STUDY PROTOCOL

CIILOS – Continuous Renal Replacement Therapy, Impact on Intensive Care Unit Length of Stay

Unique Protocol ID: CIILOS
NCT Number: Not yet assigned

Protocol Version: 1.0
Date: 2026-01-05

Principal Investigator
Max Bell, MD, PhD
Department of Perioperative Medicine and Intensive Care, Karolinska University Hospital
Department of Physiology and Pharmacology, Karolinska Institutet
Stockholm, Sweden

Sponsor: Karolinska Institutet

Ethics Approval: Swedish Ethical Review Authority, Dnr 2025-05653-02

1. Background and Objectives

This large national cohort study, including over 500,000 patients, aims to evaluate the association between time to initiation of continuous renal replacement therapy (CRRT) and intensive care unit (ICU) length of stay (LOS).

We hypothesize that earlier start of CRRT is associated with shorter length of stay among critically ill patients.

CRRT is seen as a costly intervention, and after studies failing to demonstrate a mortality benefit from earlier initiation, the trend is to push, or postpone the start of CRRT. In Sweden the additional cost of CRRT amounts to around 5000 SEK, approximately 500 dollars/euros per 24 hours. However, the 24-hour cost of staying in the ICU is around 58000 SEK or 5800 dollars/euros.

2. Primary Endpoints

The primary endpoint is ICU length of stay; this will be measured with high resolution, in hours.

3. Secondary Endpoints

Secondary endpoints include: time on mechanical ventilation, and short- and long-term mortality — specifically 30, 90 and 180 day mortality.

4. Methods

4.1 Data source

This proposed observational cohort study uses The Swedish Intensive Care Registry (SIR). This national quality register was founded in 2001, and holds high-resolution data on all patients treated in Swedish ICUs. The SIR database contains age, sex, illness severity scores, admission diagnoses, treatments and length of stay, as well as short- and long-term mortality. The number of Swedish ICUs reporting data to SIR has risen and since 2019 all Swedish ICUs continuously report data. Since 2010 SIR uses SAPS3 to categorize illness severity; previously APACHE II was used.

4.2 Study design

This is a planned observational cohort study spanning 14+ years. We will use data from the Swedish Intensive Care Registry from 2010 to today. Around 40,000 ICU treatments per year are reported to SIR, indicating that this cohort will encompass over 560,000 treatments in more than 500,000 patients.

The use of CRRT varies significantly across the nation, dependent on the size and type of ICU; the patient demographics and local traditions. Preliminary data from SIR indicate that almost 5% of the adult ICU population were/are treated with CRRT. This would mean that we have around 25,000 unique patients with CRRT. Using the SIR Open Data Report Portal (https://portal.icuregswe.org/utdata/sv/report/atgD012-7) one notes that time to CRRT-start differs significantly across Swedish ICUs. For instance, median time from admission to CRRT initiation was 20.8 hours at the Karolinska University Hospital's central ICU (centrala intensivårds-avdelningen, CIVA, where I work) and 64.3 hours in the central ICU at the university hospital in Linköping. Median/mean time to start (in 2024) was 26.1/30.1 hours from admission.

4.3 Summary

Study Design: Observational cohort study.

Two groups: Group 1 — patients with CRRT initiation time less than 30 hours; Group 2 — patients with CRRT initiation time 30 hours or more.

Data: 14 years of data, approximately 25,000 patients. ICU data from SIR include age, sex, illness severity, ICU interventions, and ICU admission diagnoses.

Analysis Plan: Compare median and mean length of stay, time on mechanical ventilation and mortality between the two groups.

Potential Results: If patients in Group 1 have a shorter median and mean LOS than patients in Group 2, this could provide support for the hypothesis that early CRRT initiation is associated with shorter hospitalization time. If patients in Group 1 have lower mortality at 30, 90 and 180 days, this provides support for the hypothesis that early CRRT initiation saves lives. It is important to note that an observational study cannot prove causation.

4.4 Sample size

Given that the largest randomized controlled trial included around 3000 patients (STARRT-AKI), this proposed study has the power to find even very small differences in the primary outcome. With a power of 80%, significance level of 0.05, and a standard deviation of LOS of 5 days (and 12,500 patients in each group) we could find a detectable effect size of around 0.3 days (or 7.2 hours) in LOS between the early and late CRRT groups.

4.5 Statistics

Descriptive statistics, boxplots and histograms will be used to analyze individual baseline variables in the two groups, allowing for adjustment. Normally or near-normally distributed, non-correlated variables will be reported as means with SD and compared using the appropriate Student's t-test. Non-normally distributed, non-correlated continuous data will be reported as medians with IQRs and compared using the Mann–Whitney U-test. Multivariable regression analyses will be used to test if outcomes differ between early and late initiation of CRRT. We will furthermore use machine learning models including (but not confined to) XGBoost, Decision Tree and Random Forest models.

4.6 Additional considerations

It is paramount to adjust for potential confounders in the analysis, such as patient age, gender, severity of illness, and other comorbidities. Moreover, we are well aware of the fact that time from admission to CRRT-start is suboptimal in defining early vs late start, as some patients may be admitted to the ICU with severe uremia or KDIGO stage 3. However, given that this investigation will entail around 25,000 patients, we believe that the ICU admission to CRRT initiation will be a working proxy for early vs late start.

5. Key Inclusion Criteria

We will only include adult patients, 18 years or older. Note that non-CRRT patients will be included for comparison, in order to analyze and then adjust for correct confounders between early and late CRRT groups.

6. Key Exclusion Criteria

Patients under the age of 18 will be excluded. We will not exclude, but separately analyze, patients in cardiothoracic and neuro/neurosurgical ICUs.