review Board exempt status.

**RESULTS**
There were total 134 adult/adult-pediatrics ICU responses from 24 (83% out of 29) states, and two (28% out of 7) UTs in 61 cities. They had median (IQR) 16 (10-25) beds and most, were mixed medical-surgical, 111(83%), with 108(81%) being adult-only ICUs. Representative responders were young, median (IQR), 38 (32-44) years age and majority, $n = 108$ (81%) were males. The consultants were, $n = 101$ (75%). A total of 77 (57%) reported to have 24 h in-house intensivist. A total of 68 (51%) ICUs reported to have either 2:1 or 2≥:1 patient:nurse ratio. More than 80% of the ICUs were open, and mixed type. Protocols followed regularly by the ICUs included sepsis care, ventilator- associated pneumonia (83% each); nutrition (82%), deep vein thrombosis prophylaxis (87%), stress ulcer prophylaxis (88%) and glycemic control (92%). Digital infrastructure was found to be poor, with only 46 % of the ICUs reporting high-speed internet availability.

**CONCLUSION**
In this large, national, semi-structured, need-assessment survey, the need for improved manpower including; in-house intensivists, and decreasing patient-to-nurse ratios was evident. Sepsis was the most common diagnosis and quality and research initiatives to decrease sepsis mortality and ICU length of stay could be prioritized. Additionally, subsequent surveys can focus on digital infrastructure for standardized care and efficient resource utilization and enhancing compliance with existing protocols.

**Key words:** Intensive care unit; Critical care; India; Survey; Intensive care unit survey; Intensive care unit needs

**Core tip:** Intensive care unit (ICU) practices are variable in a vast country like India. Most common admitting diagnosis for ICU is similar to Western reporting in literature. There is variable protocol penetration for processes of care in ICU.

## INTRODUCTION

Critical care practices vary worldwide and are a reflection of varying epidemiology and existing financial and human resources. Patient outcomes in these centers can vary dramatically due to the influence of interlinked, multiple factors[1].

A diverse country like India, may have variable intensive care units (ICUs) practices in various states, which can be due to differences in; hierarchical arrangements, allocation of resources, patient backgrounds, cultural and clinical practices, and goals or objectives of the caregivers[2]. Although it is imperative to have standardized care of practice to minimize variations and maximize the quality of care delivered to the patients, it is essential to paint a picture in the backdrop keeping in mind the epidemiological context, resource availability, and local practices[3]. In addition, it is crucial to identify and evaluate variables like prevalent clinical practices, protocols, a range of service, human resources and facilities available on a national level to bring forth a prototype which will help in quality control and unification of the care delivery. Studies have been done in developed countries[3,4], and a few more describe the practices in a multinational setting[5-7] but the information is scarce in an Indian setting[2].

Our study aimed to gain insight into clinical services, prevalent practices, processes of care and patient outcomes in ICUs across different regions of India. Studying and analyzing these patterns can potentially help prioritize quality improvement interventions, educate practicing physicians and, create a framework for further studies to fill in the knowledge gap, to further strategize best care practices and act as a paradigm for critical care delivery.

## MATERIALS AND METHODS

This was a cross-sectional pan-India survey-based study. We created a multidisciplinary, diverse team of qualified individuals who constituted the "Indian ICU needs assessment research group".

A questionnaire was designed to assess the ICU clinical practices prevalent in the institution followed by the study of the demographics of the institution and the surveyor. Questions were asked regarding the ICU being closed or open, group and type of patients catered to, number of ICU beds, protocols followed in the ICU setting, top diagnoses of the admitted patients, and availability of critical care equipment and technology. Moreover, human resource demographics were explored through variables such as the presence of certified intensivists, residents/fellows, 24-h in-house staff intensivists, patient: Nurse ratio, age of the surveyor, gender, level of training, and years of experience. Outcome variables included average ICU length of stay, mechanical ventilation duration, ICU mortality, sepsis mortality and, mechanical ventilation patient mortality. The functionality of the survey was tested as a pilot among a random group of critical care physicians prior to implementation for internal validity. A sample of the survey is depicted in the E-supplement.

A database of intensivists was identified through critical care societies, social media, and personal networks. The team carried out the study through a survey from July 23rd to August 25th, 2018, through an anonymous questionnaire designed on a Google™ form online and distributed to the critical care providers in 29 states and 7 Union territories (UTs) of India (Figure 1). Various platforms like electronic mail (e-mail), social media applications such as WhatsApp™, Facebook™ and LinkedIn™,

were used for dispatching the form and to reach out to potential collaborators for reminder and motivation.

A convenient sample of 134 ICUs was collected through the survey, and the data collected is presented as mean, with standard deviation, or median with interquartile range. Pictorial and graphical representation of the relevant data was done.

For analysis purposes, we divided India into 6 zones (Figure 2), on the basis of administrative divisions mainly – North, South, West, East, Central, Northeast[8]. Descriptive statistical analysis was used.

By completing and submitting the survey, providers gave their consent to provide pertinent information for research purposes. This study was deemed eligible for category-2 Institutional Review Board exempt status.

## RESULTS

### *Representation*
Our analysis was based on total 134 adult/adult-pediatrics ICU responses. They represented 61 cities of 24 states, and two UTs of India. The response rate was 83% states and 28% of UTs. Region-wise sample distribution revealed that 39 (29%) of entries belonged to the Northern region, whereas South Indian cities contributed to 34 (25%) entries. Thirteen (10%) from the Central; 25 (19%) from West; while 18 (13%) entries belonged to East and North-East, contributed 5 (4%) of the total of 134 entries.

### *Demographics*
A vast majority of responders in the survey were young adults, median (IQR), 38 (32-44) years age and predominantly, $n$ = 108 (80%) were males, with a median clinical ICU experience of 8.5 (IQR, 4-14) years. Likewise, most of the responses came from consultants, $n$ = 101 (75%), followed by residents (PGY-3 and above), $n$ = 19 (14%). Most of them were working in mixed medico-surgical ICUs, $n$ = 111(83%) in private academic hospitals, $n$ = 50 (37%) with median (IQR) 16 (10-25) beds. Most of the responders were working in open type of ICU setup, 110 (82%), and only 24 (18%) of them in closed ICUs (Table 1 and Figure 3).

### *Clinical resources*
Intensivist and the nurses played a major role in ICU patient care. Most responders (62%), had patient: nurse ratio of 2:1, and only (10%) responders were strictly abiding by 1:1 nursing care. Additionally, 37% of ICUs, which usually had 2:1 patient: nurse ratios, switched to 1:1 for complicated cases. Also, more than 2:1 patient: nurse's ratios were reported in 24% of ICUs. A total of 107 (80%) reported to have ICU staffed by certified intensivists and 77 (58%), had 24 h in-house intensivist coverage to take care of the patients. The majority of ICUs ($n$ = 110, 82%) ICUs had residents/fellows/medical students rotating through or cover ICU along with staff intensivists (Table 2 and Figure 4).

### *Critical care clinical protocols*
The majority of ICUs had glycemic control (92%) protocols, Advanced Cardiac Life Support (89%), deep vein thrombosis prophylaxis (87%), stress ulcer prophylaxis (87%), sepsis care (84%), ventilator-associated pneumonia (84%) and nutrition (83%) protocols. The least reported protocols included palliative care/end-of-life care (50%), delirium assessment and treatment (49%), early mobility (49%) and targeted temperature management after cardiac arrest (45%) (Table 3 and Figure 5).

### *Digital infrastructure*
In spite, of 60 (46%) hi-speed internet availability the digital infrastructure was reported to be limited. Electronic medical records, $n$ = 49 (37%), tele-ICU coverage, $n$ = 28 (21%) and 2-way communication including webcam, $n$ = 21 (16%) were reported (Table 4).

### *Admitting diagnosis*
The self-reported top admitting diagnosis in our survey study was sepsis, closely followed by respiratory failure (Table 5).

### *Outcomes*
The self-reported average ICU mortality ($n$ = 95) was *median* 18% (IQR 11-30); ICU length of stay ($n$ = 112) was 3.5 (4-6) d; mechanical ventilation (MV) duration ($n$ = 98) was *median* 4 (3-5) d; MV patient mortality ($n$ = 77) was 25% (15%-40%) and sepsis mortality ($n$ = 75) was 30% (20%-40%).

**Figure 1 Distribution of participating intensive care unit's over India's map**[17].

## DISCUSSION

Our survey describes some of the critical care practices in a convenient sample of 134 Indian ICUs, and for a better visualization we aimed to cover the whole country, and data was collected from majority of states and some union territories. We found substantial variation in the representation, with minimal participation being observed from North-East region. The majority of the responders of the survey were young adult men, practicing as intensivists, supporting the notion that the country has been training more individuals in critical care, and expanding its health infrastructure.

The Indian subcontinent has variations abound, and each geographical region in the country blending with its own cultural and regional diversity constructs a polychromatic picture. It is only natural for the country to have diversified patient care practices. While being appreciative of the uniqueness this land offers, it is imperative to be vigilant for any disparities which may compromise the delivery of quality and standardized patient care.

Most of the ICUs we surveyed were mixed (medical-surgical) in nature, open in type with an average number of beds of less than 20 per hospital. More than half of them were privately owned, academic-nonacademic institutions. Likewise, elaborating clinical resource parameters, such as a ≤ 2:1 patient-nurse ratio[9], 24-h certified intensivists, and certified intensivists, are associated with better outcomes in intensive care. The majority of Indian ICUs reported having 1 nurse for two or more patients with only few reporting 1:1 patient-nurse ratio. The new finding is that the majority of the ICUs reported having a certified intensivist, and more than half of them had 24 h-in house intensivist coverage.
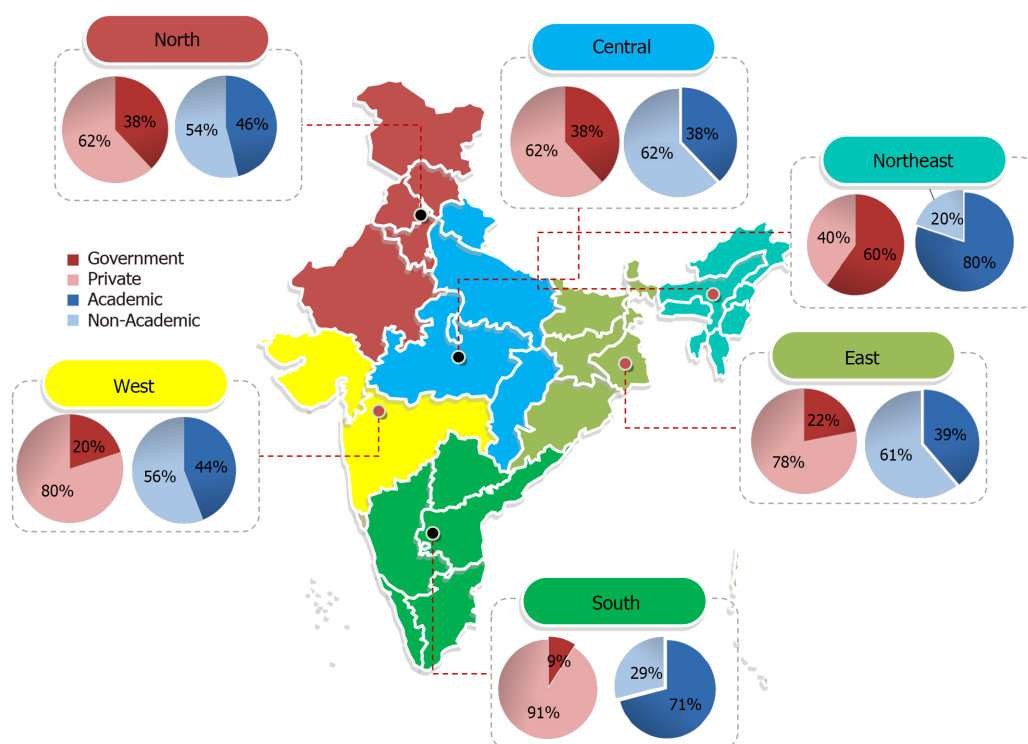
In a survey-based study done in India covering 400 ICUs, similar results were reported with average age of responders being 30-40 years, number of ICU beds 10-30, and the majority of the ICUs were open type and mixed in nature[2].

The top admitting diagnosis in our study was sepsis, which was reported across an over whelming majority of all the ICUs closely followed by respiratory failure. This follows global trends. For example, an observational study, collecting data from 10096 patients across different countries, observed the most common diagnosis on admission to be sepsis[10].

Recent reports suggest that standardized protocols and best practice guidelines in the treatment of the critically ill patients in the ICU are associated with more favorable outcomes and decreased ICU-related morbidity and mortality. In our survey, self-reported data suggested that the majority of the ICUs across India followed the glycemic control, Advanced Cardiac Life support, deep vein thrombosis prophylaxis, stress ulcer prophylaxis, severe sepsis, ventilator Associated pneumonia bundle, and nutrition protocols. Some of the protocols that still require widespread penetration and awareness in India included palliative care/end-of-life, delirium, early mobility and targeted temperature management after cardiac arrest.

With the advent of digital revolution in India, we also explored the depth of digital coverage in the ICU. Not aligning with the rapid growth observed in other sectors,

**Figure 2 Participating intensive care unit's distribution by administrative divisions of India – North, South, West, East, Central, Northeast- with type of hospital setting.**

less than half of the ICUs reported having high-speed internet with even lesser having electronic medical records, tele-ICU coverage and 2-way communication. A survey of ICUs in medium to low income countries documented an average number of beds being around 10 per ICU, almost 70% of the ICUs were staffed with certified intensivists and 69% of the hospitals had a reliable internet access[7]. In a systematic review done 18 years ago in an attempt to identify physician staffing patterns and clinical outcomes in critically ill patients, the ICU mortality rates ranged from 6%-74% in low intensity staffing and 1%-57% in high intensity staffing ICUs[11]. Outcome data in our study was well within the observed range, reflecting that the majority of the ICUs across the country are adhering to the accepted standard of care, although the self-reported outcomes decrease the validity of these results.

In a descriptive study in the United States of ICUs, the average ICU size was 11.7 ± 7.8 beds per unit, and majority of these hospitals had more than one ICU, followed standard of care protocols, had better patient care delivery, as well as better outcomes, as compared to studies done in low and middle income countries[2,12,13].

Our study has several limitations. First, we had no follow up of initial non-responders. We had a limited sample size, and we used a survey that had not been previously validated in the literature. Other limitations included the documentation of self-reported outcomes reporting, which is similar to previously reported survey-based study from one state in India[14,15]. Also, our study had a limited ability from the surveyor's side to ensure correct data entry and eliminate bias. For example, the overall penetration of tele-ICUs systems and EMRs in India is extremely low; but the reported fraction of tele-ICU penetration in our study may be higher due to selection bias. However, the strength of this survey is that the ICU data was retrieved from diverse geographical regions, which increase the external validity of the study. In addition, we were appreciated at Society of Critical Care Medicine 2019 conference abstract presentation[16] about the fact that the functionality of the survey was tested as a pilot among a random group of critical care physicians prior to implementation, which adds to the internal validity.

Understanding the epidemiology of the Indian subcontinent is incredibly complex, due to inherent variability and lack of required infrastructure to carry out such large-scale studies. At best, these trends can be used as building blocks to identify the gaps in the understructure, and identify areas to focus on, for improved financial and human resource investments.

In a large nation, semi-structured need assessment survey, the need for improved manpower including; in-house intensivists and decreasing patient-to-nurse ratios are evident. Quality and research initiatives to decrease sepsis mortality and ICU length

| Table 1 Demographic variables | |
|---|---|
| **Demographic variables** | **Responses in % (*n* = 134)** |
| **Age ( yr)** | |
| 30-40 | 41 |
| 40-50 | 30.6 |
| 20-30 | 17.2 |
| > 50 | 11.2 |
| **Gender** | |
| Male | 80.2 |
| Female | 19.4 |
| **ICU experience (yr)** | |
| < 10 | 61.9 |
| 11-20 | 28.4 |
| 20-30 | 8.2 |
| > 30 | 1.5 |
| **Designation** | |
| Consultant staff | 75.4 |
| Resident- PGY-3 and above | 14.1 |
| Resident- PGY-1 | 6.7 |
| Resident- PGY-2 | 3.7 |
| **Intensive care unit specialty wise distribution** | |
| Mixed medical-surgical | 82.8 |
| Medical | 8.2 |
| Others | 6.7 |
| Surgical | 2.2 |
| **Institution type** | |
| Private/academic | 37.3 |
| Private/non-academic | 36.5 |
| Government/academic | 14.2 |
| Government/non-academic | 11.9 |
| **Bed strength** | |
| 11-20 | 36.6 |
| < 10 | 26.9 |
| 21-30 | 22.4 |
| > 30 | 14.2 |
| **ICU type** | |
| Open | 82.1 |
| Closed | 17.9 |

ICU: Intensive care unit.

of stay can be prioritized. Our new theory would be that subsequent surveys can focus on digital infrastructure for standardized care and scarce resources utilization and enhancing the compliance of existing protocols.

**Table 2 Clinical resource parameters**

| Clinical resource parameters | Responses in % (*n* = 134) |
| --- | --- |
| Patient:nurse ratio | |
| Usually 2:1 (for complicated patients 1:1) (*n* = 49) | 36.6 |
| 2:1 (*n* = 34) | 25.4 |
| > 2:1 (*n* = 32) | 23.9 |
| 1:1 (*n* = 13) | 9.7 |
| No fixed patient:nurse (*n* = 6) | 4.5 |
| 24 h in-house intensivist (*n* = 77) | 57.5 |
| Certified intensivist (*n* = 107) | 79.9 |
| Residents/fellows/medical students rotate through or cover ICU along with staff intensivists (*n* = 110) | 82.1 |

ICU: Intensive care unit.

**Table 3 Critical care protocols self-reporting**

| High (%) | | Medium (%) | | Low (%) | |
| --- | --- | --- | --- | --- | --- |
| Glucose control | 91.8 | Daily interruption of sedation | 71.6 | Palliative care/end of life | 50.0 |
| Advanced cardiac life support | 88.8 | Acute coronary syndrome | 68.7 | Delirium | 48.5 |
| DVT prophylaxis | 87.3 | Acute lung injury | 62.7 | Early mobility | 48.5 |
| Stress ulcer prophylaxis | 87.3 | Transfusion restriction | 62 | Hypothermia after cardiac arrest | 44.8 |
| Severe sepsis | 83.5 | | | | |
| VAP bundle | 83.5 | | | | |
| Nutrition | 82.8 | | | | |

DVT: Deep vein thrombosis.

**Table 4 Digital demographics**

| Digital demographics | Responses in % (*n* = 134) |
| --- | --- |
| High speed internet | 46 |
| Electronic medical records | 37 |
| Tele-ICU Coverage | 21 |
| 2 – way communication (*e.g.*, webcam) | 16 |

ICU: Intensive care unit.

**Table 5 Common diagnoses**

| Common diagnoses (Dx) | No. | % of ICU |
| --- | --- | --- |
| Most common Dx - septic shock | 116 | 86.57 |
| Respiratory failure | 108 | 80.6 |
| Heart failure | 58 | 43.28 |
| Trauma | 57 | 42.54 |
| Post Op | 59 | 44.03 |
| COPD exacerbation | 72 | 53.73 |
| Electrolyte imbalance | 39 | 29.1 |
| Epilepsy or seizure | 21 | 15.67 |
| Renal failure | 72 | 53.73 |
| Hypotension | 37 | 27.61 |

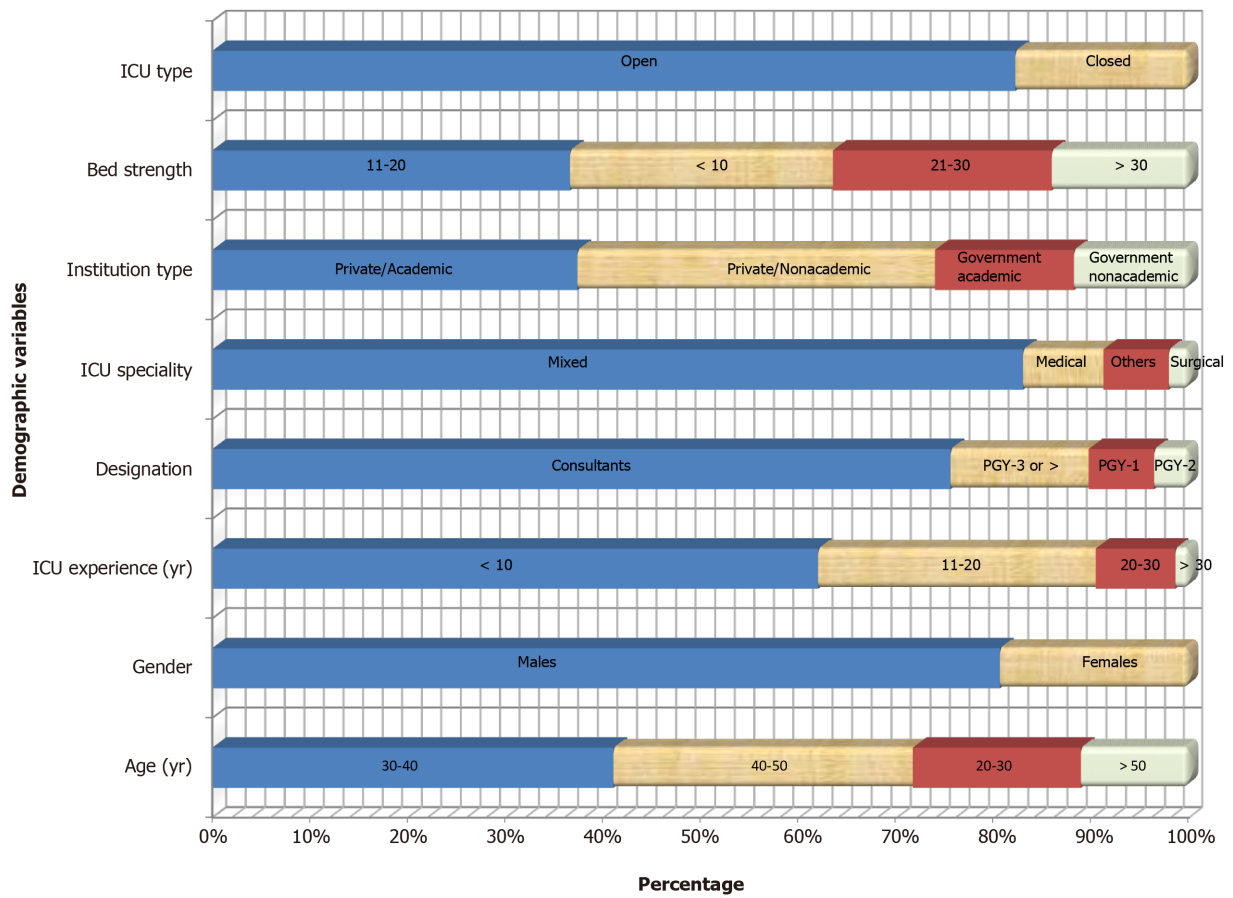| Poisoning/substance abuse | 34 | 25.37 |
|---|---|---|

ICU: Intensive care unit.



**Figure 3 Intensive care unit demographics variables.** ICU: Intensive care unit.
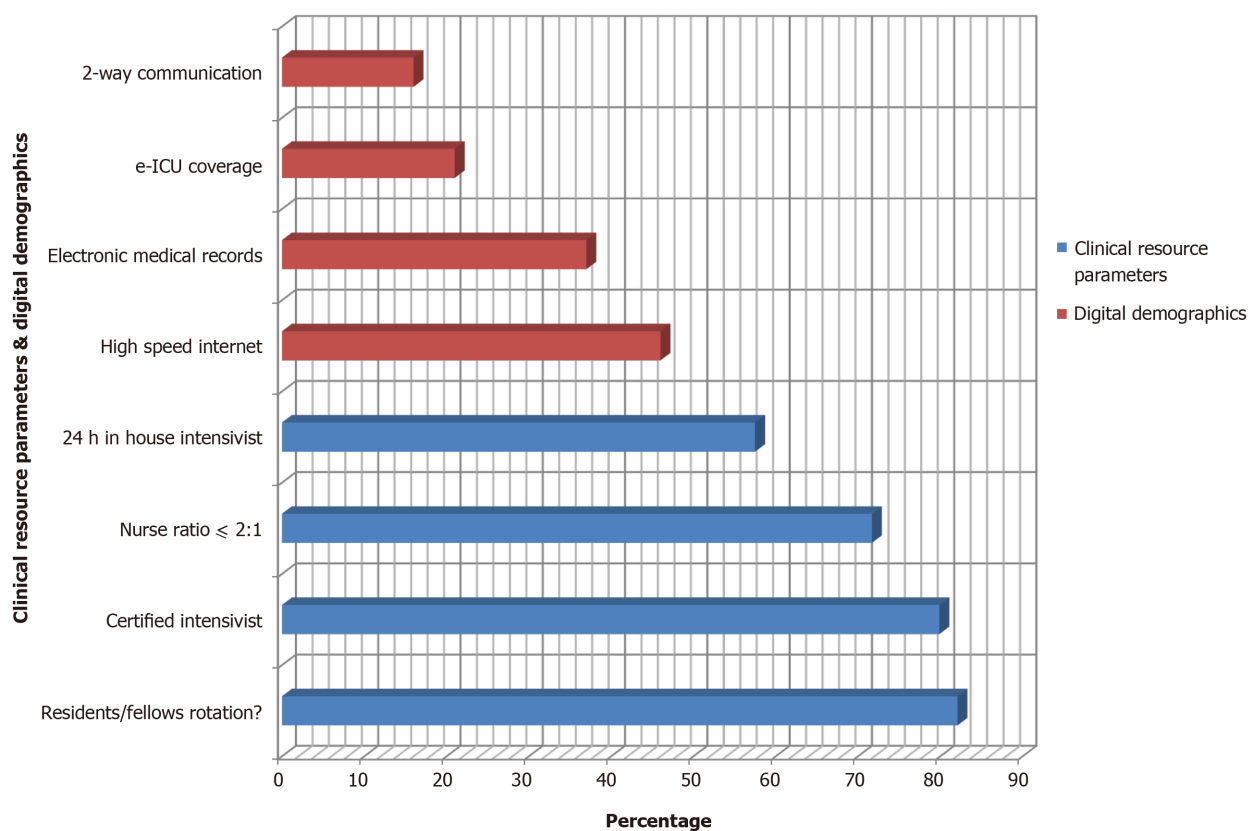
**Figure 4 Intensive care unit clinical resource parameters and digital demographics.**
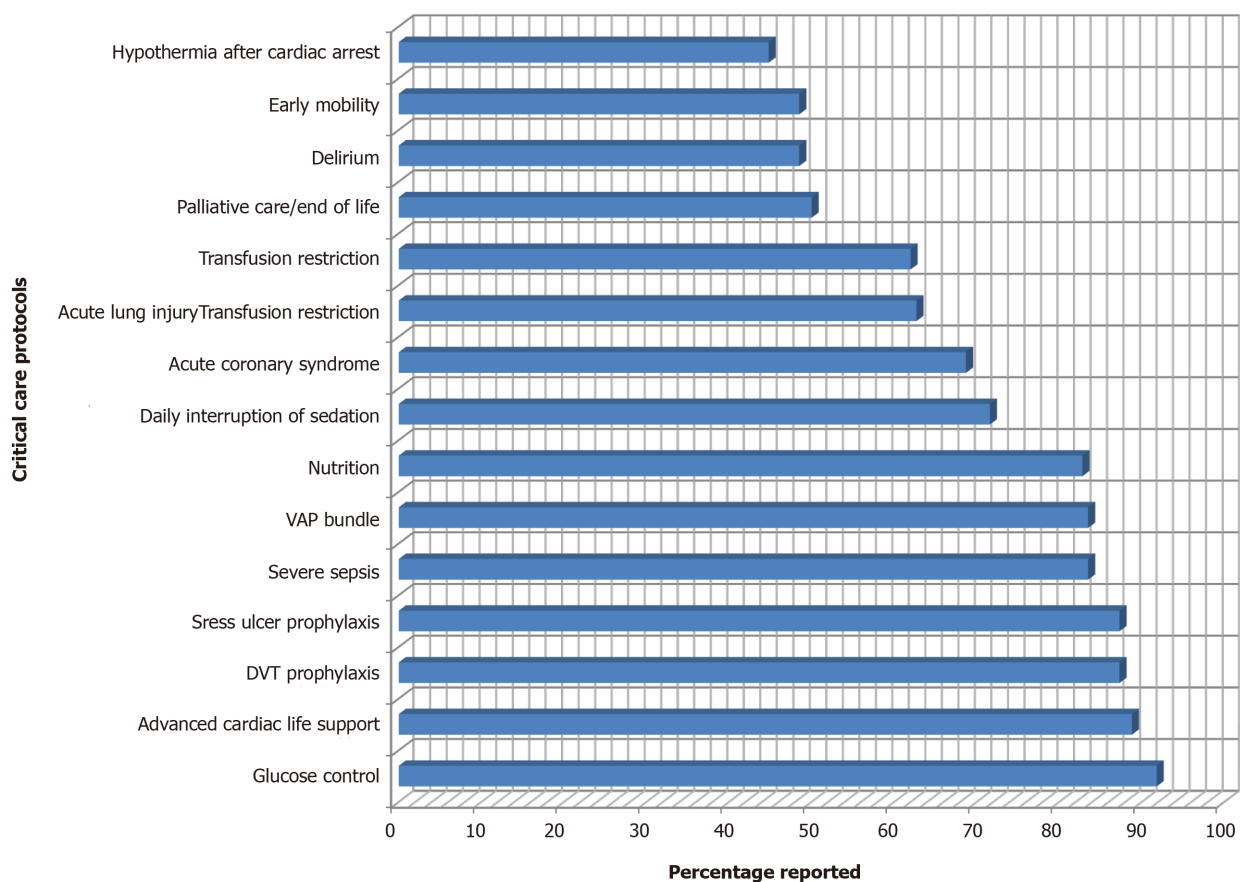


**Figure 5 Intensive care unit critical care protocols.**

## ARTICLE HIGHLIGHTS

### Research background

With the modernization of medicine and technology, the population is living longer. The patients presenting in hospital have several co-morbid factors and are critically ill on many instances. The developed countries have come with several protocol and best practices, based on the scientific facts and expert guideline. This has shown to save lives and improve the outcomes. When it comes to developing countries, though progress has been made but not much data or information is available.

### Research motivation

There is not much data out there regarding standard of practice, variations in practice, clinical services available in the different region of intensive care unit (ICU). We believe that having that knowledge will help in decreasing the variation and improve henceforth help in improving the patient care.

### Research objectives

Study was designed to understand the processes, adherence to the guidelines and clinical services available in ICU in different part of India.

### Research methods

This study was cross-sectional pan-India based survey.

### Research results

Responses were received from 134 adult/pediatric ICU were received. More than 80% of their ICU was either open or transitional. Digital infra-structure and technology was found to be marginal. More than 80% of them were utilizing sepsis care, ventilator-associated pneumonia bundle, deep venous thrombosis prophylaxis, stress ulcer prophylaxis and glycemic control. They have lower nurse to patient ratio. They also have fewer critical care specialist.

### Research conclusions

There is definitely need for improvement in the digital infra-structure, nurse to patient ratio, critical care physician availability.

### Research perspectives

Improving the practice gaps can help in improving the patient care, decreasing the hospital and ICU length of stay, decrease in mortality, and improvement in patient outcome.

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