TITLE (SHORT, 200 CHARACTERS MAX.):

THE RELATIONSHIP BETWEEN SEDATIVE CHOICE AND DELAYED AWAKENING FOLLOWING CARDIAC ARREST

MAIN HYPOTHESES TESTED (2 MAX)

Hypothermia is known to impair hepatic enzyme function. We hypothesize that those patients who receive midazolam for sedation (which is metabolized primarily by the hepatic cytochrome P450 enzymes) and are randomized to the 33°C arm will have delayed awakening as compared to those randomized to the normothermia arm. We further hypothesize that patients who receive midazolam will have delayed awakening as compared to patients sedated with propofol or volatile anesthetics.

SINGLE CENTER [ ] , MULTICENTER [X]

All TTM2 sites with at least 20% of patients receiving midazolam as their primary sedative agent.

PICO

Patients: All patients admitted to the ICU and who survive the planned 40-hours of sedation will be included. Patients who require ongoing sedation beyond 40-hours will be excluded.

Intervention/Exposure/Prognostic factor: Received midazolam for sedation vs. other sedative medications

Comparison:

1) Among patients who receive midazolam, time-to-awakening in the 33°C arm vs. the normothermia arm?
2) Time-to-awakening in patients who receive midazolam vs. other sedative agents

Outcome: Time-to-awakening (i.e. following commands)

DATA NEEDED FOR THE ANALYSIS (SPECIFY VARIABLES AND MOTIVATE ANY PROPOSED ADDITIONS TO THE ECRF)

1) Sedative(s) received during 40-hours of sedation
2) Total dose of all sedatives received
3) Randomization arm
4) Date and time of awakening (i.e. following commands)
5) Neurologic outcome at hospital discharge
6) Additional variables including arrest variables (e.g. total downtime, initial rhythm), patient variables (e.g. comorbidities) and post-arrest variables (e.g. liver/kidney failure)

LOGISTICS – HOW WILL ADDITIONAL DATA BE GATHERED?

If not already collected as part of the TTM2 eCRF, we would ask that sites collect data regarding duration and total dose of all sedatives.

BRIEF STATISTICAL ANALYSIS PLAN AND SAMPLE SIZE ESTIMATE

For the primary analysis, we will perform multivariate linear regression with time-to-awakening included as the dependent variable and randomization arm (33°C vs. normothermia) as the primary independent variable.
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Additional variable (e.g. organ failure) that are unbalanced after randomization will be included in the model. Generalized estimating equations will be used to account for clustering at the hospital level. For the secondary analysis, we will similarly perform multivariate linear regression with time-to-awakening as the dependent variable as choice of sedative (midazolam vs. other) as the binary dependent variable.

To have 90% power to detect a 20% difference in time-to-awakening between groups at an α of 0.05 we would anticipate a minimum sample size of 206 patients (103 patients per group) for both analyses.

FUNDING (IF APPLICBABLE)

None

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