

# World Journal of *Gastrointestinal Surgery*

*World J Gastrointest Surg* 2020 July 27; 12(7): 307-335



**OPINION REVIEW**

- 307 Crucial anatomy and technical cues for laparoscopic transabdominal preperitoneal repair: Advanced manipulation for groin hernias in adults

*Yasukawa D, Aisu Y, Hori T*

**ORIGINAL ARTICLE****Retrospective Study**

- 326 Neutrophil-to-lymphocyte ratio predicts acute kidney injury occurrence after gastrointestinal and hepatobiliary surgery

*Bi JB, Zhang J, Ren YF, Du ZQ, Wu Z, Lv Y, Wu RQ*

**ABOUT COVER**

Associate Editor of *World Journal of Gastrointestinal Surgery*, Dr. Zong-Ming Zhang, Professor of Capital Medical University of People's Republic of China, Director of Department of General Surgery in Beijing Electric Power Hospital of State Grid Corporation of China. Over the last 35 years, he has focused his clinical and scientific interests on General Surgery. He has extensive clinical experience in performing all kinds of general surgery operation, such as pancreaticoduodenectomy, radical resection of hilar cholangiocarcinoma, right hemihepatectomy, total gastrectomy, laparoscopic transcystic common bile duct exploration, etc. Professor Zhang has published more than 170 scientific articles in peer-reviewed journals, 15 book chapters, 20 conference abstracts. He is also the Editorial Board Member of 16 academic journals.

**AIMS AND SCOPE**

The primary aim of *World Journal of Gastrointestinal Surgery* (*WJGS, World J Gastrointest Surg*) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

*WJGS* mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, pancreatectomy, pancreaticoduodenectomy, and pancreaticojejunostomy, etc.

**INDEXING/ABSTRACTING**

The *WJGS* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, and PubMed Central. The 2020 edition of Journal Citation Reports® cites the 2019 impact factor (IF) for *WJGS* as 1.863; IF without journal self cites: 1.824; Ranking: 109 among 210 journals in surgery; Quartile category: Q3; Ranking: 77 among 88 journals in gastroenterology and hepatology; and Quartile category: Q4.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Electronic Editor: *Li-Li Wang*; Production Department Director: *Xiang Li*; Editorial Office Director: *Jia-Ping Yan*.

**NAME OF JOURNAL**

*World Journal of Gastrointestinal Surgery*

**ISSN**

ISSN 1948-9366 (online)

**LAUNCH DATE**

November 30, 2009

**FREQUENCY**

Monthly

**EDITORS-IN-CHIEF**

Shu-You Peng, Varut Lohsirirawat

**EDITORIAL BOARD MEMBERS**

<https://www.wjgnet.com/1948-9366/editorialboard.htm>

**PUBLICATION DATE**

July 27, 2020

**COPYRIGHT**

© 2020 Baishideng Publishing Group Inc

**INSTRUCTIONS TO AUTHORS**

<https://www.wjgnet.com/bpg/gerinfo/204>

**GUIDELINES FOR ETHICS DOCUMENTS**

<https://www.wjgnet.com/bpg/GerInfo/287>

**GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH**

<https://www.wjgnet.com/bpg/gerinfo/240>

**PUBLICATION ETHICS**

<https://www.wjgnet.com/bpg/GerInfo/288>

**PUBLICATION MISCONDUCT**

<https://www.wjgnet.com/bpg/gerinfo/208>

**ARTICLE PROCESSING CHARGE**

<https://www.wjgnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjgnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

<https://www.f6publishing.com>

## Retrospective Study

## Neutrophil-to-lymphocyte ratio predicts acute kidney injury occurrence after gastrointestinal and hepatobiliary surgery

Jian-Bin Bi, Jia Zhang, Yi-Fan Ren, Zhao-Qing Du, Zheng Wu, Yi Lv, Rong-Qian Wu

**ORCID number:** Jian-Bin Bi 0000-0002-9281-1999; Jia Zhang 0000-0001-7306-3350; Yi-Fan Ren 0000-0003-0907-2900; Zhao-Qing Du 0000-0003-0781-1079; Zheng Wu 0000-0002-7102-9543; Yi Lv 0000-0002-7104-2414; Rong-Qian Wu 0000-0003-0993-4531.

**Author contributions:** Bi JB and Wu RQ were involved in the design of the research; Wu Z and Lv Y provided guidance on clinical issues; Bi JB, Zhang J, Ren YF and Du ZQ collected the data; Bi JB analyzed the data; Bi JB wrote the manuscript; Wu RQ supervised the whole research; all authors have read and agreed with the final manuscript.

**Supported by** the National Natural Science Foundation of China, No. 81770491.

**Institutional review board**

**statement:** This study was reviewed and approved by the Ethics Committee of the Xi'an Jiaotong University (Permit number: XJTU1AF2015LSL-057).

**Informed consent statement:** The need for patients' informed written consent was waived due to the retrospective nature of the study.

**Conflict-of-interest statement:** All the Authors have no conflict of

**Jian-Bin Bi, Jia Zhang, Yi-Fan Ren, Zhao-Qing Du, Zheng Wu, Yi Lv, Rong-Qian Wu,** National Local Joint Engineering Research Center for Precision Surgery & Regenerative Medicine, Shaanxi Provincial Center for Regenerative Medicine and Surgical Engineering, Institute of Advanced Surgical Technology and Engineering, First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, Shaanxi Province, China

**Jian-Bin Bi, Jia Zhang, Yi-Fan Ren, Zhao-Qing Du, Zheng Wu, Yi Lv,** Department of Hepatobiliary Surgery, First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, Shaanxi Province, China

**Corresponding author:** Rong-Qian Wu, MD, PhD, Professor, National Local Joint Engineering Research Center for Precision Surgery and Regenerative Medicine, First Affiliated Hospital of Xi'an Jiaotong University, No. 76, West Yanta Road, Xi'an 710061, Shaanxi Province, China. [rwu001@mail.xjtu.edu.cn](mailto:rwu001@mail.xjtu.edu.cn)

**Abstract****BACKGROUND**

Postoperative acute kidney injury (AKI) is a complex pathological process involved in intrarenal and systemic inflammation caused by renal hypoperfusion, nephrotoxic drugs and urinary obstruction. Neutrophil-to-lymphocyte ratio (NLR) is a marker of inflammation reflecting the progress of many diseases. However, whether NLR at admission can predict the occurrence of AKI after surgery in the intensive care unit (ICU) remains unknown.

**AIM**

To clarify the relationship between NLR and the occurrence of AKI in patients with gastrointestinal and hepatobiliary surgery in the ICU.

**METHODS**

A retrospective analysis of 282 patients receiving surgical ICU care after gastrointestinal and hepatobiliary surgery in our hospital from December 2014 to December 2018 was performed.

**RESULTS**

Postoperative AKI occurred in 84 patients (29.79%) in this cohort. NLR by the multivariate analysis was an independent risk factor for occurrence of postoperative AKI in patients with gastrointestinal and hepatobiliary surgery in

interest related to the manuscript.

**Data sharing statement:** The data used to support the findings of this study are available from the corresponding author upon request.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Manuscript source:** Invited manuscript

**Received:** December 30, 2019

**Peer-review started:** December 30, 2019

**First decision:** April 12, 2020

**Revised:** May 10, 2020

**Accepted:** May 15, 2020

**Article in press:** May 15, 2020

**Published online:** July 27, 2020

**P-Reviewer:** Tajiri K, Tchilikidi KY

**S-Editor:** Wang J

**L-Editor:** MedE-Ma JY

**E-Editor:** Wang LL



the ICU. In this cohort, receiver operating characteristic curves of AKI occurrence showed that the optimal cut-off value of NLR was 8.380. NLR was found to be significantly correlated with the white blood cell count, neutrophil count, lymphocyte count, arterial lactate and dialysis ( $P < 0.05$ ). Additionally, NLR value at admission was higher in AKI patients compared with the non-AKI patients and increased with the severity of AKI. Patients with  $\text{NLR} \geq 8.380$  exhibited significantly higher incidences of postoperative AKI and severe AKI than patients with  $\text{NLR} < 8.380$  (AKI: 38.12% vs 14.85%,  $P < 0.001$ ; severe AKI: 14.36% vs 1.98%,  $P = 0.001$ ).

## CONCLUSION

NLR at admission is a predictor of AKI occurrence in patients with gastrointestinal and hepatobiliary surgery in ICU. NLR should be included in the routine assessment of AKI occurrence.

**Key words:** Neutrophil-to-lymphocyte ratio; Acute kidney injury; Gastrointestinal and hepatobiliary surgery; Surgical intensive care unit; Arterial lactate; Sepsis

©The Author(s) 2020. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** This was a retrospective study to clarify the relationship between neutrophil-to-lymphocyte ratio (NLR) and the occurrence of acute kidney injury (AKI) in patients with gastrointestinal and hepatobiliary surgery in the surgical intensive care unit (ICU). We found that patients with  $\text{NLR} \geq 8.380$  exhibited significantly higher incidences of postoperative AKI and severe AKI. NLR at admission is a predictor of AKI in patients with gastrointestinal and hepatobiliary surgery in ICU. We recommend that NLR should be included in the routine assessment of AKI occurrence.

**Citation:** Bi JB, Zhang J, Ren YF, Du ZQ, Wu Z, Lv Y, Wu RQ. Neutrophil-to-lymphocyte ratio predicts acute kidney injury occurrence after gastrointestinal and hepatobiliary surgery.

*World J Gastrointest Surg* 2020; 12(7): 326-335

**URL:** <https://www.wjgnet.com/1948-9366/full/v12/i7/326.htm>

**DOI:** <https://dx.doi.org/10.4240/wjgs.v12.i7.326>

## INTRODUCTION

Acute kidney injury (AKI) is one of the most common complications after gastrointestinal and hepatobiliary surgery. Numerous studies have reported high incidences of postoperative AKI, ranging from 22% to 66% in intensive care unit (ICU)<sup>[1-4]</sup>. Postoperative AKI and its stages are independent risk factors for the prognosis of surgical patients<sup>[5]</sup>. In addition, a large number of studies have reported that AKI significantly increases the risk of chronic renal insufficiency and end-stage kidney disease<sup>[6,7]</sup>. Patients with severe AKI often require renal replacement therapy, and once developed into end-stage kidney disease, patients would require long-term hemodialysis, which decreases quality of life<sup>[8]</sup>. Early detection of AKI is critical to the treatment of perioperative patients. Serum creatinine is a classic indicator of AKI, but changes in serum creatinine levels often occur at a later stage. Some new tests are either too expensive or too difficult to implement, making them difficult for clinical use<sup>[9]</sup>. Therefore, indicators that can predict the occurrence of AKI after surgery are urgently needed.

The neutrophil-to-lymphocyte ratio (NLR) is a marker of inflammation that can be calculated directly from a patient's complete blood count. Extensive studies have shown that NLR can predict the outcome of cardiac surgery, sepsis, and cancer<sup>[10-13]</sup>. A recent study showed that sepsis patients with  $\text{NLR} > 17.11$  were more likely to develop AKI<sup>[10]</sup>. The risk factors and early diagnosis of postoperative AKI have always been urgent problems in clinic. Nevertheless, whether NLR at admission can predict the occurrence of AKI after surgery in patients receiving ICU care remains unknown. We hypothesize that NLR is an independent risk factor for AKI after surgery, and patients with high NLR are more likely to develop postoperative AKI. The main purpose of this article was to clarify the relationship between NLR and the occurrence

of postoperative AKI in patients with gastrointestinal and hepatobiliary surgery in the ICU.

---

## MATERIALS AND METHODS

---

### **Patients and data sources**

This study retrospectively analyzed the electronic medical records of 282 patients after gastrointestinal and hepatobiliary surgery in the ICU of the First Affiliated Hospital of Xi'an Jiaotong University from December 2014 to December 2018. The inclusion criteria were: Patients admitted to the ICU after gastrointestinal or hepatobiliary surgery; aged over 18 years; hospitalized in the ICU for at least 24 hours. The exclusion criteria were: Patients admitted with known acute or chronic kidney disease; patients with liver transplantation; patients without complete clinical data. This study complied with the provisions of Declaration of Helsinki<sup>[14]</sup>. The protocol was approved by the Ethics Committee of the First Affiliated Hospital of Xi'an Jiaotong University.

### **Definition of clinical outcome**

The clinical outcomes in this study included occurrence of AKI and severe AKI, length of ICU stay, ICU re-admission, ICU mortality and 28-day overall mortality. The definition of AKI complied with Kidney Disease: Improving Global Outcomes criteria<sup>[15]</sup> as follows: The serum creatinine level increased by  $\geq 0.3$  mg/dL ( $\geq 26$  mmol/L) within 48 h, or serum creatinine levels increased by 1.5 times of the baseline within 7 d after surgery, or urine volume was less than 0.5mL/kg per h and lasted more than 6 h. The staging of AKI is defined as follows: Stage 1, serum creatinine level increased by  $\geq 0.3$  mg/dL ( $\geq 26$  mmol/L) within 48 h, or serum creatinine levels increased by 1.5-1.9 times of the baseline within 7 d after surgery; Stage 2, serum creatinine serum creatinine levels increased by 2.0-2.9 times of the baseline within 7 d after surgery; Stage 3, serum creatinine level increased by  $\geq 4.0$  mg/dL ( $\geq 354$  mmol/L) within 48 h, or serum creatinine levels increased by more than 3.0 times of the baseline within 7 d after surgery, or patients require renal replacement therapy. Severe AKI is defined as AKI of stage 2 and 3.

### **Statistical analysis**

The distribution of the continuous variables was checked for normality using the Kolmogorov-Smirnov test. Normally distributed variables were expressed as mean  $\pm$  SD, and differences between the two groups were analyzed by the *t* test. Nonnormally distributed variables were expressed as medians (interquartile range) and differences between the two groups were analyzed by the Mann-Whitney. Categorical variables were expressed as absolute numbers and percent frequencies and differences between the two groups were analyzed by  $\chi^2$  or Fisher's exact test. Univariate and multivariate analyses were performed using logistic regression models. Variables with  $P < 0.05$  in the univariate analysis were incorporated into the multivariate analysis. The receiver operating characteristic (ROC) curve was used to determine the optimal cut-off value (with the highest sum of specificity plus sensitivity). PASW 18.0 software (SPSS Inc., Chicago, Illinois, United States) was used for statistical analysis. A two-tailed  $P < 0.05$  was considered statistically significant.

---

## RESULTS

---

### **Risk factors for postoperative AKI in patients with gastrointestinal and hepatobiliary surgery in ICU**

A total of 84 patients (29.79%) developed postoperative AKI in this cohort. To identify risk factors for AKI in patients with gastrointestinal and hepatobiliary surgery in ICU, univariate and multivariate analyses were performed (Table 1). The results of univariate analysis exhibited that the following factors were significantly associated with occurrence of AKI in patients with gastrointestinal and hepatobiliary surgery in ICU, including sex (HR: 1.761, 95%CI: 1.008-3.075,  $P = 0.047$ ), drinking (HR: 0.547, 95%CI: 0.306-0.977,  $P = 0.042$ ), coexisting condition of ischemic heart disease (HR: 0.387, 95%CI: 0.166-0.901,  $P = 0.028$ ), sequential organ failure assessment score (SOFA score) at ICU admission (HR: 1.092, 95%CI: 1.030-1.157,  $P = 0.003$ ), acute physiology and chronic health evaluation (APACHE II) at ICU admission (HR: 1.038, 95%CI:

**Table 1 Risk factors of acute kidney injury occurrence by univariate and multivariate analyses**

Parameters	Univariate analysis		Multivariate analysis	
	HR (95%CI)	P value	HR (95%CI)	P value
Age (< 65 yr/≥ 65 yr)	1.010 (0.996-1.024)	0.146	-	-
Sex (male/femal)	1.761 (1.008-3.075)	0.047	0.684 (0.325-1.438)	0.316
Smoking (yes/no)	0.599 (0.351-1.021)	0.060	-	-
Drinking (yes/no)	0.547 (0.306-0.977)	0.042	0.916 (0.401-2.097)	0.836
MAP (mmHg)	1.001 (0.988-1.014)	0.923	-	-
Hypertension (yes/no)	1.218 (0.668-2.223)	0.519	-	-
Diabetes mellitus (yes/no)	0.828 (0.393-1.744)	0.619	-	-
Cirrhosis (yes/no)	0.563 (0.239-1.324)	0.188	-	-
Ischemic heart disease (yes/no)	0.387 (0.166-0.901)	0.028	1.111 (0.385-3.212)	0.845
Stroke (yes/no)	2.500 (0.834-7.493)	0.102	-	-
Malignant diseases (yes/no)	0.949 (0.514-1.751)	0.867	-	-
SOFA score at ICU admission	1.092 (1.030-1.157)	0.003	1.010 (0.937-1.088)	0.801
APACHE II at ICU admission	1.038 (1.005-1.073)	0.023	1.006 (0.954-1.060)	0.836
PLT (10 <sup>9</sup> /L)	0.999 (0.997-1.002)	0.487	-	-
WBC (10 <sup>9</sup> /L)	1.026 (0.999-1.055)	0.062	-	-
TB	1.001 (0.999-1.003)	0.216	-	-
Creatinine	1.005 (1.003-1.007)	< 0.001	1.000 (0.998-1.002)	0.989
K	1.676 (1.190-2.362)	0.003	0.918 (0.594-1.416)	0.698
Na	1.012 (0.979-1.046)	0.473	-	-
INR	1.269 (0.980-1.641)	0.070	-	-
PaO <sub>2</sub> /FiO <sub>2</sub>	0.994 (0.883-1.119)	0.920	-	-
Arterial lactate <sup>1</sup>	0.936 (0.876-1.000)	0.051	-	-
Procalcitonin <sup>2</sup>	1.003 (0.096-1.011)	0.348	-	-
Blood transfusion (yes/no)	0.898 (0.555-1.452)	0.660	-	-
NLR	1.052 (1.026-1.078)	< 0.001	1.290 (1.212-1.373)	< 0.001

<sup>1</sup>High neutrophil to lymphocyte ratio (NLR) group ( $n = 167$ ), Low NLR group ( $n = 89$ ).

<sup>2</sup>High NLR group ( $n = 154$ ), Low NLR group ( $n = 79$ ). HR: Hazard ratio; MAP: Mean arterial pressure; SOFA score: Sequential organ failure assessment score; APACH II: Acute physiology and chronic health evaluation; PLT: Platelet count; WBC: White blood cell count; TB: Total bilirubin; INR: International normalized ratio; PaO<sub>2</sub>/FiO<sub>2</sub>: Oxygen partial pressure/oxygen concentration; NLR: Neutrophil to lymphocyte ratio.

1.005-1.073,  $P = 0.023$ ), serum creatinine (HR: 1.005, 95%CI: 1.003-1.007,  $P < 0.001$ ), serum K concentration (HR: 1.676, 95%CI: 1.190-2.362,  $P = 0.003$ ) and NLR (HR: 1.052, 95%CI: 1.026-1.078,  $P < 0.001$ ). Further multivariate analysis revealed that NLR (HR: 1.290, 95%CI: 1.212-1.373,  $P < 0.001$ ) was an independent risk factor for occurrence of postoperative AKI in patients with gastrointestinal and hepatobiliary surgery in ICU.

### ROC curve analysis

ROC curves analysis with occurrence of AKI was used to determine the optimal cut-off value of NLR. The value of NLR at the maximum value of the Youden index is taken as the optimal cut-off point. As shown in **Figure 1**, the optimal cut-off value of NLR was 8.380 [sensitivity of 82.14% and specificity of 43.43%, area under the curve = 0.634, 95%CI: 0.563-0.705,  $P = 0.0004$ ]. The patients were divided into a high-NLR group ( $n = 181$ ) and a low-NLR group ( $n = 101$ ) by the optimal cut-off value of NLR (8.380).

### Patient demographics and clinical features of the high and low NLR groups

As shown in **Table 2**, the average age of 282 patients in ICU was  $60.48 \pm 17.74$  years. In

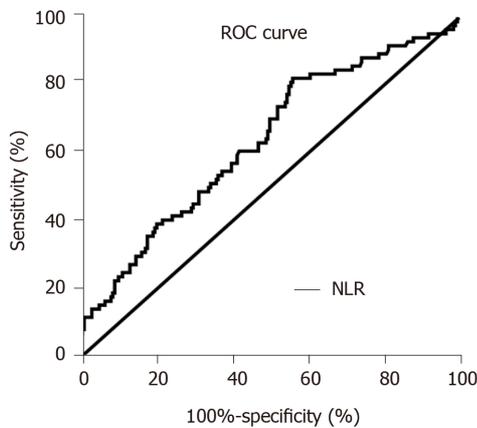
**Table 2 Patient demographics and clinical features of the high and low NLR groups**

Variables	Overall (n = 282)	High-NLR group (n = 181)	Low-NLR group (n = 101)	P value
Age (yr)	60.48 ± 17.74	62.62 ± 17.44	58.42 ± 18.17	0.146
Sex (male/female)	180/102	114/67	66/35	0.695
Operative site				0.330
Gastrointestinal surgery, n (%)	214 (75.89)	134 (74.03)	80 (79.21)	
Hepatobiliary surgery, n (%)	68 (24.11)	47 (25.97)	21 (20.79)	
Characteristics of surgery				0.398
Emergency surgery	55 (19.5)	38 (21.0)	17 (16.8)	
Non-emergency surgery	227 (80.5)	143 (79.0)	84 (83.2)	
Lab values at ICU admission				
PLT (10 <sup>9</sup> /L)	144.17 ± 112.61	146.84 ± 114.94	139.40 ± 108.70	0.596
WBC (10 <sup>9</sup> /L)	12.67 ± 9.34	14.85 ± 10.25	8.77 ± 5.65	< 0.001
ALT (U/L)	169.28 ± 356.37	194.10 ± 413.23	126.53 ± 259.71	0.140
AST (U/L)	258.83 ± 683.02	310.81 ± 822.44	169.28 ± 308.64	0.098
TB (μmol/L)	87.42 ± 132.18	90.95 ± 126.59	81.14 ± 142.01	0.554
Albumin (g/L)	28.63 ± 6.42	28.14 ± 5.90	29.49 ± 7.20	0.091
Creatinine (μmol/L)	131.44 ± 135.27	138.84 ± 122.81	118.20 ± 154.87	0.225
K (mmol/L)	3.95 ± 0.76	4.03 ± 0.77	3.82 ± 0.73	0.034
Na (mmol/L)	137.55 ± 7.72	137.68 ± 7.54	137.32 ± 8.05	0.708
Neutrophil (10 <sup>9</sup> /L)	10.68 ± 7.57	13.10 ± 7.91	6.34 ± 4.32	< 0.001
Lymphocyte (10 <sup>9</sup> /L)	1.04 ± 1.04	0.78 ± 0.50	1.49 ± 1.50	< 0.001
PaO <sub>2</sub> /FiO <sub>2</sub>	3.24 ± 2.08	3.30 ± 1.75	3.14 ± 2.63	0.576
Arterial lactate (mmol/L) <sup>1</sup>	3.43 ± 4.13	2.91 ± 3.29	4.40 ± 5.23	0.006
Procalcitonin (ng/mL) <sup>2</sup>	15.85 ± 35.73	17.11 ± 39.68	13.37 ± 26.29	0.453
SOFA score at ICU admission	7.74 ± 5.01	7.63 ± 4.11	7.93 ± 6.34	0.806
APACHE II at ICU admission	16.04 ± 7.78	15.95 ± 7.49	16.19 ± 8.31	0.630
Coexisting conditions				
Smoking (yes/no)	91/191	60/121	31/70	0.672
Drinking (yes/no)	65/217	43/138	22/79	0.706
Hypertension (yes/no)	71/211	44/137	27/74	0.653
Diabetes mellitus (yes/no)	36/246	27/154	9/92	0.147
Ischemic heart disease (yes/no)	24/258	16/165	8/93	0.791
Stroke (yes/no)	26/256	15/166	11/90	0.469
Malignant diseases (yes/no)	62/220	43/138	19/82	0.336
ICU care				
Ventilation (yes/no)	169/113	103/78	66/35	0.166
Dialysis (yes/no)	72/210	54/127	18/83	0.027
Steroids (yes/no)	81/201	52/129	29/72	0.998
CPR (yes/no)	58/224	35/146	23/78	0.494
Vasopressor (yes/no)	131/151	84/97	47/54	0.984
Transfusion	173/109	112/69	61/40	0.806

High neutrophil to lymphocyte ratio (NLR) group:  $\text{NLR} \geq 8.380$ , Low NLR group:  $\text{NLR} < 8.380$ .

<sup>1</sup>High NLR group ( $n = 167$ ), Low NLR group ( $n = 89$ ).

<sup>2</sup>High NLR group ( $n = 154$ ), Low NLR group ( $n = 79$ ). WBC: White blood cell count; PLT: Platelet count; ALT: Alanine aminotransferase; AST: Alanine aminotransferase;  $\text{PaO}_2/\text{FiO}_2$ : Oxygen partial pressure/oxygen concentration; APACHE II: Acute physiology and chronic health evaluation; SOFA score: Sequential organ failure assessment score; CPR: Cardio-pulmonary resuscitation; NLR: Neutrophil-to-lymphocyte ratio.



**Figure 1 Receiver operating characteristic analysis for optimal cutoff values of neutrophil-to-lymphocyte ratio.** Area under the receiver operating characteristic curve: 0.6338. The optimal cutoff value of neutrophil-to-lymphocyte ratio was 8.38. NLR: Neutrophil-to-lymphocyte ratio; ROC: Receiver operating characteristic.

the cohort, 24.11% of patients underwent hepatobiliary surgery. The age, sex, operative site and characteristics of surgery showed no significant differences between the high-NLR and low-NLR groups. Laboratory examination at ICU admission revealed that the high-NLR group exhibited higher white blood cell count ( $14.85 \pm 10.25$  vs  $8.77 \pm 5.65$ ,  $P < 0.001$ ) and neutrophil count ( $13.10 \pm 7.91$  vs  $6.34 \pm 4.32$ ,  $P < 0.001$ ), and lower lymphocyte count ( $0.78 \pm 0.50$  vs  $1.49 \pm 1.50$ ,  $P < 0.001$ ) and arterial lactate ( $2.91 \pm 3.29$  vs  $4.40 \pm 5.23$ ,  $P = 0.006$ ) than the low-NLR group. No significant differences were found in SOFA and APACHE II scores at ICU admission between the two groups. The most common coexisting conditions at ICU admission were smoking, hypertension and drinking. There were no differences in smoking, hypertension, drinking, diabetes mellitus, ischemic heart disease, stroke, and malignant diseases between the high and low-NLR patients. There was no significant difference in terms of ICU care, including ventilation, steroids, cardio-pulmonary resuscitation, vasopressor and transfusion, except that high-NLR patients used more dialysis.

#### **NLR levels in AKI and non-AKI patients**

To further clarify the relationship between postoperative AKI occurrence and NLR, we analyzed the NLR levels in the AKI patients and non-AKI patients. The results showed that AKI patients had higher NLR value compared with the non-AKI patients ( $18.210 \pm 14.179$  vs  $12.121 \pm 8.499$ ,  $P < 0.001$ ) (Figure 2A). Additionally, NLR increased with the severity of AKI (stage 1:  $17.356 \pm 15.686$ , stage 2:  $19.697 \pm 5.080$ , stage 3:  $20.113 \pm 13.937$ ) and was significantly higher in all three stages than that in the non-AKI group (Figure 2B).

#### **Clinical outcomes of patients with high and low NLR levels**

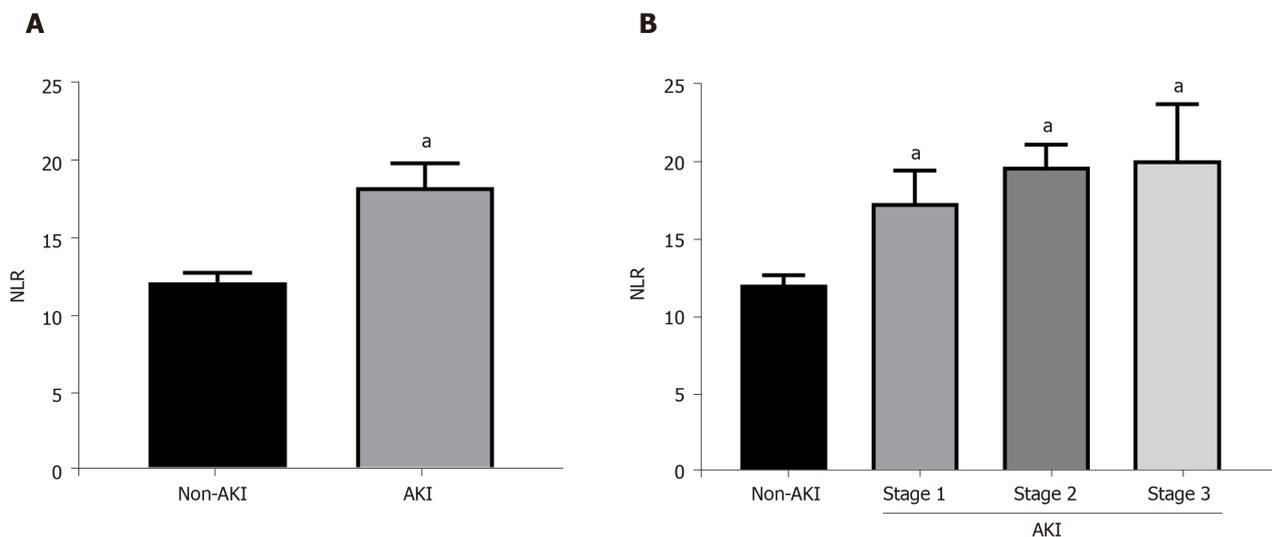
Clinical outcomes of patients in the high and low NLR groups are shown in Table 3. A total of 84 patients (29.79%) and 28 patients (9.92%) were complicated with AKI and severe AKI, respectively. The incidence of AKI and severe AKI in the high-NLR group was significantly higher than those in the low-NLR group (AKI: 38.12% vs 14.85%,  $P < 0.001$ ; severe AKI: 14.36% vs 1.98%,  $P = 0.001$ ). The difference in the occurrence of sepsis between two groups showed a strong tendency of statistical significance (17.68% vs 10.89%,  $P = 0.083$ ). Additionally, length of ICU stays, ICU re-admission, ICU mortality and 28-d overall mortality exhibited no significant differences between the high-NLR and low-NLR groups.

**Table 3 Clinical outcomes of the high and low NLR groups**

Variables	Overall (n = 282)	High-NLR group (n = 181)	Low-NLR group (n = 101)	P value
Renal				
AKI, n (%)	84 (29.79)	69 (38.12)	15 (14.85)	< 0.001
Severe AKI	28 (9.92)	26 (14.36)	2 (1.98)	0.001
Sepsis, n (%)	45 (15.96)	32 (17.68)	11 (10.89)	0.083
Length of ICU stay (d)	11.36 ± 13.37	11.36 ± 12.58	11.38 ± 14.74	0.990
ICU re-admission, n (%)	40 (14.18)	24 (13.25)	16 (15.84)	0.551
ICU mortality, n (%)	41 (14.54)	24 (13.25)	17 (16.83)	0.415
28-d overall mortality (%) <sup>1</sup>	80 (28.4)	55 (30.4)	25 (24.8)	0.314

High neutrophil to lymphocyte ratio (NLR) group: NLR ≥ 8.380, Low NLR group: NLR < 8.380; Severe AKI: AKI of stage 2 and stage 3.

<sup>1</sup>28-d overall mortality included ICU mortality and 28-d mortality after leaving ICU. AKI: Acute kidney injury; ICU: Intensive care unit.



**Figure 2 Neutrophil-to-lymphocyte ratio in acute kidney injury and non-acute kidney injury patients.** <sup>a</sup>*P* < 0.05 vs non-AKI group. NLR: Neutrophil-to-lymphocyte ratio; AKI: Acute kidney injury.

## DISCUSSION

In this study, the multivariate analysis showed NLR at admission was an independent risk factor for occurrence of postoperative AKI in patients with gastrointestinal and hepatobiliary surgery in ICU. Patients with NLR ≥ 8.380 exhibited significantly higher incidences of postoperative AKI and severe AKI. NLR at admission could be a predictor of AKI occurrence in patients with gastrointestinal and hepatobiliary surgery and should be included in the routine assessment of AKI occurrence.

AKI is one of the most common critical illnesses with high morbidity and poor prognosis. The causes of AKI are extremely complicated, including renal hypoperfusion such as hypovolemia and reduced cardiac output, nephrotoxicity drugs and urinary obstruction<sup>[16]</sup>. Different causes eventually lead to hypoxia, inflammation, oxidative stress and innate immune system activation and cell death<sup>[17]</sup>. AKI is a common complication after abdominal surgery. The mortality of patients with postoperative AKI after abdominal surgery increased by 3.5 times<sup>[18]</sup>. A large number of previous studies have shown that preoperative renal insufficiency is the most important risk factor for AKI after abdominal surgery, and other risk factors include preoperative dehydration, intra-abdominal hypertension, blood transfusion, and use of nephrotoxic drug<sup>[19]</sup>. Our study found a 29.79% incidence of postoperative AKI in patients with gastrointestinal and hepatobiliary surgery in ICU. Univariate analysis exhibited that sex, coexisting condition of ischemic heart disease, SOFA score at ICU admission, APACHE II at ICU admission, serum creatinine, serum K concentration

and NLR were significantly associated with occurrence of postoperative AKI. However, multivariate analysis revealed that only NLR was the independent risk factor for occurrence of postoperative AKI in surgical ICU.

Intrarenal and systemic response plays a key role in postoperative AKI. A large number of inflammatory factors and inflammatory cells promote oxidative stress and apoptosis, eventually leading to renal insufficiency<sup>[20]</sup>. Many anti-inflammatory drugs have significant effects on AKI and have entered clinical trials<sup>[20]</sup>. Early detection of AKI has great influence on the prognosis of postoperative patients. Examination of indicators of renal insufficiency, such as creatinine and urea nitrogen, is the most accurate test, but changes often occur at a later stage<sup>[21]</sup>. Some new tests are either too expensive or too difficult to implement, making them difficult for clinical use<sup>[9]</sup>. NLR is a marker of inflammation reflecting the progress of inflammation-related disease. Extensive studies have shown that NLR can predict the outcome of cardiac surgery, sepsis, and cancer<sup>[10-12]</sup>. Our study showed that NLR at admission was an independent risk factor for occurrence of postoperative AKI and patients with NLR  $\geq 8.380$  exhibited significantly higher incidences of postoperative AKI and severe AKI. NLR, characterized by easy accessibility, objectivity, and noninvasiveness, could be a better predictor of AKI occurrence in patients with gastrointestinal and hepatobiliary surgery.

Sepsis is life threatening organ dysfunction caused by the host's harmful response to infection. Patients with AKI significantly increased sepsis mortality<sup>[22]</sup>. Studies have shown that sepsis is associated with 50% of AKI, and up to 60% of sepsis patients develop organ dysfunction including AKI<sup>[23]</sup>. Mechanism of sepsis-induced AKI is that deleterious inflammatory cascade of sepsis causes kidney damage<sup>[10,24]</sup>. Several studies have shown that NLR is a predictor of AKI occurrence in patients with sepsis. They showed that NLR  $\geq 9.11$  in sepsis had a high risk of AKI occurrence<sup>[24]</sup>. In this study, the difference in the occurrence of sepsis between high-NLR group and low-NLR group showed a strong tendency of statistical significance (17.68% *vs* 10.89%,  $P = 0.083$ ). The high tendency of sepsis in the NLR  $\geq 8.380$  group may be one of the important reasons for NLR as an independent risk factor for AKI in patients with gastrointestinal and hepatobiliary surgery in ICU.

High levels of arterial lactate reflect tissue microcirculatory insufficiency. Numerous studies have considered lactic acid levels as a risk factor in critically ill patients<sup>[25,26]</sup>. However, in this study, the multivariate analysis showed that arterial lactate at admission was not an independent risk factor for occurrence of postoperative AKI in patients with gastrointestinal and hepatobiliary surgery in ICU. Intraoperative tissue ischemia and postoperative coagulation and sepsis may lead to changes in lactate levels<sup>[27]</sup>. In addition, severe inflammatory response in the tissue can lead to elevated lactic acid levels<sup>[28]</sup>. Our study showed that patients with NLR  $\geq 8.380$  had high arterial lactate levels ( $2.91 \pm 3.29$  mmol/L *vs*  $4.40 \pm 5.23$  mmol/L,  $P = 0.006$ ). Increased lactic acid levels may be due to postoperative inflammation under such conditions.

This study has several limitations. First, this is a single-center retrospective cohort study. The results might be influenced by selection bias, recall bias and some residual confounding. A further multiple-center data was needed to clarify the relationship between NLR and the occurrence of AKI in patients with gastrointestinal and hepatobiliary surgery in ICU. Second, this study retrospectively analyzed the electronic medical records of 282 patients after gastrointestinal and hepatobiliary surgery in the surgical ICU. The conclusion is only based on a small number of patients. A further large sample sized study is needed in the future. Additionally, this research mainly clarified the phenomenon that NLR at admission is a predictor of AKI occurrence, and the specific mechanism needs further study.

In conclusion, NLR at admission was an independent risk factor and could be a predictor for occurrence of postoperative AKI in patients with gastrointestinal and hepatobiliary surgery in ICU. NLR should be included in the routine assessment of AKI occurrence.

## ARTICLE HIGHLIGHTS

### Research background

Postoperative acute kidney injury (AKI) is one of the most common complications after gastrointestinal and hepatobiliary surgery. Neutrophil-to-lymphocyte ratio (NLR) is a marker of inflammation that can be calculated directly from a patient's complete blood count. Extensive studies have shown that NLR can predict the outcome of cardiac surgery, sepsis, and cancer.

### Research motivation

The risk factors and early diagnosis of postoperative AKI have always been urgent problems in clinic.

### Research objectives

To clarify the relationship between NLR and the occurrence of AKI in patients with gastrointestinal and hepatobiliary surgery in the intensive care unit (ICU).

### Research methods

This study retrospectively analyzed the electronic medical records of 282 patients after gastrointestinal and hepatobiliary surgery in ICU to clarify the relationship between NLR at admission and the postoperative AKI occurrence.

### Research results

Postoperative AKI occurred in 29.79% of patients receiving ICU care. NLR value at admission was higher in AKI patients compared with the non-AKI patients and increased with the severity of AKI. Patients with  $NLR \geq 8.380$  exhibited significantly higher incidences of postoperative AKI and severe AKI than patients with  $NLR < 8.380$ . The multivariate analysis showed that NLR at admission was an independent risk factor for occurrence of postoperative AKI in patients with gastrointestinal and hepatobiliary surgery in ICU.

### Research conclusions

NLR at admission is a predictor of AKI occurrence in patients with gastrointestinal and hepatobiliary surgery in ICU.

### Research perspectives

NLR should be included in the routine assessment of AKI occurrence.

---

## ACKNOWLEDGEMENTS

We are indebted to all individuals who participated in or helped with this research project.

---

## REFERENCES

- 1 **Thakar CV**, Christianson A, Freyberg R, Almenoff P, Render ML. Incidence and outcomes of acute kidney injury in intensive care units: a Veterans Administration study. *Crit Care Med* 2009; **37**: 2552-2558 [PMID: 19602973 DOI: 10.1097/CCM.0b013e3181a5906f]
- 2 **Srisawat N**, Sileanu FE, Murugan R, Bellomod R, Calzavacca P, Cartin-Ceba R, Cruz D, Finn J, Hoste EE, Kashani K, Ronco C, Webb S, Kellum JA; Acute Kidney Injury-6 Study Group. Variation in risk and mortality of acute kidney injury in critically ill patients: a multicenter study. *Am J Nephrol* 2015; **41**: 81-88 [PMID: 25677982 DOI: 10.1159/000371748]
- 3 **Bellomo R**, Kellum JA, Ronco C. Acute kidney injury. *Lancet* 2012; **380**: 756-766 [PMID: 22617274 DOI: 10.1016/S0140-6736(11)61454-2]
- 4 **Wang Y**, Li Q, Ma T, Liu X, Wang B, Wu Z, Dang S, Lv Y, Wu R. Transfusion of Older Red Blood Cells Increases the Risk of Acute Kidney Injury After Orthotopic Liver Transplantation: A Propensity Score Analysis. *Anesth Analg* 2018; **127**: 202-209 [PMID: 28863026 DOI: 10.1213/ANE.0000000000002437]
- 5 **Trongtrakul K**, Sawawiboon C, Wang AY, Chitsomkasem A, Limphunudom P, Kurathong S, Prommool S, Trakarnvanich T, Srisawat N. Acute kidney injury in critically ill surgical patients: Epidemiology, risk factors and outcomes. *Nephrology (Carlton)* 2019; **24**: 39-46 [PMID: 29124867 DOI: 10.1111/nep.13192]
- 6 **Coca SG**, Singanamala S, Parikh CR. Chronic kidney disease after acute kidney injury: a systematic review and meta-analysis. *Kidney Int* 2012; **81**: 442-448 [PMID: 22113526 DOI: 10.1038/ki.2011.379]
- 7 **Chawla LS**, Kimmel PL. Acute kidney injury and chronic kidney disease: an integrated clinical syndrome. *Kidney Int* 2012; **82**: 516-524 [PMID: 22673882 DOI: 10.1038/ki.2012.208]
- 8 **Jiang L**, Zhu Y, Luo X, Wen Y, Du B, Wang M, Zhao Z, Yin Y, Zhu B, Xi X; Beijing Acute Kidney Injury Trial (BAKIT) workgroup. Epidemiology of acute kidney injury in intensive care units in Beijing: the multicenter BAKIT study. *BMC Nephrol* 2019; **20**: 468 [PMID: 31842787 DOI: 10.1186/s12882-019-1660-z]
- 9 **Odutayo A**, Wong CX, Farkouh M, Altman DG, Hopewell S, Emdin CA, Hunn BH. AKI and Long-Term Risk for Cardiovascular Events and Mortality. *J Am Soc Nephrol* 2017; **28**: 377-387 [PMID: 27297949 DOI: 10.1681/ASN.2016010105]
- 10 **Bu X**, Zhang L, Chen P, Wu X. Relation of neutrophil-to-lymphocyte ratio to acute kidney injury in patients with sepsis and septic shock: A retrospective study. *Int Immunopharmacol* 2019; **70**: 372-377 [PMID: 30852292 DOI: 10.1016/j.intimp.2019.02.043]
- 11 **Bartlett EK**, Flynn JR, Panageas KS, Ferraro RA, Sta Cruz JM, Postow MA, Coit DG, Ariyan CE. High

- neutrophil-to-lymphocyte ratio (NLR) is associated with treatment failure and death in patients who have melanoma treated with PD-1 inhibitor monotherapy. *Cancer* 2020; **126**: 76-85 [PMID: 31584709 DOI: 10.1002/cncr.32506]
- 12 **Green J**, Bin Mahmood SU, Mori M, Yousef S, Mangi AA, Geirsson A. Stability across time of the neutrophil-lymphocyte and lymphocyte-neutrophil ratios and associations with outcomes in cardiac surgery patients. *J Cardiothorac Surg* 2019; **14**: 164 [PMID: 31511078 DOI: 10.1186/s13019-019-0988-6]
  - 13 **Du Z**, Dong J, Bi J, Bai R, Zhang J, Wu Z, Lv Y, Zhang X, Wu R. Predictive value of the preoperative neutrophil-to-lymphocyte ratio for the development of hepatocellular carcinoma in HBV-associated cirrhotic patients after splenectomy. *PLoS One* 2018; **13**: e0195336 [PMID: 29621282 DOI: 10.1371/journal.pone.0195336]
  - 14 **World Medical Association**. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 2013; **310**: 2191-2194 [PMID: 24141714 DOI: 10.1001/jama.2013.281053]
  - 15 **Okusa MD**, Davenport A. Reading between the (guide)lines--the KDIGO practice guideline on acute kidney injury in the individual patient. *Kidney Int* 2014; **85**: 39-48 [PMID: 24067436 DOI: 10.1038/ki.2013.378]
  - 16 **Ronco C**, Bellomo R, Kellum JA. Acute kidney injury. *Lancet* 2019; **394**: 1949-1964 [PMID: 31777389 DOI: 10.1016/S0140-6736(19)32563-2]
  - 17 **Hultström M**, Becirovic-Agic M, Jönsson S. Comparison of acute kidney injury of different etiology reveals in-common mechanisms of tissue damage. *Physiol Genomics* 2018; **50**: 127-141 [PMID: 29341864 DOI: 10.1152/physiolgenomics.00037.2017]
  - 18 **Kim M**, Brady JE, Li G. Variations in the risk of acute kidney injury across intraabdominal surgery procedures. *Anesth Analg* 2014; **119**: 1121-1132 [PMID: 25191972 DOI: 10.1213/ANE.0000000000000425]
  - 19 **An Y**, Shen K, Ye Y. Risk factors for and the prevention of acute kidney injury after abdominal surgery. *Surg Today* 2018; **48**: 573-583 [PMID: 29052006 DOI: 10.1007/s00595-017-1596-5]
  - 20 **Rabb H**, Griffin MD, McKay DB, Swaminathan S, Pickkers P, Rosner MH, Kellum JA, Ronco C; Acute Dialysis Quality Initiative Consensus XIII Work Group. Inflammation in AKI: Current Understanding, Key Questions, and Knowledge Gaps. *J Am Soc Nephrol* 2016; **27**: 371-379 [PMID: 26561643 DOI: 10.1681/ASN.2015030261]
  - 21 **Gameiro J**, Fonseca JA, Neves M, Jorge S, Lopes JA. Acute kidney injury in major abdominal surgery: incidence, risk factors, pathogenesis and outcomes. *Ann Intensive Care* 2018; **8**: 22 [PMID: 29427134 DOI: 10.1186/s13613-018-0369-7]
  - 22 **Bouchard J**, Acharya A, Cerda J, Maccariello ER, Madarasu RC, Tolwani AJ, Liang X, Fu P, Liu ZH, Mehta RL. A Prospective International Multicenter Study of AKI in the Intensive Care Unit. *Clin J Am Soc Nephrol* 2015; **10**: 1324-1331 [PMID: 26195505 DOI: 10.2215/CJN.04360514]
  - 23 **Poston JT**, Koyner JL. Sepsis associated acute kidney injury. *BMJ* 2019; **364**: k4891 [PMID: 30626586 DOI: 10.1136/bmj.k4891]
  - 24 **Ni J**, Wang H, Li Y, Shu Y, Liu Y. Neutrophil to lymphocyte ratio (NLR) as a prognostic marker for in-hospital mortality of patients with sepsis: A secondary analysis based on a single-center, retrospective, cohort study. *Medicine (Baltimore)* 2019; **98**: e18029 [PMID: 31725679 DOI: 10.1097/MD.00000000000018029]
  - 25 **Lokhandwala S**, Andersen LW, Nair S, Patel P, Cocchi MN, Donnino MW. Absolute lactate value vs relative reduction as a predictor of mortality in severe sepsis and septic shock. *J Crit Care* 2017; **37**: 179-184 [PMID: 27771598 DOI: 10.1016/j.jcrc.2016.09.023]
  - 26 **Bou Chebl R**, El Khuri C, Shami A, Rajha E, Faris N, Bachir R, Abou Dagher G. Serum lactate is an independent predictor of hospital mortality in critically ill patients in the emergency department: a retrospective study. *Scand J Trauma Resusc Emerg Med* 2017; **25**: 69 [PMID: 28705203 DOI: 10.1186/s13049-017-0415-8]
  - 27 **O'Connor E**, Fraser JF. The interpretation of perioperative lactate abnormalities in patients undergoing cardiac surgery. *Anaesth Intensive Care* 2012; **40**: 598-603 [PMID: 22813486 DOI: 10.1177/0310057X1204000404]
  - 28 **Pucino V**, Bombardieri M, Pitzalis C, Mauro C. Lactate at the crossroads of metabolism, inflammation, and autoimmunity. *Eur J Immunol* 2017; **47**: 14-21 [PMID: 27883186 DOI: 10.1002/eji.201646477]



Published by **Baishideng Publishing Group Inc**  
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

**Help Desk:** <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

