Predictive Value of Pre-Transplant Monocyte-to-Lymphocyte Ratio for Delayed Graft Function in Kidney Transplant Recipients

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Abstract

Background: Delayed graft function (DGF) after kidney transplantation (KT) negatively impacts long-term allograft survival. Inflammatory and immune response markers in transplant recipients have been linked to allograft outcomes. However, the association between the pre-transplant monocyte-to-lymphocyte ratio (MLR) and DGF following KT has not been previously investigated.

Methods: This study included 162 patients who underwent KT between January 1989 and December 2023. The optimal pre-transplant MLR cutoff for predicting DGF was identified using receiver operating characteristic (ROC) curve analysis. Univariate and multivariate logistic regression analyses were performed to identify factors associated with DGF.

Results: DGF occurred in 58 patients (35.8%). The optimal MLR cut-off for predicting DGF was 0.255 (Area under the curve (95% confidence interval) = 0.686 (0.603–0.769), P < 0.001), with a sensitivity of 81.0% and specificity of 55.8%. In multivariate analysis, MLR ≥ 0.255 was independently associated with DGF (Odds ratio (95% confidence interval) = 3.74 (1.55–9.02), P = 0.003). Higher MLR values were also correlated with longer hospital stays.

Conclusions: An elevated pre-transplant MLR was a significant predictor of DGF following KT. MLR may serve as a useful, non-invasive biomarker for risk stratification and prediction of post-transplant outcomes.

Keywords: slow graft function; allograft dysfunction; white blood cell; monocyte; lymphocyte

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Received: 22 March 2025; Revised: 24 April 2025; Accepted: 27 April 2025
https://doi.org/10.63555/jnst.2025.278215

การใช้อัตราส่วนโมโนไซต์ต่อลิมโฟไซต์ก่อนการปลูกถ่ายเพื่อทำนายภาวะการทำงานล่าช้าในผู้ป่วยที่ได้รับการปลูกถ่ายไต

ไอริณ จริยะโยธิน, ศิริลักษณ์ อินค้า, ปิยะณัฐ แก้วดวงเทียน

หน่วยโรคไต, กลุ่มงานอายุรกรรม, โรงพยาบาลตำรวจ

บทคัดย่อ

บทนำ: ภาวะการทำงานล่าช้าของไตที่ปลูกถ่าย (delayed graft function) ส่งผลเสียต่อการอยู่รอดของไตในระยะยาว จากการศึกษาพบว่าตัวบ่งชี้การอักเสบและการตอบสนองของระบบภูมิคุ้มกันในผู้ป่วยที่ได้รับการปลูกถ่ายมีความสัมพันธ์กับผลลัพธ์ของไตที่ปลูกถ่าย อย่างไรก็ตามยังไม่เคยมีการศึกษาถึงความสัมพันธ์ระหว่างอัตราส่วนโมโนไซต์ต่อลิมโฟไซต์ (Monocyte-to-Lymphocyte Ratio: MLR) ก่อนการปลูกถ่ายไตของผู้ป่วยที่จะได้รับการปลูกถ่ายไต กับภาวะการทำงานล่าช้าของไตที่ได้รับการปลูกถ่าย

ระเบียบวิธีวิจัย: งานวิจัยนี้ได้รวบรวมผู้ป่วยจำนวน 162 รายที่ได้รับการปลูกถ่ายไประหว่างเดือนมกราคม พ.ศ. 2532 ถึงเดือนธันวาคม พ.ศ. 2566 ค่าตัดขอบของ MLR ก่อนการปลูกถ่ายที่เหมาะสมที่สุดในการทำนายภาวะการทำงานล่าช้าของไตได้รับการวิเคราะห์โดยวิธี Receiver Operating Characteristic นอกจากนี้ยังใช้การวิเคราะห์ถดถอยลอจิสติกแบบตัวแปรเดียวและและแบบพหุตัวแปรเพื่อระบุปัจจัยที่เกี่ยวข้องกับภาวะการทำงานล่าช้าของไตที่ปลูกถ่าย

ผลการวิจัย: ภาวะการทำงานล่าช้าของไตที่ปลูกถ่ายเกิดขึ้นในผู้ป่วย 58 ราย (ร้อยละ 35.8) ค่าตัดขอบของ MLR ที่เหมาะสมที่สุดในการทำนายภาวะการทำงานล่าช้าของไตที่ได้รับการปลูกถ่าย คือ 0.255 (Area under the curve (95% confidence interval) = 0.686 (0.603–0.769), P < 0.001) โดยมีความไวที่ร้อยละ 81.0 และความจำเพาะที่ร้อยละ 55.8 ในการวิเคราะห์แบบพหุตัวแปรพบว่า MLR ≥ 0.255 มีความสัมพันธ์อย่างอิสระกับการเกิดภาวะการทำงานล่าช้าของไตที่ได้รับการปลูกถ่าย (Odds ratio (95% confidence interval) = 3.74 (1.55–9.02), P = 0.003). นอกจากนี้ค่า MLR ที่สูงขึ้นยังสัมพันธ์กับระยะเวลาการนอนโรงพยาบาลที่นานขึ้น

สรุป: ค่า MLR ก่อนการปลูกถ่ายที่เพิ่มขึ้นสามารถทำนายภาวะการทำงานล่าช้าของไตที่ได้รับการปลูกถ่าย ดังนั้น MLR อาจเป็นตัวบ่งชี้ทางชีวภาพที่มีประโยชน์ในการประเมินความเสี่ยงและการทำนายผลลัพธ์ของไตที่ได้รับการปลูกถ่าย

คำสำคัญ: เปลี่ยนไต; ไตวาย; เม็ดเลือดขาว; โมโนไซต์; ลิมโฟไซต์

Background

Kidney transplantation (KT) remains the preferred form of renal replacement therapy for most patients with end-stage renal disease, offering improved quality of life and extended survival compared to dialysis.[1-4] However, delayed graft function (DGF) after transplantation significantly hinders optimal outcomes. DGF, defined as a temporary impairment of graft function requiring dialysis within the first week post-transplantation, is associated with prolonged hospitalization and reduced long-term graft survival.[5,6]

Identifying reliable predictors of DGF is crucial for early detection and timely intervention, which may mitigate its adverse effects on graft survival and patient outcomes.

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รับบทความ: 22 มีนาคม 2568; ปรับปรุงแก้ไข: 24 เมษายน 2568; รับตีพิมพ์: 27 เมษายน 2568

Although the exact pathogenesis of DGF is not fully understood, it is believed to involve a combination of donor and recipient factors. Donor-related ischemia-reperfusion injury, caused by the interruption and subsequent restoration of blood flow, triggers inflammation and contributes to graft dysfunction.[7-9] Additionally, recipient-related immune responses, both innate and adaptive, may exacerbate systemic inflammation and impair graft function.[5,10] Previous studies have shown that elevated inflammatory biomarkers in the early post-transplantation period are associated with increased long-term mortality in kidney transplant recipients.[11,12]

Recently, there has been growing interest in biomarkers that reflect the interplay between inflammation and immune response in systemic inflammation, including erythrocyte sedimentation rate, C-reactive protein (CRP), procalcitonin, and the monocyte-to-lymphocyte ratio (MLR). While CRP is widely used, its elevation can result from a variety of causes, such as infection, tissue injury, or abnormal liver and kidney function, and it requires specialized testing beyond routine laboratory work.[13]

Among these biomarkers, MLR has emerged as a promising, readily available, and cost-effective marker of systemic inflammation. MLR has demonstrated predictive potential in various pathological conditions, particularly as an indicator of inflammation in cancer and coronary artery disease.[14-16] Elevated MLR levels have been linked to poor clinical outcomes, likely reflecting underlying immune dysregulation and heightened inflammatory response. However, the potential of MLR to predict DGF in kidney transplant recipients has not yet been explored. This retrospective cohort study aims to evaluate the association between MLR and DGF, and to determine the predictive value of MLR in identifying patients at risk for DGF. Additionally, the study will examine the relationship between MLR and post-transplant complications, as well as hospital length of stay.

Materials and Methods

Study Design and Population

This retrospective cohort study included adult patients (aged ≥18 years) who underwent kidney transplantation at Police General Hospital, Bangkok, Thailand, between January 1989 and December 2023. Patients with missing or incomplete medical records were excluded. A total of 162 patients met the inclusion criteria and were analyzed. The study flow diagram is presented in **Figure 1**.

Ethical approval was obtained from the Institutional Review Board of Police General Hospital. All data were handled in accordance with patient confidentiality regulations. Informed consent was waived due to the retrospective nature of the study.

Data Collection and Definitions

Demographic and laboratory data were retrieved from the electronic medical record system. For kidney transplant recipients, the laboratory values used were pre-transplantation results. DGF was defined as a temporary impairment of allograft function requiring dialysis within the first week post-transplantation.

Sample Size Calculation

Using a previously established MLR cut-off value of 0.2168, as reported by Yang et al. in a study investigating MLR in peritoneal dialysis patients, the sample size was calculated based on a comparison of proportions between two groups. The analysis indicated that at least 62 patients with DGF would be required for sufficient statistical power.[17]

Statistical Analysis

Data are presented as mean ± standard deviation, median (interquartile range), or number (percentage), as appropriate. The optimal pre-transplant MLR cut-off value was determined using a Receiver Operating Characteristic (ROC) curve. Categorical variables were compared using the Chi-square test. Continuous variables were analyzed using the unpaired t-test or the Mann–Whitney U test, depending on distribution. Pearson and Spearman correlation analyses were used to assess relationships between continuous variables. Univariate and multivariate logistic regression models were employed to evaluate the association between pre-transplant MLR and DGF. All statistical analyses were performed using SPSS software.

Results

Baseline characteristics of the study population.

A total of 162 patients were included in the study. **Figure 1** shows the study flow diagram. **Table 1** presents kidney transplant recipients' baseline demographic and laboratory data, donor characteristics, transplant parameters, and outcomes. The average pre-transplant MLR was 0.34 ± 0.22. Most patients underwent deceased donor KT with a standard criteria donor. Thirty percent had a positive panel reactive antibody (PRA), and 97% had at least one HLA mismatch. Induction therapy with anti-interleukin-2 antibody was administered in 56% of patients, while 80% received tacrolimus-based maintenance therapy. DGF occurred in 35.8% of cases. The average serum creatinine and estimated glomerular filtration rate (eGFR) at 1 and 3 years were 1.5 mg/dL and 59 mL/min/1.73 m², respectively.

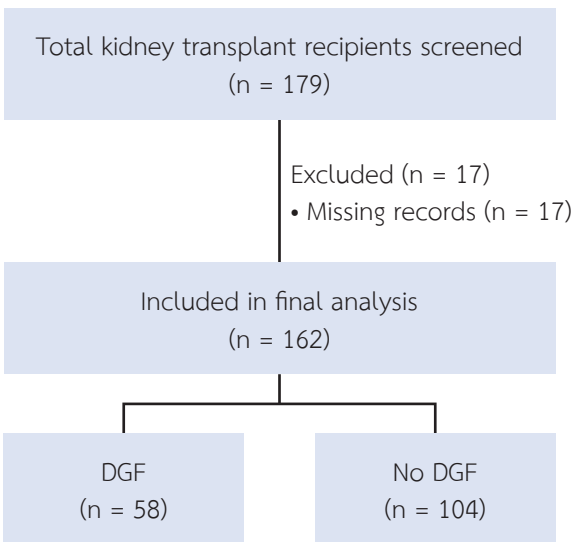

Figure 1 Study Flow Diagram
DGF, delayed graft function

Table 1 Baseline data of kidney transplant recipients, donors, transplant parameters, and outcomes of all patients

Parameters	N = 162	Parameters	N = 162
Recipients' parameters		Donors' parameters	
Male sex, n (%)	102 (63.0)	Male sex, n (%)	142 (87.7)
Age at transplantation (years)	42.22±8.92	Age (years)	36.79±12.59
Weight (kg)	62.38±12.98	Donor criteria, n (%)	
Height (m)	1.64±0.09	Standard criteria	110 (67.9)
Body mass index (kg/m^2)	23.01±3.87	Acute kidney injury	61 (37.7)
Dialysis vintage (years)	5.01±3.74	Extended criteria	0 (0)
Dialysis mode, n (%)		Types of donors, n (%)	
Hemodialysis via AV fistula	152 (93.8)	Deceased donor	144 (88.9)
Hemodialysis via AV graft	5 (3.1)	Living donor	18 (11.1)

Table 1 Baseline data of kidney transplant recipients, donors, transplant parameters, and outcomes of all patients (continue)

Parameters	N = 162	Parameters	N = 162
Hemodialysis via TCC	1 (0.6)	Induction therapy, n (%)	
CAPD	4 (2.5)	No induction	68 (42.0)
Underlying diseases, n (%)		Anti-interleukin-2 antibody	90 (55.6)
None	24 (14.8)	Others	4 (2.5)
Diabetes Mellitus	21 (13.0)	Maintenance therapy, n (%)	
Hypertension	127 (78.4)	Tacrolimus	129 (79.6)
Dyslipidemia	42 (25.9)	Cyclosporine	33 (20.4)
Coronary artery disease	5 (3.1)	Panel reactive antibody, n (%)	
Cerebrovascular accident	3 (1.9)	Negative	114 (70.4)
Smoking, n (%)		Positive	48 (29.6)
Non-smoker	149 (92.0)	HLA-mismatch, n (%)	
Current smoker	2 (1.2)	None	5 (3.1)
Former smoker	11 (6.8)	≥ 1	157 (96.9)
Causes of end-stage renal disease, n (%)		Transplantation outcomes	
Unknown	34 (21.0)	Delayed graft function, n (%)	58 (35.8)
Diabetic nephropathy	16 (9.9)	Serum creatinine (mg/dL)	
Hypertension	65 (40.1)	1 year (n=150)	1.46±0.54
Glomerular diseases	37 (22.8)	3 years (n=134)	1.50±0.81
Kidney stones	6 (3.7)	eGFR (ml/min/1.73m^2)	
Genitourinary abnormalities	3 (1.9)	1 year (n=150)	59.31±21.08
Others	12 (7.4)	3 years (n=134)	59.09±20.45
Pre-transplantation labs results			
Hemoglobin (g/dL)	11.57±1.56		
Hematocrit (%)	35.54±4.61		
White blood cells (cell/mm^3)	7,500±2,931		
Neutrophil (%)	63.52±12.52		
Lymphocyte (%)	20.40±8.86		
Monocyte (%)	6.23±3.39		
Platelet (cells/mm^3)	222,028±73,638		
MLR	0.34±0.22		
Albumin (g/dL)	4.30±0.44		
Globulin (g/dL)	3.50±0.49		

AV, arteriovenous; TCC, tunneled cuffed catheter; CAPD; continuous ambulatory peritoneal dialysis; MLR, monocyte-to-lymphocyte ratio; KT, kidney transplantation; HLA, human leukocyte antigen; eGFR, estimated glomerular filtration rate

Pre-transplant Monocyte-to-lymphocyte ratio and delayed graft function

The ROC curve of the recipient's pre-transplant MLR for predicting DGF showed an area under the curve (AUC) of 0.686 (95% confidence interval: 0.603–0.769), as illustrated in **Figure 2**. This AUC was significantly higher than the reference value of 0.5 ($P < 0.001$), indicating meaningful predictive value. The optimal pre-transplant MLR cutoff point was determined to be 0.255, based on the highest Youden index of 0.368. The corresponding sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy for predicting DGF at this threshold are summarized in **Table 2**.

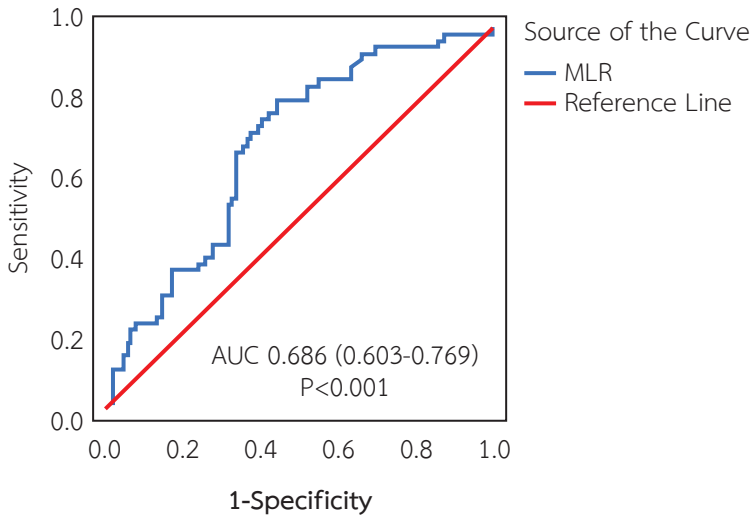

Figure 2 Receiver Operating Characteristic curve of the recipient's pre-transplant monocyte-to-lymphocyte ratio in predicting delayed graft function
MLR, monocyte-to-lymphocyte ratio

Table 2 The cut-off value for monocyte-to-lymphocyte ratio in predicting delayed graft function

Parameters	DGF (n=58)	No DGF (n=104)
MLR < 0.255 (n=69), n (%)	11 (19.0%)	58 (55.8%)
MLR ≥ 0.255 (n=93), n (%)	47 (81.0%)	46 (44.2%)
Sensitivity (95%CI)	81.03 (68.59, 90.13)	
Specificity (95%CI)	55.77 (45.70, 65.50)	
Positive predictive value (95%CI)	50.54 (44.33, 56.73)	
Negative predictive value (95%CI)	84.06 (75.10, 90.22)	
Accuracy (95%CI)	64.81 (56.93, 72.14)	
Odds ratio (95%CI)	5.39 (2.51, 11.54)	

DGF, delayed graft function; CI, confidence interval; MLR, monocyte-to-lymphocyte ratio

Factors associated with delayed graft function

Univariate analyses of factors associated with DGF are presented in **Table 3**. Increased recipient's pre-transplant white blood cell count (WBC) and MLR, deceased donor KT, donor acute kidney injury, and longer hospital stays were positively associated with DGF. In contrast, standard

criteria donor was a protective factor. Multivariate analysis, which included variables with a p-value < 0.1 from the univariate analyses, is shown in **Table 4**. High MLR (≥0.255) and elevated WBC were identified as independent predictors of DGF. Standard criteria donor remained a protective factor.

Table 3 Univariable analysis of factors associated with delayed graft function

Variables	DGF (N=58)	Non-DGF (N=104)	Odds Ratio (95%CI)	P-value
Recipients' parameters				
Male sex, n (%)	36 (62.1)	66 (63.5)	0.94 (0.49, 1.83)	0.860
Age at transplantation (years)	42.55±7.73	42.04±9.55	1.01 (0.97, 1.04)	0.725
Body mass index (kg/m^2)	23.66±3.84	22.66±3.87	1.07 (0.98, 1.16)	0.117
Dialysis vintage (years)	5.31±3.94	4.85±3.63	1.03 (0.95, 1.13)	0.449
HD via AVF (vs. others), n (%)	54 (93.1)	98 (94.2)	0.83 (0.22, 3.06)	0.775
Underlying diseases, n (%)				
None	10 (17.2)	14 (13.5)	1.34 (0.55, 3.24)	0.517
Diabetes Mellitus	8 (13.8)	13 (12.5)	1.12 (0.44, 2.88)	0.814
Hypertension	45 (77.6)	82 (78.8)	0.93 (0.43, 2.02)	0.852
Dyslipidemia	15 (25.9)	27 (26.0)	0.99 (0.48, 2.07)	0.989
Coronary artery disease	3 (5.2)	2 (1.9)	2.78 (0.45, 17.15)	0.270
Cerebrovascular disease	2 (3.4)	1 (1.0)	3.68 (0.33, 41.47)	0.292
Smoker (vs. non-smoker)	5 (8.6)	8 (7.7)	1.13 (0.35, 3.64)	0.835
Causes of end-stage renal disease, n (%)				
Unknown	12 (20.7)	22 (21.2)	0.97 (0.44, 2.14)	0.945
Diabetic nephropathy	8 (13.8)	8 (7.7)	1.92 (0.68, 5.42)	0.218
Hypertension	24 (41.4)	41 (39.4)	1.09 (0.56, 2.09)	0.808
Glomerular diseases	10 (17.2)	27 (26.0)	0.59 (0.26, 1.34)	0.208
Kidney stones	3 (5.2)	3 (2.9)	1.84 (0.36, 9.41)	0.466
Genitourinary abnormalities	2 (3.4)	1 (1.0)	3.68 (0.33, 41.47)	0.292
Others	6 (10.3)	6 (5.8)	1.89 (0.58, 6.14)	0.293
Recipients' labs before transplantation				
Hemoglobin (g/dL)	11.57±1.57	11.56±1.56	1.00 (0.82, 1.23)	0.986
Hematocrit (%)	35.50±4.51	35.56±4.69	0.99 (0.93, 1.07)	0.943
WBC (cell/mm^3)	8,132±3,209	7,148±2,716	1.12 (1.00, 1.25)	0.046
Neutrophil (%)	65.56±14.12	65.19±11.60	0.99 (0.99, 1.00)	0.774
Lymphocyte (%)	19.09±9.12	21.13±8.67	0.97 (0.94, 1.01)	0.162
Monocyte (%)	6.67±2.75	5.99±3.68	1.06 (0.97, 1.17)	0.222

Table 3 Univariable analysis of factors associated with delayed graft function (continue)

Variables	DGF (N=58)	Non-DGF (N=104)	Odds Ratio (95%CI)	P-value
Platelet (cell/mm^3)	234,966±74,167	214,813±72,699	1.45 (0.94, 2.24)	0.098
MLR	0.41±0.21	0.31±0.21	9.63 (1.81, 51.24)	0.008
MLR ≥0.255 (vs. <0.255), n (%)	47 (81.0)	46 (44.2)	5.39 (2.51, 11.54)	<0.001
Albumin (g/dL)	4.33±0.50	4.27±0.41	1.35 (0.64, 2.85)	0.425
Globulin (g/dL)	3.51±0.58	3.49±0.43	1.08 (0.56, 2.10)	0.812
Donor characteristics				
Male donor, n (%)	52 (89.7)	90 (86.5)	1.35 (0.49, 3.72)	0.564
Age (years)	38.74±12.91	35.70±12.33	1.02 (0.99, 1.05)	0.141
Standard criteria, n (%)	27 (46.6)	83 (79.8)	0.22 (0.11, 0.45)	<0.001
Acute kidney injury, n (%)	32 (55.2)	29 (27.9)	3.18 (1.63, 6.23)	0.001
Transplantation parameters, n (%)				
DDKT (vs. LDKT)	58 (100.0)	18 (17.3)	N/A[a]	0.001[b]
No Induction therapy (vs. Induction)	28 (48.3)	40 (38.5)	1.49 (0.78, 2.86)	0.226
Tacrolimus (vs. cyclo-A)	47 (81.0)	82 (78.8)	1.15 (0.51, 2.57)	0.740
No PRA (vs. positive PRA)	41 (70.7)	73 (70.2)	1.02 (0.51, 2.07)	0.947
No HLA mismatch (vs. ≥ 1)	2 (3.4)	3 (2.9)	1.20 (0.20, 7.41)	0.843
Post-transplant complications, n (%)				
Graft failure (vs. functioning graft)	1 (1.7)	1 (1.0)	1.81 (0.11, 29.44)	0.678
1-year mortality	0 (0.0)	1 (1.0)	N/A[a]	1.000[b]
Urinary tract infection	5 (8.6)	23 (22.1)	0.33 (0.12, 0.93)	0.036
Obstructive uropathy	1 (1.7)	0 (0.0)	N/A[a]	0.358[b]
Lymphocele	0 (0.0)	1 (1.0)	N/A[a]	1.000 [b]
Urinoma	0 (0.0)	3 (2.9)	N/A	0.553[b]
Perigraft hematoma	2 (3.4)	1 (1.0)	3.68 (0.33, 41.47)	0.292
Vascular complication	5 (8.6)	4 (3.8)	2.36 (0.61, 9.16)	0.215
Other surgical complication	5 (8.6)	6 (5.8)	1.54 (0.45, 5.29)	0.492
Length of hospital stay (days)	30.03±13.60	21.94±8.47	1.07 (1.04, 1.11)	<0.001*

[a]Odds ratio is not provided because the number in the contingency table is 0

[b]Data were analyzed with Simple binary logistic regression and Fisher exact test

DGF, delayed graft function; CI, confidence interval; HD, hemodialysis; AVF, arteriovenous fistula; WBC, white blood cells; MLR, monocyte-to-lymphocyte ratio; HLA, human leukocyte antigen; PRA, panel reactive antibody; cyclo-A, cyclosporin A; DDKT, deceased donor kidney transplantation; LRKT, living donor kidney transplantation

Table 4 Multivariable analysis of factors associated with delayed graft function

Variables	Odds Ratio (95%CI)	P-value
White blood cells (x 1,000 cells/mm^3)	1.18 (1.03, 1.35)	0.020*
Platelets (x 100,000 cell/mm^3)	1.52 (0.88, 2.61)	0.133
MLR ≥0.255 (vs. <0.255)	3.74 (1.55, 9.02)	0.003*
Standard criteria donor	0.09 (0.01, 0.95)	0.045*
Donor with acute kidney injury	0.26 (0.02, 2.75)	0.260

MLR, monocyte-to-lymphocyte ratio; CI, confidence interval

Allograft function at 1 and 3 years after kidney transplantation

Allograft function at 1 and 3 years for the DGF and non-DGF groups is presented in **Table 5** and **Figure 3**. The DGF group had significantly higher serum creatinine levels and lower eGFR at both 1 and 3 years post-KT compared to the non-DGF group. Within each group, there were no significant changes in allograft function between the 1- and 3-year time points.

Table 5 Allograft function at 1 and 3 years after kidney transplantation

Parameters	DGF	Non-DGF	P-value
Serum creatinine (mg/dL) (median (interquartile range))			
1 year	1.47 (1.29, 1.80)	1.32 (1.08, 1.59)	0.022
3 years	1.45 (1.16, 1.76)	1.30 (1.07, 1.46)	0.012
P-value	0.495	0.130	
eGFR (ml/min/1.73m^2) (median (interquartile range))			
1 year	52.70 (39.15, 65.68)	61.50 (47.73, 73.48)	0.017
3 years	52.80 (39.40, 65.70)	61.00 (50.80, 73.40)	0.011
P-value	0.933	0.564	

DGF, delayed graft function; eGFR, estimated glomerular filtration rate

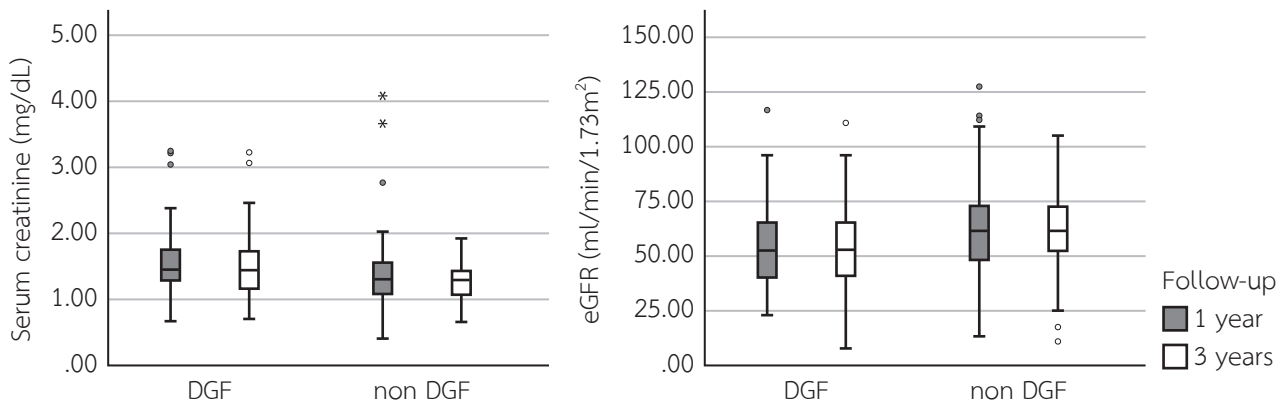

Figure 3 Allograft function at 1 and 3 years after kidney transplantation
Left, serum creatinine; Right, Estimated glomerular filtration rate

Monocyte-to-lymphocyte ratio and post-transplant complications

The associations between pre-transplant MLR and post-transplant complications, as well as length of hospital stay, were analyzed using Pearson and Spearman correlation methods and are presented in **Table 6**. MLR showed a negative correlation with urinary tract infections and a positive correlation with length of hospital stay.

Table 6 Correlations between monocyte-to-lymphocyte ratio with post-transplant complications and length of hospital stays

Parameters	Correlation coefficients	P-value
Urinary tract infection	-0.188	0.016*
Obstructive uropathy	0.112	0.156
Lymphocele	0.097	0.220
Urinoma	0.148	0.060
Perigraft hematoma	0.031	0.697
Vascular complication	0.070	0.376
Other surgical complication	0.041	0.607
Length of hospital stay	0.159	0.044

Discussion

The findings of this retrospective cohort study provide valuable insights into the potential role of pre-transplant MLR as a predictor of DGF following kidney transplantation. Our analysis demonstrated, for the first time, a significant association between elevated pre-transplant MLR levels and an increased risk of DGF, independent of other clinical variables. This highlights the role of systemic inflammation in the pathogenesis of DGF and supports the use of pre-transplant MLR as a readily accessible biomarker for risk stratification in kidney transplant recipients.

The robustness of pre-transplant MLR as a predictive marker is further supported by its performance in ROC curve analysis, which identified an optimal cut-off value of 0.255. This threshold showed reasonable sensitivity and specificity for identifying individuals at increased risk of DGF. A prior study by Yang et al. also identified an optimal pre-transplant MLR cut-off of 0.2168 for predicting all-cause mortality and cardiovascular events in peritoneal dialysis patients[17], reinforcing the relevance of MLR in clinical prognostication.

The observed association between pre-transplant MLR and DGF suggests a mechanistic link between systemic inflammation and graft dysfunction. Elevated MLR may reflect immune dysregulation, where increased monocytes contribute to the inflammatory environment, while decreased lymphocytes may signal a weakened immunosuppressive state. This imbalance could heighten susceptibility to ischemia-reperfusion injury and alloimmune responses, both of which are implicated in the development of DGF. Although donor with AKI was significantly associated with DGF in univariate analysis, this was not retained in the multivariate model. This may be due to confounding factors, strict donor selection (only mild AKI allowed), and a small sample size in the AKI group, which may have limited statistical power and contributed to the wide confidence interval.

To our knowledge, no prior study has specifically investigated the relationship between pre-transplant MLR and DGF. However, a study by Pilichowska et al. found a correlation between a higher neutrophil-to-monocyte ratio and DGF in renal transplant recipients[18]. Similarly, Siddiqui et al. reported that a lower pre-transplant

platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio were associated with an increased incidence of DGF in pediatric kidney transplant patients[19]. Outside the transplant setting, Urbanowicz et al. showed that an elevated MLR on the first postoperative day predicted late mortality following off-pump coronary artery bypass graft surgery[20], further supporting the association between heightened inflammation and adverse clinical outcomes.

Despite these novel findings, several limitations should be acknowledged. The retrospective design of the study introduces the possibility of residual confounding and selection bias. As a single-center study, the generalizability of the results to broader populations is limited. Although the sample size was adequate to detect significant associations, it may not have provided sufficient power for the identification of potential effect modifiers. Furthermore, reliance on routine pre-transplant blood tests may not capture dynamic changes in systemic inflammation over time. Serial MLR measurements throughout the transplant process could offer deeper insights into its prognostic value and its temporal relationship with DGF. Lastly, while MLR serves as a surrogate marker of systemic inflammation, its direct mechanistic role in the development of DGF remains speculative. Future studies incorporating functional immune assays and molecular profiling are needed to elucidate the biological pathways linking elevated MLR to graft dysfunction.

In conclusion, this is the first study to evaluate the association between pre-transplant MLR and DGF in KT. Our findings support the potential utility of pre-transplant MLR as a predictive biomarker for DGF. Elevated pre-transplant MLR may serve as a promising prognostic tool for risk stratification and allograft outcome prediction.

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