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Original Article

The prognostic values of platelet to lymphocyte ratio for predicting mortality in patients with acute mesenteric ischemia: a cross-sectional study

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Abstract

Introduction: Acute mesenteric ischemia (AMI) is a life-threatening disease that can cause multi-organ damage and ultimately lead to death. Early diagnosis and treatment significantly reduce morbidity and mortality rates in high-risk patients. This study aimed to explore the prognostic values of platelet to lymphocyte ratio (PLR) in predicting mortality in patients with mesenteric ischemia.

Methods: This prospective study included 126 patients with a complaint of acute abdominal pain, suggesting mesenteric ischemia. Demographic data and measured variables were determined using a pre-designed questionnaire. Statistical analysis was conducted using *t* test analysis, Spearman correlation analysis, and receiver operating characteristic (ROC) curve.

Results: Of 126 studied cases, mesenteric ischemia was confirmed in 47 patients. The mean age in patients with mesenteric ischemia (68 years) was significantly higher than that of non-ischemic patients (65 years). Mean blood bicarbonate level in non-ischemic patients (13.53 mmol/L) was higher than ischemic patients (11.15 mmol/L) ($P<0.0001$). PLR in patients with mesenteric ischemia and non-ischemic patients was 159 and 151, respectively; this difference was not statistically significant ($P=0.14$). The overall mortality rate in this study was 61%.

Conclusion: Even though the PLR increases in patients with systemic inflammation, it cannot distinguish between patients with mesenteric ischemia and other inflammatory conditions.

Introduction

Acute mesenteric ischemia (AMI) occurs as a result of insufficient blood supply. AMI prevents sufficient cellular nutrition and prevents the supply of metabolic requirements to abdominal organs; naturally, cell death and tissue damage follow as an outcome of ischemia.[1,2] being a life-threatening condition, it can lead to multi-organ failure and even death. Early diagnosis and appropriate treatment can significantly affect patients' health and mortality rates in high-risk groups.[3]

AMI occurs by obstructive and non-obstructive mechanisms. In both situations, rapid rehabilitation of blood vessels can lead to revascularization of intestinal tissue. Intestinal ischemia and reperfusion cause damage to the mucous membrane. Reperfusion facilitates the transmission of micro-organisms and endotoxins from the intestinal lumen to the internal tissues, combined with free radicals derived from oxygen and other intestinal factors such as pro-inflammatory cytokines, which can start a destructive process.[4-7]

Various methods have been suggested to diagnose mesenteric ischemia in a faster and more accurate way. In the recent decade, the development of duplex ultrasonography has given promising results in diagnosing chronic mesenteric ischemia. Of course, duplex ultrasonography's limitation is its dependence on the operator's experience.[1,8]

Magnetic resonance angiography has a specificity of 95% to diagnose, but it has many limitations.[1,9] CT scan also has limited use in the diagnostic process, except in suspected acute mesenteric vein thrombosis cases.[6]

Although imaging is necessary for diagnosing the disease, laboratory tests also help diagnose the patient and predict its prognosis. Serum lactate has a diagnostic sensitivity of 96% in mesenteric ischemia cases; even so, lactic acidosis is a late-stage finding in these patients and is usually accompanied by shock, intestinal necrosis cut-off of blood circulation.[1] Recently, D-dimer plasma level is mentioned as an early diagnostic factor in AMI.[4,5]

Platelet to lymphocyte ratio (PLR) has been studied in acute vascular disorders. Various studies have shown that this ratio varies rapidly in patients with acute coronary artery thrombosis, pulmonary embolism, and acute ischemia; and that it can be used as a predictive factor. Mesenteric ischemia is a type of acute vascular obstruction that can change this ratio in patients. Looking at the

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diagnostic problems in mesenteric ischemia, the PLR can be useful for early diagnosis; however, there have been no studies in patients with mesenteric ischemia.

Also, there is no study demonstrating the disease's prognosis in emergency departments (EDs) and hospitalization time. Thus, this study aims to evaluate PLR's relationship with diagnosis and short-term prognosis in patients with mesenteric ischemia referring to ED.

Methods

In this cross-sectional study, sampling was done by the census method. All patients referred to the Imam Reza hospital in Tabriz during 2018 with a complaint of abdominal pain with a probability of mesenteric ischemia were included in the study.

An emergency specialist examined patients with abdominal pain complications. Patients with a high probability of mesenteric ischemia were selected. During the initial phase of the study, patients who had no other diagnosis and were considered to have mesenteric ischemia were enrolled. Patients older than 60 years old with cardiac atrial fibrillation rhythm and metabolic acidosis had a higher risk of AMI.

Patients who left the hospital during treatment with a self-consent were excluded. Notably, patients with any history of hematologic disorders like leukemia, blood cell decreases, lymphomas were excluded from the study. Patients with a history of recent infectious diseases, patients undergoing blood transfusion, and immunosuppressed patients were excluded from the study. A total of 126 patients were included in the study. Due to the limitation of the study duration, the sample size was limited.

Blood samples were taken routinely from all patients at the time of admission to the ED. Blood samples were analyzed by Sysmex KX-21. Blood analysis results were categorized, and diagnostic points were extracted, and then the surgeon's confirmation and pathology results were used to prove the diagnosis and address detection bias. After this stage, patients were classified into two groups. Patients with a definitive diagnosis of mesenteric ischemia and patients for whom mesenteric ischemia was ruled out were split into two groups. The lymphocyte/platelet ratio was compared between the two groups.

To avoid selection bias, only the self-referred patients were enrolled in the study.

The data analyses were performed using SPSS 18.0 software (SPSS Inc, Chicago, IL). The data with a normal distribution were expressed as the mean ± standard deviation, and data with a non-normal distribution were expressed as the median. A Spearman correlation analysis was also performed. T-test analysis was used to compare the mean in two groups. The receiver operating characteristic (ROC) curve was used to predict the diagnostic value of different elements. In all items, $P < 0.05$ was considered statistically significant. Power of the study was set at 80%.

All patients signed a written, explicit, informed consent. The collected data were anonymously entered into this study. Only general data about our study population were provided. The collected data were recorded in real and non-perverted forms without selecting particular individuals to achieve the desired results.

Results

This study was consisted of 126 patients; 52.3% of them were males and remaining 46.8% were females. Minimum age among patients was 49 years old and oldest patients was 80 years old. And the mean ± standard deviation of age for the participants in the study was 66.91 ± 6.73 years. From 126 studied patients, for a total of 47 of them mesenteric ischemia was confirmed and in 79 cases it was not.

In Table 1, Measured variables in association with mesenteric ischemia in both groups are listed. Statistical evaluation results have shown that average differences in bicarbonate between two groups are statistically significant, the same cannot be said for platelet counts, lymphocyte counts and PLR.

Overall, in both groups more than 61% of patients expired. Also, another noticeable result is the survival rate of patients with confirmed mesenteric ischemia, that was only 6.3%.

Figure 1 shows number of surviving and expired patients in both groups. Of 47 patients with mesenteric ischemia in this study, only 3 survived; for the other group this was 46 out of 79 patients. Mortality rates in these groups were 93.7% and 41.8% respectively.

Figure 2 depicts the ROC curve for lymphocytes. The area under the curve for lymphocytes is equal to 0.311.

Table 1. Measured variables in association with mesenteric ischemia in both groups

Variables	Groups						*P* value
	Without AMI			With AMI			
	Mean	Max.	Min.	Mean	Max.	Min.	
Age	65.73	79	49	68.87	80	51	0.011
Bicarbonate	13.53	21	6	11.15	21	4	<0.0001
Platelet	301676	605000	110000	334566	756800	104500	0.237
Lymphocyte	1909	2950	1250	2072	51000	950	0.19
PLR	151.43	220	80	159.51	220	92	0.142

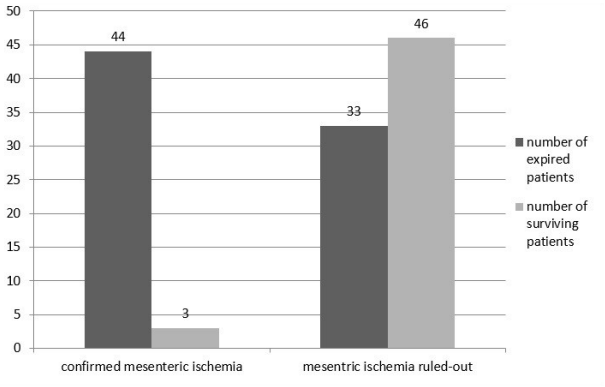

Figure 1. Number of surviving and expired patients in both groups.

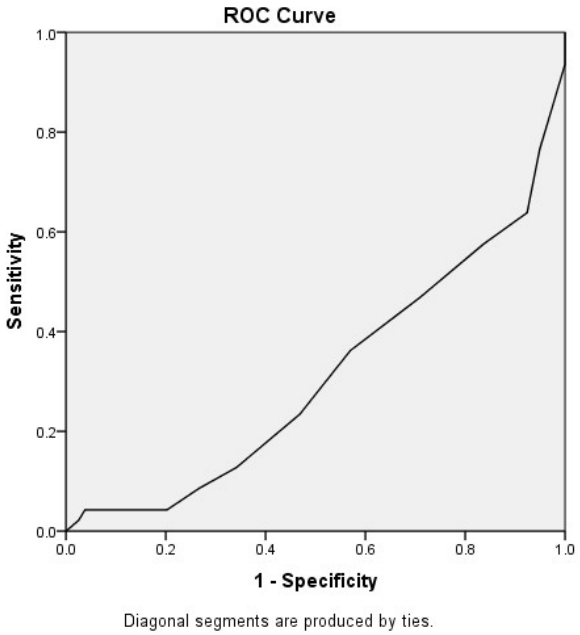

Figure 2. ROC curve for lymphocytes. Illustrating the diagnostic ability of lymphocytes in mesenteric ischemia created by plotting true positive rate (sensitivity – vertical segment) against the false positive rate (1-specificity – horizontal segment). The area under the curve (AUC) gives a combined measure of performance for all possible classification thresholds. Here it equals 0.311. However an acceptable AUC should be at least 0.7 ($P=0.36$).

In addition in Figure 3, showing the ROC curve for blood platelets, the area under the curve is 0.534. Hence the diagram for platelet/lymphocyte proportion is what depicted in Figure 4 and the area under the curve for platelet/lymphocyte proportion is equals to 0.580.

Discussion

In this study, 47 patients with AMI were studied, and in the remaining 79 patients, AMI was ruled-out. There was no significant difference in gender between the two groups of patients. The mean age for the group of patients with mesenteric ischemia was higher and this difference was a statistically significant one. Of course, the incidence of AMI increases drastically after the age of 60, so that the prevalence of AMI in patients over 80 years old is ten times higher than that of patients over 60 years.[10,11]

Comparison of bicarbonate levels between the two groups showed that the level of blood bicarbonate in

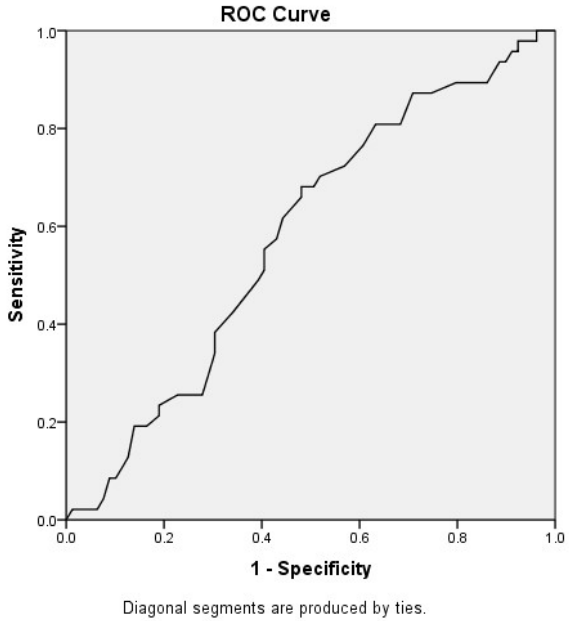

Figure 3. ROC curve for blood platelets. Illustrating the diagnostic ability of lymphocytes in mesenteric ischemia created by plotting true positive rate (sensitivity – vertical segment) against the false positive rate (1-specificity – horizontal segment). The area under the curve (AUC) gives a combined measure of performance for all possible classification thresholds. Here it equals 0.534. An AUC of 0.5 suggests no discrimination and an acceptable AUC should be at least 0.7 ($P=0.134$).

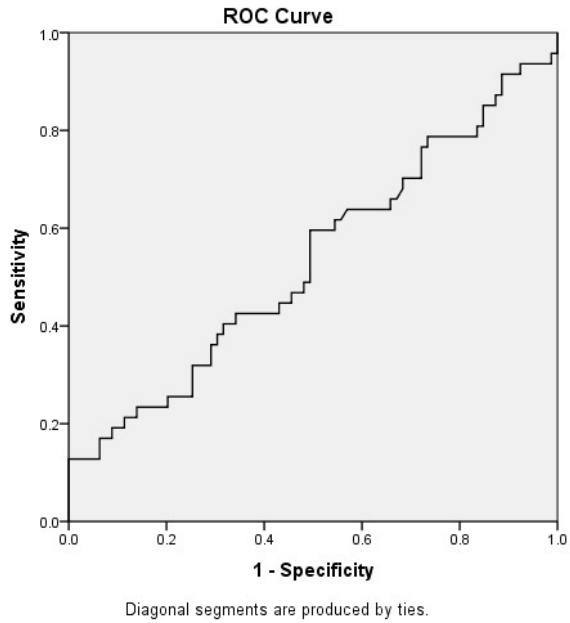

Figure 4. ROC curve for lymphocytes. Illustrating the diagnostic ability of lymphocytes in mesenteric ischemia created by plotting true positive rate (sensitivity – vertical segment) against the false positive rate (1-specificity – horizontal segment). The area under the curve (AUC) gives a combined measure of performance for all possible classification thresholds. Here it equals 0.580 (P = 0.045).

the group in which AMI was ruled-out for them was significantly higher than that of patients with AMI in group 1. Acidosis and low blood bicarbonate is a common finding in patients with AMI. However, lower bicarbonate's cause seems to be the severity of the disease in patients with AMI. As Huang et al[12] showed, plasma bicarbonate can be a marker for evaluating patients' deterioration,

so that in patients with lower levels of bicarbonate, the mortality rate is significantly higher. Our study also found that mortality was significantly higher in patients with mesenteric ischemia; it seems that lower levels of bicarbonate are associated with higher mortality rates.

The platelets' and blood lymphocytes' count in patients with confirmed AMI was slightly higher than patients in group 2. Previous studies have shown that in systemic inflammation, the lymphocytes' and platelet count increases due to the secretion of inflammatory factors in the patient's peripheral blood circulation. In inflammatory conditions, there is a strong link between platelets and lymphocytes, causing vascular wall inflammation and even thrombosis in collaboration with endothelial cells.[13,14]

This study's main goal was to examine the PLR in two groups of patients as a predictive factor. Results have shown that the average PLR in patients with mesenteric ischemia was 159, while in the patients for whom AMI was ruled-out, this was 151. Statistical evaluations have demonstrated that this difference in proportion between the two groups was not statistically significant. One study reported that the proportion of platelet against lymphocytes rises drastically in patients with ischemic extremities.[13] Multiple studies have shown that PLR also rises in different vascular diseases like pulmonary embolism and coronary artery disorders.[15] The exact mechanism and causes of this phenomenon are not clear. We need to determine the value of this ratio in the diagnosis of mesenteric ischemia in patients. Our study showed that this ratio could not help differentiate between patients with mesenteric ischemia from non-ischemic patients. It is worth noting that the current study was not performed between healthy people and patients with an ischemic condition, but it wanted to distinguish between two groups that both were dealing with an inflammatory condition. PLR also will rise in patients with systemic inflammation.[16] due to this and because of already existent systemic inflammation signs in these patients and also being critically ill; in patients in both groups, the PLR was increased and as a result of this increase, said ratio could not help us distinguish between patients with and without mesenteric ischemia in our study.

Our study showed a higher level of mortality among patients with confirmed mesenteric ischemia when compared with patients for whom mesenteric ischemia was ruled-out. Overall, the mortality rate was 61% in the study. The survival rate of patients with confirmed mesenteric ischemia was 6.3%. Our study's mortality rates were considerably higher than the rate at similar studies; various studies have reported multiple deaths in patients with mesenteric ischemia. The mortality rates were 60% to 100%.[17] For instance, a study by Chang et al[18] found that the mortality rate was 58% in patients with mesenteric ischemia. There could have been multiple reasons for the higher mortality rate in our study, in which the quality of post-operation care and late diagnosis of disease are the two effective factors that could account for the main causes of this issue.

The area under the ROC curve for the PLR is 0.580, larger than the area below the platelet count and lymphocyte count, indicating a high sensitivity to this ratio in patients diagnosed with mesenchymal ischemia. Before us, in the study of Leone et al,[19] it was determined that the PLR in detecting ischemic vascular disorders was more sensitive to lymphocytes and platelets alone.

Before our study, many studies were performed on the PLR in patients with vascular disorders. However, no similar studies assessing the relationship between PLR and mesenteric ischemia and its predictive power was available. Hence, further studies are recommended to confirm the results of our study. Future studies should aim to include a larger number of patients in the study. Also, all the patients in the study were patients admitted to a single care facility. Multicentral studies will be more reliable.

Conclusion

Investigating the PLR to predict mesenteric ischemia in patients showed that the ratio of platelets to lymphocytes, despite an increase in both groups of patients, could not distinguish between patients who had mesenteric ischemia and does who did not. Nevertheless, bicarbonate levels were significantly lower in patients with mesenteric ischemia.

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Author Contributions

Concept – AAl, HY; Design – AAl, JG.; Supervision – AAl, JG; Resources – HY, AAd; Materials – AAl, AAd; Data collection and/or Processing – HY, AAd; Data analysis and/or interpretation – AAd, JG; Literature search – HY, AAd; Writing manuscript – AAd, JG, HY; Critical review – AAl, JG.

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Ethical Approval

The current study was approved by the Ethical Board of Tabriz University of Medical Sciences (ethics code No. 95/3-5/2).

Study Highlights

What is current knowledge?

- PLC maybe can help us in diagnose of mesenteric ischemia disease

What is new here?

- Even though the PLR increases in patients with systemic inflammation, it cannot distinguish between patients with mesenteric ischemia and other inflammatory conditions

Conflict of Interest

No conflict of interest was declared by the authors.

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