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REPORTS OF ORIGINAL INVESTIGATIONS

The PROTROPIC feasibility study: prognostic value of elevated troponins in critical illness

L'étude de faisabilité PROTROPIC : valeur pronostique de l'élévation des troponines dans une maladie critique

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Abstract

Purpose *Elevated cardiac troponin concentrations in people with critical illness are associated with an increased risk of death. We aimed to assess the feasibility of a larger study to ascertain the utility of cardiac troponin as a prognostic tool for mortality in critically ill patients.*

Methods *Patients admitted to participating intensive care units during the one-month enrolment period were eligible. We excluded cardiac surgical patients and patients who were admitted and either died or were discharged within 12 hr. In enrolled patients, we measured high-sensitivity cardiac troponin I (hs-cTnI) and obtained electrocardiograms to ascertain the incidence of myocardial infarction (MI) and isolated troponin elevation. Our feasibility objectives were to measure recruitment rate, the proportion of patients who consented under a deferred consent model, and time required for data collection and study procedures.*

Results *Over a four-week enrolment period, 280 patients were enrolled using a deferred consent model. We obtained subsequent consent from 81% of patients. Study procedures and data collection required 1.7 hr per participant. Overall, 86 (38%) suffered a MI, 23 (10%) had an isolated hs-cTnI elevation, and 117 (52%) had no hs-cTnI elevation. The crude hospital mortality rate was 10%*

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without an hs-cTnI elevation, 29% with an isolated hs-cTnl elevation (relative risk [RR]) 2.2; 95% confidence interval [CI], 1.0 to 6.0) and 29% with an MI (RR, 2.6; 95% CI, 1.4 to 5.1).

Conclusion *Myocardial injury with elevated hs-cTnI concentrations and MIs occur frequently during critical illness. This pilot study has established the feasibility of conducting a large-scale investigation addressing this issue.*

Résumé

Objectif *Des concentrations élevées de troponine cardiaque chez des personnes présentant une maladie critique sont associées à un plus grand risque de décès. Nous avons cherché à évaluer la faisabilité d'une plus grande étude confirmant l'intérêt de la troponine cardiaque comme outil pronostique de décès chez des patients dans un état critique.*

Méthodes *Les patients admissibles étaient les patients hospitalisés dans les unités de soins critiques participantes pendant la période de recrutement d'un (1) mois. Nous avons exclu les patients chirurgicaux cardiaques et ceux qui avaient été admis dans l'unité et étaient décédés ou avaient eu un congé dans les 12 heures suivantes. Chez les patients inclus, nous avons mesuré la troponine I cardiaque de haute sensibilité (hs-cTnI) et avons obtenu des électrocardiogrammes pour vérifier l'incidence de l'infarctus du myocarde (IM) et de l'élévation isolée de la troponine. Nos objectifs de faisabilité étaient de mesurer le taux de recrutement, le pourcentage de patients donnant leur consentement selon un modèle de consentement différé, ainsi que le temps nécessaire à la collecte des données et aux procédures de l'étude.*

Résultats *Sur une période de recrutement de quatre semaines, nous avons inclus 280 patients avec un modèle de consentement différé. Nous avons obtenu ultérieurement le consentement de 81 % des patients. Les procédures d'étude et la collecte des données ont nécessité 1,7 heure par participant. Globalement, 86 patients (38 %) ont présenté un IM, 23 (10 %) avaient une élévation isolée du taux de hs-cTnI tandis que 117 patients (52 %) n'en avaient pas. Le taux de mortalité hospitalière a été de 10 % en l'absence d'augmentation de la hs-cTnI, de 29 % en cas d'augmentation isolée de la hs-cTnl (risque relatif [RR]) 2,2; intervalle de confiance [IC] à 95 % : 1,0 à 6,0) et de 29 % en cas d'IM (RR, 2,6; IC à 95 %, 1,4 à 5,1).*

Conclusion *Les atteintes myocardiques avec augmentation de la concentration de hs-cTnI et les IM sont fréquents au cours des maladies critiques. Cette étude pilote a établi la faisabilité d'une enquête à grande échelle sur cette question.*

Critically ill patients frequently have elevated cardiac troponin concentrations. Previous systematic screening studies suggest incidences of troponin elevations as high as 84% in this population.[1,2] Critically ill patients often receive life-support interventions such as mechanical ventilation, renal replacement therapy, vasopressors, and/or inotropes, which in combination with the underlying illness, result in extremely high levels of physiologic stress. Excess sympathetic activity with an imbalance of myocardial oxygen supply and demand is hypothesized to be the cause of troponin elevations in a variety of critical illnesses such as sepsis, intracranial catastrophes, and severe burns.[3-5] Troponins can be elevated in conditions associated with increased cardiac preload or afterload such as pulmonary embolism, pulmonary hypertension, and heart failure.[6-8] Nevertheless, critical illness is an inflammatory and pro-coagulant condition, therefore the risk of coronary thrombotic events is theoretically higher.[9]

Whether fulfilling criteria for myocardial infarction (MI) or not, observational evidence suggests that elevated cardiac troponin concentrations in critical illness are associated with an increased risk of death even when adjusted for confounding factors.[10] We conducted a pilot study to assess the feasibility of a large cohort study to

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evaluate whether troponin elevations have independent prognostic value for mortality in critically ill patients.

Methods

Study design

The PROTROPIC feasibility study (Prognostic value of elevated troponins in critical illness, NCT02285686) was a multicentre prospective cohort of consecutive critically ill patients conducted in four medical-surgical intensive care units (ICUs) at three university-affiliated hospitals in Hamilton, ON (St. Joseph's Healthcare Hamilton, Hamilton General Hospital, and Juravinski Hospital).

Study objectives

The pre-defined pilot study objectives were to assess the feasibility of recruiting patients efficiently in four ICUs, to evaluate the time required for data collection and study procedures, and to assess the deferred consent success rate. Pre-specified feasibility criteria were: 1) average recruitment rate (defined as the number of patients enrolled in the study per week) of 50 patients/week or more, 2) if the deferred consent rate (defined as the number of patients or substitute decision makers who provided consent divided by the total number of approached patients) was $\geq$ 80%, and 3) average time for completion of data collection of six hours or less. *A posteriori*, we measured compliance with study procedures (ability to assess serum high-sensitivity cardiac troponin I [hs-cTnI] levels and electrocardiograms [ECG] screening at the protocolized time points) as an additional feasibility objective (calculated as the number of tests obtained as a proportion of the number that should have been obtained based on the study protocol).

Secondary objectives of the PROTROPICS pilot study were the primary objectives of a larger future study—to describe the incidence of hs-cTnI elevations and their impact on crude in-hospital mortality, to evaluate the proportion of critically ill patients with elevated hs-cTnI who met the Third Universal Definition for Myocardial Infarction,[11] and to assess the association of hs-cTnI elevation with in-hospital mortality (meeting MI criteria or not) upon adjusting for confounders known to influence mortality.

Eligibility criteria

All adult patients admitted to participating ICUs during the study enrolment period were eligible. We excluded cardiac surgical patients, patients who were not expected to be alive or in the ICU for at least 12 hours, and patients re-admitted to the ICU during the study period. The Hamilton Integrated Research Ethics Board approved the study and allowed either *a priori* or deferred informed consent.

Patient recruitment

During the one-month study enrolment period, the research team in the participating ICUs screened all new admissions, including during weekends. We enrolled eligible patients using deferred consent, and obtained explicit consent from the patients or their substitute decision makers at the earliest possible time following enrolment. We recorded when study participation was declined and the reasons why patients or substitute decision makers were not approached.

Procedures

Study data points were entered into a REDCap database.[12] Upon enrolment into the study, we collected demographic and baseline clinical data (diagnosis for admission, Acute Physiology and Chronic Health Evaluation II [APACHE II] score,[13] comorbidities, cardiovascular risk factors, and home medications). During the ICU stay, we collected data on life support (mechanical ventilation, vasopressors and/or inotropes, and dialysis), treatments (medications, blood product transfusions), laboratory tests (creatinine, hemoglobin) and cardiovascular events (MI, stroke, arrhythmia, major bleeding, pulmonary edema, and non-fatal cardiac arrest). For the duration of hospital stay or up to three months after study enrolment, we collected data on vital status, ICU discharge, and risk stratification strategies (echocardiograms, stress tests, myocardial perfusion scans, and cardiac catheterization). The time required for data collection was measured every day upon completion of study procedures by all data collectors during the fourth week of recruitment. Collecting these data in the fourth week allowed research staff sufficient time to familiarize themselves with the study procedures.

Upon admission to and while participants were in the ICU, we obtained hs-cTnI measurements and ECGs daily for one week, every other day for three weeks, and then weekly for two months. The hs-cTnI assay (a chemiluminescent microparticle assay from Abbott Diagnostics) was performed using fresh EDTA plasma on the ARCHITECT i2000SR analyzers at all three centres with laboratory performance in agreement with the latest recommendations.[14] We collected data on all cardiac troponin measurements and ECGs ordered based on clinical care and data on whether patients had associated cardiac symptoms. We followed patients until hospital discharge, death, or for a maximum of three months.

Patients transferred to other hospitals were censored at the time of transfer.

The clinical team had access to all hs-cTnI results and ECGs that they ordered for clinical purposes, but were blinded to the non-clinical hs-cTnI and ECGs taken per the study protocol. If a non-clinical research ECG showed significant new ST depressions or ST elevations, a copy of the ECG was immediately provided to the clinical team.

Adjudication

An hs-cTnI result > 30 ng·L^{-1} was considered elevated, which corresponds to the 99th percentile upper limit of normal based on healthy populations.[15,16] Physicians who were blinded to the hs-cTnI results adjudicated all ECGs independently and in duplicate. They evaluated ECGs chronologically for ischemic changes meeting the Third Universal Myocardial Infarction Definition criteria.[11] A cardiologist, also blinded to hs-cTnI results, resolved any disagreements. Patients were considered to have had an MI if they had an elevated hs-cTnI with a rise and/or fall pattern in combination with either ischemic symptoms, ischemic ECG changes, new Q waves, new loss of viable myocardium, new regional wall motion abnormalities, or evidence of intracoronary thrombus.[11] We divided the patients into three groups: MI, isolated hs-cTnI elevation, and no hs-cTnI elevation.

Statistical analyses

We included a convenience sample to inform our feasibility objectives. We used descriptive statistics to report the feasibility outcomes and baseline characteristics of participants: mean and standard deviation (SD), median and interquartile range (IQR), and counts with associated proportions. For crude comparisons, we compared proportions using Pearson's Chi-square or Fisher's exact test and continuous variables using two-sample t test or Wilcoxon rank-sum test as appropriate for the data distribution. We built a logistic regression model to assess the relationship between isolated hs-cTnI elevations, MI, and mortality with adjustment for known prognostic factors. We chose the adjustment variables based on previous literature[17,18] and limited them to ensure a ratio of ten events per variable; we forced them in the model. The APACHE II was an obvious choice as it allowed adjustment for multiple factors at once. We added troponin elevation and MI as they were the focus of the study. For the final variable, we chose to include vasopressor at baseline as opposed to another variable because it is not captured in the APACHE II score and may cause myocardial injury. A P value < 0.05 was considered statistically significant. We report crude associations using relative risk and adjusted associations using adjusted odds ratio (aOR) with the associated 95% confidence interval (CI).

Results

Recruitment and feasibility objectives

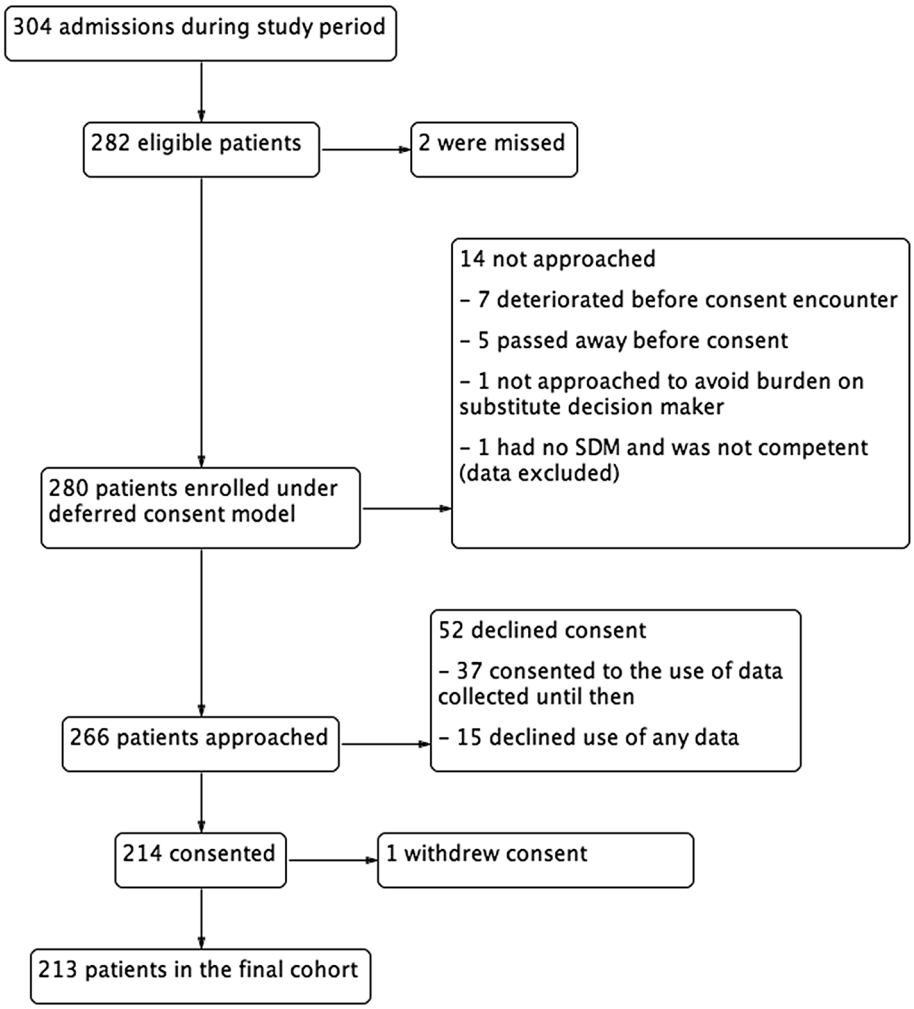
Over four consecutive weeks in the four ICUs, we screened 304 admissions; 282 patients were eligible but two were missed. Full consent was provided by 80.5% (214/266) of patients/substitute decision makers. One patient initially consented, but later withdrew consent. Of approached patients, 13.9% (37/266) consented to the use of data that had already been collected but declined further study participation. No consent was sought for 14 patients: 13 because of perceived substitute decision maker burden and imminent death (these patients are included in the cohort) and one patient because no substitute decision maker was identified. Details on the consent model and rate are published separately.[19] The patient flow chart is reported in the Figure.

During the four-week recruitment, we enrolled 266 patients, corresponding to 66.5 patients/week. Data collection took an average of one hour on a patient's first study day and 20 min on subsequent study days, for a median data collection time per patient of 1.7 hr throughout the entire study. One thousand and seventy-six hs-cTnI measurements were completed, which represents 74.6% of the troponin measurements that were supposed to be done based on the protocol. One thousand, two hundred and thirty-two ECGs were performed, which represents 85.4% of the ECGs that were supposed to be done based on the protocol.

Baseline characteristics

Of the 226 participants with complete follow-up, the mean (standard deviation [SD]) age was 61.5 (17.3) yr and 133 (58.8%) were males. The mean (SD) APACHE II score was 14.9 (7.6). Most patients were admitted with medical diagnoses (54.4%), while 38.1% were within 72 hr of a surgery, and 7.5% had suffered a trauma. Of the participants, 54.9% had hypertension, 27.4% had diabetes, 33.6% had hypercholesterolemia, and 16.4% had a history of coronary artery disease. On the first ICU day, 43.4% of participants received invasive mechanical ventilation, 19.0% received vasopressors, and 1.8% received intermittent hemodialysis or continuous renal replacement therapy (Table 1). A table comparing the characteristics of patients with full consent and those who declined follow-up is presented in the Appendix.

Figure Patient flow chart



Clinical outcomes

The median [interquartile range (IQR)] length of ICU stay was three (2–7) days. Of the participants with complete follow-up, 97.8% (221/226) had at least one research hs-cTnI result with the median [IQR] number of research hs-cTnI results being 5 (2–8). All participants with complete follow-up had at least one clinical or research hs-cTnI result. Of the patients with any data (those with complete follow-up and those who allowed us to use the data we had already collected, but declined further participation), 99.6% (262/263) had at least one hs-cTnI result, with the median [IQR] number of research hs-cTnI results being 4 (2–8). Of 226 participants with complete follow-up, 109 patients (48.0%) had at least one hs-cTnI concentration exceeding the upper limit of normal cutoff (30 $ng \cdot L^{-1}$) during their ICU stay. Of these patients, 86 (38.1%) met MI criteria and 23 (10.2%) had an isolated hs-cTnI elevation; 117 patients (51.7%) had no hs-cTnI elevation. Patient characteristics based on whether they suffered an MI, had an isolated hs-cTnI elevation, or neither are presented in Table 1. APACHE II, vasopressors requirement on day 1, and invasive and non-invasive ventilation differed significantly when the three groups were compared.

The crude hospital mortality rate was 9.5% in those without hs-cTnI elevation, 28.6% for those with isolated hs-cTnI elevation (RR, 2.2; 95% CI, 0.98 to 6.0) and 29.1% in those with MI (RR, 2.6; 95% CI, 1.4 to 5.1) (Table 2). Neither isolated hs-cTnI elevation (aOR, 0.5; 95% CI, 0.21 to 1.22) nor MI (aOR, 1.38; 95% CI, 0.44 to 4.35) were found to be independent predictors of hospital mortality after adjusting for confounders (Table 3).

Discussion

The PROTROPICS pilot study has three key findings. First, cardiac troponin elevations are common in the ICU, occurring in 48% of patients enrolled. Second, such elevations may be associated with a threefold increase in mortality. Finally, this pilot study shows the feasibility of a large-scale cohort aiming to determine the threshold at

Table 1 Baseline characteristics of participants with complete follow-up

	Total	Myocardial infarction	Isolated troponin elevation	No troponin elevation	*P* value for three-group comparison
n (%)	226	86 (38.0)	23 (10.2)	117 (51.8)	
Age, yr (SD)	61.5 (17.3)	63.4 (17.3)	65.5 (17.8)	59.4 (16.2)	0.12
Male sex, *n* (%)	133 (58.8)	48 (55.8)	13 (56.5)	72 (61.5)	0.66
BMI, $kg \cdot m^{-2}$ (SD)	30.2 (8.4)	28.4 (5.3)	26.8 (4.0)	31.7 (10.0)	0.21
APACHE II (SD)	14.9 (7.6)	18.2 (7.5)	19.2 (8.0)	11.5 (5.9)	< 0.001
Patient type, *n* (%)					
Medical	123 (54.4)	59 (68.6)	16 (69.6)	48 (41.0)	0.002*
Surgical	86 (38.1)	22 (25.6)	6 (26.1)	58 (49.6)	
Trauma	17 (7.5)	5 (5.8)	1 (4.3)	11 (9.4)	
Diagnosis category on admission, *n* (%)					
Cardiovascular	34 (15.0)	18 (20.9)	4 (17.4)	12 (10.2)	**
Respiratory	67 (29.6)	21 (24.4)	7 (30.4)	39 (33.3)	
Gastrointestinal	33 (14.6)	13 (15.1)	1 (4.3)	19 (16.2)	
Neurologic	45 (19.9)	17 (18.9)	3 (13.0)	25 (21.4)	
Sepsis	19 (8.4)	11 (12.8)	3 (13.0)	5 (4.3)	
Metabolic	11 (4.8)	4 (4.7)	2 (8.7)	5 (4.3)	
Other	17 (7.5)	2 (2.3)	3 (13.0)	12 (10.2)	
Past medical history, *n* (%)					
Smoker	34 (15.0)	15 (17.4)	1 (4.3)	18 (15.3)	0.35*
Hypertension	124 (54.9)	50 (58.1)	15 (65.2)	59 (50.4)	0.29
Diabetes	62 (27.4)	29 (33.7)	8 (34.8)	25 (21.3)	0.10
Atrial fibrillation	28 (12.4)	17 (19.8)	2 (8.7)	9 (7.7)	0.03*
Hypercholesterolemia	76 (33.6)	31 (36.0)	11 (47.8)	34 (29.1)	0.17
Coronary artery disease	37 (16.4)	17 (19.8)	3 (13.0)	17 (14.5)	0.54*
Venous thromboembolism	10 (4.4)	3 (3.5)	0 (0)	7 (6.0)	0.57*
Congestive heart failure	26 (11.5)	14 (16.3)	3 (13.0)	9 (7.7)	0.14*
Moderate or severe valvular heart disease	5 (2.2)	3 (3.5)	0 (0)	2 (1.7)	0.80*
Peripheral vascular disease	14 (6.2)	5 (5.8)	1 (4.3)	8 (6.8)	1.00*
Stroke/transient ischemic attack	34 (15.0)	22 (25.6)	4 (17.4)	8 (6.8)	0.001*
Chronic obstructive pulmonary disease/asthma	51 (22.6)	18 (20.9)	7 (30.4)	26 (22.2)	0.62
Baseline life support, *n* (%)					
Inotropes	1 (0.4)	1 (1.2)	0 (0)	0 (0)	0.48*
Vasopressors	43 (19.0)	28 (32.6)	3 (12.0)	12 (10.2)	<0.001*
Non-invasive ventilation	29 (12.8)	17 (19.8)	0 (0)	12 (10.2)	0.02*
Invasive mechanical ventilation	98 (43.4)	45 (52.3)	15 (65.2)	38 (32.5)	0.001
Intermittent dialysis	2 (0.9)	2 (2.3)	0 (0)	0 (0)	0.34*
Continuous renal replacement therapy	2 (0.9)	2 (2.3)	0 (0)	0 (0)	0.34*

APACHE II = Acute Physiology and Chronic Health Evaluation II; BMI = body mass index; SD = standard deviation

*At least one cell count with an expected count less than 5, Fisher's exact test used

**Not calculated

Table 2 Clinical outcomes with complete follow-up

	Total	Myocardial infarction	Isolated troponin elevation	No troponin elevation	*P* value for three-group comparison
Hospital mortality, *n* (%)	42 (18.8)	25 (29.1)	6 (28.6)	11 (9.5)	0.001*
Intensive care unit length of stay, days [IQR]	3 [2–7]	6 [2–12]	4 [2–5]	2 [1–5]	0.02
Hospital length of stay, days [IQR]	11 [5–22]	16 [8–35]	12 [4–18]	9 [4–14]	0.28

IQR = interquartile range

*At least one cell count with an expected count less than 5, Fisher's exact test used

Table 3 Logistic regression model for in-hospital mortality

	B	SE	Wald	df	*P*	Odds ratio	95% CI
Isolated troponins elevation	0.69	0.46	2.30	1	0.13	0.50	0.21 to 1.22
Myocardial infarction	0.32	0.59	0.30	1	0.58	1.38	0.44 to 4.35
APACHE II	0.05	0.03	3.88	1	0.049	1.05	1.0 to 1,11
Vasopressor on day 1	1.44	0.42	11.99	1	0.001	4.21	1.87 to 9.50
Constant	2.45	0.59	17.13	1	0.000	0.09	

APACHE II = Acute Physiology and Chronic Health Evaluation II; B = beta coefficient; CI = confidence interval; df = degrees of freedom; SE = standard error

which cardiac troponin elevation is an independent prognostic factor for mortality in critically ill patients.

Despite improvements in mechanical ventilation,[20] new technologies for hemodynamic support,[21] and implementation of interventions that have been proven to decrease complications of critical illness,[22] about 15% of patients die during their ICU stay.[23] More than a fifth of patients admitted to the ICU die in hospital. Risk prediction models for mortality have been validated but their discrimination is imperfect.[13,24] A better understanding of the relationship between widely available laboratory tests and mortality in the ICU may lead to identification of patients at risk of poor outcomes, and evaluation of therapies in these patients at risk of poor outcomes, potentially decreasing the risk of death.

Studying cardiac troponin elevations during critical illness should be a priority. Clinicians need to understand a phenomenon that, based on our pilot study results, affects nearly half of all critically ill patients and is associated with an almost threefold increase in hospital mortality. The estimates seen in our pilot study are consistent with previous reports on prospective systematic screening studies,[1,2,25] systematic reviews,[4,10,26,27] and more recent non-systematic/retrospective cohorts.[28-31]

Currently, whether troponin elevations in the ICU hold an etiologic prognostic value of their own, or whether they are a marker of higher illness severity in general remains unclear. In many critically ill patients, cardiac symptoms cannot be elicited because of sedation or other distracting factors such as postoperative analgesic medications and delirium, making the distinction between isolated troponin elevations and MI in this population problematic and potentially spurious. If cardiac troponin elevation and MI identified in critically ill patients share the pathophysiology of type 1 (spontaneous, due to ruptured atherosclerosis plaque) or type 2 (secondary, caused by an imbalance of myocardial oxygen supply and demand) MI,[11]—and they likely do—then these two conditions underscore the need for evaluation of treatments to improve the short- and long-term outcomes of patients in the ICU. Cardiac troponin elevation as a potentially modifiable mediator of death is the focus of the OVATION65 trial (NCT03431181), which is evaluating whether permissive hypotension in vasodilatory shock (by sparing catecholaminergic agents) decreases myocardial injury and, consequently, improves survival. As a parallel, cardiac troponin elevations after non-cardiac surgery are independently associated with mortality at 30 days as demonstrated in a large cohort study.[32] In a subsequent randomized-controlled trial,[33] dabigatran was shown to lower the risk of major vascular complications when administered to patients with cardiac troponin elevations after non-cardiac surgery. Meanwhile,

in the absence of ICU specific trials, applying data from the acute coronary syndrome literature in the ICU population could be considered given the strength of the evidence supporting the treatment of patients with MI whether perceived to be primary or secondary.[34]

A large multicentre prospective cohort study with built-in ancillary mechanistic studies will improve our understanding of cardiac troponin elevations in critical illness. Such a cohort study with systematic laboratory testing and ECG screening will confirm if elevated cardiac troponins in patients with critical illness, whether meeting other criteria for MI or not, are independently associated with a worse prognosis. Given the multiplicity of confounding factors, a large cohort is required to adjust for these confounders. The current literature consists of relatively small single centre observational studies spread over almost 20 years using different types of cardiac troponin assays that have either been taken off the market or are bound to disappear in the future, with the majority of the major diagnostic companies producing hs-cTn assays.[35] A contemporary evaluation of the prevalence, incidence, and risk factors for elevated cardiac troponin concentrations, how patients with elevated concentrations are treated as a baseline, and the incidence of MI in critically ill patients are needed. Knowing the prognosis of these conditions and understanding current management will guide researchers and clinicians in evaluating potential risk-modifying therapies.

Our results show that conducting such a large cohort study with systematic cardiac troponin and ECG screening is feasible. The high consent rate is reassuring for the main cohort's external validity. The rapid accrual of participants confirms that a large cohort can be recruited efficiently. With data collection requiring on average less than two hours per participant, the study procedures are pragmatic. While compliance with screening cardiac troponin and ECG was suboptimal, we have identified these as key study procedures to monitor in the main cohort.

Strengths and limitations

Strengths of this study include demonstrating feasibility of a study to ascertain the utility of cardiac troponin as a prognostic tool for mortality in critically ill patients, using a larger sample size than previous studies with a similar design.[1,2] The study also estimated the incidence of cardiac troponin elevation and MI that will inform a rigorous future evaluation. Using a deferred consent model, we avoided selection bias enrolling consecutive patients fulfilling eligibility criteria in four ICUs. Blinded adjudicators assessed serial ECGs for ischemia.

The study also has several limitations. We evaluated feasibility in teaching centres; different practical issues may occur in community hospitals. In addition, this pilot study was not powered to evaluate clinical outcomes and thus should generate further hypotheses rather than change practice.

Conclusions

Myocardial injury and MI are frequent during critical illness and these patients have an unadjusted higher risk of mortality compared with patients who do not have a cardiac troponin elevation. Whether the association of cardiac troponin elevation with death in the ICU is independent of other prognostic factors remains uncertain. This pilot study has established the feasibility of conducting a large-scale investigation addressing this issue.

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Competing interest Dr. Peter Kavsak has received grants/reagents/consultant/advisor/honoria from Abbott Laboratories, Abbott Point of Care, Abbott Diagnostics Division Canada, Beckman Coulter, Ortho Clinical Diagnostics, Randox Laboratories, Roche Diagnostics, and Siemens Healthcare Diagnostics related to cardiac biomarker testing. McMaster University has filed patents with Dr. Kavsak listed as an inventor in the acute cardiovascular biomarker field, in particular, a patent has been filed on aspects related to the data presented in this study "A laboratory score for risk stratification for patients with possible cardiac injury".

Editorial responsibility This submission was handled by Dr. Sangeeta Mehta, Associate Editor, *Canadian Journal of Anesthesia.*

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Appendix: Comparison of patients with complete follow-up and patients with partial consent

	Total	Complete follow-up	Partial consent with data	*P* value
n (%)	261	226	35	-
Age, yr (SD)	61.4 (17.8)	61.5 (17.3)	60.2 (23.1)	0.69
Male sex, *n* (%)	145 (55.6)	133 (58.8)	12 (34.3)	0.006
BMI, $kg \cdot m^{-2}$ (SD)	29.7 (8.1)	30.2 (8.4)	26.2 (4.4)	0.17
APACHE II (SD)	15.1 (7.7)	14.9 (7.6)	16.7 (8.6)	0.19
Patient type, *n* (%)				
Medical	142 (54.2)	123 (54.4)	18 (51.4)	0.39*
Surgical	98 (37.4)	86 (38.1)	12 (34.3)	
Trauma	22 (8.4)	17 (7.5)	5 (14.3)	
Diagnosis category on admission, *n* (%)				
Cardiovascular	38 (14.5)	34 (15.0)	4 (11.4)	0.95*
Respiratory	77 (29.4)	67 (29.5)	10 (28.6)	
Gastrointestinal	37 (14.1)	33 (14.6)	4 (11.4)	
Neurologic	53 (20.2)	45 (19.9)	8 (22.9)	
Sepsis	23 (8.8)	19 (8.4)	4 (11.4)	
Metabolic	12 (4.6)	11 (4.8)	1 (2.9)	
Other	22 (8.4)	17 (7.5)	4 (11.4)	
Past medical history, *n* (%)				
Smoker	38 (14.5)	34 (15.0)	4 (11.4)	0.80*
Hypertension	141 (53.8)	124 (54.9)	17 (48.6)	0.50
Diabetes	71 (27.1)	62 (27.4)	9 (25.7)	0.84
Atrial fibrillation	31 (11.8)	28 (12.4)	3 (8.6)	0.78*
Hypercholesterolemia	89 (34.0)	76 (33.6)	13 (37.1)	0.67
Coronary artery disease	40 (15.3)	37 (16.4)	3 (8.6)	0.24
Venous thromboembolism	11 (4.2)	10 (4.4)	1 (2.9)	1.00*
Congestive heart failure	30 (11.5)	26 (11.5)	4 (11.4)	1.00*
Moderate or severe valvular heart disease	5 (1.9)	5 (2.2)	0 (0)	0.75
Peripheral vascular disease	17 (6.5)	14 (6.2)	3 (8.6)	0.59*
Stroke/Transient ischemic attack	38 (14.5)	34 (15.0)	4 (11.4)	0.58*
Chronic obstructive pulmonary disease/ Asthma	60 (22.9)	51 (22.6)	9 (25.7)	0.67*
Baseline life support, *n* (%)				
Inotropes	2 (0.8)	1 (0.4)	1 (2.9)	0.25*
Vasopressors	58 (22.1)	43 (19.0)	15 (42.9)	0.002
Non-invasive ventilation	32 (12.2)	29 (12.8)	3 (8.6)	0.48*
Invasive mechanical ventilation	120 (45.8)	98 (43.4)	22 (62.9)	0.03
Intermittent dialysis	3 (1.1)	2 (0.9)	1 (2.9)	0.35*
Continuous renal replacement therapy	2 (0.8)	2 (0.9)	0 (0)	0.75*
Outcomes				
Isolated troponin elevation	31	23 (10.1)	8 (22.9)	0.045*
Myocardial infarction	99	86 (37.9)	13 (37.1)	0.93

*At least one cell count with an expected count less than 5, Fisher's exact test used

APACHE II = Acute Physiology and Chronic Health Evaluation II; BMI = body mass index; SD = standard deviation

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