INTRODUCTION

Parotid gland carcinoma (PGC) represents 0.3% of all cancers and 1% to 3% of all head and neck cancers, and has different malignant phenotypes and prognoses.1,2 Owing to its low incidence and histological diversity, the prognoses of patients with PGC remain unclear. Previous studies have revealed that prognostic factors for such patients include age,3 TNM classification,1,4 preoperative facial paralysis,5 high-risk histology,6 perineural invasion,5 lymphovascular invasion,4 and surgical margin.8

Recent studies have demonstrated the relevance of inflammatory, nutritional, and immunological markers as predictors of prognosis in patients with various cancers.7–13 These markers include the modified Glasgow prognostic score (mGPS),11 C-reactive protein (CRP)-to-albumin ratio (CAR),14,15 neutrophil-to-lymphocyte ratio (NLR),12 platelet-to-lymphocyte ratio (PLR),13 and lymphocyte-to-monocyte ratio (LMR).7–9 Previous investigations have explored the prognostic value of the NLR in pediatric patients with PGC16 as well as the mGPS, CRP, and NLR in patients with salivary duct carcinoma.17 However, the importance of these prognostic markers in patients with PGC overall (ie, not specific subgroups) has not been fully established.

In the present study, we investigated the role of blood test–derived inflammatory, nutritional, and immunological markers as predictors of prognoses in patients with PGC who underwent curative treatment.
because they lacked blood test data acquired within 1 month prior to surgery. Two patients with distant metastasis at diagnosis and one with clinical evidence of acute infection were also excluded. Finally, 101 patients were included in this study. Their characteristics (age, sex, TNM classification, surgical findings, pathologic characteristics, any pretreatment for facial nerve paralysis, and follow-up examinations) were collected from their medical records. The TNM classification was based on the eighth edition of the American Joint Committee on Cancer staging manual. The patients were histologically diagnosed using the World Health Organization (WHO) criteria. The high-risk histology was defined based on the description of WHO criteria; if not described, we did not define as high-risk histology. Postoperative follow-up was performed at regular intervals (1- to 3-month intervals during the first 3 postoperative years, 3- to 6-month intervals during the fourth and fifth years, and 6- to 12-month intervals from the sixth year onward). Computed tomography or magnetic resonance imaging was performed every 3-6 months in year one and every 6-12 months from year two onward.

Treatment
All patients underwent partial parotidectomy, total parotidectomy, extended total parotidectomy, or parotidectomy plus neck dissection as a primary treatment. Facial nerves that were directly involved with the tumor were sacrificed; all others were preserved. Neck lymph node dissection was concurrently performed for patients with positive neck nodes. In principle, adjuvant radiotherapy or chemoradiotherapy was administered to patients with adverse features such as high histological grade, close or positive margins, perineural invasion, lymph node metastases, and/or lymphatic/vascular invasion. Patients were generally irradiated at 2.0 Gy/fraction, five times a week for a total dose of 50–60 Gy, although their performance statuses and any comorbidities were considered before treatment. Patients in whom resectable locoregional recurrences or neck metastases were detected during follow-up underwent additional resections immediately. Some patients received chemotherapy as palliative treatment for persistent disease or after the discovery of distant metastases; these included tegafur/uracil; tegafur/gimeracil/oteracil; hereceptin and docetaxel; and docetaxel, cisplatin, and fluorouracil.

Scoring Systems
The LMR was defined as the absolute lymphocyte count (ALC) divided by the absolute monocyte count (AMC). The NLR was defined as the absolute neutrophil count (ANC) divided by the ALC. The PLR was defined as the absolute platelet count (APC) divided by the ALC. The CAR was defined as the absolute monocyte count (AMC) divided by the ALC. The NLR was defined as the absolute platelet count (APC) divided by the ALC. The CAR was defined as the ALC divided by the absolute monocyte count (AMC). The LMR was defined as the serum albumin (< 3.5 g/dL) and elevated CRP level (≥ 0.5 mg/dL) were allocated a score of 2, while all others were assigned a score of 1. All markers levels were obtained during blood tests performed within 1 month before surgery.

Statistical Analysis
The 5-year overall survival (OS) and disease-free survival (DFS) rates were determined using the Kaplan–Meier method under various conditions. All survival periods were calculated from the date of surgery to that of the event or of the latest follow-up visit. The following variables were included: age, sex, T classification, N classification, TNM stage, existence of pretreatment facial nerve paralysis, high-risk histology, perineural invasion, surgical margin, LMR, NLR, PLR, CAR, mGPS, ALC, AMC, ANC, APC, CRP, and albumin. On univariate analysis, the OS and DFS of patients in the different subgroups were assessed using the log-rank test. Factors that were significant on univariate analysis were then analyzed using multivariate analyses, which were performed using a Cox proportional hazards model with a backward-selection procedure. To avoid multicollinearity, the correlations between variables were evaluated using Pearson’s correlation coefficient. When two or more variables were strongly correlated, the most significant representative of that group was selected. The distributions of categorical variables between the two groups were compared using the chi-square or Fisher’s exact test. Associations between continuous variables were assessed using the Mann–Whitney test. All statistical analyses were performed using SPSS.

| TABLE I. Patient Characteristics. |
|-----------------------------------|
| Variables | Cases (N = 101) | % |
| Age       | 59 (13–85) | 62%/38% |
| Sex       | 63/38 | 62%/38% |
| Histology | 35 | 35% |
| Mucoepidermoid carcinoma | 15 | 15% |
| Acinic cell carcinoma | 14 | 14% |
| Salivary duct carcinoma | 9 | 9% |
| Adenoid cystic carcinoma | 9 | 9% |
| Carcinoma ex pleomorphic adenoma | 8 | 8% |
| Adenocarcinoma, not otherwise specified | 6 | 6% |
| Basal cell adenocarcinoma | 3 | 3% |
| Squamous cell carcinoma | 3 | 3% |
| Sebaceous carcinoma | 1 | 1% |
| Carcinosarcoma | 1 | 1% |
| Lymphoepithelial carcinoma | 1 | 1% |
| Small cell carcinoma | 1 | 1% |
| Unclassified | 1 | 1% |
| T classification | 15/31/15/40 | 15%/31%/31%/40% |
| N classification | 74/8/18/1 | 73%/8%/1%/1% |
| TNM stage | 13/29/15/44 | 13%/29%/15%/44% |
| Pretreatment facial nerve paralysis | 23/78 | 23%/77% |
| Yes/No | 62/39 | 61%/39% |
| High-risk histology | 38/63 | 38%/62% |
| Perineural invasion | 43/58 | 43%/57% |

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TABLE II. Univariate Analyses of Prognostic Factors for OS and DFS in PGC Patients.

| Variables                        | Cases | 5-year OS (%) | P-value | 5-year DFS (%) | P-value |
|----------------------------------|-------|---------------|---------|----------------|---------|
| Overall                          | 101   | 73.1%         |         | 62.8%          |         |
| Age                              |       |               |         |                |         |
| < 60                             | 55    | 86.8%         | 0.001   | 75.9%          | 0.002   |
| ≥ 60                             | 46    | 56.4%         |         | 47.5%          |         |
| Sex                              |       |               |         |                |         |
| Male                             | 63    | 63.0%         | 0.018   | 61.7%          | 0.394   |
| Female                           | 38    | 90.7%         |         | 65.0%          |         |
| T classification                 |       |               |         |                |         |
| 1,2                              | 46    | 91.8%         | < 0.001 | 81.4%          | < 0.001 |
| 3,4                              | 55    | 59.4%         |         | 48.7%          |         |
| N classification                 |       |               |         |                |         |
| 0                                | 74    | 89.4%         | < 0.001 | 78.5%          | < 0.001 |
| 1,2,3                            | 27    | 27.3%         |         | 19.0%          |         |
| TNM stage                        |       |               |         |                |         |
| I, II                            | 42    | 96.9%         | < 0.001 | 85.9%          | < 0.001 |
| III, IV                          | 59    | 57.7%         |         | 47.8%          |         |
| Pretreatment facial nerve paralysis |     |               |         |                |         |
| Yes                              | 23    | 29.2%         | < 0.001 | 21.9%          | < 0.001 |
| No                               | 78    | 86.2%         |         | 75.9%          |         |
| High-risk histology              |       |               |         |                |         |
| Yes                              | 62    | 59.2%         | < 0.001 | 50.6%          | 0.001   |
| No                               | 39    | 97.2%         |         | 82.9%          |         |
| Perineural invasion              |       |               |         |                |         |
| Yes                              | 38    | 49.7%         | < 0.001 | 35.1%          | < 0.001 |
| No                               | 63    | 88.2%         |         | 80.8%          |         |
| Surgical margin                  |       |               |         |                |         |
| Positive                         | 43    | 61.4%         | 0.011   | 49.0%          | 0.010   |
| Negative                         | 58    | 83.3%         |         | 74.2%          |         |
| LMR                              |       |               |         |                |         |
| ≥5.54                            | 58    | 89.5%         | < 0.001 | 79.5%          | < 0.001 |
| <5.54                            | 41    | 52.1%         |         | 42.6%          |         |
| NLR                              |       |               |         |                |         |
| ≥2.43                            | 59    | 84.6%         | 0.004   | 74.7%          | 0.004   |
| <2.43                            | 40    | 54.7%         |         | 47.8%          |         |
| PLR                              |       |               |         |                |         |
| ≥209                             | 86    | 76.1%         | 0.013   | 66.8%          | 0.106   |
| <209                             | 13    | 43.1%         |         | 26.4%          |         |
| CAR                              |       |               |         |                |         |
| ≥0.077                           | 75    | 76.9%         | 0.001   | 68.1%          | 0.021   |
| <0.077                           | 18    | 41.2%         |         | 37.7%          |         |
| mGPS                             |       |               |         |                |         |
| 0                                | 76    | 74.8%         | 0.024   | 66.2%          | 0.208   |
| 1,2                              | 16    | 45.6%         |         | 39.7%          |         |
| ALC                              |       |               |         |                |         |
| ≥1742                            | 47    | 83.5%         | 0.019   | 78.5%          | 0.010   |
| <1742                            | 52    | 62.7%         |         | 49.9%          |         |
| AMC                              |       |               |         |                |         |
| ≥231                             | 26    | 95.2%         | 0.004   | 86.4%          | 0.029   |
| <231                             | 73    | 65.0%         |         | 55.9%          |         |

(Continues)
with OS. In addition, T classification (HR 0.317, \( P = 0.030 \)), N classification (HR 0.266, \( P = 0.001 \)), perineural invasion (HR 0.428, \( P = 0.044 \)), and LMR (HR 3.005, \( P = 0.010 \)) were independently associated with DFS. Since there were strong correlations between T classification and TNM stage, as well as between CAR and CRP, only the T classification and CRP were selected as prognostic factors. The Kaplan–Meier curves for OS and DFS divided by significant prognostic factors are shown in Figures 1 and 2.

### DISCUSSION

Our study demonstrated that the 5-year OS and DFS among patients with PGC who underwent curative treatment were 73.1% and 62.8%, respectively. These rates were previously reported to be 46% to 82.9\%1,3-6,21-24 and 60.2% to 74.4\%,3-5,25 respectively; our results are consistent with those of previous studies, given that the treatment protocol at our institution is based on the National Comprehensive Cancer Network guidelines for head and neck cancers.26

Multivariate analysis revealed that N classification, perineural invasion, and LMR were significant predictors of OS and DFS in our study; moreover, T classification was a significant predictor of DFS. In previous studies, TNM classification 1,3,21,23,24 and perineural invasion21,24 were also found to be significant prognostic factors; however, in contrast to such studies, in our study age,3,6,23 high-risk histology,3,21 preoperative facial paralysis,21,23 and surgical margin5 showed no consistent association with survival. The \( P \)-values of high-risk histology and preoperative facial paralysis were close to significant (\( P = 0.057 \) and 0.084 for OS, respectively); therefore, these factors may be found to be statistically significant in a larger case series. It has also been reported that age,1 high-risk histology,6 preoperative facial paralysis,1

### TABLE III.
Multivariate Analyses of Prognostic Factors for OS and DFS in PGC Patients.

| Variables                  | OS          | DFS          |
|----------------------------|-------------|--------------|
|                            | HR 95% CI   | \( P \)-value| HR 95% CI   | \( P \)-value |
| Age                        | 0.569 0.200–1.615 .289 |               | 0.507 0.243–1.058 .07 |
| Sex                        | 0.409 0.108–1.555 .190 | -            | -            |
| T classification           | 0.799 0.174–3.683 .772 | 0.317 0.113–0.892 .030 |
| N classification           | 0.214 0.085–0.540 .001 | 0.266 0.122–0.581 .001 |
| Pretreatment facial nerve paralysis | 0.417 0.155–1.123 .084 | 0.592 0.243–1.438 .247 |
| High-risk histology        | 0.133 0.017–1.065 .557 | 0.620 0.190–2.019 .427 |
| Perineural invasion        | 0.286 0.109–0.754 .111 | 0.428 0.188–0.977 .044 |
| Surgical margin            | 0.658 0.147–2.936 .583 | 0.948 0.319–2.816 .923 |
| LMR                        | 3.658 1.286–10.403 .015 | 3.006 1.306–6.912 .010 |
| NLR                        | 1.643 0.415–6.502 .479 | 1.773 0.609–5.156 .293 |
| PLR                        | 0.531 0.123–2.281 .394 | -            | -            |
| mGPS                       | 2.252 0.806–6.293 .122 | -            | -            |
| ALC                        | 0.353 0.097–1.286 .114 | 2.065 0.764–5.581 .153 |
| AMC                        | 0.377 0.043–3.333 .380 | 1.108 0.327–3.756 .869 |
| CRP                        | 0.549 0.228–1.317 .179 | 1.130 0.475–2.687 .783 |

Statistically significant values are marked in bold.

ALC = absolute lymphocyte count; AMC = absolute monocyte count; CRP = C-reactive protein; DFS = disease-free survival; LMR = lymphocyte-to-monocyte ratio; mGPS = modified Glasgow prognostic score; NLR = Neutrophil-to-lymphocyte ratio; OS = Overall survival; PLR = Platelet-to-lymphocyte ratio.

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and surgical margin\textsuperscript{3,21} were not significant prognostic factors. As such, the prognostic values of these factors remain controversial.

We found that the LMR was a significant predictor of the OS and DFS in patients with PGC who were receiving curative treatment. To the best of our knowledge, we are the first to report a correlation between a low LMR and poor prognosis in patients with this disease. Our results are consistent with those of previous studies showing LMR to be a prognostic factor in B cell lymphoma,\textsuperscript{7} colon cancer,\textsuperscript{8} and renal cell carcinoma.\textsuperscript{9} The specific mechanism underlying how LMR influences prognosis remains unclear; however, both lymphocytes and monocytes are related to the tumor microenvironment, as tumor-infiltrating lymphocytes and tumor-associated macrophages\textsuperscript{8} play critical roles in tumor immunity. Zhu et al. reported that the preoperative peripheral LMR is correlated with the tumor-infiltrating lymphocytes-to-tumor-associated macrophage ratio in the tissues of postoperative patients with esophageal squamous cell carcinoma.\textsuperscript{27} The presence of tumor-infiltrating lymphocytes indicates the activation of an effective anti-tumor cellular immune response\textsuperscript{28} that includes the induction of active tolerance and apoptosis.\textsuperscript{29} Tumor-associated macrophages play a role in secreting pro-inflammatory cytokines (interleukin [IL]-1, IL-4, IL-6, IL-10, IL-13, tumor necrosis factor, and transforming growth factor-\(\beta\)); this promotes tumor-associated angiogenesis, invasion, and migration while suppressing anti-tumor immunity.\textsuperscript{30,31} LMR might represent the balance of host immune status and tumor malignancy, and is an inexpensive and easily measurable marker calculated from parameters obtained during routine blood tests. Therefore, patients with PGC who have low LMRs and are amenable to treatment may be recommended to undergo adjuvant treatments such as radiotherapy to improve their prognoses after a thorough evaluation of the patients’ immunological, nutritional, and performance status.

The roles of other blood test-derived inflammatory, nutritional, and immunological markers in PGC were unclear. As in previous studies of pediatric patients with PGC and patients with salivary duct carcinoma,\textsuperscript{16,17} the NLR and mGPS were significant prognostic predictors according to our univariate analysis; however, in contrast to these studies, the NLR and mGPS were not significant prognostic predictors on multivariate analysis. These discrepancies may be attributable to the pathological variations in this study. It was previously reported that malignant bladder cancer,\textsuperscript{32} renal cell carcinoma,\textsuperscript{33} PGC,\textsuperscript{34} and epithelial ovarian cancer\textsuperscript{35} of high pathological grades exhibit higher NLR and GPS than do those with low pathological grades. Our study included PGCs of all pathological grades; as such, the ANC, ALC, CRP, and albumin might be more closely associated with the prognosis of patients with salivary duct carcinoma than are the ALC and AMC.

There were several limitations in this study. First, this was a retrospective investigation conducted at a single institution; as such, the sample size was small and may have been subject to inevitable bias. Second, we could not fully evaluate lymphovascular invasion, a potentially important prognostic factor, due to a lack of data in the records. Third, this study did not investigate

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\text{Disease Free Survival (\%)}
\]

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\begin{array}{cccccccc}
\text{T = 1,2} & \text{T = 3,4} & \text{Number at risk} & \text{Months} & \text{Disease Free Survival (\%)} \\
\text{T = 1,2} & \text{T = 3,4} & \text{Number at risk} & \text{Months} & \text{Disease Free Survival (\%)} \\
46 & 55 & 0 & 12 & 24 & 36 & 48 & 60 & 100 \\
38 & 37 & 4 & 38 & 35 & 30 & 25 & 25 & 21 \\
51 & 30 & 8 & 51 & 47 & 40 & 36 & 32 \\
47 & 24 & 14 & 47 & 18 & 15 & 14 & 10 \\
40 & 24 & 7 & 40 & 18 & 15 & 14 & 10 \\
36 & 14 & 4 & 36 & 18 & 15 & 14 & 10 \\
32 & 7 & 3 & 32 & 18 & 15 & 14 & 10 \\
\end{array}
\]

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\begin{array}{cccccccc}
\text{N = 0} & \text{N \geq 1} & \text{Number at risk} & \text{Months} & \text{Disease Free Survival (\%)} \\
\text{N = 0} & \text{N \geq 1} & \text{Number at risk} & \text{Months} & \text{Disease Free Survival (\%)} \\
74 & 27 & 0 & 12 & 24 & 36 & 48 & 60 & 100 \\
63 & 12 & 5 & 63 & 7 & 5 & 4 & 3 \\
57 & 8 & 1 & 57 & 7 & 5 & 4 & 3 \\
50 & 5 & 1 & 50 & 7 & 5 & 4 & 3 \\
46 & 4 & 1 & 46 & 7 & 5 & 4 & 3 \\
39 & 3 & 1 & 39 & 7 & 5 & 4 & 3 \\
27 & 2 & 1 & 27 & 7 & 5 & 4 & 3 \\
\end{array}
\]

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\begin{array}{cccccccc}
\text{LMR \leq 5.54} & \text{LMR > 5.54} & \text{Number at risk} & \text{Months} & \text{Disease Free Survival (\%)} \\
\text{LMR \leq 5.54} & \text{LMR > 5.54} & \text{Number at risk} & \text{Months} & \text{Disease Free Survival (\%)} \\
58 & 54 & 0 & 12 & 24 & 36 & 48 & 60 & 100 \\
58 & 54 & 4 & 58 & 47 & 41 & 36 & 36 & 30 \\
54 & 47 & 8 & 54 & 41 & 26 & 22 & 18 & 13 \\
50 & 41 & 12 & 50 & 26 & 22 & 18 & 13 & 12 \\
46 & 36 & 16 & 46 & 26 & 22 & 18 & 13 & 12 \\
39 & 30 & 20 & 39 & 26 & 22 & 18 & 13 & 12 \\
32 & 16 & 12 & 32 & 26 & 22 & 18 & 13 & 12 \\
\end{array}
\]
the effect of the adjusted treatment according to LMR. In the future, larger, multi-institutional prospective investigations are required to validate the findings of this study, and to investigate the effect of adjusted treatment protocols, which consider LMR as a factor, on the prognosis of patients with PGC.

CONCLUSION

Our study revealed that the LMR, T classification, N classification, and perineural invasion status are useful for predicting the prognosis of patients with PGC who have undergone curative treatment. The LMR is an inexpensive and easily measurable marker calculated from routine blood test data before treatment. Patients with PGC who are diagnosed with low LMRs and are amenable to treatment may be recommended to receive adjuvant treatment for improving their prognoses after a thorough evaluation of the patients’ immunological, nutritional, and performance status.

BIBLIOGRAPHY

1. Mercante G, Marchese C, Giannarelli D, et al. Oncological outcome and prognostic factors in malignant parotid tumours. J Craniofac Surg 2014;42:59–65.
2. Renzhan AG, Gleave EN, Slevin NJ, McGurk M. Clinicopathological and treatment-related factors influencing survival in parotid cancer. Br J Cancer 1999;80:1296–1300.
3. Ervinc BM, Shah MD, Bruch G, et al. Outcome analysis of 215 patients with parotid gland tumors: a retrospective cohort analysis. J Otolaryngol Head Neck Surg 2015;44:43.
4. Kim YH, Chung WK, Jeong JU, et al. Evaluation of prognostic factors for the parotid cancer treated with surgery and postoperative radiotherapy. Clin Exp Otorhinolaryngol 2019;13:69–76.
5. Vander Poorten VL, Hart AA, van der Laan BP, et al. Prognostic index for patients with parotid carcinoma: external validation using the nationwide 1985-1994 Dutch Head and Neck Oncology Cooperative Group database. Cancer 2003;97:1453–1463.
6. Shang J, Wu Y, Wang W, Wang K, Ge M. Analysis of prognostic risk factors and treatment of parotid cancer. Oncol Lett 2012;3:1307–1310.
7. Li ZM, Huang JJ, Xia Y, et al. Blood lymphocyte-to-monocyte ratio identifies high-risk patients in diffuse large B cell lymphoma treated with R-CHOP. PLoS One 2012;7:e41658.
8. Stutz M, Pichler M, Absenger G, et al. Preoperative lymphocyte to monocyte ratio predicts clinical outcome in patients with stage III colon cancer. Br J Cancer 2014;110:435–440.
9. Luca I, de Martino M, Hofbauer SL, Zamani N, Shariat SF, Klutte T. Comparison of the prognostic value of pretreatment measurements of systemic inflammatory response in patients undergoing curative resection of clear cell renal cell carcinoma. World J Urol 2015;33:2045–2052.
10. Kimoshita A, Onoda H, Imai N, et al. The Glasgow prognostic score, an inflammation based prognostic score, predicts survival in patients with hepatocellular carcinoma. BMC Cancer 2013;13:52.
11. Nakayama M, Tabuchi K, Hara A. Clinical utility of the modified Glasgow prognostic score in patients with advanced head and neck cancer. Head Neck 2015;37:1745–1749.
12. Wang DS, Luo HY, Qiu MZ, et al. Comparison of the prognostic values of various inflammation based factors in patients with pancreatic cancer. Med Oncol 2012;29:3092–3100.
13. Zheng RR, Huang M, Jin C, Wang HC, Yu JT, Zeng LC, Zheng FY, Lin P. Zn12-acetyl-L-aspartate: a novel predictor of prognosis. Oncotarget 2016;7:35219–35224.
14. Mikoshi T, Ozawa H, Saito S, et al. Usefulness of hematological inflammatory markers in predicting severe side effects from induction chemotherapy in head and neck cancer patients. Anticancer Res 2019;39:3059–3065.
15. Tominaa T, Nonaka T, Sumida Y, Hidaka S, Sawai T, Nagayaasu T. The C-reactive protein to albumin ratio as a predictor of severe side effects of adjuvant chemotherapy in stage III colorectal cancer patients. PLoS One 2016;11:e0167967.
16. Seng D, Fang Q, Li P, Liu F, Liu S. Prognostic value of the pretreatment neutrophil-to-lymphocyte ratio in pediatric parotid cancer. Front Pediatr 2019;7:207.
17. Kawakita D, Tada Y, Imanishi Y, et al. Impact of hematological inflammatory markers on clinical outcome in patients with salivary duct carcinoma: a multi-institutional study in Japan. Oncotarget 2017;8:10833–10841.
18. Edge SB, Byrd DR, Compton CC, Fritx AG, Greene FL, Trotti A. AJCC Cancer Staging Manual 8th ed. New York, NY: Springer; 2018.
19. El-Naggar AK, JCC J, Grandis JR, Takata T, Grandis J, Shotreg P. WHO Classification of Head and Neck Tumours. 4th ed. Lyon: IARC; 2017.
20. Toiyama Y, Miki C, Inoue Y, Tanaka K, Mohri Y, Kusunoki M. Evaluation of an inflammation-based prognostic score for the identification of patients requiring postoperative adjuvant chemotherapy for stage II colorectal cancer. Exp Ther Med 2011;2:95–101.
21. Paderno A, Tomaselli M, Mattavelli D, Battocchio S, Lombardi D, Nicolai P. Primary parotid carcinoma: analysis of risk factors and validation of a prognostic index. Eur Arch Otorhinolaryngol 2018;275:2829–2841.
22. Parry J, Cummins C, Redman V, Wilson S, Woodman C. Incidence and survival of malignant parotid tumours in the west midlands region 1977-1986. Clin Oncol (R Coll Radiol) 1995;3:150–153.
23. Vander Poorten VL, Balm AJ, Hilgers FJ, et al. The development of a prognostic score for patients with parotid carcinoma. Cancer 1999;83:2057–2067.
24. Lu CH, Liu CT, Chang PH, et al. Validation and comparison of the 7th edition of the American joint committee on cancer staging system and other prognostic models to predict relapse-free survival in Asian patients with parotid cancer. J Cancer 2016;7:1833–1841.
25. Molteni G, Molinari G, Ghirelli M, et al. Oncological outcomes of parotid gland malignancies: a retrospective analysis of 74 patients. J Stomatol Oral Maxillofac Surg 2019;120:310–316.
26. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Head and Neck cancers, Version 3 2019. Sep 16, 2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf.
27. Zhu Y, Li M, Bo C, et al. Prognostic significance of the lymphocyte-to-monocyte ratio and the tumor-infiltrating lymphocyte to tumor-associated macrophage ratio in patients with stage III/N0 esophageal squamous cell carcinoma. Cancer Immunol Immunother 2017;66:343–354.
28. Rabinovich H, Cohen R, Bruderman I, Steiner Z, Klajman A. Functional analysis of mononuclear cells infiltrating into tumors: lysis of autologous human tumor cells by cultured infiltrating lymphocytes. Cancer Res 1987;47:173–177.
29. Rosenberg SA. Progress in human tumour immunology and immunotherapy. Nat Rev Cancer 2004;4:380–394.
30. Fridman WH, Pages F, Sautes-Fridman C, Galon J. The immune contexture of human tumours: impact on clinical outcome. Nat Rev Cancer 2011;11:298–306.
31. Pollard JW. Tumour-educated macrophages promote tumour progression and metastasis. Nat Rev Cancer 2004;4:71–78.
32. Tang X, Wang S, An C, Du P, Yang Y. Preoperative high neutrophil-to-lymphocyte ratio is associated with high-grade bladder cancer. Anticancer Res 2017;37:4659–4663.
33. Calisank S. Elevated neuron to lymphocyte and platelet to lymphocyte ratios predict high grade and advanced stage renal cell carcinoma. Int J Biol Markers 2019;34:15–19.
34. Damar M, Dinç AE, Erdem D, et al. Pretreatment neutrophil-lymphocyte ratio in salivary gland tumors is associated with malignancy. Otolaryngol Head Neck Surg 2016;155:988–996.
35. Zhu J, Wang H, Liu CC, Lu Y, Tang H. The Glasgow prognostic score (GPS) is a novel prognostic indicator in advanced epithelial ovarian cancer: a multicenter retrospective study. J Cancer Res Clin Oncol 2016;142:2389–2395.