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ORIGINAL ARTICLE

Prognostic value of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio on low-grade appendiceal mucinous neoplasm: A single tertiary hospital experience

Tai-Chuan Kuan[a,b,c], Wen-Yi Liang[c,d], Chun-Chi Lin[a,c], Hung-Hsin Lin[a,c], Sheng-Chieh Huang[a,c], Ho-Shuan Cheng[a,c], Shih-Ching Chang[a,c], Jeng-Kai Jiang[a,c], Yuan-Tzu Lan[a,c,*]

[a]Division of Colon & Rectal Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [b]Division of Colon & Rectal Surgery, Department of Surgery, Far Eastern Memorial Hospital, New Taipei City, Taiwan, ROC; [c]Department of Surgery, Faculty of Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; [d]Department of Pathology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

Abstract

Background: Low-grade appendiceal mucinous neoplasm (LAMN) is a rare disease, which prognostic factors were difficult to evaluate. Inflammation markers, like neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), were used as prognosticators for various cancers. This study aimed to investigate the prognostic value of pretreatment NLR and PLR on LAMN.

Methods: From January 2000 to September 2018, there were 57 patients diagnosed with LAMN in Taipei Veterans General Hospital. Patients diagnosed with mucinous cystadenoma, mucinous tumor with uncertain malignant potential before 2010 were also included based on previous classification. Clinical and pathological data were collected. Patients were separated into high-NLR (NLR-H) and low-NLR (NLR-L) groups according to cutoff value of 3. Similarly, they were separated into high-PLR (PLR-H), and low-PLR (PLR-L) groups with cutoff value of 300. Overall survival (OS) and recurrence-free survival (RFS) were analyzed.

Results: Among all patients, the median follow-up time was 42 months. Age, gender, clinical manifestations, type of surgery, and T stage were similar in different NLR and PLR groups. Both NLR-H and PLR-H groups had higher rate of M1 stage of diseases (22.7% vs 9.4%, $p = 0.04$; 57.1% vs 8.8%, $p < 0.01$, respectively). PLR-H group had more presence of pseudomyxoma peritonei (PMP) (57.1% vs 15.2%, $p = 0.03$). In univariate analysis, factors such as age, gender, tumor perforation, and operation did not have impact on OS nor RFS. On the other hand, M1b stage is the only significantly poor prognostic factor on RFS (hazard ratio, 57.96, 95% CI, 5.16-651.23, $p < 0.01$).

Conclusion: Both NLR-H and PLR-H had more M1 stage of diseases, but they were not correlated to OS nor RFS. PLR-H group had higher rate of presence PMP. Nevertheless, patients with LAMN and cellular PMP (M1b stage) had a higher rate of recurrence, and other factors showed no statistical difference in OS nor RFS.

Keywords: Appendix; Lymphocyte; Neoplasm; Neutrophil; Pseudomyxoma Peritonei

1. INTRODUCTION

Mucinous appendiceal tumors are rare and involve a wide spectrum of diseases. They are classified according to degree of invasion and cytologic atypia. Of these, low-grade appendiceal tumors or mucinous neoplasms (LAMN) account for about 73%.[1] The terminology for LAMN has varied considerably over the decades,[2] and its presenting characteristics were clarified after the Peritoneal Surface Oncology Group (PSOGI) conference in 2015.[3] LAMN is defined as a mucinous neoplasm with intraluminal low-grade cytologic atypia and a noninvasive, pushing margin. LAMNs are relatively benign but have potential to spread to the peritoneal cavity, a condition that is called pseudomyxoma peritonei (PMP). According to the American Joint Committee on Cancer staging manual, eighth edition, acellular peritoneal deposit is classified as M1a, whereas a deposit with malignant cells is M1b. M1b disease signifies a higher rate of recurrence, and most recurrence happens within three after surgery.[4,5] Management of LAMN has been discussed for many years. Although treatment strategies for LAMN with PMP are still being debated, appendectomy (AP) is considered a sufficient surgical treatment.[6,7] Cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) was shown to be an independent predictor of progression-free survival (hazard ratio [HR], 0.65; $p = 0.03$), with a 5-year progression-free survival rate of 96% and 69.8% in the presence of peritoneal acellular mucin and peritoneal cellular mucin, respectively.[8,9]

Address correspondence. Dr. Yuan-Tzu Lan, Division of Colon & Rectal Surgery, Department of Surgery, Taipei Veterans General Hospital, 201, Section2, Shi-Pai Road, Taipei 112, Taiwan, ROC. E-mail address: ytlan@vghtpe.gov.tw (Y.-T. Lan).

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Investigation of prognostic factors for LAMN is important in order that high-risk patients can be closely followed up. Previous studies proposed that the following factors, including positive resection margin, elevated serum carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), and CA12-5 result in higher recurrence and mortality.[6,10] However, systemic/local inflammatory response has prognostic value in various cancers. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been identified as inflammation markers, which are also used as prognostic factors in cancer.[11,12] A previous study proposed that NLR and PLR were not predictive of overall survival (OS) in advanced appendiceal carcinoma[13]; this study combined all malignant appendiceal tumors. However, the prognostic values of NLR and PLR are still unclear in LAMN. This study aimed to investigate them.

2. METHODS

2.1. Pathological diagnosis and definition

Our hospital defined appendiceal tumors with mucin-filled, partial, low-grade neoplastic epithelium, and possible extra-appendiceal mucin-component invasion as LAMN, based on the World Health Organization (WHO) classification, fourth edition, in 2010. Before this, these tumors were called appendiceal mucinous cystadenomas (AMC) or mucinous tumors with uncertain malignant potential (MT-UMP) according to prior classification. Meanwhile, the incidence of extra-appendiceal mucin-component distribution is defined as PMP.

2.2. Patients and clinical data

A total of 81 cases diagnosed as mucocele, AMC, MT-UMP, and LAMN from January 2000 to September 2018 were retrieved from the database of the Department of Pathology and Laboratory Medicine, Taipei Veterans General Hospital, Taiwan. This study was approved by the Hospital Review Board (Institutional Review Board [IRB] 2021-03-001BC). After a pathological review using the latest WHO criteria[14] and tumor, node, metastasis staging according to the eighth version of American Joint Committee on Cancer staging criteria,[15] 57 patients were enrolled in this study. Of them, 28 were diagnosed before 2010. All patients underwent surgeries, including appendectomy ileocecal resection, right hemicolectomy, and tumor excision with regional lymphadenectomy.

Clinical information collected from electronic medical records included age, gender, clinical manifestations, pretreatment white blood counts, neutrophil counts, lymphocyte counts, platelet counts, initial diagnoses, types of surgery, initial CEA, date of last follow-up, adjuvant treatment, date of recurrence, and therapy for recurrence. Surgery details obtained included the type of procedures, presence of perforation, and presence of PMP. Tumor size information was obtained from pathological reports. The follow-up protocol differed between surgeons, and imaging studies, such as abdominal computerized tomography (CT) scan and ultrasonography, and CEA were arranged accordingly. Recurrence was defined as pathological evidence from a biopsy or surgical specimen or new lesions presented in follow-up imaging studies, which were confirmed by radiologists. OS was defined as the time from the date of operation to the date of the last follow-up or the date of death, whereas recurrence-free survival (RFS) was the time from the date of operation to the date of recurrence.

2.3. NLR and PLR

Our sample size was too small to determine the cutoff values of NLR and PLR properly by receiver operating characteristic curve analysis. Therefore, we determined the cutoff values 3 and 300 for NLR and PLR, respectively, which were based on prior colorectal cancer studies.[16,17] Patients with NLR >3 were defined as high-NLR (NLR-H) group and others as low-NLR (NLR-L) group. Similarly, patients with PLR >300 were in high-PLR (PLR-H) group and others in low-PLR (PLR-L) group.

2.4. Statistical analysis

All statistical analyses were conducted using IBM SPSS Statistics for Windows, version 22 (IBM Corp., Chicago, IL). The χ^2 test was used for categorical variables, and Fisher exact test was used for count <5. Continuous variables were analyzed using the Student *t* test. The Kaplan-Meier curve and Cox regression analysis were used for univariate analysis to compare differences in OS and RFS. Furthermore, risk factors which *p* value was <0.1 in univariate analysis were applied to multivariate analysis with Cox regression model. p value < 0.05 was considered statistically significant.

3. RESULTS

3.1. Patients' characteristics

The mean age of all patients was 65.1 ± 14.5 years old, and the median follow-up time was 42.0 months (range, 0.33-225.13 months) (Table 1). The study population was composed of 24 males (42.1%) and 33 female (57.9%). Of the preoperative diagnoses, 13 (22.8%) were appendicitis, 27 (47.3%) were unknown appendiceal tumors, 10 (17.5%) were unknown right lower abdominal tumors that were mostly initially diagnosed as ovarian tumors, and 7 (12.3%) were synchronous appendectomies with other abdominal surgeries, including gynecologic and colorectal surgeries. The most common clinical presentation was abdominal pain (n = 27, 47.4%). About one-third of the patients were asymptomatic (n = 20, 35.1%). Although the preoperative CEA level was not checked in about half of the patients, 12 (21.1%) were found with elevated CEA levels (>5 mg/dL). Forty-four (77.2%) patients underwent elective surgeries, while 13 (22.8%) had emergent surgeries. AP was performed for 35 (61.4%) patients, whereas other radical surgeries were done for the remaining 22 (38.6%) cases. Furthermore, 14 (24.6%) patients had a perforated appendix during operation. For tumor staging, 50 cases (87.7%) had carcinoma in situ (Tis), and T3, T4 were 4 (7.0%) and 3 (5.3%) cases, respectively. Six (10.5%) patients had M1a, and 2 (3.5%) had M1b disease. The mucus deposit samples of two patients with PMP were not sent for cytological analysis, so their M stages could not be evaluated. Three cases (5.3%) showed recurrence, two of which had M1b disease initially. The other one underwent laparoscopic drainage surgery at another hospital. No PMPs were noted during the open appendectomy procedures at our hospital.

3.2. Comparison between NLR-H (>3) and NLR-L (<3)

The comparison of the NLR-H and NLR-L groups is shown in Table 1. Three patients did not have available data on NLR and were not included in the following analysis. The NLR-L and NLR-H groups were composed of 32 and 22 patients, respectively. The mean age of the two groups was similar (65.3 ± 14.4 years vs 64.6 ± 15.3 years; p = 0.86) and so was gender distribution. Many factors, including clinical presentation, preoperative diagnosis, CEA level, surgery type, tumor size showed no difference between the two groups. NLR-H group had higher rate of perforation than NLR-L group (40.9% vs 15.6%, p = 0.04). Furthermore, NLR-H group was not significantly associated with presence of PMP but had higher rate of M1 stage (22.7% vs 9.4%, p = 0.04). Nevertheless, the recurrence rate and mortality rate were similar. The medians of RFS and OS were not reached. The survival curves are shown in Fig. 1.

Table 1

Patient characteristics and comparison of NLR and PLR

		NLR (n = 54)			PLR (n = 53)		
	Total	**NLR-L (<3)**	**NLR-H (>3)**	***p***	**PLR-L (<300)**	**PLR-H (>300)**	***p***
Number	57	32 (59.3%)	22 (40.7%)		46 (86.8%)	7 (13.2%)	
Age (year-old, mean± SD)	65.1 ± 14.5	65.3 ± 14.4	64.6 ± 15.3	0.86	64.6 ± 14.9	67.6 ± 14.5	0.63
Gender				0.17			0.76
Male	24 (42.1%)	10 (31.3%)	11 (50.0%)		17 (37.0%)	3 (42.9%)	
Female	33 (57.9%)	22 (68.7%)	11 (50.0%)		29 (63.0%)	4 (57.1%)	
Clinical presentation				0.35			0.85[a]
Pain	27 (47.4%)	13 (40.6%)	12 (54.5%)		20 (43.5%)	4 (57.1%)	
Palpable mass	6 (10.4%)	4 (12.5%)	2 (9.1%)		6 (13.0%)	0	
Asymptomatic	20 (35.1%)	11 (34.4%)	8 (36.4%)		16 (34.8%)	3 (42.9%)	
Others	4 (7.1%)	4 (12.5%)	0		4 (8.7%)	0	
Preoperative diagnosis				0.12			0.11[a]
Appendicitis	13 (22.8%)	6 (18.8%)	7 (31.8%)		10 (21.7%)	2 (28.6%)	
Unknown appendiceal tumor	27 (47.3%)	19(59.4%)	6 (27.3%)		24 (52.2%)	1 (14.3%)	
Operation for RLQ tumor	10 (17.5%)	5 (15.6%)	5 (22.7%)		8 (17.4%)	2 (28.6%)	
Operation for other disease	7 (12.3%)	2 (6.2%)	4 (18.2%)		4 (8.7%)	2 (28.6%)	
Tumor size, cm (mean+ SD)	6.5 ± 3.0	5.95 ± 2.6	7.23 ± 3.5	0.13	6.45 ± 3.0	6.14 ± 3.4	0.81
CEA level				0.50[a]			0.01[a]
CEA>5 mg/dL	12 (21.1%)	9 (28.1%)	3 (13.6%)		14 (30.4%)	6 (85.7%)	
CEA<5 mg/dL	20 (35.1%)	11 (34.4%)	9 (40.9%)		11 (23.9%)	1 (14.3%)	
NA	25 (43.8%)	12 (37.5%)	10 (45.5%)		21 (45.7%)	0	
Emergent surgery, %				0.10[a]			1.00[a]
Emergent surgery	13 (22.8%)	4 (12.5%)	7 (31.8%)		37 (80.4%)	6 (85.7%)	
Elective surgery	44 (77.2%)	28 (87.5%)	15 (68.2%)		9 (19.6%)	1 (14.3%)	
Surgery type, %				0.41			0.10[a]
Appendectomy	35 (61.4%)	21 (65.6%)	12 (54.5%)		30 (65.2%)	2 (28.6%)	
Other radical surgery	22 (38.6%)	11 (34.4%)	10 (45.5%)		16 (34.8%)	5 (71.4%)	
Perforation, %				0.04			0.07[a]
Yes	14 (24.6%)	5 (15.6%)	9 (40.9%)		10 (21.7%)	4 (57.1%)	
No	43 (75.4%)	27 (84.4%)	13 (59.1%)		36 (78.3%)	3 (42.9%)	
T stage, %				0.33[a]			1.00
Tis	50 (87.7%)	26 (81.3%)	21 (95.5%)		39 (73.6%)	7 (100%)	
T3	4 (7.0%)	3 (9.4%)	1 (4.5%)		4 (7.5%)	0	
T4	3 (5.3%)	3 (9.4%)	0		3 (5.7%)	0	
M stage, %				0.04[a]			<0.01
M0/NA	49 (86.0%)	29 (90.6%)	17 (77.3%)		42 (91.3%)	3 (42.9%)	
M1a	6 (10.5%)	1 (3.2%)	5 (22.7%)		2 (4.4%)	4 (57.1%)	
M1b	2 (3.5%)	2 (6.2%)	0		2 (4.4%)	0	
PMP, %				0.10[a]			0.03[a]
Yes	10 (17.5%)	4 (12.5%)	6 (27.3%)		7 (15.2%)	4 (57.1%)	
No	46 (82.5%)	28 (87.5%)	16 (72.7%)		39 (84.8%)	3 (42.9%)	
Recurrence, %				1.00[a]			1.00[a]
Yes	3 (5.3%)	2 (6.2%)	1 (4.5%)		3 (6.5%)	0	
No	54 (94.7%)	30 (93.8%)	21 (95.5%)		43 (93.5%)	7 (100%)	
Status, %				0.51			0.47
Alive	53 (93.0%)	29 (90.6%)	21 (95.5%)		43 (93.5%)	6 (85.7%)	
Expired	4 (7.0%)	3 (9.4%)	1 (4.5%)		3 (6.5%)	1 (14.3%)	
Follow-up time (median, mo)	42 (0.33–225.13)	…	…	…	…	-	-

CEA = carcinoembryonic antigen; NA = not available; NLR = neutrophil-to-lymphocyte ratio; NLR-H = high-NLR; NLR-L = low-NLR; PLR = platelet-to-lymphocyte ratio; PLR-H = high-PLR; PLR-L = low-PLR; PMP = pseudomyxoma peritonei; RLQ = right lower quadrant of abdomen; Tis = carcinoma in situ.

[a]Calculation using Fisher exact test

3.3. Comparison between PLR-H (>300) and PLR-L (<300)

The comparison of the PLR-H and NLR-L groups is shown in Table 1. Four patients did not have available data on NLR and were not included in the following analysis. The PLR-L and PLR-H groups were composed of 46 and 7 patients, respectively. The mean age of the two groups was similar (64.6 ± 14.9 years vs 67.6 ± 14.5 years; $p = 0.63$) and so was gender distribution. Many factors, including clinical presentation, preoperative diagnosis, surgery type, and tumor size, showed no difference between the two groups. The distribution of PMP between the two groups differed (PLR-H vs PLR-L: 57.1% vs 15.2%, $p = 0.03$) and so did M stage (PLR-H vs PLR-L: 57.1% vs 8.8%, $p < 0.01$). Nevertheless, the recurrence rate and mortality rate were similar. The medians of RFS and OS were not reached. The survival curves are shown in Fig. 1.

3.4. Univariate analysis/ Multivariate analysis

There were four mortalities during follow-up. Univariate analysis for OS showed no significant difference between the two groups for age, gender, type of operation, NLR, and PLR. For

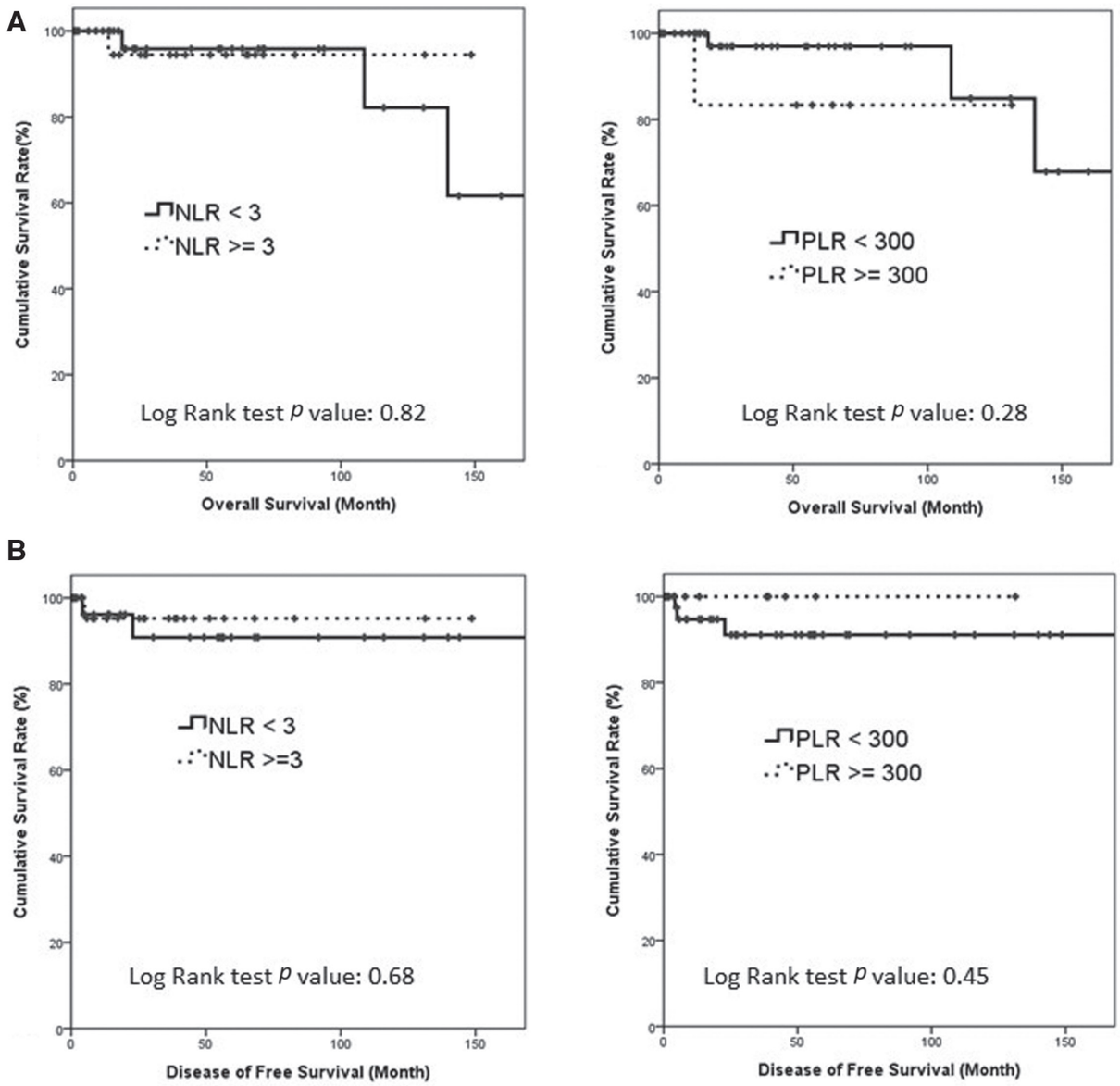

Fig. 1 Kaplan-Meier curve of overall survival between NLR-H and NLR-L (A); PLR-H and PLR-L (B); disease-free survival between NLR-H and NLR-L (C); PLR-H and PLR-L (D). NLR = neutrophil-to-lymphocyte ratio; NLR-H = high-NLR; NLR-L = low-NLR; PLR = platelet-to-lymphocyte ratio; PLR-H = high-PLR; PLR-L = low-PLR.

RFS, age, type of surgery, presence of PMP, NLR, and PLR showed no statistically significant differences. However, M1b disease was significantly different between the two groups for RFS (hazard ratio, 57.96, 95% CI, 5.16-651.23, $p < 0.01$). However, only M1b disease reached p value <0.1 in univariate analysis, so we did not perform multivariate analysis.

4. DISCUSSION

The terminology and definition for LAMN have changed across the decades, from AMC, to MT-UMP, to LAMN. WHO published the latest classification for mucinous appendiceal tumors in 2019. However, some hospitals still used the MT-UMP classification even after 2010.[10] Some researchers reevaluated prior AMC and MT-UMP cases according to the cancer staging manual of American Joint Committee on Cancer, Eighth edition, and they overturned the diagnoses of 47.4% (9/19) cases.[2] In the current study, our pathologist reviewed all slides of cases diagnosed as AMC, MT-UMP, and LAMN and excluded cases with other diagnoses. This allowed us to avoid misdiagnosis and enhanced the accuracy of our findings. However, our patient characteristics presented no lymph node metastasis, more Tis but less T4 stage disease, and our results disclosed type of surgery, perforation, and PMP showed no statistical difference in OS or RFS. These patient characteristics and treatment outcomes were compatible to other larger cohort studies.[18,19] However, due to indolence, and low malignancy of LAMN, complete cytoreduction brought lower recurrent rate than other gastrointestinal tract cancers, even in M stage diseases.[5,20] Therefore, we used RFS instead of disease-free survival or progression-free survival in our series.

There were three cases with recurrence in our study. Two cases were incidentally diagnosed after debulking surgery performed

Table 2

Univariate analysis of overall survival and disease-free survival

	Overall survival			Recurrence-free survival		
	HR	95% CI	*p*	HR	95% CI	*p*
Age (>mean/<mean)	2.16	0.22-20.95	0.51	0.39	0.04-4.33	0.44
Gender (male/female)	1.02	0.13-7.78	0.99	NA	NA	NA
Emergent surgery (yes/no)	1.59	0.16-15.64	0.69	1.77	0.16-19.59	0.64
Operation (RS/AP)	0.58	0.06-5.67	0.64	0.02	0-329.59	0.44
Perforation (yes/no)	NA	NA	NA	6.22	0.56-68.61	0.14
CEA level (>5/ <5)	1.38	0.09-22.0	0.822	NA	NA	NA
NLR (>3/ <3)	0.76	0.08-7.65	0.82	0.60	0.05-6.64	0.68
PLR (>300/ <300)	3.46	0.31-38.31	0.31	0.04	0-26012.47	0.63
PMP (yes/no)	NA	NA	NA	NA	NA	NA
M stage				…	…	<0.01
M0	NA	NA	NA	1.00	…	…
M1a	NA	NA	NA	…	…	…
M1b	NA	NA	NA	57.96	5.16-651.23	<0.01

AP = appendectomy; CEA = carcinoembryonic antigen; HR = hazard ratio; NA = not available; NLR = neutrophil-to-lymphocyte ratio; PLR = platelet-to-lymphocyte ratio; PMP = pseudomyxoma peritonei; RS = radical surgeries.

by gynecologists. They got pT4aM1b LAMN, but they did not receive followed treatment. Recurrences were found 4 and 22 months after initial surgery by abdominal CT. One of them received salvage folinic acid, flourouracil, irinotecan (5-flourouracil, leucovorin, and irinotecan) and bevacizumab treatment, and followed right hemicolectomy and HIPEC. No recurrence developed in following 10 months. The other case got lost follow-up. The third case was referred from other hospital after drainage right lower quadrant intraabdominal abscess which was caused by ruptured appendix. She underwent appendectomy in our hospital, and the pathological report showed LAMN, pathological carcinoma in situ (pTis). Recurrence developed 5 months later, and right hemicolectomy was performed. She refused further treatment then. For the last case, though we did not have pathological data of ascites, we highly suspected the presence of M1b disease of LAMN or malignant cell spillage due to perforation.

The link between local/systemic inflammation and solid tumors has been researched for many years,[21] and these inflammations were used for predicting prognosis in different cancers.[11,12] In a previous study, for malignant appendiceal tumors, NLR and PLR did not appear to be predictive of OS, but the sample size was also relatively small.[13] Their result demonstrated histological grade was more important than inflammatory markers. Our conclusion is compatible with their study. Furthermore, our univariate analysis showed M1b stage was the only significant factor for RFS, which is also compatible with another study.[5] In our opinion, the reason may be that there were 23% patients diagnosed with acute appendicitis, which increased NLR. However, not every patient with appendicitis presented cellular PMP, which mean M1b stage, so NLR-H could not be predictive of OS or RFS in this series.

PMP is associated with inflammation and fibrosis, and many circulating cytokines, such as interleukin (IL)-6, IL-8, and macrophage inflammatory protein-1b (MIP-1b) play a central role in its biology.[22] NLR and PLR were inexpensive and inflammation could be easily estimated in PMP patients. In a previous study, Kusamura et al[23] proposed that NLR could be a prognosticator for OS in patients with PMP treated with CRS and HIPEC. For appendix-originated PMP, high-NLR (>2.79) predicts worse OS after CRS and HIPEC treatment.[24] The selected cutoff value of NLR was similar to ours, but the two results were distinct. A previous study[22] proposed that infection or damage-related inflammatory cytokines, such as IL-1, IL-2, tumor necrosis factor (TNF)-a, and interferon (IFN)-γ, do not elevate in PMP, whereas IL-6, IL-8, and MIP-1b are more prominent in PMP formation. In our study, some patients underwent emergent operations due to acute appendicitis. Therefore, they were not proper to be compared to patients who received elective surgery for LAMN by pretreatment NLR or PLR. Furthermore, it was too difficult to analyze OS and RFS in a small size patient pool.

Appendiceal perforation sometimes happens during surgery, which causes PMP and may lead to peritoneal recurrence. In our study, NLR-H group had higher rate of perforation ($p = 0.04$). In total, 14 patients (24.6%) had perforation, but this did not influence the RFS ($p = 0.14$). However, our two M1b cases developed recurrence, and M1b staging is the only significantly poor prognostic factor of RFS ($p < 0.01$). Such developments indicated that cellular mucinous caused peritoneal recurrence. This conclusion was compatible with other studies.[5,10,18] PLR-H may indicate higher rate of PMP ($p = 0.01$); however, unfortunately, both NLR-H and PLR-H could not be used as predictors of cellular ascites. Therefore, cautious handling of mucinous appendiceal tumors during surgery is crucial to avoiding perforation. Once perforation occurs, the complete removal of all mucinous ascites becomes almost impossible. Intraoperative frozen sections may be needed to assess the cellularity of ascites. Secondary or even serial operations are possible, and this should be communicated to patients. This has led some researchers to propose CRS combined with HIPEC for malignant, mucinous appendiceal tumors, but only one of our patients received this treatment. Long-term follow-up is needed.

This retrospective study, to our knowledge, is the first study investigating the association between NLR, PLR, and LAMN specifically. However, some limitations to the study should be noted. This is a retrospective study, which inevitably incurred selection biases. Second, most of our cases were pTis diseases, which have excellent prognosis, and we lacked representative cases of diseases at other stages. Due to a relative benign nature course of LAMN, only three patients had recurrence during follow-up and four mortality cases did not die of LAMN. Thus LAMN-specific survival could not be evaluated. Third, histological data were lacking in two PMP cases because of emergent surgeries. Fourth, the study was performed on a small sample size, which is unavoidable due to the rarity of LAMN. Lastly, some data were missing because of incomplete surveys during emergent surgeries or missing data in our electronic database.

In conclusion, in this study, NLR and PLR levels did not influence OS and RFS. Perforated LAMN and type of surgery were

not significant prognosticators in OS and RFS. Cellular mucin PMP (M1b disease) was the only crucial factor that influenced RFS in our study.

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