Appendix to the AID-ICU cohort study statistical analysis plan for investigating physical restraint in critically ill patients

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Prevalence and risk factors for the use of physical restraint in the adult intensive care unit – a sub-study to the multinational AID-ICU inception cohort study

Introduction

In critically ill patients, physical restraint is used to ensure safety i.g. applied to prevent patients from accidently or purposefully removing lifesaving medical devices[1]. However the prevalence of physical restraint varies from 0% to 100% in intensive care units (ICU) across different countries[2]. Risk factors for physical restraint have been suggested to include mechanical ventilation, coma, delirium, agitation, use of anti-psychotics, benzodiazepines and renal replacement therapy[3,4]. Physical restraint has been an accepted and integrated intervention in several countries for many years and has rarely not been considered, a variable in the analysis of pain, sedation and delirium.

We will conduct a secondary analysis of all patients in the AID-ICU cohort to assess the association between physical restraint and selected variables. The STROBE statement will be used to report the results of this study[5].

Research question

1. What is the prevalence of physical restraint in a mixed contemporary multinational cohort?
2. Which factors are associated with physical restraint for patients admitted to an ICU including nurse-patient ratios?
3. How many patients without delirium are under physical restraint?

Hypothesis: We hypothesize that physical restraints are common in some countries during the ICU stay and that older age, delirium, coma, mechanical ventilation, sedatives, benzodiazepines and atypical antipsychotics in the ICU are associated with use of physical restraints. We also hypothesize that physical restraint is used more frequently in some countries than others and in ICUs with lower nurse-to-patient ratio[6].

Aim: The aim of this study is to describe the prevalence and variables associated with application of physical restraint in patients admitted to the ICUs participating in the AID-ICU cohort study.

Power analysis

The sample of the AID-ICU restraint cohort is fixed. The AID-ICU cohort included 1260 ICU patients. The actual power of the primary analysis will be expressed through the width of the confidence intervals.

Primary outcome: Number of patients that were physically restrained at some point during their ICU stay (% (95% Confidence Interval)).

Secondary outcomes:

- Number of days physical restraint was applied
- Number of days physical restraint was applied when the patient also was in coma, delirious or mechanical ventilated
- Days alive without use of restraint, mechanical ventilation, coma and delirium

Definition of variables

Physical restraint

Any manual method, physical, or mechanical device, material, or equipment that immobilizes or limits the patient´s ability to move the head or extremities freely. This was assessed daily in the AID-ICU study in all patients (physical restraint during this day (y/n)).

Delirium

We considered patients as delirious if they were screened delirium positive at any point during the ICU stay using a validated tool.

Subtypes

We divided delirium into subtypes defined as hypoactive, hyperactive and mixed on the first day with delirium[8,9].

Mechanical Ventilation

We considered a patient mechanically ventilated (MV) if they were MV the first day in ICU.

Coma

Defined as coma the first day in ICU.

Length of ICU and hospital stay

Number of days in ICU from time of admission to time of discharge from ICU. The time for hospital stay is the time the patient was admitted to the hospital and discharged home (or other e.g. care facility) from the hospital. Additional hospitalisations will be added to hospital length of stay.

Data presentation

Numeric data will be shown as medians with inter-quartile ranges (IQR) or ranges where relevant. Frequencies will be shown as numbers with percentages and 95% confidence intervals (CI) where relevant.

Descriptive statistics

Exposure:

Restraint within 72 hours: all patients physically restrained within the first 72 hours of ICU admission.

Restraint after 72 hours: all patients physically restrained after 72 hours of ICU admission.
No restraint: all patients not physically restrained with in the first 24 hour of ICU admission. If a patient subsequently is physically restrained within the 24 to 72 hours after ICU admission the patient will be moved to the group "Restraint within 72 hours". If a patient is physically restrained after 72 hours of ICU admission the patient will be moved to the group "Restraint after 72 hours".

Competing events
Death and ICU discharge is competing event to be physically restraint.

We will use Cox model to analysis time to restraint in the ICU censoring for death and ICU discharge. We will separately report total days of physical restraint.
We will report how many patients that were mechanically ventilated, delirious, comatose, sedated, treated with benzodiazepines or anti-psychotics at the time of physical restraint. We will also report the time of MV, delirium and coma as median (IQR) or mean (SD) where relevant.

We will compare differences in baseline (day 1 (first- and second-day form)) characteristics between patients physically restraint and non-restraint using the Wilcoxon's or Chi-square test.

We will present the number of patients with restraint that received anti-psychotics (haloperidol, olanzapine and quetiapine), benzodiazepines, and sedatives at any time during ICU stay as frequencies (% with 95% CI).

We will present the number of patients with a hyperactive, hypoactive and mixed type of delirium, and use of physical restraint as frequencies (% with 95% CI) at baseline.

We will present the number of patients without delirium and use of physical restraint as frequencies (% with 95% CI) at baseline.

Analysis for the risk of being physically restraint
For the analysis of risk factors for the use of physical restraint in ICU, the outcome measures will be compared between the dynamically updated groups (No restraint, Restraint within 72 hours and Restraint after 72 hours) using Cox model with delayed entry, censoring at death and ICU discharge. This is comparable to Cox model with time varying exposure, where the time varying exposure is the dynamic group for each patient. We will adjust the analysis for the following confounders: age (in quartiles), presence of delirium as no, hyper, hypo or mixed, coma, use of dialysis (y/n), shock (y/n), use of mechanical ventilation (y/n)), use of sedation (y/n) and ICU characteristic (university hospital, guidelines for identifying and/or treating delirium and average staff-patient ratio as 1:1, 1:2, 1:3 or 1:3+, and country.

All statistical tests will be 2-tailed and $p<.05$ considered statistically significant.

Missing data will be presented in the appendix of the main manuscript. We expect only few individuals with missing data therefore we will employ complete case analyses after logical imputations. All details will be presented in a supplement to the primary publication.

Reference

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