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LETTER TO THE EDITOR

Are endothelial damage and inflammation level demonstrated clearly in liver transplant patients?

To the Editor,

We read with great interest the recently published article by Hayashi et al[1] in which the authors aimed to evaluate the relationship between neutrophil-to-lymphocyte ratio (NLR) and adult small-for-size grafts, along with an analysis of other clinical factors. As a result, although the neutrophil and lymphocyte absolute counts in groups did not differ significantly, the NLR showed significant differences between the two groups from Postoperative Day 3 to Postoperative Day 10. In conclusion, the elevation of postoperative NLR has been claimed to reflect suggestive pathophysiology of endothelial injuries that related to small-for-size graft syndrome in living donor liver transplantation. However, there are some points that we would like to address about this study.

Firstly, as is known, NLR combines the antagonistic effects of neutrophilia (an indicator of inflammation) and lymphopenia (an indicator of physiologic stress). There are several clinical conditions and comorbidities that possibly affect the distribution of white blood cell (WBC) counts, which should be excluded to avoid possible confounders for the NLR results.[2] Also, the WBC cut-off values may vary depending on many factors such as the population studied, the individual laboratory, and the instruments or measurement methods used.[3] Studies evaluating inflammation underlying endothelial injuries, initially, in the patients included inflammation in this study or at least the WBC levels should be assessed, it should be exclude those over a certain cut-off. Moreover, as done before in similar studies, adding C-reactive protein (CRP), which is a very common marker of inflammation, it can be excluded in high level NLR patients caused by comorbidities.

Secondly, although the authors assert that postoperative NLR elevation reflects pathophysiology of endothelial injuries, they did not submit any data that may support this theory.

In the current study, one of the signs commonly used in endothelial damage, or at least used in the evaluation of the endothelial wall thickness and the image type to use one of radiological methods could increase the reliability of data.[4] In addition, evaluation of the correlation between markers of endothelial injury and postoperative NLR level would be useful.

Finally, NLR alone without other inflammatory markers cannot give exact information in this patient group. Possible causes affecting WBC counts and the confounding factors, which have a considerable effect on the clinical availability of NLR, should be discussed in more detail. In addition, evaluation and comparison of endothelial damage markers would provide more reliable results.

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Conflicts of interest: The authors state that there are no conflicts of interest regarding the publication of this paper.

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Endothelial injury is the most compelling theory for inflammatory changes in living donor liver transplant recipients

Thank you for your interest in our study.[1] In this case series, we emphasize the clinical importance of graft size in living donor liver transplantation (LDLT). This importance is demonstrated by inflammatory changes such as elevated neutrophil-to-lymphocyte ratio (NLR) after LDLT, especially in cases of small-for-size LDLT grafts.

As previously reported, complex pathophysiology occurs during the immediate post-surgical phase in cases of small-for-size LDLT grafts.[2] Better outcomes for both recipients and grafts after LDLT can be achieved only by understanding the recipient's pathophysiology, including comorbidities. Therefore, we chose not to exclude various clinical conditions and comorbidities from the analysis. In addition, we correctly considered white blood cells (WBCs), WBC differentiation, and C-reactive protein (CRP) levels in preliminary analyses, and found no statistically significant findings according to graft size. WBC count and CRP levels are easily influenced by various conditions such as graft failure, rejection, and infections. We therefore chose not to consider these variables as clinical markers. Simple and concise clinical markers are needed after LDLT. For this reason, we analyzed NLR in the present case series.

In the acute phase of the postoperative period following LDLT, strong inflammatory changes were observed as mentioned above. In the case of prolonged graft dysfunction, graft liver biopsy specimens revealed sinusoid endothelial cell injury and bleeding in the space of Disse. We discussed this phenomenon as being a result of the graft endothelial injury mentioned above.[3] However, we did not take additive blood samples or perform radiological examination, which may have suggested the etiology of these inflammatory changes. Therefore, further detailed discussion and examination of this particular pathophysiology is required.

Finally, what we wish convey in this case series is that NLR is a simple and reliable marker for LDLT recipient status, and that endothelial injury is the most compelling theory for inflammatory changes in LDLT recipients. This recipient status was influenced by various pathophysiological factors, as might be expected. NLR elevation is, therefore, the result of these post-operative changes, and graft endothelial injury is the most often considered post-operative change after LDLT with respect to graft size.

Conflicts of interest

The authors declare no conflicts of interest.

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