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Risk factors for acute kidney injury requiring renal replacement therapy based on regional registry data

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Abstract

Background: Acute kidney injury (AKI) is a common problem in critically ill patients treated in the intensive care unit (ICU) and is associated with high mortality, particularly when renal replacement therapy (RRT) is required. Our aim was to investigate the risk factors for AKI requiring RRT (AKI-RRT).

Methods: In our retrospective, multi-centre, observational study, we analysed 14,672 consecutive AKI-RRT patients hospitalized in ICUs in the Silesian Region (Poland) between October 2011 and December 2014. Demographic and clinical data were derived from the Silesian Registry of Anaesthesiology and Intensive Care Departments. Logistic regression was used to select final risk factors for AKI-RRT. The ROC method was used to analyse the value of clinical parameters to predict the risk of AKI-RRT.

Results: Of a total of 14,672 patients, 1,234 (8.4%) developed AKI requiring RRT. Overall 59% of patients were males and the median age in the group was 66 (IQR 55–76) years. There were 16 variables that modified the risk of AKI-RRT. The AUROC for the test scored 0.845 (95% CI: 0.84–0.85; $P < 0.0001$).

Conclusions: We found multiple factors that modified the risk of AKI requiring RRT. Chronic kidney disease (CKD) and cardiogenic shock increased, whereas neurological disorders decreased the risk. Measures directed towards AKI prevention should be aimed specifically at patients with cardiological disorders and CKD.

Key words: acute kidney injury; risk factors; renal replacement therapy; intensive care unit

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Acute kidney injury (AKI) is a common problem in patients who are hospitalized in intensive care units (ICUs) [1]. According to the Do-Re-Mi study, almost 4% of AKI patients required renal replacement therapy (RRT) [2]; in the international, multi-centre BEST study this percentage was found to be 6% [3].

AKI is a prognostically unfavourable syndrome. Regardless of the extent of kidney injury or concomitant disorders and diseases AKI increases the risk of transition into chronic kidney disease (CKD) or end-stage renal failure, as well as early and late mortality [4, 5]. AKI generates higher costs of treatment [6, 7] and deteriorates patients' quality of life [8]. The mortality of AKI patients requiring RRT reaches 60% [2, 3].

Numerous risk factors for AKI have been implicated in critically ill patients. In the multi-centre PICARD study, Mehta and colleagues [9] demonstrated that AKI patients have higher incidences of CKD, coronary artery disease, type 2 diabetes and chronic liver disease. According to the authors 64% of AKI patients required RRT [9]. In the prospective, multi-centre FINNAKI study, the independent risk factors for AKI included CKD, hypovolaemia before admission to an ICU and use of diuretics and colloids [10]. In the study involving the patients > 75 years of age hospitalized in ICU, the risk factors for AKI included sepsis, arterial hypertension and treatment with nephrotoxic drugs [11].

The data regarding the risk factors for AKI in patients treated in Polish ICUs are sparse. Therefore an attempt was made to determine the risk factors for AKI requiring RRT in critically ill patients hospitalized in ICUs in the Silesian Region.

METHODS

This retrospective, multi-centre observational study included patients hospitalized in ICUs in the Silesian Region. Considering the retrospective and anonymous nature of the study, the Bioethical Committee of the Medical University of Silesia in Katowice waived the requirement for informed consent.

The data regarding hospitalization of patients in the multi-profile ICUs of the Silesian Region were derived from the Silesian Registry of Anaesthesiology and Intensive Care Departments. The Registry is an online platform that has been available on the Internet since October 2011. The Registry is operated by the Silesian Division of the Polish Society of Anaesthesiology and Intensive Therapy. The process of data reporting is completely voluntary. Although the Registry is available to all 37 ICUs in the Silesian Region that treat adults and have 270 beds available, regular reports are submitted by 40–50% of the ICUs. The platform is only accessible to registered users, i.e. physicians from the ICUs that participate in the programme. The data are entered by marking the boxes or by describing in case of non-standard data. In response to questions, multiple boxes can be marked. A registered user status allows only to enter and modify the user's own entries. The identification of individual patients is impossible. The Registry gathers clinical data from the period prior to admission, upon admission, during the ICU stay and the outcome. The registry contains 100 variables in total grouped into 24 categories.

Consecutive patients hospitalized in ICUs in the Silesian Region and reported in the Registry (since creation) were enrolled into the study. On the data extraction date (December 31, 2014), the Registry contained information regarding 15030 patients. The patients undergoing RRT before ICU admission (no history of end-stage renal disease [ESRD] on dialysis; n = 172) and those with ESRD on dialysis (n =186) were excluded.

AKI was defined as an acute deterioration of kidney function requiring RRT, corresponding to AKI stage 3 according to the Acute Kidney Injury Network (AKIN) [11].

To determine the factors predisposing patients to the development of AKI requiring RRT, the study population was divided into 2 groups: AKI+ patients who required RRT during ICU hospitalization (n = 1234; 8.4%) and AKI– patients who did not require RRT during ICU hospitalization (n = 13,438; 91.6%).

The statistical analysis was performed using the licenced MedCalc software (version 16.1 2016, MedCalc Software bvba, Ostend, Belgium). The quantitative variables were presented as a mean ± SD or a median (IQR). The qualitative variables were expressed as a percentage. The intergroup differences for quantitative variables were analysed using parametric tests (Student's t-test, ANOVA) or non-parametric tests (U Mann-Whitney, Kruskal-Wallis), based on the type of distribution. The distribution of the data was verified using the Smirnow-Kołmogorow conformity test. For qualitative variables, a chi-square or Fisher's exact test was applied. The results of simple analyses were re-used in the multivariate model of logistic regression, accepting only variables for which $P < 0.05$ in intergroup comparisons. The odds ratios (ORs) and their 95% confidence intervals (95% CIs) were calculated. $P < 0.05$ was considered statistically significant.

RESULTS

After the exclusion criteria were applied, the study population consisted of 14,672 individuals. The percentage of AKI patients requiring RRT was 8.4%. The data regarding the pre-admission period in the individual groups are presented in Table 1; whereas relating to ICU admission and ICU stay are listed in Tables 2 and 3, respectively.

The majority of patients were males (59%) with a median age of 66 (IQR 55–76) years. The most common direct cause of admission was respiratory failure (90.6%), followed by circulatory insufficiency (58.7%) and obtunded consciousness (57.5%). Almost 44% of the patients were on catecholamines upon admission; during the entire hospitalization this percentage increased to 72.6%. Upon admission 76.9% of the patients were mechanically ventilated and this number increased to 80.4% during the entire stay. The median APACHE II score was 22 (IQR 17–28), whereas the median SAPS III score was 61 (IQR 42-76).

By analysing intergroup comparisons we found fifty-four variables that were the potential risk factors for AKI requiring RRT (Tables 1–3). Based on the multivariate analysis, 16 parameters that modified the risk of AKI-RRT were finally selected (Fig. 1). The diagnostic accuracy of the model was satisfactorily high with the area under the ROC curve (AUROC) of 0.845 (95% CI 0.84–0.85; $P < 0.0001$).

DISCUSSION

AKI requiring RRT is a significant clinical problem in the population of ICU patients. The aim of the study was to select from a wide range of variables associated with ICU hospitalization the factors that modified the risk of AKI requiring RRT the most. The study population is an extremely interesting but clinically diverse group characterized by very poor prognoses. Our analysis is the first multi-centre study of

Table 1. Pre-ICU admission clinical data in all patients and in AKI–RRT patients

Variable	All (n = 14,672)	AKI+ (n = 1234)	AKI– (n = 13,438)	OR (95% CI)	*P* value
Age (years)	66 (55–76)	66 (56–75)	66 (55–76)	1.00 (0.99–1.00)	0.99
Female gender	6,013 (41%)	444 (35.9%)	5,569 (41.4%)	0.79 (0.70–0.89)	< 0.001
Hospitalization prior to ICU (days)	1 (0–5)	2 (1–7)	1 (0–5)	1.01 (1.00–1.01)	< 0.001
Coronary artery disease	6,241 (42.5%)	609 (49.3%)	5,632 (41.9%)	1.35 (1.22–1.52)	< 0.001
Chronic circulatory failure	4,926 (33.6%)	556 (45.1%)	4,370 (32.5%)	1.70 (1.51–1.91)	< 0.001
Arterial hypertension	6,915 (47.1%)	648 (52.5%)	6,267 (46.6%)	1.26 (1.13–1.42)	< 0.001
Atherosclerosis	4,977 (33.9%)	465 (37.7%)	4,512 (33.6%)	1.19 (1.06–1.35)	0.0036
Alcohol abuse	1,342 (9.1%)	132 (10.7%)	1,210 (9.0%)	1.21 (1.00–1.46)	0.049
Auto-aggressive systemic disease	157 (1.1%)	35 (2.8%)	122 (0.9%)	3.19 (2.18–4.66)	< 0.001
Malignancies	938 (6.4%)	59 (4.8%)	879 (6.5%)	0.72 (0.55–0.94)	0.016
Diabetes mellitus	3,366 (22.9%)	384 (31.1%)	2,982 (22.2%)	1.58 (1.39–1.79)	< 0.001
Cachexia (BMI < 18.5)	531 (3.6%)	51 (4.1%)	480 (3.6%)	1.16 (0.87–1.56)	0.31
Previous stroke	1,026 (7.0%)	67 (5.4%)	959 (7.1%)	0.75 (0.58–0.96)	0.025
Solid organ transplantation	29 (0.2%)	8 (0.6%)	21 (0.2%)	4.17 (1.84–9.43)	< 0.001
Chronic kidney disease	1,830 (12.5%)	384 (31.1%)	1,446 (10.8%)	3.75 (3.28–4.28)	< 0.001
Chronic respiratory failure	1,749 (11.9%)	120 (9.7%)	1,629 (12.1%)	0.78 (0.64–0.95)	0.013
Chronic neurologic disease	1,150 (7.8%)	53 (4.3%)	1,097 (8.2%)	0.51 (0.38–0.67)	< 0.001
Obesity (BMI > 35)	756 (5.1%)	83 (6.7%)	673 (5.0%)	1.37 (1.08–1.73)	0.009

BMI — body mass index (kg m^{-2})

this type involving a large cohort of Polish ICU patients. The incidence of AKI requiring RRT in ICUs in the Silesian Region is high (8.4%) and significantly higher than that reported in the Do-Re-Mi study (3.6%) [2] and the BEST study (5–6%) [3], although our finding is lower than the incidence reported in the FINNAKI study (10%) [10].The general health status of patients hospitalized in ICUs in the Silesian Region is often poorer than that of patients included in the aforementioned studies, which is evidenced by high APACHE II and SAPS III scores (22.9 ± 8.6 and 59.1 ± 22.8, respectively).

Numerous variables affect the risk of AKI. These variables are associated with clinical comorbidities, demographic characteristics and the treatment administered. Many AKI risk factors selected in our study are consistent with those reported by other authors. One of the most important risk factors was cardiogenic shock, which is evidenced by a high risk associated with catecholamine therapy (OR = 4.61) and intra-aortic counterpulsation (OR = 3.51). In the KDIGO guidelines, cardiogenic shock is one of the cardinal determinants of AKI [12]. Both the use of catecholamines and intra-aortic counterpulsation balloons are considered risk factors for AKI [13]. Moreover, according to the guidelines mentioned above [12] and in other studies [14], an extensive surgical procedure is an AKI-inducing factor. This finding is consistent with our data as surgery performed during the ICU stay doubled the risk of AKI (OR = 2.05). In the FINNAKI [10] and PICARD [9] studies, an essential predictor of AKI was CKD. According to the KDIGO guidelines, CKD was a predisposing factor [12]. In the study by Wijeysundera and colleagues [15], CKD with an estimated glomerular filtration rate below 30 mL min^{-1} scored 2 points on the eight-point scale evaluating the risk of AKI requiring RRT after cardiac surgery. In our analysis the odds ratio for AKI requiring RRT in patients with CKD was 1.69, renal failure as a direct admission diagnosis was the strongest predictor of the end point (OR = 5.77).

The severity of disease, as evaluated by recognized prognostic scales used in ICU, considerably affected the risk of AKI [15], what in our study was evidenced by an increased risk of AKI associated with increasing APACHE II scores (OR = 1.12 for each 5 points).

Our findings suggest that neurologic diseases reduce the risk of AKI in the ICU (i.e. history of chronic neurologic disease or traumatic brain injury as a primary admission diagnosis), what is consistent with the data reported by other authors [16]. These results are understandable considering the pathophysiology and natural course of this group of diseases; in most cases neurologic diseases are not associated with impaired kidney function. The additional risk factors selected in our study may result from the specificity of the population studied [13]. The diagnostic accuracy of the statistical model we used is very good as 16 variables enabled a prediction of the end-point in more than 80% of cases.

There are some potential limitations to the present study. First, these limitations result predominantly from the retrospective nature of the study that affects the quality of data and increases the possibility of making a systematic error.

Table 2. Direct ICU admission diagnosis, primary ICU admission diagnosis and status upon admission in all patients and in AKI-RRT patients

Variable	All (n = 14,672)	AKI+ (n = 1234)	AKI– (n = 13,438)	OR (95% CI)	*P* value
Direct admission diagnosis					
Circulatory insufficiency	8,617 (58.7%)	952 (77.1%)	7665 (57.0%)	2.54 (2.22–2.91)	< 0.001
Renal failure	2,307 (15.7%)	691 (56.0%)	1616 (12.0%)	9.31 (8.22–10.53)	< 0.001
Respiratory failure	13,299 (90.6%)	1087 (88.1%)	12212 (90.9%)	0.74 (0.62–0.89)	0.001
Multiple trauma	791 (5.4%)	38 (3.1%)	753 (5.6%)	0.53 (0.38–0.74)	< 0.001
Metabolic disorders	2,759 (18.8%)	516 (41.8%)	2243 (16.7%)	3.59 (3.17–4.05)	< 0.001
Obtunded consciousness	8,434 (57.5%)	695 (56.3%)	7739 (57.6%)	0.95 (0.84–1.07)	0.388
Primary admission diagnosis					
Severe sepsis	948 (6.5%)	232 (18.8%)	716 (5.3%)	4.11 (3.50–4.83)	< 0.001
Severe metabolic disorder	748 (5.1%)	123 (10.0%)	625 (4.6%)	2.27 (1.85–2.78)	< 0.001
Infection	2,513 (17.1%)	277 (22.4%)	2236 (16.6%)	1.45 (1.26–1.67)	< 0.001
Circulatory insufficiency	6,457 (44.0%)	656 (53.2%)	5,801 (43.2%)	1.49 (1.33–1.68)	< 0.001
MODS	1,552 (10.6%)	323 (26.2%)	1,229 (9.1%)	3.53 (3.06–4.05)	< 0.001
Sudden cardiac arrest (SCA)	3,753 (25.6%)	253 (20.5%)	3,500 (26.0%)	0.73 (0.63–0.84)	< 0.001
Acute respiratory failure	10,848 (73.9%)	815 (66.0%)	10,033 (74.7%)	0.66 (0.58–0.75)	< 0.001
Acute neurologic diseases	1,174 (8.0%)	36 (2.9%)	1,138 (8.5%)	0.32 (0.23–0.45)	< 0.001
Acute pancreatitis	230 (1.6%)	56 (4.5%)	174 (1.3%)	3.62 (2.66–4.93)	< 0.001
Postsurgical status	4,215 (28.7%)	377 (30.6%)	3,838 (28.6%)	1.10 (0.97–1.25)	0.139
Traumatic Brain Injury	805 (5.5%)	17 (1.4%)	788 (5.9%)	0.22 (0.14–0.36)	< 0.001
Multiple trauma	639(4.4%)	35 (2.8%)	604 (4.5%)	0.62 (0.44–0.88)	0.0068
Shock	4,442 (30.3%)	492 (39.9%)	3,950 (29.4%)	1.59 (1.41–1.79)	< 0.001
Obtunded consciousness	6,033 (41.1%)	446 (36.1%)	5,587 (41.6%)	0.79 (0.70–0.89)	< 0.001
Acute chronic respiratory failure	1,136 (7.7%)	63 (5.1%)	1,073 (7.9%)	0.62 (0.48–0.80)	< 0.001
Intoxication	250 (1.7%)	24 (1.9%)	226 (1.7%)	1.16 (0.76–1.77)	0.495
Status upon admission					
Catecholamines	6,418 (43.7%)	718 (58.2%)	5,700 (42.4%)	1.89 (1.68–2.12)	< 0.001
Unconscious	10,384 (70.8%)	798 (64.7%)	9,586 (71.3%)	0.73 (0.65–0.83)	< 0.001
Endocavitary stimulation	224 (1.5%)	19 (1.5%)	205 (1.5%)	1.00 (0.63–1.62)	0.97
Mechanically ventilated	11,283 (76.9%)	882 (71.5%)	10,401 (77.4%)	0.73 (0.64–0.83)	< 0.001
Intubated	11,673 (79.6%)	71.9%	80.3%	0.63 (0.55–0.72)	< 0.001
GCS (score)*	5 (3–11)	7 (3–13)	5 (3–10)	1.06 (1.04–1.08)	< 0.001
APACHE II (score)**	22 (17–28)	26 (20–32)	22 (17–28)	1.05 (1.04–1.06)	< 0.001
SAPS III (score)***	61 (42–76)	64 (45–81)	60 (42–76)	1.01 (1.00–1.01)	0.001
TISS–28 (score)****	35 (30–40)	39 (33–45)	34 (29–40)	1.07 (1.07–1.08)	< 0.001

*data available for 10414 patients; **data available for 8,113 patients; ***data available for 5,066 patients; ****data available for 11,686 patients; MODS — multiple organ dysfunction syndrome; GCS — Glasgow Coma Scale; SAPS — Scale for the Assessment of Positive Symptoms; TISS — Therapeutic Intervention Scoring System

Table 3. Clinical data of ICU stay in all patients and in AKI-RRT patients

Variable	All (n = 14,672)	AKI+ (n = 1234)	AKI– (n = 13,438)	OR (95% CI)	*P* value
Length of stay (days)	6 (2.2–12.8)	10 (4.0–18.8)	6 (2.1–12.1)	1.01 (1.01–1.02)	< 0.001
Catecholamines	10,655 (72.6%)	1,158 (93.8%)	9,497 (70.7%)	6.32 (4.99–7.99)	< 0.001
Antibiotic therapy	12,087 (82.4%)	1,146 (92.9%)	10,941 (81.42%)	2.97 (2.38–3.71)	< 0.001
Treatment with activated protein C	12 (0.08%)	7 (0.57%)	5 (0.04%)	15.33 (4.86–48.36)	< 0.001
Hypothermia	191 (1.3%)	7 (0.57%)	184 (1.37%)	0.41 (0.19–0.88)	0.02
Intra-aortic counterpulsation	407 (2.8%)	79 (6.4%)	328 (2.4%)	2.73 (2.12–3.52	< 0.001
Intubation	9,270 (63.2%)	877 (71.1%)	8,393 (62.5%)	1.48 (1.29–1.68)	< 0.001
Surgery during ICU stay	1,382 (9.4%)	275 (22.3%)	1,107 (8.2%)	3.19 (2.76–3.70)	< 0.001
Tracheostomy	24,44 (16.7%)	287 (23.3%)	2,157 (16.0%)	1.58 (1.38–1.82)	< 0.001
Invasive ventilation	11,794 (80.4%)	1,070 (86.7%)	10,724 (79.8%)	1.65 (1.39–1.96)	< 0.001
Non-invasive ventilation	653 (4.5%)	81 (6.6%)	572 (4.3%)	1.58 (1.24–2.00)	< 0.001

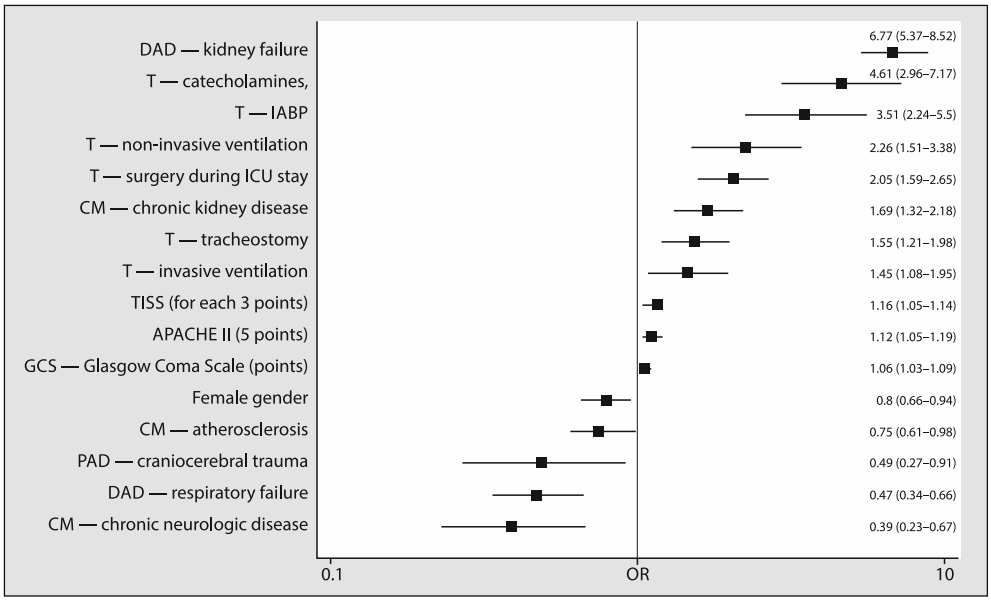

Figure 1. Risk factors of AKI requiring RRT in ICU (multivariate analysis). DAD — direct admission diagnosis; IABP — intra-aortic balloon pump; T — treatment; CM — comorbidity; PAD — primary admission diagnosis; TISS — Therapeutic Intervention Scoring System

The optimal method to identify AKI risk factors would be a prospective, randomized study. However, the advantage of our project (as with any registry) is the size of the population studied, what is difficult to achieve in randomized studies conducted in ICU. Second, not all ICUs in the Silesia Region report regularly to the Registry, hence our analysis does not fully reflect the extent of an AKI problem in ICUs in the Silesian Region. Moreover, the Registry data are entirely declarative in nature, we lack data for creatinine concentrations and urine output, i.e. the parameters used to define AKI. Therefore the analysis was narrowed to patients with substantially impaired kidney function who required RRT. The above-mentioned example reveals the universal problem of possible verification of registry data as their quality depends on meticulosity of the users who provide data. Vague terms used in the Registry is another limitation, i.e. "circulatory insufficiency" or "respiratory failure". Moreover, the Registry is a regional platform therefore the results cannot be extrapolated to a wider population. Finally, the Registry contains the clinical data of a specific group of patients hospitalized in ICU, i.e. severely ill patients frequently presenting with symptoms of multiple organ failure dysfunction syndrome. Great caution should be exercised while extrapolating our results to other groups of patients.

The present project constitutes the first comprehensive analysis of this issue at the regional level. It demonstrates that there is a wide range of factors affecting the risk of AKI requiring RRT in critically ill patients. CKD and cardiogenic shock significantly increase, whereas neurologic diseases substantially reduce the risk of AKI. Strategies directed towards AKI prevention should be aimed primarily at patients with cardiological disorders and those with pre-existing kidney disease.

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