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***Retrospective study***

**Prognostic significance of the lymphocyte-to-monocyte ratio in patients with metastatic colorectal cancer**

Shibutani M *et al*. The lymphocyte to monocyte ratio

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**Abstract**

**AIM**: To evaluate the prognostic significance of the lymphocyte to monocyte ratio (LMR) in patients with unresectable metastatic colorectal cancer who received palliative chemotherapy.

**METHODS**: A total of 104 patients with unresectable metastatic colorectal cancer who underwent palliative chemotherapy were enrolled. The LMR was calculated from blood samples by dividing the absolute lymphocyte count by the absolute monocyte count. The pretreatment LMR values were measured within one week before the initiation of chemotherapy and the posttreatment LMR values were measured eight weeks after the initiation of chemotherapy.

**RESULTS**: The median pretreatment LMR was 4.16 (range: 0.58-14.06). We set 3.38 as the cut-off level based on the receiver operating characteristic curve. Based on the cut-off level of 3.38, 66 patients were classified into the high pretreatment LMR group and 38 patients were classified into the low pretreatment LMR group. The low pretreatment LMR group had a significantly worse overall survival rate (*P =* 0.0011). Moreover, the patients who demonstrated a low pretreatment LMR and normalization after treatment exhibited a better overall survival rate than the patients with low pretreatment and posttreatment LMR values.

**CONCLUSION**: The lymphocyte to monocyte ratio is a useful prognostic marker in patients with unresectable metastatic colorectal cancer who receive palliative chemotherapy.

**Key words**: Colorectal cancer; Prognosis; Unresectable; chemotherapy; Lymphocyte to monocyte ratio

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**Core tip**: We retrospectively analyzed 104 patients who had unresectable metastatic colorectal cancer. This study indicated that patients with the low pretreatment lymphocyte to monocyte ratio (LMR) had a significantly worse overall survival rate. Moreover, the patients who demonstrated a low pretreatment LMR and normalization after chemotherapy exhibited a better overall survival rate than the patients with low pretreatment and posttreatment LMR values.

Shibutani M, Maeda K, Nagahara H, Ohtani H, Sakurai K, Yamazoe S, Kimura K, Toyokawa T, Amano R, Tanaka H, Muguruma K, Hirakawa K. Prognostic significance of the lymphocyte-to-monocyte ratio in patients with metastatic colorectal cancer. *World J Gastroenterol* 2015; In press

**INTRODUCTION**

Colorectal cancer (CRC) is the third leading cause of cancer-related death worldwide[1]. In particular, patients with unresectable metastatic CRC have a worse prognosis. Despite the recent major advances in new cytotoxic and molecular targeted therapies for unresectable CRC developed within the last 10 years[2-5], the median survival time of patients with unresectable metastatic CRC is only approximately 30 mo[6,7]. According to the guidelines of the European Society for Medical Oncology (ESMO), it is recommended to individualize the treatment of patients with metastatic CRC based on the tumor- and disease-related characteristics[8]. Therefore, it is necessary to detect biomarkers for predicting survival.

 It is well known that the systemic inflammatory response plays an important role in cancer progression[9]. Markers based on systemic inflammation, such as the neutrophil to lymphocyte ratio (NLR) and Glasgow prognostic score, have been reported to be useful for predicting the prognosis in patients with various types of cancer[10-14]. Recently, the lymphocyte to monocyte ratio (LMR), which also reflects the degree of systemic inflammation, has been reported to correlate with survival in various types of malignancies. However, the prognostic value of the LMR has been investigated mainly in patients with hematological malignancies and there have been only a few reports focusing on patients with solid tumors, such as colon, bladder and lung cancer[15-22]. Moreover, to the best of our knowledge, no studies regarding the prognostic significance of the LMR in patients with unresectable metastatic CRC are available. The aim of this retrospective study was to evaluate the prognostic significance of the LMR in patients with unresectable metastatic CRC.

**MATERIALS AND METHODS**

***Patients***

We retrospectively reviewed a database of 104 patients who underwent palliative combination chemotherapy for unresectable metastatic colorectal cancer at the Department of Surgical Oncology of Osaka City University between 2005 and 2010.

The patient characteristics are listed in Table 1. The patient population consisted of 59 males and 45 females, with a median age of 64 years (range: 27-86). According to the definition of the Eastern Cooperative Oncology group performance status (PS), 96 patients were classified as having a PS of 0, six patients were classified as having a PS of 1 and two patients was classified as having a PS of 2. Sixty patients had primary tumors located in the colon and 44 had primary tumors located in the rectum. A total of 42 patients had metachronous unresectable cancer, and 62 patients had synchronous unresectable cancer. Fifty-eight patients had only one organ affected by metastasis and 46 patients had more than one organ affected by metastasis. Among the 104 patients, 88 patients underwent resection of a primary tumor. All patients underwent combination chemotherapy with oxaliplatin or irinotecan plus 5-fluorouracil/leucovorin or a prodrug of 5-fluorouracil as first-line chemotherapy. There was no initiation of palliative chemotherapy for recurrence while undergoing adjuvant chemotherapy. In particular, 64 patients received 5-fluorouracil+leucovorin+oxaliplatin (FOLFOX), 26 patients received capecitabine+oxaliplatin (CapeOX), nine patients received 5-fluorouracil+leucovorin+irinotecan (FOLFIRI) and five patients received S-1+oxaliplatin (SOX). Seventy-six patients underwent chemotherapy combined with molecular targeted therapy. The median follow-up period in the survivors was 22.4 mo (range: 2.6-69.5). During the follow-up period, a total of 67 patients died.

***Evaluation***

Response evaluations were performed every eight weeks. A variation of approximately one week was regarded as an allowable error. All patients were followed up with a physical examination, blood tests, including measurements of the levels of tumor markers, such as carcinoembryonic antigen (CEA), computed tomography and ultrasonography.

 We adopted the response evaluation criteria in solid tumors (RESIST)[23] to classify the treatment response of each patient as one of the following: complete response (CR), partial response (PR), stable disease (SD) or progressive disease (PD). An objective response was defined as either CR or PR, while disease control was defined as CR, PR or SD.

The pretreatment blood samples were obtained within one week before the initiation of chemotherapy and the posttreatment blood samples were obtained eight weeks after the initiation of chemotherapy. The differential white blood cell count was analyzed using an XE-5000 hematology analyzer (Sysmex, Kobe, Japan) based on the manufacturer’s protocol. In each case, the LMR was calculated from a blood sample by dividing the absolute lymphocyte count by the absolute monocyte count. The neutrophil to lymphocyte ratio (NLR) was calculated from a blood sample by dividing the absolute neutrophil count by the absolute lymphocyte count.

***Statistical analysis***

The significance of correlations between the pretreatment LMR and the clinicopathological characteristics were analyzed using the *χ2* test, *t*-test and Mann-Whitney *U*-test. The duration of survival was calculated according to the Kaplan-Meier method. Differences in the survival curves were assessed using the log-rank test. A multivariate analysis was performed according to the Cox proportional hazard model. All statistical analyses were conducted using the SPSS software package for Windows (SPSS Japan, Tokyo, Japan). Statistical significance was set at a value of *P* < 0.05.

***Ethical consideration***

This research conformed to the provisions of the Declaration of Helsinki established in 1995. All patients were informed of the investigational nature of the study and provided their written informed consent. This retrospective study was approved by the ethics committee of Osaka City University.

**RESULTS**

***Classification according to the pretreatment LMR/NLR***

We used the LMR, which was a continuous variable, as the test variable and the 24.8-mo survival (median survival time: 24.8 mo) as the state variable. When we investigated the cut-off value for the LMR using the receiver operating characteristic (ROC) curve, we found that the appropriate cut-off value for the LMR was 3.38 (sensitivity: 90.0%; specificity: 52.1%) (Figure 1). We therefore set 3.38 as the cut-off value and the patients were classified into the high-LMR (*n =* 66) and low-LMR (*n =* 38) groups. We also set the cut-off value for the NLR at 2.8 in accordance with the findings of a previous report[10].

***Survival analysis according to the pretreatment LMR***

The overall survival rate was significantly worse in the low pretreatment LMR group than in the high pretreatment LMR group (*P =* 0.0011) (Figure 2A).

***Correlation between the pretreatment LMR and the clinicopathological factors***

The correlations between the pretreatment LMR and the clinicopathological factors are shown in Table 2. The pretreatment LMR had no significant relationships with any of the clinicopathological factors except for the pretreatment NLR.

***Chemotherapeutic response***

The distribution of the chemotherapeutic response after the administration of first-line chemotherapy with reference to the LMR/NLR subgroup is shown in Table 3. The objective response rate did not differ according to the LMR (34.4% *vs* 28.9%, *P =* 0.664). However, the disease control rate of the high-LMR group was significantly higher than that of the low-LMR group (82.8% *vs* 63.2%, *P =* 0.033). On the other hand, there was no significant relationship between the NLR and the chemotherapeutic response.

***Prognostic factors influencing long-term survival***

The correlations between overall survival and the various clinicopathological factors are shown in Table 4. According to the results of a univariate analysis, overall survival exhibited significant relationships with the performance status (*P* < 0.001), the number of organs affected by metastasis (*P =* 0.045), the response to molecular targeted therapy (*P =* 0.011), the response to chemotherapy (*P =* 0.006), the pretreatment LMR (*P =* 0.002) and the pretreatment NLR (*P* < 0.001). A multivariate analysis indicated that the performance status (HR = 3.345, 95%CI: 1.558-7.182, *P =* 0.002) and the response to molecular targeted therapy (HR = 0.462, 95%CI: 0.263-0.813, *P =* 0.007) and the response to chemotherapy (HR = 0.432, 95%CI: 0.244-0.765, *P =* 0.004) were independent prognostic factors for survival.

***Correlation between normalization of the LMR/NLR eight weeks after chemotherapy and survival***

We evaluated the prognostic significance of normalization of the LMR/NLR eight weeks after the initiation of chemotherapy. We categorized the patients into three groups according to the combination of their pretreatment and posttreatment LMR values. Patients with a high pretreatment LMR were categorized into group A. Patients with a low pretreatment LMR and normalization of the LMR eight weeks after the initiation of chemotherapy were categorized into group B. Patients with low pretreatment and posttreatment LMR value were categorized into group C. The patients in group C exhibited a worse prognosis than those in groups A and B (A *vs* C, *P* < 0.0001; B *vs* C, *P =* 0.0308) (Figure 2B). We categorized the patients into three groups according to the combination of their pretreatment and posttreatment NLR values. Patients with a low pretreatment LMR were categorized into group D. Patients with a high pretreatment NLR and normalization of the NLR eight weeks after the initiation of chemotherapy were categorized into group E. Patients with high pretreatment and posttreatment NLR value were categorized into group F. There was no significant difference between groups E and F (Figure 2C).

***pretreatment and posttreatment absolute neutrophil/lymphocyte/monocyte counts***

The absolute neutrophil count tended to decrease after chemotherapy. However, the absolute lymphocyte count did not change after chemotherapy while the absolute monocyte count tended to increase after chemotherapy (Table 5).

**DISCUSSION**

In this study, we investigated the prognostic significance of the pretreatment LMR as a marker for predicting the chemotherapeutic response and survival time in patients with unresectable metastatic CRC. Moreover, we demonstrated that normalization of the LMR after chemotherapy resulted in improved overall survival. Recently, systemic inflammation has been recognized to correlate with tumor progression and inflammatory markers have been reported to be useful for predicting the prognosis[9-13]. The LMR is an inflammatory marker, and a correlation between the LMR and survival has been reported[14-21]. However, most analyses in previous studies targeted patients with hematological malignancies[14-18]. To the best of our knowledge, this is the first study to assess the prognostic significance of the LMR in patients with unresectable metastatic CRC who received palliative chemotherapy.

Lymphocytes play an important role in the antitumor immunity of the host, including cytotoxic cell death and the inhibition of tumor cell proliferation and migration[9,24-26]. The absolute lymphocyte count is assumed to reflect the degree of responsiveness of the immune system of the host[26-28]. Therefore, a decreased number of lymphocytes is considered to be responsible for an insufficient immunologic reaction to the tumor, thus promoting tumor progression and metastasis[20].

On the other hand, monocytes play an important role in tumor progression and metastasis[9,29]. Tumor-associated macrophages (TAMs), which are derived from circulating monocytes, suppress the adaptive immunity and promote angiogenesis, invasion, migration and tumor growth[9,30-32]. The circulating level of monocytes in the peripheral blood is reported to reflect the formation and/or presence of TAMs[20,22]. Therefore, an increased level of monocytes reflects a high tumor burden in patients with cancer.

As mentioned above, the LMR reflects both the immune status of the host and the degree of tumor progression. Because both a low lymphocyte count and high monocyte count reflect insufficient antitumor immunity and an elevated tumor burden, a low LMR is associated with a poorer prognosis.

In this study, normalization of the LMR eight weeks after the initiation of chemotherapy tended to correlate with an improvement in the overall survival. Based on this result, the posttreatment LMR is considered to reflect the responsiveness of chemotherapy. Therefore, the LMR is a useful marker for monitoring tumor progression in patients with unresectable metastatic CRC who receive palliative chemotherapy.

The NLR, which has been reported to correlate with the survival in patients with CRC, is quite similar to the LMR because we can easily obtain both results from an examination of the peripheral blood. Although the pretreatment NLR significantly correlated with the pretreatment LMR and similar results regarding the long-term survival were obtained, only the LMR significantly correlated with the chemotherapeutic response. Moreover, in relation to the normalization of the value after chemotherapy, only the LMR significantly correlated with the survival. Because the absolute neutrophil count tends to decrease after chemotherapy, the NLR tends to improve regardless of whether the tumor is controlled. On the other hand, because the absolute monocyte count tends to increase, the LMR tends to worsen regardless of whether the tumor progresses. The normalization of the LMR after chemotherapy despite such situations is considered to reflect the tumor control. This is because the prognostic significance of the normalization after chemotherapy varied between the LMR and NLR. Therefore, the LMR is considered to be superior to the NLR.

There are some possible limitations associated with this study. First, we evaluated a relatively small number of patients and the study design was retrospective. Second, factors such as infection, ischemia and coronary syndrome, which may affect the white blood cell count, were not taken under consideration. Third, the appropriate cut-off value for the LMR is not uniform in previous studies, although we set 3.38 as the cut-off value in the current study based on the ROC curve. Therefore, large prospective studies should be performed to confirm our findings.

**COMMENTS**

***Background***

Despite recent major advances in the development of new cytotoxic and molecular targeted therapies, patients with unresectable metastatic colorectal cancer (CRC) still have a poor prognosis. According to the guidelines of the European Society for Medical Oncology, it is recommended that the treatment of patients with metastatic CRC be individualized based on the tumor- and disease-related characteristics. It is therefore necessary to detect biomarkers for predicting survival.

***Research frontiers***

The lymphocyte to monocyte ratio (LMR) is a useful marker for predicting the survival and chemotherapeutic response. This marker can therefore be used for the individualization of treatment in patients with unresectable metastatic CRC. By using this marker, we can identify the patients with a high risk of a poor prognosis and thus choose the most appropriate intensive therapy.

***Innovations and breakthroughs***

It is difficult to predict the prognosis of patients with unresectable metastatic CRC. A few markers for predicting patient survival have been reported previously. Survival prediction is important for planning an appropriate course of treatment. The LMR was revealed to correlate with both the survival and the chemotherapeutic response in the present study. The LMR makes a useful clinical biological marker because its measurement by peripheral blood cell count is a quick and easy assay to perform.

***Applications***

The results of the present study suggest that the LMR is a useful prognostic marker for predicting the survival and chemotherapeutic response in patients with unresectable metastatic CRC who undergo palliative chemotherapy.

***Terminology***

The LMR was calculated from a blood sample by dividing the absolute lymphocyte count by the absolute monocyte count. The LMR reflects the immune status and the systemic inflammatory response of the host. The immune status and systemic inflammation have been reported to correlate with tumor progression, invasion and metastasis. The LMR is thus considered to correlate with the survival of patients with CRC.

***Peer-review***

This is a good descriptive study in which the authors evaluated the prognostic significance of the lymphocyte to monocyte ratio in patients with unresectable metastatic colorectal cancer who underwent palliative chemotherapy. The study is well structured and the subject is clear and interesting. The manuscript is correctly written and the conclusions are justified by the results found in the study.

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**P-Reviewer:** Lakatos pl, Liu xe, Nishida t, Wang G **S-Editor:** Ma YJ **L-Editor:** **E-Editor:**

**Table 1 Patient characteristics**

|  |  |
| --- | --- |
| Age (yr) | 　 |
|  Median (range) | 64 (27-86) |
| Gender |  |
|  Male | 59 |
|  Female | 45 |
| Performance Status |  |
|  0 | 96 |
|  1 | 6 |
|  2 | 2 |
| Location of primary tumor |  |
|  Colon | 60 |
|  Rectum | 44 |
| Histological type |  |
|  Well, moderately | 81 |
|  Poorly, mucinous | 14 |
| KRAS |  |
|  Wild type | 25 |
|  Mutant type | 25 |
|  Unknown | 54 |
| Detection of unresectable tumor |  |
|  Synchronous | 62 |
|  Metachronous | 42 |
| The number of organs affected by metastasis |  |
|  One organ | 58 |
|  More than one organ | 46 |
| Resection of primary tumor |  |
|  No | 16 |
|  Yes | 88 |
| Regimen of first-line chemotherapy |  |
|  FOLFOX | 64 |
|  CapeOX | 26 |
|  FOLFIRI | 9 |
|  SOX | 5 |
| Molecular targeted therapy |  |
|  No | 28 |
|  Yes | 76 |
| The pretreatment LMR |  |
|  (mean ± SD) | 4.548 ± 2.314 |
| The pretreatment NLR |  |
|  (mean ± SD) | 3.204 ± 2.284 |

FOLFOX: 5-fluorouracil + leucovorin + oxaliplatin; CapeOX: capecitabine + oxaliplatin; FOLFIRI: 5-fluorouracil+leucovorin+irinotecan; SOX: S-1+oxaliplatin; LMR: Lymphocyte to monocyte ratio; NLR: Neutrophil to lymphocyte ratio.

**Table 2 Correlations between the pretreatment lymphocyte to monocyte ratio and clinicopathological factors**

|  |  |
| --- | --- |
|  | **Pretreatment LMR** |
|  | **High** | **Low** | ***P*-value** |
| Performance status |  |  |  |
| 0 | 62 | 34 |  |
| 1, 2 | 4 | 4 | 0.459  |
| Location of primary tumor |  |  |  |
| Colon | 39 | 21 |  |
| Rectum | 27 | 17 | 0.837  |
| Detection of unresectable tumor |  |  |  |
|  Synchronous | 39 | 23 |  |
|  Metachronous | 27 | 15 | 1.000  |
| Resection of primary tumor |  |  |  |
| No | 8 | 8 |  |
| Yes | 58 | 30 | 0.264  |
| Histological type |  |  |  |
| Well, Moderately | 51 | 30 |  |
| Poorly, Mucinous | 10 | 4 | 0.764  |
| KRAS |  |  |  |
| Wild type | 15 | 10 |  |
| Mutant type | 15 | 10 | 1.000  |
| Peritoneal dissemination |  |  |  |
| Negative | 53 | 32 |  |
| Positive | 13 | 6 | 0.793  |
| The number of organs affected by metastasis |  |  |
|  One organ | 39 | 19 |  |
|  More than one organ | 27 | 19 | 0.416  |
| Pretreatment CEA (ng/ml) |  |  |  |
| ≤ 5 | 10 | 3 |  |
| > 5 | 54 | 35 | 0.362  |
| Average relative dose intensity (%) |  |  |  |
| median (range) | 100 (60.0-100) | 96.2 (50.0-100) | 0.697  |
| Molecular targeted therapy |  |  |  |
| No | 15 | 13 |  |
| Yes | 51 | 25 | 0.253  |
| Pretreatment NLR |  |  |  |
| < 2.8 | 48 | 5 |  |
| ≥ 2.8 | 18 | 33 | < 0.001 |

CEA: Carcinoembryonic antigen; LMR: Lymphocyte to monocyte ratio; NLR Neutrophil to lymphocyte ratio.

**Table 3 Treatment response to chemotherapy according to the pretreatment lymphocyte to monocyte ratio/neutrophil to lymphocyte ratio**

|  |  |  |  |
| --- | --- | --- | --- |
|  | LMR |  | NLR |
| Response | High (*n =* 64) | Low (*n =* 38) | *P*-value | 　 | High (*n =* 51) | Low (*n =* 51) | *P*-value |
| CR | 2 | 2 |  |  | 2 | 2 |  |
| PR | 20 | 9 |  |  | 12 | 17 |  |
| SD | 31 | 13 |  |  | 22 | 22 |  |
| PD | 11 | 14 | 　 | 　 | 15 | 10 | 　 |
| Objective response rate | 34.4% | 28.9% | 0.664 |  | 27.5% | 37.3% | 0.397 |
| Disease control rate | 82.8% | 63.2% | 0.033  |  | 70.6% | 80.4% | 0.357 |

CR: Complete response; PR: Partial response; SD: Stable disease; PD: Progressive disease; LMR: Lymphocyte to monocyte ratio; NLR: Neutrophil to lymphocyte ratio.

**Table 4 Correlations between the overall survival and various clinicopathological factors**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Univariate analysis |  | Multivariate analysis |
| 　 | HR | 95% CI | *P*-value | 　 | HR | 95% CI | *P*-value |
| Performance status (≥ 1) | 3.821 | 1.805-8.087 | < 0.001 |  | 3.345  | 1.558-7.182 | 0.002 |
| Location of primary tumor (Colon) | 1.405  | 0.857-2.304 | 0.177  |  |  |  |  |
| Detection of unresectable tumor (Synchronous) | 1.407 | 0.852-2.312 | 0.182  |  |  |  |  |
| Histological type (Poorly, Mucinous) | 1.283 | 0.644-2.556 | 0.478  |  |  |  |  |
| Peritoneal dissemination (Yes) | 0.981 | 0.534-1.802 | 0.951  |  |  |  |  |
| The number of organs affected by metastasis (≥ 2) | 1.637 | 1.012-2.648 | 0.045  |  | 1.270  | 0.737-2.187 | 0.389  |
| Pretreatment CEA (> 5 ng/ml) | 1.949 | 0.841-4.521 | 0.120  |  |  |  |  |
| Resection of primary tumor (No) | 1.716 | 0.948-3.104 | 0.074  |  | 1.736  | 0.871-3.459 | 0.117  |
| Molecular targeted therapy (Yes) | 0.496 | 0.289-0.853 | 0.011  |  | 0.462  | 0.263-0.813 | 0.007  |
| Response to chemotherapy (CR, PR) | 0.459 | 0.264-0.797 | 0.006  |  | 0.432  | 0.244-0.765 | 0.004  |
| Pretreatment LMR (< 3.38) | 2.273 | 1.368-3.777 | 0.002  |  | 1.734  | 0.942-3.192 | 0.077  |
| Pretreatment NLR (< 2.8) | 2.578 | 1.569-4.237 | < 0.001 | 　 | 1.734  | 0.947-3.178 | 0.075  |

CEA: Carcinoembryonic antigen; CR: Complete response; PR: Partial response; LMR: Lymphocyte to monocyte ratio; NLR: Neutrophil to lymphocyte ratio.

**Table 5 pretreatment and posttreatment absolute neutrophil/lymphocyte/monocyte counts**

|  |  |  |  |
| --- | --- | --- | --- |
| 　 | **Pretreatment value** | **Posttreatment value** | ***P*-value** |
| All patients |  |  |  |
| Neutrophil (mean ± SD) | 4538.5 ± 200.4 | 2798.0 ± 190.0 | < 0.001 |
| Lymphocyte (mean ± SD) | 1664.3 ± 649.1 | 1610.5 ± 671.0 | 0.247 |
| Monocyte (mean ± SD) | 422.1 ± 19.0 | 471.7 ± 24.6 | 0.027 |
| Patients receiving chemotherapy based on oxaliplatin |  |  |  |
| Neutrophil (mean ± SD) | 4455.8 ± 1962.6 | 2791.7 ± 1859.9 | < 0.001 |
| Lymphocyte (mean ± SD) | 1694.9 ± 695.4 | 1639.2 ± 677.8 | 0.365 |
| Monocyte (mean ± SD) | 412.4 ± 181.0 | 457.3 ± 248.4 | 0.001 |
| Patients receiving chemotherapy based on irinotecan |  |  |  |
| Neutrophil (mean ± SD) | 4567.6 ± 1873.2 | 2879.4 ± 2007.3 | 0.038 |
| Lymphocyte (mean ± SD) | 1307.5 ± 440.8 | 1238.6 ± 342.1 | 0.394 |
| Monocyte (mean ± SD) | 466.9 ± 221.0 | 427.0 ± 134.2 | 0.174 |

****

**Figure 1 receiver operating characteristic curve analysis of the lymphocyte to monocyte ratio in the patients with unresectable metastatic colorectal cancer.** The area under the curve = 0.703, 95%ci: 0.594-0.812, *P =* 0.001, positive predictive value = 80.65%, negative predictive value = 59.65%.



A



*P =* 0.0208

*P* < 0.0001

B



C

**Figure 2 Overall survival.** a: according to the pretreatment lymphocyte to monocyte ratio.The overall survival rate was significantly worse in the low pretreatment LMR group than in the high pretreatment LMR group (*P =* 0.0011); b: according to the combination of the pretreatment and posttreatment lymphocyte to monocyte ratio values. The patients in group C exhibited a worse prognosis than those in groups A and B; C: according to the combination of the pretreatment and posttreatment neutrophil to lymphocyte ratio values. There was no significant difference between groups E and F. LMR: Lymphocyte to monocyte ratio.