ICCR PROJECT PROTOCOL
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Study Title:
A Case-Control Study of Outcomes Among Patients Readmitted to a Medical ICU

Study Purpose and Rationale:
Intensive care services are among the most invasive and costly of all care strategies in US hospitals. However, defining which patients stand to benefit most from these aggressive, costly services has proved difficult. It has been reported that over half of intensive care resources are expended on patients who do not survive to hospital discharge.[1] Transfer to an intensive care unit (ICU) is very common during a terminal hospitalization. It has been estimated that 17% of all deaths in the United States occur during hospitalizations that include triage to an ICU.[2] Further, of the 37% of all deaths in the United States that occur in acute-care hospitals, 47% involve intensive care services.[2]

Given the high costs and limited benefits attributable to ICU-level care during a terminal hospitalization, there is interest in defining risk factors to help physicians identify and appropriately triage those patients who are least likely to survive an ICU admission. However, while existing in-hospital mortality prediction scales perform well on a population basis, they perform only with moderate predictive value when applied to individual patients. In fact, despite the routine use of prediction scales at the time of ICU admission, observational studies have suggested that attending ICU physicians discriminate between survivors and non-survivors more accurately than do scoring systems.[3]

Beyond costs, it is also unclear whether routine triage to ICU-level care during terminal hospitalizations is in accordance with the wishes of patients and their families. A study at one teaching hospital investigating all in-hospital deaths over a two-year period showed that none of the 78% of patients who underwent transfer to an ICU prior to death had had discussions with their physicians regarding palliation or end-of-life care as an alternative to aggressive treatment. Of the 22% of in-hospital decedents who were not transferred to an ICU, 25% had had such discussions. Experienced physicians were more likely to have had discussions regarding alternatives to aggressive care than were house staff, suggesting that the inability to confidently prognosticate serves as a barrier to transitioning patients from aggressive to palliative measures.[4]

Enhancing the ability of physicians to predict in-hospital death and communicate that risk to patients and their families may therefore influence triage decisions to bring them more in line

[1] Durbin CG Jr, Kopel RF. A case-control study of patients readmitted to the intensive care unit. *Crit Care Med*. 1993 Oct;21(10):1547-53.

[2] Wunsch H, *et al*. Use of intensive care services during terminal hospitalizations in England and the United States. *Am J Respir Crit Care Med*. 2009 Nov 1;180(9):875-80.

[3] Sinuff T, *et al*. Mortality predictions in the intensive care unit: comparing physicians with scoring systems. *Crit Care Med*. 2006 Mar;34(3):878-85.

[4] Rady MY, Johnson DJ. Admission to intensive care unit at the end-of-life: is it an informed decision? *Palliat Med*. 2004 Dec;18(8):705-11.

with patient and family wishes. Identifying risk factors for in-hospital mortality is an important component of this pursuit, especially given the prominent roles of relatively inexperienced house staff in establishing goals of care and making decisions regarding ICU triage.

This study proposes to investigate whether readmission to the medical ICU during a single hospitalization is itself a risk factor of in-hospital death. Readmission to an ICU is a common occurrence, with the average readmission rate among ICU discharges estimated to be about 7%.[5,6] In-hospital mortality among these patients is known to be high, with prior studies demonstrating mortality rates of about 40%.[1,7] Prior studies have aimed at demonstrating the increased mortality among patients readmitted to ICUs as compared to those who are not readmitted, and at identifying risk factors for readmission at the time of ICU discharge.[1,7,8] While it has been shown that the in-hospital mortality of patients readmitted to ICUs is 5- to 8-fold greater than those not readmitted,[1,7,8] whether the prior ICU admission *per se* confers an independent risk of mortality at the time of readmission has not been studied. Whether the prior ICU admission confers risk beyond what would otherwise be predicted based on a patient's cross-sectional characteristics is an important question when considering the appropriateness of a possible transfer back to the ICU. Our hypothesis is that the prior ICU admission is in fact an independent risk factor of in-hospital death among those readmitted to the medical ICU. This hypothesis is based on the principle that the need for ICU readmission is an indicator of "poor response to treatment."[7] We therefore propose to conduct a case-control trial comparing outcomes of patients readmitted to a medical ICU versus matched controls admitted to a medical ICU for the first time.

Study Design, Subjects, and Statistical Analysis
The proposed study is a retrospective case-control chart review, investigating outcomes of admissions to MICU-A and MICU-B at the Columbia University Medical Center, from January 1, 2009 through December 31, 2009. The cases will comprise all patients transferred from the general medicine wards to MICU-A or MICU-B following a prior admission to either MICU during the same hospitalization. Two controls will be selected for each case, and will be drawn from the cohort of patients transferred to MICU-A or MICU-B from the general medicine wards, who were not previously admitted to either MICU. Those patients who were subsequently readmitted to either MICU will be excluded from the cohort of possible controls, in order to avoid using the same patient as both a case and a control. The controls will be selected to match cases on the following criteria: age, sex, unit, ICU admission diagnosis, and APACHE II score 24 hours following ICU admission. MICU admissions directly from the Emergency Department (ED) will be excluded from the cohort from which controls are selected, as direct admissions from the ED are likely a disparate group of patients, as compared to patients who undergo clinical deterioration during their hospitalizations requiring transfer to a higher level of care.

[5] Rosenberg AL, Watts C. Patients readmitted to ICUs* : a systematic review of risk factors and outcomes. *Chest*. 2000 Aug;118(2):492-502.

[6] Elliott M. Readmission to intensive care: a review of the literature. *Aust Crit Care*. 2006 Aug;19(3):96-8, 100-4.

[7] Rosenberg AL, *et al*. Who bounces back? Physiologic and other predictors of intensive care unit readmission. *Crit Care Med*. 2001 Mar;29(3):511-8.

[8] Chen LM, *et al*. Patients readmitted to the intensive care unit during the same hospitalization: clinical features and outcomes. *Crit Care Med*. 1998 Nov;26(11):1834-41.

The primary outcome for comparison will be in-hospital mortality. Secondary outcomes will be (1) time to death among decedents, (2) length of ICU stay and post-ICU hospitalization among survivors, and (3) discharge destination among survivors (*ie*, to home, skilled nursing facility, or hospice). All demographic data will be analyzed using t-test for continuous variables and Chi-square analysis for categorical variables, to determine whether there are differences between the cases and controls. To evaluate the primary outcome (in-hospital mortality), a Chi-square analysis will be performed. The anticipated in-hospital mortality rates are as follows: 40% among cases (as derived from the literature),[1,6] and 20% among controls (as estimated from experience). The number of subjects needed to detect this difference with a power of 80% and an alpha of 0.05, using 2 matched-controls for each case, is 66 cases and 132 controls. Given the anticipation of 1.5 MICU readmissions per week, a review period of 12 months should produce an adequate number of cases.

If, as per the hypothesis, APACHE-II does not accurately predict the in-hospital mortality among the MICU readmissions, a multiple logistic regression will be performed to generate a more accurate predictive model.

Study Procedures/Drugs/Medical Devices/Questionnaires
No procedures, drugs, medical devices, or questionnaires are associated with this study.

Recruitment of Subjects and Confidentiality of Study Data
Given the study design utilizing chart review, and the corresponding minimal anticipated harm to subjects, we propose that the need for informed consent among subjects or their survivors be waived for this study. In order to preserve the confidentiality of the study data, all data extracted from the medical record will be de-identified. Data will be stored in a secure location, accessible only to the investigators.

Potential Conflict of Interest
There are no potential conflicts of interest to report.

Location of the Study
MICU-A & MICU B, Milstein Hospital, Columbia University Medical Center

Potential Risks/Benefits/Alternative Therapies
As a retrospective chart review, there are no potential benefits or alternative therapies. Potential risks are limited to the possible release of confidential data.

Compensation/Costs to Subjects
None

Minors as Research Subjects
No minors will be included as research subjects

Radiation or Radioactive Substances
No exposure to radiation or radioactive substances will result as a consequence of this study.

References
1. Durbin CG Jr, Kopel RF. A case-control study of patients readmitted to the intensive care unit. *Crit Care Med*. 1993 Oct;21(10):1547-53.
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3. Sinuff T, Adhikari NK, Cook DJ, Schünemann HJ, Griffith LE, Rocker G, Walter SD. Mortality predictions in the intensive care unit: comparing physicians with scoring systems. *Crit Care Med*. 2006 Mar;34(3):878-85.
4. Rady MY, Johnson DJ. Admission to intensive care unit at the end-of-life: is it an informed decision? *Palliat Med*. 2004 Dec;18(8):705-11.
5. Rosenberg AL, Watts C. Patients readmitted to ICUs* : a systematic review of risk factors and outcomes. *Chest*. 2000 Aug;118(2):492-502.
6. Elliott M. Readmission to intensive care: a review of the literature. *Aust Crit Care*. 2006 Aug;19(3):96-8, 100-4.
7. Rosenberg AL, Hofer TP, Hayward RA, Strachan C, Watts CM. Who bounces back? Physiologic and other predictors of intensive care unit readmission. *Crit Care Med*. 2001 Mar;29(3):511-8.
8. Chen LM, Martin CM, Keenan SP, Sibbald WJ. Patients readmitted to the intensive care unit during the same hospitalization: clinical features and outcomes. *Crit Care Med*. 1998 Nov;26(11):1834-41.