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CONTINUOUS RENAL REPLACEMENT THERAPY IN ELDERLY PATIENTS WITH ACUTE KIDNEY INJURY

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Acute kidney injury is one of the most intriguing challenges in medicine, as it is followed by high mortality rates despite the progress in understanding and treating the condition. Elderly patients form a particularly sensitive group, due to the complications that come with age and various comorbid conditions. The aim of the study was to analyse the outcome of patients on CRRT, specifically mortality, loss or recovery of kidney functions, along with parameters which could influence outcome and which could be improved during therapy for a better outcome.

The study included all patients that were treated for acute kidney injury at the Clinical Hospital Centre Rijeka in the last 5 years. Total number of patients was 178, of which 64 were female, and 114 were male. Average age was 74,35 ± 5,46 (65-89). All analyzed patients were treated with continuous renal replacement therapy. Patients were divided into three groups in relation to the outcome (group that passed away, group with the loss and group with the recovery of kidney function).

The most common indications for continuous renal replacement therapy were of cardiogenic (n=89, 50,0%) and infectious etiology (n=52, 29,2%). Mortality in patients with acute kidney injury that were treated with continuous renal replacement therapy in our study was 70,79% (n=126), while recovery of renal function occurred in 6,18% (n=11) of the patients. Permanent loss of renal function was more common than recovery, and it occurred in 23,03% (n=41) of the patients. Analysis of parameters revealed that initial creatinine levels, 24-hour diuresis, glomerular filtration, potassium levels and multiple organ failure can be predictors of acute kidney injury outcome in elderly patients.

Key words: continuous renal replacement therapy, acute kidney injury, elderly, mortality

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INTRODUCTION

Acute kidney injury (AKI) is one of the most intriguing challenges in medicine, as it is accompanied by high mortality rates despite the progress in understanding and treating the condition. AKI is defined as a rapid and varied loss of kidney function which results in a wide spectrum of injuries, ranging from mild to severe (1). Resulting kidney dysfunction leads to the accumulation of waste products as well as a volume and electrolyte disbalance which causes systemic damage (2). AKI is usually clinically diagnosed by RIFLE classification, given by ADQI group, and AKIN classification, given by AKIN group (3). Elderly patients form a particularly sensitive group, due to lower renal reserves and complications which come with age and various comorbid conditions such as hypertension, diabetes, atherosclerosis and heart failure (4). Continuous renal replacement therapy (CRRT) is a variety of extracorporeal blood purification technique used to substitute impaired renal function for a prolonged period (5). Despite the advance in CRRT, it is still characterized by high mortality, especially in elderly patients with AKI (6). It bears some risks, including access-related complications, extracorporeal circuit-associated complications, hemodynamic compromise, electrolyte and metabolic complications together with human factors (7). There is no consensus regarding the right time to

initiate CRRT and it remains an important question for the treatment (8). The aim of the study was to analyze the state of patients treated with CRRT, specifically regarding mortality and loss or recovery of kidney functions, along with parameters which could affect the outcome and which could be improved during therapy for better results.

AIM OF THE RESEARCH

Acute kidney injury is associated with excess mortality rates and information for elderly patients are limited. Therefore, the primary goal of this retrospective study was to determine the mortality of the elderly patients with AKI who underwent CRRT. Comorbidities, etiology and parameters were also observed as a potential predictor of mortality.

METHODS

Patient selection

A retrospective study was conducted in Clinical Hospital Center Rijeka on the elderly patients (≥ 65 years) with AKI. 178 patients were admitted to the intensive care unit between January 1st 2010 and December 31st 2015, including 64 female and 114 male patients. The average age was 74,35 ± 5,46 (65 to 89 years). All participants of the study were treated with continuous renal replacement therapy, which include 147 patients with CVVHD, 20 patients with CVVHDF, 8 patients with CVVH and 3 patients with CVVHDF + OXIRIS. The average time on CRRT was 58.95 ± 53.01 (2-259) hours. This retrospective study was approved by Ethics Committee of Clinical Hospital Center Rijeka and it was conducted according to the principles of the Declaration of Helsinki.

Inclusion criteria

According to the Kidney Disease Improving Global Outcomes (KIDIGO) criteria, AKI is defined as any of the following: increase in SCr by ≥ 26.5 μmol/l (≥ 0.3 mg/dl) within 48 hours; or increase in Scr to ≥ 1.5 times baseline in prior 7 days; or urine volume < 0.5 ml/kg/h for 6 hours (9). Patients with chronic kidney disease (CKD) stage 4 and 5, kidney transplantation and patients younger then 65 years were excluded from the study.

Limitations

Limitations in interpreting the results mostly stem from the fact that the three outcome groups of patients and different in number, especially the dialysis outcome group with a small sample size. Furthermore, future studies should objectivize patient state using standard scoring used in intensive medicine (APACHE II, SPAS II, SOFA) to improve the possible analysis.

Data collection

The data was collected from the Integral hospital information system. The following indicators were recorded: general information, such as age, sex, primary disease, complications; vital signs, such as blood pressure, urine output, temperature, oxygenation; laboratory parameter such as kidney function, blood routine, electrolytes. Patients were divided into three groups and then compared according to the outcome and their baseline characteristics. Groups were non-survival group (n=126), renal recovery group (n=42) and dialysis group (n=11). Mortality was calculated according to the statistical survival time of patients 4 weeks after CRRT, with renal recovery being based on creatinine clearance (30 ml per hour urine flow increase or spontaneous serum creatinine fall).

Statistical analysis

Statistical analysis was performed using descriptive statistics, expressed as the mean ± standard deviation of minimal and maximum value. One-way ANOVA was used for normally distributed samples, which were additionally verified using the Kruskal-Wallis test due to the low sample count in one of the groups. Kruskal-Wallis test was also used for comparing the non-parametric samples of independent groups. P value of <0.05 has been considered statistically significant. Statistical analysis was performed using the MedCalc 10 software (MedCalc, Mariakerke, Belgium).

RESULTS

Total number of analyzed patients was 178, consisting of 114 male (64.04%) and 64 female (35.96%) patients, mean age 74.35 ± 5.46 (65-89), who were treated with continuous renal replacement therapy due to AKI. The most common indication for CRRT was of cardiac (n=89) and infective etiology (n= 52). The mean time of CRRT in patients was 58.95 ± 53.01 hours. The mortality rate was 70.79% (126 patients), 23.03% (41 patients) recovered renal function with no need for further renal replacement therapy, while 6.18% (11 patients) required renal replacement therapy. There were no statistical significant differences among groups in the gender (p=0.677) and the mean age (p=0.634)(Table 1).

Table 1.
Characteristics of patients treated with CRRT.

Demographics	Total patients	178
	Age (y)	74.35 ± 5.46 (65-89)
	Sex (M/F)	114 (64.04%) / 64 (35.96%)
Causes of AKI/ CRRT indication (%)	Ischemia	76 (42.70%)
	Sepsis/Infection	62 (34.83%)
	Surgery	40 (22.47%)
Comorbidities (%)	Diabetes	59 (33.15%)
	Hypertension	124 (69.66%)
	Cardiopathies	145 (81.46%)
Outcome (%)	Death (non-survival)	126 (70.79%)
	Dialysis	11 (6.18%)
	Renal function recovery	41 (23.03%)

Initial levels of serum creatinine were statistically higher in the dialysis outcome group (649.81 ± 332.89) compared to the renal recovery group (341.05 ± 164.05) and non-survival group (420.07 ± 200.78), which had no mutually significant difference (Figure 1A). Creatinine levels at the end of CRRT were highest in the dialysis group (407.00 ± 227.92) and non-survival group (294.06 ± 158.82), which were both statistically higher than the renal recovery group (185.82 ± 108.6). However, there was no statistically significant differences between the two former groups in end creatinine levels (Figure 1B). Furthermore, measured 24-hour diuresis was only significantly higher in the renal recovery group (782.33 ± 675.05) compared to the non-survival group (541.76 ± 863.73) (Figure 1C). Interestingly, initial glomerular filtration rates were rather different between all three groups. The renal recovery group had significantly higher GFR (19.25 ± 9.94) compared to both groups, while the dialysis group had the lowest GFR of the three groups (8.00 ± 5.47) (Figure 1D). Measuring initial potassium revealed a mild, statistically significant, hyperkalemia in the non-survival group (5.30 ± 1.06) compared to the renal recovery group (4.77 ± 0.83). The renal recovery and the dialysis groups (5.01 ± 0.84) had normal potassium levels, although the latter had borderline levels (Figure 1E). Finally, the analysis of multiple organ dysfunction revealed a greatly increased incidence in the non-survival group (n=57. 45%) compared to the renal recovery group (n=9. 23%) and the dialysis group (n=2. 18%) (Figure 1F).

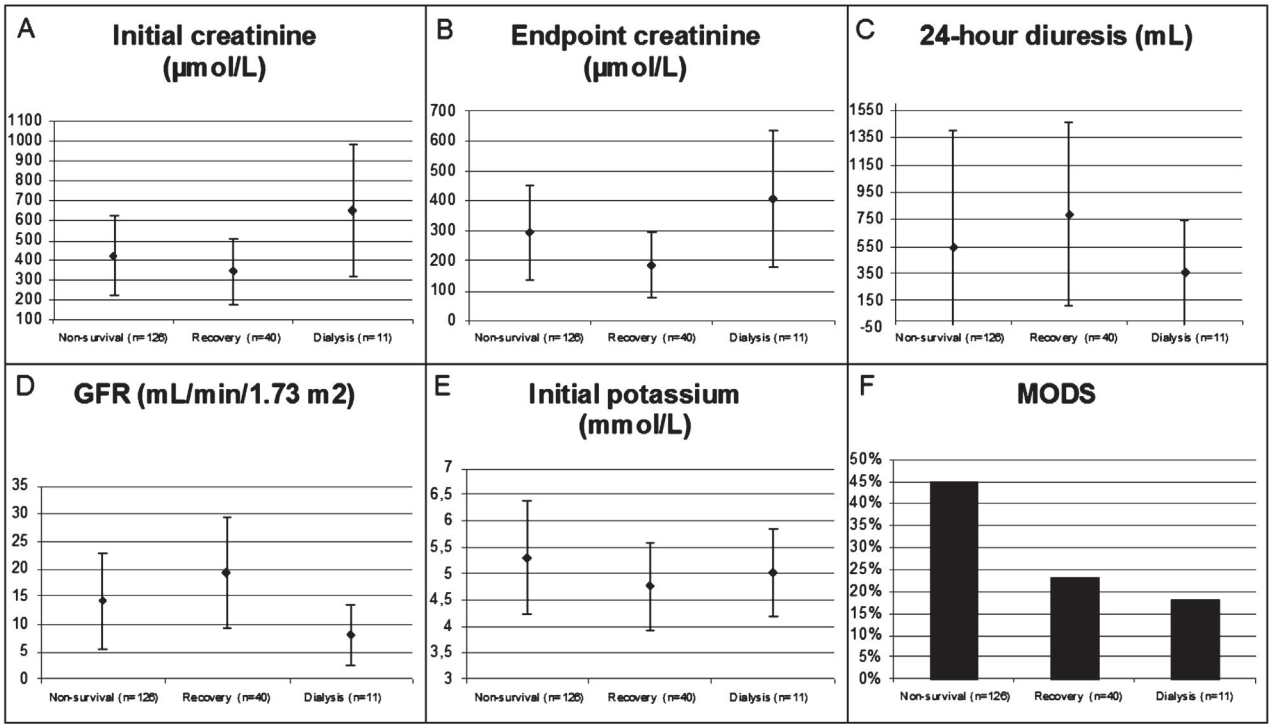

Fig. 1. *Results of the kidney function, postassium and MODS.*
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DISCUSSION

In 1977 the continuous arteriovenous hemofiltration, which was the predecessor od today's CVVHDF, was described by Kramer for the first time. (10). Although further improvement of the continuous replacement therapy contributed to greater survival rates, mortality is still high. Particularly sensitive and vulnerable group are elderly patients (≥65 years). Due to their physiological aging, anatomic and structural changes in the kidney lead to the functional deterioration, which presents itself as a decrease in glomerular filtration rate and renal blood flow (11). Age-related changes occur in every organ system and they vary from one individual to another (12). A mixture of aging, complications and various comorbidities lead to a condition susceptible for diseases.

Acute kidney injury is related to the high mortality rate, which amount from 40% to 70% in general population (13). Metnitz *et al.* performed a prospective, multicenter study in Austria to explore the association between AKI and the mortality rate. The prevalence of patients with AKI, who underwent CRRT, was 4,9% in the intensive care unit. Their mortality rate was 62.8% with mean age 65.2 ± 15.2 years (14). Uchino *et al.* conducted a prospective, multicenter and multinational study about AKI in critically ill patients in intensive care unit. The mean age of observed patients was 67 years (53-75 years) and the overall mortality rate was 60,3%.One of the goals was to determine the prevalence of AKI requiring RRT and it was from 5% to 6% (15). Liu *et al.* have reported 60,98% mortality rate for elderly patients, mean age 88,65 ± 4,76 years (16), while Gong *et al.* have reported 42% mortality rate with mean age 77.89 ± 7.86 years (4). In this study, despite the younger average age (74.35 ± 5.46 years), the analyzed patients had a higher mortality rate (70.79%). The Eurostat statistical information shows that the European population is aging and the life expectancy is increasing. The percentage of elderly people in 2015 in France was 18,4%, in Austria and Spain 18.5%, in Croatia 18.8, in Germany 21.0% and in Italy 21.7% (17). Therefore, studying diseases and differences in connection with age is needed and relevant.

Furthermore, no difference was found in gender and age among analyzed groups, which is in accordance with the studies performed by Gong *et al.* and Liu *et al.* (4)(16). As in this study, Yokota *et al.* also did not find any correlation between concomitant diseases, like hypertension, diabetes mellitus, and cardiovascular diseases, and an excess risk of death (18). Interestingly, Gong *et al.* reveal that concomitant diseases present in elderly patients with AKI are an independent risk factor for death and the most frequent ones are cardiovascular diseases, diabetes, sepsis and hypertension. The main causes of AKI in this study with elderly patients, who underwent CRRT, were ischemia (n=76, 42.70%), sepsis/infection (n=62, 34.83%) and surgery (n=40, 22.47%), while Gong *et al.* had a smaller number of sepsis (n=10, 10.10%), but more ischemic causes (n=53. 54%), then surgery (n=33, 33.33%) and nephrotoxic drug (n=3, 3.03%)(4).

Creatinine levels measured initially and creatinine levels measured at the end of CRRT were the highest in the dialysis group, compared to the other groups, which had no mutually significant differences. High serum creatinine in the dialysis group was elucidated with etiology of AKI, which is chronic kidney disease, stage 1 to 3 (stages 4 and 5 were excluded). However, the difference among the non-survival and the renal recovery group is consistent with results from Liu *et al,* who completely excluded patients with chronic kidney disease (stage 1 to 5) (16). Furthermore, a significantly higher urine output measured over a 24-hour period was present only in the renal recovery group, compared to the non-survival group, which tells us that 24-hour diuresis can be one of the predictors of outcome in AKI. Beside diuresis, glomerular filtration rate provides information about kidney function. Initial glomerular filtration rates were significantly different between analyzed groups. The renal recovery group had the highest GFR among all three groups, while the dialysis group had the lowest GFR, due to the chronic kidney disease (stage 1 to 3) in the background. Therefore, initial GFR can be one of the predictors of outcome. Interestingly, statistically significant difference in initial potassium was noticed between non-survival and renal recovery group, but not between non-survival and dialysis group. However, Gong *et al.* have reported normal potassium levels in the non-survival group (4.0 mmol/L, 3.7-4.9), as well as in the survival group (4.2 mmol/L, 3.7-4.7) (4), which is more preferable, because inadequate potassium regulation can precipitate or result in life-threatening condition (19). According Gong et al., MODS was independent risk factor in the death of patients with AKI. The mean mortality rate for elderly patients was 42% and it was increasing with the number of failed organs. With the dysfunction of 2 organs, the mortality rate was 39%, 3 organs was 50%, 4 organs was 60% and 100% for the dysfunction of 5 organs (4). In this study the non-survival group had higher incidence of MODS (45%) compared to the renal recovery group (23%) and the dialysis group (18%). Therefore, MODS is one of the predictors of mortality. Liu *et al.* also reported that MODS increased incidence of mortality (16). Yokota *et al.* found that elderly patients with septic complications are prone to develop MODS, which increases the risk of mortality (18).The results summary between the three analyzed groups were shown in Table 2.

Table 2.
Results summary between the three groups.

	NON-SURVIVAL (N=126)	RENAL RECOVERY (N=41)	DIALYSIS (N=11)	P
Age (y)	74,45 ± 5,54	74,29 ± 5,42	72,81 ± 4,91	0,634
Sex (% M)	82 (65)	24 (58)	6 (54)	0,677
24-hour diuresis (mL)	541,76 ± 863,73	782,33 ± 675,05	357,00 ± 389,35	<0,05
Initial creatinine (μmol/L)	420,07 ± 200,78	341,05 ± 164,05	649,81 ± 332,89	<0,05
Endpoint creatinine (μmol/L)	294,06 ± 158,82	185,82 ± 108,6	407,00 ± 227,92	<0,05
Initial potassium(mmol/L)	5,30 ± 1,06	4,77 ± 0,83	5,01 ± 0,84	<0,05
Initial urea (mmol/L)	26,05 ± 12,63	22,39 ± 11,48	26,34 ± 12,76	0,262
GFR (ml/min/1.73 m2)	14,21 ± 8,65	19,25 ± 9,94	8,00 ± 5,47	<0,05
MODS [(n)%]	57 (45)	9 (23)	2 (18)	<0,05
Surgical procedure [(n)%]	67 (53)	25 (61)	4 (45)	0,565

Abbreviations: CRRT – continuous renal replacement therapy; GFR – glomerular filtration rate; MODS – multiple organ dysfunction syndrom;

CONCLUSIONS

This study found out that the mortality rate of elderly patients with AKI, who underwent CRRT, was 70,79%, and that 24-hour diuresis, GFR and MODS were independent risk factors for the death.

REFERENCES

1. Case J, Khan S, Khalid R, Khan A. Epidemiology of acute kidney injury in the intensive care unit. Crit Care Res Pract. 2013; 2013: 479730.

2. Abdel-Kader K, Palevsky PM. Acute kidney injury in the elderly. Clin Geriatr Med 2009; 25: 331-58.

3. Lopes JA, Jorge S. The RIFLE and AKIN classifications for acute kidney injury: a critical and comprehensive review. Clin Kidney J 2013; 6: 8-14.

4. Gong Y, Zhang F, Ding F, Gu Y. Elderly patients with acute kidney injury (AKI): clinical features and risk factors for mortality. Arch Gerontol Geriatr 2012; 54: e47-e51.

5. Pannu N, Gibney RN. Renal replacement therapy in the intensive care unit. The Clin Risk Manag 2005; 1: 141-50.

6. Coca SG. Acute kidney injury in elderly persons. Am J Kidney Dis 2010; 56: 122-31.

7. Palevsky PM, Baldwin I, Davenport A, Goldstein S, Paganini E. Renal replacement therapy and the kidney: minimizing the impact of renal replacement therapy on recovery of acute renal failure. Curr Opin Crit Care 2005; 11: 548-54.

8. Kellum JA, Mehta RL, Angus DC, Palevsky P, Ronco C. The first international consensus conference on continuous renal replacement therapy. Kidney Int 2002; 62(5):1855-63.

9. Kellum JA, Lameire N, Uhlig K *et al*. Diagnosis, evaluation and management of acute kidney injury: a KIDIGO summary (Part 1). Crit Care 2013; 17: 204.

10. Kramer P, Wigger W, Rieger J, Matthaei DSF. Arteriovenous hemofiltration: a new and simple method for treatment of overhydrated peatients resistant to diuretics. Klin Wochenschr 1977; 55: 1121-25.

11. Weinstein JR, Anderson S. The Aging Kidney: Physiological Changes. Adv. Chronic Kidney Dis 2010; 17: 302-7.

12. Boss GR, Seegmiller JE. Age-related physiological changes and their clinical significance. West J Med 1981; 135: 434-40.

13. Bae WK, Lim DH, Jeong JM *et al*. Continuous renal replacement therapy for treatment of acute kidney injury. Korean J Intern Med 2008; 23: 58-63.

14. Metnitz PGH, Krenn CG, Steltzer H *et al*. Effect of aute renal failure requiring renal replacement therapy on outcome in critically ill patients. Crit Care Med 2002; 30: 2051-58.

15. Uchino S, Kellum JA, Bellomo R *et al*. Acute Renal Failure in Critically ill Patients; A Multinational, Multicenter Study. JAMA 2005; 294: 813.

16. Liu S, Cheng Q-L, Zhang X-Y *et al*. Application of continuous renal replacement therapy for acute kidney injury in elderly patients. Int J Clin Exp Med. 2015; 8: 9973-8.

17. Eurostat. Population age structure by major age groups, 2005 and 2015. http://ec.europa.eu/eurostat/statistics-explained/index.php/Population_structure_and_ageing.

18. Yokota LG, Sampaio BM, Rocha E, Balibi AL, Ponce D. Acute kidney injury in elderly intensive care patients from a developing country: clinical features and outcome. Int J Nephrol Renovasc Dis 2017; 10: 27-33.

19. Lenhardt A, Kamper MJ. Pathogenesis, diagnosis and management of hyperkalemia. Pediatr Nephrol 2011; 263 77-84.

SAŽETAK

KONTINUIRANO NADOMJEŠTANJE BUBREGA KOD STARIJIH BOLESNIKA S AKUTNOM OZLJEDOM BUBREGA

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Akutna bubrežna ozljeda je jedan od intrigantnijih problema medicine, budući da je i dalje prati visok mortalitet unatoč napretku u liječenju i razumijevanju same bolest. Posebno osjetljivu skupinu čine stariji pacijenti, koji su zbog same dobi i svih komorbiditeta posebno ugroženi. Cilj studije bio je analizirati ishod pacijenata na CRRT-u, odnosno mortalitet, gubitak i oporavak bubrežne funkcije, kao i parametre koji bi potencijalno mogli upućivati na mogući ishod, no na koje bi se ujedno moglo i utjecati u svrhu boljeg preživljenja.

U ispitivanju su sudjelovali pacijenti oboljeli od ABO liječeni u Kliničkom bolničkom centru Rijeka u razdoblju od 5 g. Ukupan broj ispitanika bio je 178, od toga 64 osoba ženskog i 114 osobe muškog spola. Prosječna dob iznosila je 74,35 ± 5,46 (65-89) godina. Svi analizirani pacijenti su se liječili kontinuiranim nadomještanjem bubrežne funkcije. Pacijenti su raspoređeni u tri skupine ovisno o ishodu bolesti, odnosno smrt, gubitak i oporavak bubrežne funkcije. Najčešće indikacije za primjenu kontinuiranog nadomještanja bubrežne funkcije bile su kardiogene etiologije (n=89, 50,0 %) te infektivne etiologije (n=52, 29,2 %). Mortalitet pacijenata oboljelih od ABO koji su bili na kontinuiranom nadomještanju bubrežne funkcije iznosi 70,79 % (n=126), dok se renalna funkcija oporavila u 6,18 % pacijenata (n=11), a 23,03 % pacijenata je moralo nastaviti jednom od metoda nadomještanja bubrežne funkcije (n=41). Analizom podataka dobiveno je da vrijednosti inicijalno mjerenog kreatinina, 24-satne diureze, glomerularne filtracije, kalija, kao i višestruko zatajenje organa, mogu biti jedan od prediktora ishoda ABO u starijih pacijenata.

Ključne riječi: **kontinuirano nadomještanje bubrežne funkcije, akutna bubrežna ozljeda, stariji, mortalitet**