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COMPARISON BETWEEN EARLY INITIATION AND STANDARD STRATEGY OF RENAL REPLACEMENT THERAPY IN THE CRITICALLY ILL ACUTE KIDNEY INJURY PATIENTS

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ABSTRACT

Introduction: Acute kidney injury is a medical condition with multiple etiologies that affects 5% of hospital admissions and 30% of intensive care unit (ICU) admissions. The relationship between early initiation of renal replacement therapy or delay in renal replacement therapy in critically ill patients with non-life-threatening kidney damage due to renal failure is a major issue faced by clinicians . In this study, the average age of the research participants in the early intervention group was 47.1±8.76 years, and the average age of the participants in the delayed intervention group was 46.04±7.34 years. Primary and secondary outcomes were not significantly different. **Materials and Methods**: This prospective observational study was conducted after getting approval from institutional ethical committee. We included patients >18 years of age with Stage 3 AKI according to KDIGO guidelines in our study. Patients with CKD and previous exposure to RRT were excluded from the study .The clinical profile, lab investigations and outcome of study participants were recorded. This study was done over a period of 6 months i.e, from July 2023 to December 2023. **Results:** The study had 100 participants. The average age of the study participants was 47.1± 8.76 years in early strategy group and 46.04±7.34 years in standard strategy group. The current study reported no statistically significant association between the timing of dialysis in the critically ill acute kidney injury patients in terms of primary and secondary outcome for the same. **Conclusion:** Renal replacement should be individualized.

KEYWORDS: Acute kidney injury,Renal replacement therapy, Early strategy, Standard strategy, Mechanical ventilation.

INTRODUCTION

Acute kidney injury is one of the most feared complications in patients admitted to the intensive care unit (ICU) and is associated with an increased risk of death or serious complications and a high resource utilization.[1,2] Short-term dialysis rate is highest among critically ill patients , septic patients, and patients who have undergone cardiovascular surgery.[3,4] Initiating dialysis before the onset of any major complications can be beneficial for the patients having severe acute renal dysfunction . It may help restore and maintain acid –base balance, reduce fluid retention and reduce accumulation of metabolic end products in untreated patients.[5] In patients with complications (e.g; uremic complications, excess fluid, hyperkalemia and metabolic acidosis) which are refractory to medical treatment and can prove fatal for the patient, dialysis can be started early. Initiating organ support therapy and shifting patients to intensive care unit (ICU) is a difficult decision. While this decision can normalize the patient, it can cause more harm than benefit to the patients.[6] Starting RRT presumptively can be beneficial but it can expose patients to unnecessary complications which can prove fatal for the patient.[7]

When dialysis is started early for acute kidney injury, critical care is required as the patient may receive unnecessary treatment or its associated complications and costs.[8,9] In some cases the decision making is relatively clear and starting early dialysis can prove beneficial for the patient. RRT is also inappropriate when inconsistent with patient preferences and clinical goals. However, many critically ill patients still meet stage 3 AKI criteria but lack immediate dialysis or evidence of recovery. For these patients, doctors face a dilemma: Should RRT be started as early as possible (risk of over-treatment), or delayed as long as possible (possibility of excess fluid and increased risk of abnormalties)?

However, when severe acute renal dysfunction is not accompanied by one of above problems, benefits of dialysis can be highly controversial.[10,11]

AIMS AND OBJECTIVES

AKI is the leading cause of hospital associated mortality. The precise timing of starting dialysis in patients who are critically ill is highly controversial .Therefore, primary objective of this study was to see if early initiation of RRT can be beneficial to patients than the standard RRT considering the complex issues associated with critically ill patients (sepsis, electrolyte derangement, fluid overload, etc.)

1) To Compare outcomes of early initiation and standard strategy of dialysis in patients who are critically ill with stage 3 AKI in terms of primary outcome and secondary outcome. 2) To evaluate the primary outcome in terms of mortality at 90 days. 3) To evaluate the secondary outcomes in terms of Dialysis dependence among survivors at 90 days, requirement of mechanical ventilation ,SOFA score, hospital stay, length of ICU stay among survivors and non survivors and complications like electrolyte imbalance and thrombosis.

MATERIAL AND METHODS

The present prospective observational study was conducted in General Medicine department of Acharya Shri Chander College of Medical Sciences and Hospital, Jammu after getting the ethical clearance from the institutional ethical committee for period of 6 months (July 2023- December 2023). A total of 100 patients diagnosed with stage 3 acute kidney injury (according to KIDIGO classification) who attended OPD/IPD were included after obtaining their informed written consent.

INCLUSION CRITERIA

1. Age more than 18 years.
2. Stage 3 AKI based on KDIGO classification.

EXCLUSION CRITERIA

1. Previous cases with renal-replacement therapy.
2. Patients with CKD (chronic kidney disease).

We randomly distributed patients among two groups (early initiation of RRT and standard RRT group) in ratio of 1:1. We categorized patients into stages of AKI according to Kidney Disease: Improving Global Outcomes (KDIGO) classification with stages ranging from 1-3. Baseline serum creatinine, eGFR, serum potassium, serum bicarbonate and SOFA score (for critically ill septic patients) were recorded and then monitored serially at 12 hrs, 24 hrs and subsequently. In early strategy group, dialysis was started at the earliest after randomisation was done and in standard strategy group, dialysis was withheld until one or more of following criteria was met: refractory hyperkalemia (Potassium ≥6 mmol /L), pH ≤ 7.20 or bicarbonate ≤ 12 mmol /L, or persistent Acute renal dysfunction for at least 72 hours.

The primary outcome of interest was all-cause mortality at 90 days after randomisation. The secondary outcomes of interest were Dialysis dependence in the survivors at 90 days, requirement of mechanical ventilation, severity of SOFA score (with lower score indicating better outcome), duration of hospital stay, duration of ICU stay and complications like electrolyte imbalance and thrombosis.

Patients were followed up and contacted 30 days after randomization to assess vital status, and if readmission to the hospital or emergency department. We also contacted patients at end of 90 days to assess vital status.

We recorded the data in Microsoft Excel and analysed with the help of SPSS 22.0 version. Findings were presented in number and percentage and inspected by mean, standard deviation,mean difference with confidence interval of 95% , p-value and T-tests. T- test was used to assess the association among variables.. A p-value was used to find statistical significance among the various variables.

OBSERVATIONS AND RESULTS

In this study, the average age of the study participants was 47.1± 8.76 years in early strategy group and 46.04±7.34 years in standard strategy group. Patients were randomly distributed into two study groups (early initiation and standard strategy groups) in ratio of 1:1.The male to female ratio was 26:24 in early strategy group and 23:27 standard strategy group respectively.

The base line characteristics of patients were recorded in terms of age(years), kidney function test in terms of serum creatinine and eGFR and pre existing risk factors such as hypertension, heart failure, diabetes mellitus and coronary artery disease. Hypertension was seen in majority of patients in both the groups (87% in early intervention group and 88% in standard RRT group) followed by diabetes (77% in early strategy group and 80% in standard strategy group).(table 1)

The clinical conditions of patients were noted at the time of randomisation in terms of sepsis, septic shock, requirement of mechanical ventilation, urine output, serum potassium and serum creatinine. Mean serum potassium was 4.6±0.8 in early intervention group and 5.1±0.9 in standard RRT group. Mean serum creatinine was 5.4±1.2 in early intervention group and 5.2±1.1 in standard RRT group. (Table 2)

Primary outcomes- recorded in terms of death at 90 days (p-value 0.65which was statistically insignificant). Secondary outcomes of interest were -RRT dependence among survivors at 90 days (p-value=0.73), requirement of mechanical ventilation days (p-value=0.29), hospital stay, length of ICU stay in days among survivors (p-value=0.23) and non survivors (p-value=0.38). No significant difference was present in the primary and the secondary outcomes in both the groups. (Table 3)

The adverse effects occurred in 25 patients in the early strategy group and 20 patients in standard strategy group. The adverse effects were reported in terms of those associated with RRT, associated with dialysis catheter use and anxiety and depression. Among adverse events associated with RRT hypotension was observed in maximum patients in both the groups (10% in early strategy group and 8% in standard strategy group) followed by hypoglycaemia(8% in early strategy and 6%in standard strategy group). Among adverse events associated with dialysis catheter use bleeding was observed in majority of patients in both the groups(14% in early strategy group and 16% in delayed strategy group). (Table 4)

In early group RRT was initiated soon after randomisation and in standard group after meeting the criteria as explained above. At The end of 90 Days RRT dependance was seen in ten patients and eight patients among the survivors in early and standard strategy group respectively .GRAPH 1shows the Decreasing Trend Of RRT dependence at 90 days in both Early Strategy(10 patients) and Standard Strategy Group(8 patients).

Table 1: Base Line Characteristics Of Patients.

CHARACTERISTICS	ACCELERATED STRATEGY (N=50)	STANDARD STRATEGY (N=50)
AGE IN YRS	47.1±8.7	46.04±7.3
SEX IN NO. (%)	MALE=52	MALE=46
	FEMALE=48	FEMALE=54
SERUM CREATININE IN MG/DL	0.9 ± 0.5	0.8 ± 0.5
ESTIMATED GLOMERULAR FILTERATION RATE IN ML / MIN / 1.73 M^2	84.1 ± 20.2	86.8 ± 20.1
HOSPITAL ACQUIRED RISK FACTORS FOR AKI (inNO.%)		
POST OPERATIVE	30	31
EXPOSURE TO RADIOCONTRAST MATERIAL (IN %)	85	87
NEPHROTOXIC DRUGS	25	23
PRE EXISTING CONDITIONS (inNO.%)		
HYPERTENSION	87	88
HEART FAILURE	65	66
DIABETES MELLITUS	77	80
LIVER DISEASE	15	20
CORONARY ARTERY DISESE	25	19
MALIGNANCIES	5	7

Table 2: Clinical Conditions At Randomization.

CONDITION	ACCELERATED STRATEGY (N=50)	STANDARD STRATEGY (N=50)	RELATIVE RISK OR DIFFERENCE (95% CI)	P- VALUE
SEPSIS(in no.)	30	28		
SEPTIC SHOCK	17	18	-0.02 (-0.067-0.107)	0.65
MECHANICAL VENTILLATION (No.)	10	12		
VASOPRESSOR SUPPORT (No.%)	34	36	0.02 (-0.09-0.134)	0.73
SERUM CREATININE (MG/DL)	5.4 ± 1.2	5.2 ± 1.1	0.06 (-0.05-0.17)	0.29
SERUM POTASSIUM(MEQ/L)	4.6 ± 0.8	5.1 ± 0.9	-0.52 (-0.98-2.0)	0.49
SERUM BICARBONATE (MEQ/L)	19.13±4.4	18.36±4.29	-1.23(-0.81-3.28)	0.23
MEDIAN URINE OUTPUT (ML/24HRS)	400 (100 – 850)	490 (150 -900)	1.00(-1.49-3.49)	0.38

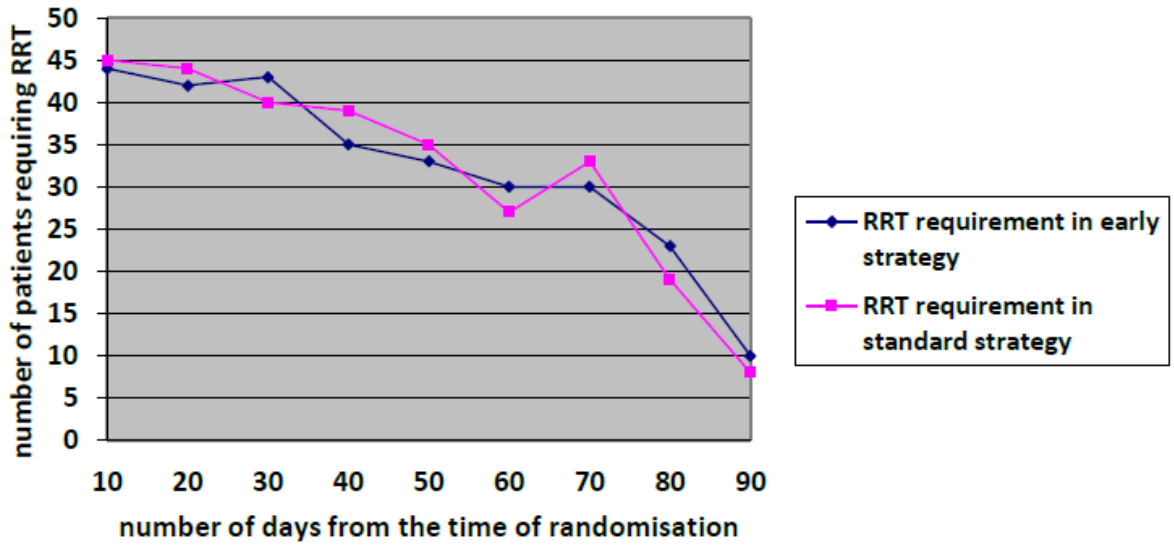
Table 3: Primary and Secondary Outcome.

CHARACTERISTIC	ACCELERATED STRATEGY (N=50)	STANDARD STRATEGY (N=50)	RELATIVE RISK OR DIFFERENCE (95% CI)	P-VALUE
PRIMARY OUTCOME				
DEATH AT 90 DAYS IN NO. (%)	4	6	-0.02 (-0.067-0.107)	0.65
SECONDARY OUTCOMES				
RRT DEPENDENCE AMONG SURVIVORS AT 90 DAYS IN NO. (%)	10	8	0.02 (-0.09-0.134)	0.73
MV REQUIRED IN NO. (%)	12	6	0.06 (-0.05-0.17)	0.29
MEAN HOSPITAL STAY IN DAYS	17.98±3.84	18.50±3.71	-0.52(-0.98-2.0)	0.49
MEAN LENGTH OF ICU STAY IN SURVIVORS	14.13±4.4	15.36±5.29	-1.23(-0.81-3.28)	0.23
MEAN LENGTH OF ICU STAY IN	8.5±1.29	7.5±1.8	1.00(-1.49-3.49)	0.38

NON SURVIVORS				
MEAN CREATININE AT 90 DAY MG/DL	1.58±O.4	1.55±0.35	0.028(-0.1401-0.1961)	0.77
ESTIMATED GLOMERULAR FILTERATION RATE IN ML / MIN / 1.73 M^2 AT 90 DAYS	65.1 ± 29.1	65.8 ± 30.8	0.32(-3.9-0.08)	0.7

Table 4: Major Adverse Events.

ADVERSE EVENTS	ACCELERATED STRATEGY (N=50)	STANDARD STRATEGY (N=50)
ASSOCIATED WITH RRT (in NO.)		
HYPOTENSION	5	4
ARRYTHMIA	2	1
SEIZURE	1	1
ALLERGIC REACTION	1	1
HYPOGLYCEMIA	4	3
ASSOCIATED WITH DIALYSIS CATHETER USE (in NO.)		
BLEEDING	7	8
THROMBUS (CONFIRMED ON USG)	1	0
ANXIETY AND DEPRESSION (in NO.)	**4**	**2**



Graph 1: Showing The Decreasing Trend Of RRT Dependence In Both Early Strategy and Standard Strategy Group. Graph Is Plotted At An Interval Of 10 Days. At The End of 90 Days Rrt Dependance Was Seen In 10 Patients and 8 Patients Among The Survivors In Early And Standard Strategy Group.

DISCUSSION

All AKI patients who had not previously received RRT were included in our study and were divided into two groups according to the time of starting RRT. The exact time of starting dialysis in patients with acute renal dysfunction is highly uncertain. Our study supports individual RRT in AKI patients rather than random distribution of RRT in AKI patients. There was no difference in RRT duration or renal recovery/RRT dependence in the early or late RRT group. In this study, 100 patients were examined and analyzed. There was no difference in results between the two groups after 90 days of observation from the date of admission (p value = 0.65). The average age of the study participants was 47.1±8.76 years in the early strategy group and 46.04±7.34 years in the standard strategy group. At 90 days after randomization, the mean dependence of RRT in the early RRT group and the delayed strategy group was 0.1 ± 0.303 and 0.08 ± 0.274, respectively, with a p value of 0.65. Complications such as ventilator dependence and thrombosis occurred in both groups.

The study conducted by El-Sharqawy OA , et al.,(2019) did not favor early initiation of RRT versus late intuition in terms of allcauses mortality reported (RR = 0.88; 95% confidence interval (CI), 0.68, 1.14; P = 0.33), RRT dependence (RR = 0.81; 95% CI, 0.46, 1.42; P = 0.46), duration of stay in ICU (SMD, −0.28; 95% CI, −0.58, 0.03; P = 0.08), and duration of stay in hospital (SMD, −0.40; 95% CI, −0.83, 0.03; P = 0.07).The systematic review and meta-analysis shows that early initiation of dialysis does not improve survival outcomes and hospital stay among patients with acute renal dysfunction , in comparison with late start of dialysis .[12] In another study conducted by Inês Castro , et al.,(2022) it was found that Early initiation of dialysis did not improve the 28-

day and overall mortality, but increased the risk for dialysis associated complications like hypotension and infection.[13] The current study reported no statistically significant association between timing of start of dialysis in early intervention and the standard group in the critically ill patients with acute renal dysfunction and in the primary and secondary outcome for the same.

Our study also has limitations. We may have predisposed the patients in accelerated strategy group to adverse events related to RRT, which could have been avoided. Compared to other multicentric trials our study only included 100 patients but the results were similar to other studies.

CONCLUSION

The present study concluded that early initiation and standard strategy of dialysis in the critically ill patients with acute renal dysfunction is insignificant in terms of primary and secondary outcomes among both the groups . Low blood volume being the major cause of admission and hypertension being the main risk factor among both the groups. Complications were seen equally distributed among both the groups.It can be concluded that RRT should be individualised and should be provided according to base line laboratory investigations and underlying risk factors. It should not be randomised as it may expose patients to unwanted RRT or RRT related infections.

REFERENCES

1. Hoste EA, Bagshaw SM, Bellomo R, et al. Epidemiology of acute kidney injury in critically ill patients: the multinational AKI- EPI study. Intensive Care Med., 2015; 41: 1411-1423.
2. R.L. Mehta, J. Cerda, E.A. Burdmann, et al.
3. International Society of Nephrology's 0by25 initiative for acute kidney injury (zero preventable deaths by 2025): a human rights case for nephrology.
4. R.K. Hsu, C.E. McCulloch, R.A. Dudley, L.J. Lo, C.Y. Hsu , et al. Temporal changes in incidence of dialysis-requiring AKI J Am Soc Nephrol, 2013; 24(1): 37-42.
5. Libório AB, Leite TT, Neves FM, Teles F, Bezerra CT. AKI complications in critically ill patients: association with mortality rates and RRT. Clin J Am Soc Nephrol., 2015; 10: 21-28.
6. N.V. Kolhe, A.W. Muirhead, S.R. Wilkes, R.J. Fluck, M.W. Taal , et al. National trends in acute kidney injury requiring dialysis in England between 1998 and 2013 Kidney Int, 2015; 88(5): 1161-1169.
7. Santos MJ, Martins MS, Santana FLP, Furtado MCSPC, Miname FCBR, Pimentel RRS, et al. COVID-19: instruments for the allocation of mechanical ventilators—a narrative review. Crit Care, 2020; 24: 582.
8. Feinstein MM, Niforatos JD, Hyun I, Cunningham TV, Reynolds A, Brodie D, et al. Considerations for ventilator triage during the COVID-19 pandemic. Lancet Respir Med., 2020; 8: e53.
9. Clark EG, Bagshaw SM., et al. Unnecessary renal replacement therapy for acute kidney injury is harmful for renal recovery. Semin Dial., 2015; 28: 6–11.
10. Gaudry S, Quenot J-P, Hertig A, Barbar SD, Hajage D, Ricard J-D, et al. Timing of renal replacement therapy for severe acute kidney injury in critically Ill patients. Am J Resp Crit Care, 2019; 199: 1066–75.
11. Karvellas CJ, Farhat MR, Sajjad I, Mogensen SS, Leung AA, Wald R, et al. A comparison of early versus late initiation of renal replacement therapy in critically ill patients with acute kidney injury: a systematic review and meta-analysis. Crit Care., 2011; 15: R72.
12. El-Sharqawy OA, Gaballah KM, Elshahat MS. Earlier start versus standard start dialysis in patients with acute kidney injury: systematic review and meta-analysis. Menoufia Med J [serial online] 2019 [cited 2024 Jan 23]; 32: 1163-8.
13. Inês Castro, Miguel Relvas, Joana Gameiro, José António Lopes, Matilde Monteiro-Soares, Luís Coentrão, et al.The impact of early versus late initiation of renal replacement therapy in critically ill patients with acute kidney injury on mortality and clinical outcomes: a meta-analysis .Clinical Kidney Journal, October 2022; 15(10): 1932–1945.