Prevalence of Acute and Chronic Kidney Disease treated by Renal Replacement Therapy in the ICU Environment (PEACE)

A prospective international, multi-centre, prevalence study on the epidemiology of the use of renal replacement therapy for ICU patients who have acute kidney injury and chronic end stage kidney disease.

Study protocol version 1.9
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Introduction:

Acute kidney injury (AKI) is a common finding in intensive care unit (ICU) patients. Approximately 30 to 65% of patients experience an episode of AKI, and 5% of ICU patients are treated with renal replacement therapy [1-4]. AKI is associated with important short term and long-term morbidity as well as mortality, and therefore also with costs. Finally, there is a close link between chronic kidney disease (CKD) and AKI. CKD patients are at greater risk for developing AKI, and survivors of AKI treated with renal replacement therapy (AKI-RRT), may develop chronic kidney disease (CKD) and end stage kidney disease (ESKD).

Different aspects of RRT modality may impact on outcomes, and data that have emerged over the last decade have improved evidence and also rejected commonly accepted dogma. Initial data suggested a better outcome when a higher dose of treatment was applied [5,6]. However, one small and two large prospective randomised controlled trials failed to reproduce these earlier findings [7-9]. Observational data seems to suggest that continuous RRT (CRRT) modalities are associated with better outcomes[10]. However, relative small, randomized studies and meta-analyses do not demonstrate such a benefit [11-16]. Observational data suggests that CRRT is associated with improved renal recovery, and also examining the data from the 2 large randomized studies on intensity of RRT suggest that CRRT confers a benefit [8,9,17-19]. Also, despite RRT being available for over 50 years there are no clear consensus guidelines for the initiation of RRT. A recent survey found that up to 89 different combinations of indications are used[20]. Recently, the Acute Kidney Injury Network and the Kidney Disease: Improving Global Outcomes (KDIGO) group, formulated recommendations for this[21,22]. Recent observational studies indicated that commonly accepted cut offs such as serum urea concentration are probably not that important [23-25]. Furthermore, timing of initiation may have an effect on outcome. Some studies suggest that early initiation is associated with better outcome, on the other hand others could not demonstrate a benefit and have even demonstrated inferior outcomes[7,26-29]. The most recent survey in Europe showed that CRRT is the preferred modality among intensivists, and that despite the recently published evidence treatment doses are similar to those of a decade ago [30].
Data on the use of renal replacement therapy (RRT) for AKI and for CKD in ICU patients are either on specific patient groups, such as cardiac surgery patients, based on surveys, or dates back for at least a decade[2,20,30-34]. Furthermore, these studies suffered from exclusion bias, as patients who fulfilled criteria for initiation of RTT, but who were denied RRT, were not considered. That this may be an important consideration is illustrated by findings from a recent small single centre study that demonstrated similar mortality rate between RIFLE-F patients who were and who were not treated with RRT [35]. Therefore, the Acute Kidney Injury Network (AKIN) recommended measuring the epidemiology of AKI[36,37]. We anticipate that the evidence that has been generated on different topics of RRT for ICU patients may have influenced current practice. Also, we anticipate regional differences in RRT practice.

Aims:

Assessment of the prevalence of severe AKI (defined as KDIGO class 3) and CKD (defined by treatment with renal replacement therapy (RRT)), in ICU patients, present at time of the study inclusion day.

Assessment of modalities of RRT used for treatment of AKI.

Assessment of indications for initiation of RRT currently described in literature.

Assessment on who is performing RRT.

Assessment of severity of illness at time of data recording.

Assessment of renal outcomes and ICU, hospital, 30-d, and 60-d mortality.

Methods:

Prospective observational study in a cohort of patients present in the ICU at time of the index date.

Recording of prevalence of CKD-RRT at time of the index study day, and AKI stage 3 (according to KDIGO)[38], including AKI-RRT during ICU stay with a maximum follow up till day 28 following the index study day.

Recording of outcomes at time:

- AKI stage 3 (without RRT)
- AKI-RRT
- ICU discharge
- Hospital discharge
- 30-d follow up
- 60-d follow up

Coded data registry in paper case record forms (CRF). Code lists will be kept in the participating hospital in a locked room. Only the site principle investigator has access to the code lists. Data will be recorded anonymously in an electronic CRF through a secured website.

**Ethics committee approval**

The study will be conducted according to Good Clinical Practice guidelines. Ethics committee approval is required according to local regulations.

**Inclusion criteria:**

1. Patients present in the ICU at time of the study data (date starting at 0:00 h, and ending at 23:59 h) (index ICU stay), either March 25th 2015 or April 22nd 2015.
2. ≥18 y
3. When required by local EC regulations and EC approval, informed consent (written or oral) by the patient or relative.

**Exclusion criteria:**

None

**Data recording (this is a not yet definitive list)**

**ICU data:**

Type of ICU, number of beds, nurse/patient ratio day and night, ...
Data on the patients present in the ICU at time of the study date (March 25th or April 22nd 2015)

- Age
- Gender
- Race (for CKD-EPI/MDRD)
- Body weight at time of admission to the ICU or hospital
- Height
- Baseline creatinine, defined as a stable/representative creatinine concentration recorded within a 6-month period before ICU admission.
  - When this is not available the electronic CRF will propose a baseline based on serum creatinine at time of hospital admission, ICU admission, or a back-calculated serum creatinine concentration based on demographic criteria and the CKD-EPI equation. As the creatinine concentrations at time of hospital and ICU admission may represent an episode of AKI, the investigator is asked what value is most representative. If none of these 3 alternative values are acceptable, e.g. because the patient is admitted with AKI, and also has chronic kidney disease, the investigator can indicate a most representative value e.g. a nadir concentration obtained during hospital stay.
  - Creatinine at time of hospital admission
  - Creatinine at time of ICU admission

These data will generate for each patient the creatinine and urine output cut off values for meeting AKI stage 3 criteria. This will allow the investigator to easily identify AKI stage 3 in the index patients during ICU stay.

Admission data:

- Admission date hospital and ICU
- Referred from home, ER, ward, other ICU
- Reason for ICU admission and main admission diagnosis (medical, emergency surgical, elective surgical, to be expanded)
Recording of data on severity of illness and processes of care for RRT, at time:

- First meeting AKI stage 3 criteria based upon creatinine or urine output criteria
- Initiation of RRT.

For patients who progress from AKI stage 3 to initiation of RRT during the study period, data will be recorded at both time points.

When RRT was already initiated at time of the index study date, the investigator needs to record data at time of initiation.

Dataset:

- Date of first meeting AKI -3 criteria / Date of initiation of RRT
- Kidney function at time of AKI stage 3 without RRT and at time of initiation of RRT
  - Urine volume preceding 24-h
  - Urine output criterion oliguria or anuria
  - Cumulative ICU volume balance/body weight as a proportion [39]? We can ask for in units who are able to report this (those with electronic records)
  - Serum creatinine
  - Serum urea/BUN
  - Na
  - K
  - Cl
  - Ca
  - P
  - Mg
  - Uric Acid
  - pH
  - HCO₃⁻
  - Albumin (cfr [40])
  - Base deficit
- Date of initiation
- Who made the decision (you can tick more than 1)
- **Nephrologist**
- **Intensivist**
- **Indication(s) – tick boxes and values (you can tick more than 1)**
  - Hyperkalaemia
  - Anuria/oliguria with/without volume overload
  - Acidosis – low pH - BD
  - Urea concentration
  - Creatinine
  - Phosphorus
  - Lactate
  - Low Creatinine clearance (indicate figure)
  - FE sodium
  - FE urea
  - Chronic end stage kidney disease
  - Other …
- **In case of AKI-3: why did you not initiate RRT?**
- **Modality at time of initiation/ study date in tick boxes**
  - CVVH
  - CVVHD
  - CVVHDF
  - CAVH
  - CAVHD
  - SLEDD – indicate duration
  - Intermittent dialysis - indicate duration
  - Peritoneal dialysis
  - …
- **For continuous therapies - Replacement fluid buffer:**
  - bicarbonate
  - lactate
  - acetate
  - other: …
- **For continuous therapies – replacement fluid:**
- Pre-dilution
- Post dilution
- Both, indicate proportion

- For PD
  - Machine/manual
  - Acute intermittent PD/chronic equilibrated PD/Tidal PD/High volume PD/continuous flow PD
  - Who placed the PD catheter
    - Intensivist/nephrologist/surgeon
    - And where: OR, ICU, other
  - Dwell time
  - Dwell volume
  - Number of exchanges per 24 h
  - Type of PD fluid used

- Who sets up the RRT machine (you can tick more than 1)
  - Renal nurse/doctor
  - ICU nurse/doctor

- Who monitors the RRT machine (you can tick more than 1)
  - Renal nurse
  - ICU nurse

- Duration of RRT
  - prescribed:
  - administered:

- Dose of RRT:
  - Not known
  - Intermittent therapies: Kt/V (indicate also prescribed Kt/V) and frequency per week, urea reduction ratio, ...
  - Continuous therapies: UF = ... mL/kg/h
  - Other:
    - How is body weight assessed for Kt/V, mL/kg/h
- Actual, estimated, at time of hosp admission, at time of ICU admission, ...

- Net fluid removal:
  - Prescribed
  - Actual net fluid removal

- Anticoagulation strategy (you can tick more than 1)
  - Unfractionated Heparin
    - Monitoring:
      - ACT
      - APTT
      - antiXa
      - None
  - LMWH
    - Monitoring
      - antiXa
      - none
  - Citrate
    - Monitoring
      - Ca-i patient
      - Total calcium patient
      - Ca-i circuit
      - none

- Saline flushes
- Prostaglandin
- None
- Other ...

- Vascular access:
  - Double lumen catheter
  - Single lumen catheter
  - ... French/gauge
Organ dysfunction according to SOFA at time of meeting AKI-3 criteria (when no AKI-RRT) and at time AKI-RRT

- Serum bilirubin
- Lowest mean blood pressure
- Highest dose of vaso-active therapy (NOR-ADR-DOPA-VASO-DOBU)
- Worst SOFA resp score
- Mechanical ventilation / non invasive mech vent
- Serum creatinine, 24 h urine output, serum urea/BUN, diuretic therapy
- Thrombocytes
- GCS
- Sedation

Outcomes for all patients included in the study (present at time of the index date)

a) For all patients included in the study:

At time of ICU discharge, or when ICU stay is longer than 60-d after the index study date, at time of index study date +60:

- Date and status of ICU discharge (alive/death).
- RRT at time of ICU discharge (Y/N)
- Creatinine at time of ICU discharge(this allows also calculation of eGFR)
- Date and status of Hospital discharge (alive/death),
- RRT at time of hospital discharge (Y/N)
- Creatinine at time of hospital discharge(this allows also calculation of eGFR)
- Status at time of index study date +30 (alive/death, RRT Y/N)
• Creatinine at time of index study date +30
• Status at time of index study date +60 (alive/death, RRT Y/N)
• Creatinine at time of index study date +60

The combination of these data will also allow reporting on Major Adverse Kidney Events (MAKE) at time 30 and 60 days (MAKE30/60).

**Publication policy**

**Publications**

Several papers will be published from this dataset:

• Primary paper on the primary aim
• Secondary papers on the secondary aims
• Tertiary papers on analyses proposed by investigators
  - Investigators who adequately fulfilled study obligations may propose such an analysis to the steering committee, which will judge on this.

**Authorship**

• Requirements for authorship will follow AMA guidelines
• Writing committees: formed on basis of contribution (enrolment, intellectual contribution etc.)
• Group authorship – the PEACE study group – includes all investigators who adequately fulfilled study obligations.
References


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