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Monocyte to Lymphocyte Ratio and Tacrolimus Levels at 2 weeks after Kidney Transplantation as Predictors of Mortality among Kidney Transplant Recipients at Dr. Sardjito Hospital, Indonesia

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INTRODUCTION

- Kidney transplantation (KT) remains the main renal replacement therapy option for end-stage renal disease.
- Recipient survival rates are an important issue of interest after KT.
- Kidney transplantation has been developing rapidly in Indonesia in recent years.
- However, data regarding mortality predictor factors has not been widely studied

This study aims to analyze predictor factors for recipient mortality after KT.

METHODS

Type of Study

Retrospective Cohort Study

Subject

60 patients who underwent KT with a living kidney donor at Dr Sardjito Hospital, Indonesia

Parameters

Recipient, Donor, Ischemic Time, and Laboratory Parameters

Data Analysis

- The cut-off values of Tacrolimus through, Monocyte-Lymphocyte Ratio (MLR), Netrophil-Lymphocyte Ratio (NLR), and Platelet-Lymphocyte Ratio (PLR) were assessed with receiver operating characteristic (ROC) curves.
- Predictor factor analysis used bivariate tests followed by multivariate tests

Table 1. Baseline characteristics of subjects (n=60)

VARIABLE		Mean ± SD	Median (min-max)	n	%
DONOR:					
Age (years)		37.83±10.51	36.0 (22.0-61.0)		
Gender	Male			39	65
	Female			21	35
Donor and Recipient Relationship	Related			18	30.5
	Unrelated			41	69.5
RECIPIENT:					
Age (years)		39±12.89	38.50 (19.0-65.0)		
Gender	Male			45	75
	Female			15	25
BMI (kg/m^2)		24.58±5.63	23.99 (15.20-35.43)		
Diabetes Mellitus	Yes			18	30
	No			42	70
Hepatitis C	Yes			7	11.7
	No			53	88.3
Azathioprine	Yes			2	3.3
	No			58	96.7
Mycophenolic Acid	Yes			52	86.7
	No			8	13.3
Mycophenolic Mofetil	Yes			6	10
	No			54	90
ISCHEMIC TIME:					
1st Warm time (minute)		3.94±2.03	3.28 (1.02-9.73)		
Cold time (minute)		31.42±11.61	27.37 (8.30-69.48)		
2nd Warm time (minute)		52.29±18.50	50.0 (15.0-120.0)		
Total ischemic (minute)		91.07±24.53	87.0 (59.0-169.0)		
Urine time (minute)		4.68±5.22	2.58 (0.07-20.0)		
LABORATORY PARAMETERS (at 2 weeks):					
BUN (mg/dL)		30.06±14.90	25.05 (11.30-81.0)		
Creatinine (mg/dL)		1.92±1.77	1.27 (0.60-7.86)		
Tacrolimus trough		7.62±2.74	7.20 (2.70-15.0)		
Hemoglobin (mg/dL)		9.91±1.44	9.80 (6.40-13.40)		
Hematocrit (%)		30.38±4.54	29.80 (19.0-40.20)		
Erythrocyte count (10^6/mL)		3.48±0.56	3.49 (2.0-4.76)		
Leukocyte count (10^3/mL)		12.61±4.41	11.90 (6.24-31.83)		
Platelet count (10^3/mL)		349.23±122.21	348.50 (88.0-625.0)		
Neutrophil (%)		78.96±7.98	81.25 (60.30-94.0)		
Lymphocyte (%)		11.80±6.35	10.15 (1.30-31.20)		
Monocyte (%)		7.04±2.47	6.85 (2.50-16.70)		
NLR		9.97±9.92	8.04 (1.93-72.31)		
PLR		39.04±28.57	31.38 (7.56-189.39)		
MLR		0.78±0.52	0.65 (0.22-3.23)		
Sodium (mEq/L)		135.53±5.08	136.0 (123.0 – 148.0)		
Potassium (mEq/L)		4.65±0.93	4.57 (2.46-7.42)		

BMI: body mass index, NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio, MLR: monocyte/lymphocyte

RESULTS

- **Gender:** Male (75% for recipient, 65% for donor)
- **Mean age :** 39±12.89 yr (recipient), 37.83±10.51 yr (donor)
- **Relationship:** unrelated (69,5%)

- **NLR > 9.58**: RR 2.0 (95% CI, 0.65-6.11), p=0.278
- **PLR > 45.17**: RR 1.56 (95% CI, 0.59-4.86), p=0.468)

NLR > 9.58 and PLR > 45.17 at 2 weeks after KT can increase the risk of mortality but is **not statistically significant**

Table 2. Bivariate analysis of predictor mortality

VARIABLE		Death		Survived		p	RR (95%CI)
		n (10)	%	n (50)	%		
Gender of Donor	Male	5	12.28	34	87.2	0.298	0.54 (0.17-1.65)
	Female	5	23.8	16	76.2		
Gender of Recipient	Male	9	20	36	80	0.426	3.00 (0.41-21.76)
	Female	1	6.7	14	93.3		
Diabetes Mellitus	Yes	3	16.7	15	83.3	1.000	1.00 (0.29-3.44)
	No	7	16.7	35	83.3		
Hepatitis C	Yes	0	0.0	7	100	0.589	-
	No	10	18.9	43	81.1		
BUN (mg/dL)	>20	10	22.2	35	77.8	0.054	-
	<20	0	0.0	15	100		
Creatinine (mg/dL)	>0.9	10	19.6	41	80.4	0.333	-
	<0.9	0	0.0	9	100		
Tacrolimus trough at 2 weeks	<7.74	9	27.3	24	72.7	0.017*	7.36 (0.99-54.54)
	>7.74	1	3.7	26	96.3		
Haemoglobin (mg/dL) at 2 weeks	<12	8	14.8	46	85.2	0.259	0.44 (0.12-1.63)
	>12	2	33.3	4	66.7		
Hematocrit (%) at 2 weeks	<35	8	16.3	46	83.7	1.000	0.89 (0.22-3.66)
	>35	2	18.2	4	81.8		
Erythrocyte count (10^6/mL) at 2 weeks	<4	10	17.2	48	82.8	1.000	-
	>4	0	0.0	2	100		
Leukocyte count (10^3/mL) at 2 weeks	>11.5	6	18,2	27	81.8	1.000	1.23 (0.38-3.91)
	<11.5	4	14,8	23	85.2		
Platelet count (10^3/mL) at 2 weeks	>450	3	21.4	11	78.6	0.685	1.41 (0.42-4.72)
	<450	7	15.2	39	84.4		
Neutrophil (%) at 2 weeks	>70	8	16	42	84	0.668	0.80 (0.19-3.22)
	<70	2	20	8	80		
Lymphocyte (%) at 2 weeks	<18	8	16.3	41	83.7	1.000	0.89 (0.22-3.66)
	>18	2	18.2	9	81.8		
Monocyte (%) at 2 weeks	>11	0	0.0	2	100	1.000	-
	<11	10	17.2	48	82.8		
NLR at 2 weeks	>9.58	5	25	15	75	0.278	2.00 (0.65-6.11)
	<9.58	5	12.5	35	87.5		
PLR at 2 weeks	>45.17	4	22.2	14	77.8	0.468	1.56 (0.59-4.86)
	<45.17	6	14.3	36	85.7		
MLR at 2 weeks	>0.99	5	38.5	8	61.5	0.031*	3.62 (1.23-10.61)
	<0.99	5	10.6	42	89.4		

RESULTS (cont')

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Table 3. The Result of Multivariate and ROC Analysis

VARIABLE	Multivariate Analysis				Receiver Operating Characteristics (ROC)		
	p	OR	95% CI		AUC	p	95%CI
			Lower	Upper			
Tacrolimus trough <7.74 at 2 weeks	0.026	13.229	1.358	128.920	0.806	0.002	0.643-0.969
MLR >0.99 at 2 weeks	0.019	7.478	1.398	40.011			

MLR: monocyte/lymphocyte ratio

Tacrolimus <7.74 ng/mL

(OR: 13.229, 95% CI:1.358-128.920)

MLR >9.58

(OR: 7.478, 95% CI: 1.398-40.011)

significantly increased the risk of mortality (p<0.05) at 2 weeks after KT among recipients

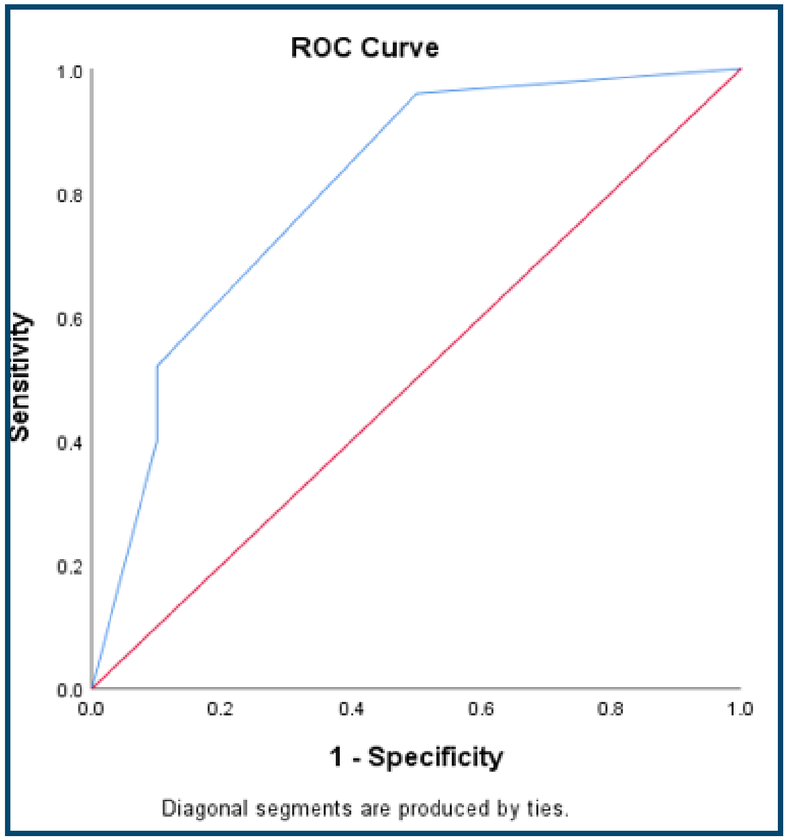

Figure 1. ROC Curve

Tacrolimus through and MLR levels at 2 weeks after kidney transplantation can **strongly predict** mortality with **an AUC of 80.6%** (95%CI 0.643-0.963, p=0.002) (Table 3 and Fig.1)

DISCUSSION

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Tacrolimus trough level <7.74 ng/mL at 2 weeks after transplantation was significantly associated with higher mortality risk (p=0.026).

- Ryu *et al*. (2021): Tacrolimus level <7 ng/mL within 1 month after renal transplantation was associated with worse death-censored graft survival (p=0.000).
- Israni *et al*. (2013): Use 8-15 ng/mL of tacrolimus level within 0-3 months after transplantation to minimise acute rejection.
- Agur *et al.* (2022): Tacrolimus level below 6 ng/mL above 14 days post-transplant was associated with an increased rate of graft loss and reduced kidney graft survival.
- Staatz *et al.*(2001): Tacrolimus levels greater than 10ng/ml should be achieved in 1st mo. after KT.

MLR level was >0.99 at 2 weeks post-transplant was significantly increased the risk of higher mortality (p=0.019).

- Yang *et al.* (2023): The high MLR group (MLR >0.2168) was significantly and independently associated with all-cause mortality and CVD events in RRT (p=0.002).
- Pilichowska *et al.* (2023): NMR and LMR parameters can be predictive factors with the risk of DGF.

NLR values >9.58 and PLR >45.17 at 2 weeks after KT were not statistically significant but both can increase the risk of mortality. → Contrary to studies by Liao *et al*., (2022), Sayilar *et al* (2020)., and Ergin *et al* (2019).

CONCLUSION

Tacrolimus trough levels <7.74 ng/mL and MLR >9.58 at 2 weeks after kidney transplantation can be predictors of mortality in kidney transplant recipients.

REFERENCES