Impact of serum albumin concentration and neutrophil–lymphocyte ratio score on gastric cancer prognosis

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Abstract
Introduction/aim Serum albumin concentration (COA) and neutrophil–lymphocyte ratio (NLR) could reflect immunological and nutritional status. We aim to evaluate the impact of COA-NLR score on the prognosis of gastric cancer (GC).

Material and methods We perform a retrospective analysis on a database of 637 GC cases, between January 2010 and December 2017. In 396 patients, the inclusion criteria for this study were met (non-resectional or palliative surgery were excluded). Analytic data was only available in 203 patients. COA-NLR score was defined as follows: COA under 35 g/L and NLR value of 2.585 or higher, score 2; one of these conditions, score 1; and neither, score 0.

Results In our population (n = 203), 87 patients were classified as score 0, 82 as score 1 and 34 as score 2. COA-NLR score was significantly associated with DFS (HR 1.674; CI 95% 1.115–2.513; p = 0.013) and with OS (HR 2.072; CI 95% 1.531–2.805; p < 0.001). Kaplan–Meier curve analysis (log rank test) revealed that a higher score of COA-NLR predicted a worse OS (p < 0.001) and DFS (p = 0.03). COA-NLR was an independent prognostic factor for OS when adjusted to pStage and age (adjusted HR 1.566; CI 95% 1.145–2.143; p = 0.005).

Conclusions Preoperative COA-NLR score was significantly associated with worse OS and DFS and, in this way, with worse prognosis on GC patients submitted to curative-intent resectional surgery.

Keywords Serum albumin concentration · Neutrophil-to-lymphocyte ratio · Gastric cancer prognosis · Curative-intent resectional surgery

Introduction

Gastric cancer (GC) is the fifth most common malignancy and the third leading cause of cancer-related death worldwide, according to GLOBOCAN 2018 [1].

Surgical resection alongside with an appropriate lymphadenectomy remains the most effective therapy for gastric cancer. Despite the improvement of surgical techniques and medical therapies, GC prognosis remains unfavourable [2]. Therefore, predictors of GC prognosis could support a better multidisciplinary clinical decision, founded in a more tailored perioperative management, treatment and follow-up strategies [2–5].

Diverse predictors of prognosis based on tumour behaviour, surgery approach and host-related features are being acknowledged [6–10]. Regarding host-related features, patients’ immunological, nutritional status and systemic inflammatory response (SIR) have been associated with cancer prognosis. NLR is an easy, routinely and inexpensive marker of SIR that has been reported as a predictor of prognosis, in various clinical situations, namely on malignancy disorders [11–13]. Commonly, cancer patients are malnourished, either due to SIR and catabolic status that can induce muscle wasting and weight loss, or due to gastrointestinal tumour symptoms, as food intake impairment [14–16].
Serum albumin concentration (COA) reflects nutritional status and SIR [17–19]. Regarding gastric cancer, lower COA was associated with worse GC prognosis [20–23] and a recent meta-analysis showed an association between higher NLR and worse GC patient’s prognosis [13].

Sun et al. hypothesized and evidenced the COA-NLR score as an predictor of worse postoperative survival after curative-intent surgery [24]. Concerning the simplicity and reproductible applicability of this score to evaluate preoperative risk of poor GC patient’s prognosis, our aim for this study is evaluate the impact of COA-NLR score on the prognosis of GC patients, submitted to curative-intent resectional surgery in our centre.

Materials and methods

Study design and population

We performed a retrospective analysis on a prospective database of GC patients (n = 637), submitted to surgical treatment in an Upper GI Surgery Unit Tertiary Medical Center, between January 2010 and December 2017. The institutional review board approved this study (CES 298–12).

In this study, only patients with gastric adenocarcinoma who were submitted to curative-intent surgery were included. The exclusion criteria were palliative, prophylactic and completion gastrectomy (gastric stump cancer cases), non-resectional surgery, atypical resections, post-endoscopic resections, pathological stage (pStage) IV, histologic types other than adenocarcinoma and R2 resections. Patients lost to follow-up were not included in this analysis. According to this selection criteria, a total of 396 cases were included and 203 were analysed (patients with analytical data available) (Fig. 1).

Data collection

Demographic characterization of our population was based on the following parameters: age at time of surgery, gender, presence of comorbidities, American Society of Anaesthesiologists (ASA), physical status classification and body mass index (BMI) score.

Therapy approach characterization was based on the type of surgical resection and lymphadenectomy; quantification of lymph nodes retrieved; presence of conversion; presence of neoadjuvant therapy; and resection classification (R). Resection was defined as curative (R0) when all gross disease was removed with negative margins and as incomplete when verified presence of positive surgical margins (R1) and when verified residual gross disease (R2).

For clinicopathological profile description, several parameters were evaluated, as the tumour location, size (cm) and type; macroscopic type, histologic type (Laurén classification) and growth pattern (Ming classification); TNM staging (7th edition, 2010); serum C-reactive protein (CRP); and lymphatic, venous and perineural invasion. COA-NLR score analysis was based on pre-operative blood analysis, obtained until 3 weeks before the surgery, with data of serum concentration of albumin (g/L) and absolute count of neutrophils and lymphocyte (10⁹/L) to calculate NLR (neutrophil absolute count/lymphocyte absolute count). Several studies tried to determine the optimal cut-off value for several biomarkers, including NLR. In a recent systematic review,
Schiefer et al. proposed a NLR cut-off of 4.5 to be used for research purposes [25].

In our study, COA-NLR score was calculated based in our optimal cut-off values for NLR and on the standard cut-off for COA (35 g/L), as previously described [20]. The optimal cut-off value of NLR (2.585) for predicting overall survival (OS) (sensitivity 0.597 and specificity 0.574) was calculated based on the ROC curve (AUC 0.594, CI 95% 0.534–0.654, \( p = 0.002 \)) and Youden method (Fig. 2).

On that account, COA-NLR score was categorized as score COA-NLR 2 when COA under 35 g/L and NLR value equal or higher than 2.585; score COA-NLR 1 when one of these conditions was present (COA under 35 g/L or NLR value equal or higher than 2.585); and score COA-NLR 0 when neither of these conditions were present (COA equal or higher that 35 g/L and NLR lower 2.585) (Fig. 3). We also performed an analysis of the predictive value of COA-NLR according to the proposed cut-off of 4.5 for NLR (supplementary material).

Survival analysis assessed overall survival (OS) and disease-free survival (DFS). OS was defined as the period between surgery date and patient death date. For patients who had survived until the end of the observation period, their last follow-up visit data was considered for OS analysis. DFS was considered the period between the surgery and the first evidence of disease recurrence. Disease

![Fig. 2 ROC curve for NLR. Optimal cut-off value of NLR (2.585) for predicting OS, based on Youden method](image)

![Fig. 3 The fundamentals and distribution of COA-NLR score. COA-NLR score 0 \((n = 87)\), COA-NLR score 1 \((n = 82)\) and COA-NLR score 2 \((n = 34)\) ](image)

| COA-NLR 0 | COA \( \geq 35 \) g/L + NLR \( < 2.585 \) | \( n = 87 \) |
|---|---|---|
| COA-NLR 1 | COA \( \geq 35 \) g/L + NLR \( \geq 2.585 \) | \( n = 82 \) |
| COA-NLR 2 | COA \( < 35 \) g/L + NLR \( < 2.585 \) | \( n = 34 \) |
recurrence was based on clinical, radiologic or endoscopic indicators of the disease.

Median (range) follow-up was 37 (0–113) months and the last follow-up review, for the entire study population, was in September of 2019.

**Perioperative management and surgical procedure**

For the diagnosis of GC, all patients underwent upper gastrointestinal endoscopy alongside biopsy and computerized tomography (CT). Tumour staging was established according to clinical, radiological (CT) or endoscopic (endoscopic ultrasonography) features and staging laparoscopy when considered necessary (mostly in locally advanced tumours with uncertain resectability).

Preoperative clinical stage of the patient was important to determine the surgical approach and the extent of lymphadenectomy. For diffuse and proximally located tumours, the surgery approach performed was a total gastrectomy with Roux-en-Y reconstruction. Additionally, for distally located tumours, the surgery approach performed was a subtotal distal gastrectomy, using Billroth II and sporadically Roux-en-Y reconstruction, according to the patient age and comorbidities. The extent of lymphadenectomy, according to the type of gastrectomy indicated, was classified based on the third version of Japanese Gastric Treatment Guidelines from 2010. Namely, D1 or D1 + was preferably performed in cT1N0 tumours and D2 in cN + or cT2-T4 tumours [26].

After surgical intervention, all patients were admitted on a post-surgical intensive care unit for early extubation, pain control management, vigorous respiratory therapy, early mobilization and ambulation. Food intake was determined by postoperative clinical evolution. Patients were re-evaluated by the surgical team at 3-month intervals during the first year after surgery, every 6 months during the second year and annually thereafter.

**Statistical analysis**

Normal distribution of continuous variables was assessed by visual analysis of histograms, normal Q-Q plots and both Kolmogorov–Smirnov and Shapiro–Wilk tests of normality. Non-parametric test Kruskal–Wallis was used to compare means and chi-square or Fisher’s exact test was used to compare proportions, as appropriate.

ROC curves of NLR were plotted for OS and the optimal NLR cut-off value for predicting OS was determined using the Youden method.

Cumulative survival curves for OS and DFS were analysed by Kaplan–Meier (KM) method and adjusted to possible confounders, namely to pStage. Log rank test was performed to assess differences between COA-NLR score subgroups.

Univariate and multivariate analysis were performed to identify independent prognostic factors for OS and DFS. Variables significantly associated to OS and DFS in a univariate analysis were considered in a multivariate Cox proportional hazards model.

Statistical analysis was performed using SPSS® 26.0 for Windows (IBM Co., Armonk, NY, USA). Significance was assumed for p values inferior to 0.05. All p values given are results of 2-sided tests.

**Results**

**Demographics and clinicopathological characteristics**

Of the patients included (n = 396), 203 were eligible (completed analytical data) and had a mean (range) age of 66 (54–78) years and 59.6% were males. Patients were categorized according to the COA-NLR score—87 (42.9%) to score 0, 82 (40.4%) to score 1 and 34 (16.7%) to score 2. Population demographics and clinicopathological characteristics are described in Table 1. COA-NLR score subgroups differed significantly on the mean age, ASA score, tumour size, pathological T stage, pathological stage, lymphatic permeation, perineural invasion, serum CRP concentration, surgery approach, type of lymphadenectomy and mean of lymph nodes retrieved (Table 1).

**Survival analysis**

Regarding Kaplan–Meier curves (Fig. 4a, b), our population presented a mean (± SD) OS of 70.0 (± 6.8) months and a mean DFS of 86.4 (± 6.6) months. Mean OS was significantly shorter in patients with higher COA-NLR score (34.3 versus 73.3 versus 82.7 months on score 2, 1 and 0, respectively) (Table 2). When adjusted to pathological stage, mean OS was still significantly shorter in patients with higher COA-NLR score (Table 2). Furthermore, mean DFS was also significantly shorter in higher COA-NLR score patients (69.3 versus 83.9 versus 94.13 months for score 2, 1 and 0, respectively) (Table 2).

**Prognostic factors for OS and DFS**

A univariate analysis (Table 3) revealed that age, tumour size, open surgery, type of lymphadenectomy, advanced pathological stage, presence of lymphatic permeation, venous invasion and perineural invasion and higher score of COA-NLR were significantly associated with OS. A multivariate analysis (Table 3) identified age, pathological stage, type of surgical approach and COA-NLR score 2 as independent prognostic factors for OS.
| Table 1: Demographics and clinicopathological profile | All (n = 203) (%) | COA-NLR score | p value |
|-----------------------------------------------------|------------------|--------------|---------|
|                                                     |                  | 0 (n = 87)   | 1 (n = 82) | 2 (n = 34) |
| Demographics                                        |                  |              |          |           |
| Age at surgery (years), mean ± SD                  | 66.1 ± 12.5      | 61.2 ± 12.5  | 68.01 ± 11.6 | 74.0 ± 8.5 | <0.001 |
| Gender, n (%)                                       |                  |              |          |           |
| Male                                                | 121 (59.6)       | 45 (51.7)    | 53 (64.6) | 23 (67.6) | 0.134 |
| Female                                              | 82 (40.4)        | 42 (48.3)    | 29 (35.4) | 11 (32.4) |
| Comorbidities, n (%)                                |                  |              |          |           |
| Presence                                            | 166 (81.8)       | 68 (78.2)    | 68 (82.9) | 30 (88.2) | 0.409 |
| Absence                                             | 37 (18.2)        | 19 (21.8)    | 14 (17.1) | 4 (11.8)  |
| ASA score, n (%)                                    |                  |              |          |           |
| I                                                    | 29 (14.3)        | 14 (16.1)    | 11 (13.4) | 4 (11.8)  | 0.040 |
| II                                                   | 110 (54.2)       | 50 (57.5)    | 49 (59.8) | 11 (32.4) |
| III                                                  | 59 (29.1)        | 22 (25.3)    | 19 (23.2) | 18 (52.9) |
| IV                                                   | 5 (2.5)          | 1 (1.1)      | 3 (3.7)   | 1 (2.9)   |
| BMI (kg/m²) mean ± SD                               | 25.86 ± 4.19     | 26.09 ± 4.28 | 25.36 ± 3.95 | 24.84 ± 5.64 | 0.278 |
| Therapeutic approach                                |                  |              |          |           |
| Surgery approach, n (%)                             |                  |              |          |           |
| Open                                                | 113 (55.7)       | 43 (49.4)    | 43 (52.4) | 27 (79.4) | 0.009 |
| Laparoscopic                                        | 90 (44.3)        | 44 (50.6)    | 39 (47.6) | 7 (20.6)  |
| Type of resection, n (%)                            |                  |              |          |           |
| Total gastrectomy                                   | 84 (41.4)        | 41 (47.1)    | 34 (41.5) | 9 (26.5)  | 0.069 |
| Distal gastrectomy, Billroth II                     | 109 (53.7)       | 39 (44.8)    | 46 (56.1) | 24 (70.6) |
| Distal gastrectomy, Roux-en-Y                       | 10 (4.9)         | 7 (8.1)      | 2 (2.4)   | 1 (2.9)   |
| Type of lymphadenectomy, n (%)                       |                  |              |          |           |
| D1                                                  | 55 (27.1)        | 13 (14.9)    | 24 (29.3) | 18 (52.9) | <0.001 |
| D1 +                                                | 75 (36.9)        | 33 (37.9)    | 30 (36.6) | 12 (35.3) |
| D2                                                  | 73 (36.0)        | 41 (47.2)    | 28 (34.1) | 4 (11.8)  |
| Resection classification n (%)                      |                  |              |          |           |
| R0                                                  | 197 (97.0)       | 86 (98.9)    | 80 (97.6) | 31 (91.2) | 0.076 |
| R1                                                  | 6 (3.0)          | 1 (1.1)      | 2 (2.4)   | 3 (8.8)   |
| Neoadjuvant treatment, n (%)                        |                  |              |          |           |
| Presence                                            | 31 (15.3)        | 17 (19.5)    | 10 (12.2) | 4 (11.8)  | 0.342 |
| Absence                                             | 172 (84.7)       | 70 (80.5)    | 72 (87.8) | 30 (88.2) |
| Clinicopathological                                 |                  |              |          |           |
| Tumour size (cm), mean ± SD                         | 4.31 ± 2.82      | 3.84 ± 2.20  | 4.85 ± 3.14 | 5.85 ± 2.91 | <0.001 |
| Tumour location, n (%)                              |                  |              |          |           |
| Proximal third (fundus)                             | 2 (1.0)          | 1 (1.2)      | 1 (1.2)   | 0 (0.0)   | 0.798 |
| Middle third (body)                                 | 62 (30.7)        | 24 (27.9)    | 29 (35.4) | 9 (26.5)  |
| Distal third (antrum/pylorus)                       | 131 (64.9)       | 59 (68.6)    | 48 (58.5) | 24 (70.6) |
| Extensive                                           | 7 (3.5)          | 2 (2.3)      | 4 (4.9)   | 1 (2.9)   |
| Macroscopic type, n (%)                             |                  |              |          |           |
| Fungating                                           | 32 (17.0)        | 10 (12.5)    | 15 (19.7) | 7 (21.9)  | 0.133 |
| Ulcerated                                           | 54 (28.7)        | 29 (36.3)    | 18 (23.7) | 7 (21.9)  |
| Infiltrative                                        | 22 (11.7)        | 13 (16.3)    | 7 (9.2)   | 2 (6.3)   |
| Ulcero-fungating                                    | 21 (11.2)        | 5 (6.3)      | 13 (17.1) | 3 (9.4)   |
| Ulcero-infiltrative                                 | 59 (31.4)        | 23 (28.7)    | 23 (30.3) | 13 (40.6) |
| Histologic type (Lauren), n (%)                     |                  |              |          |           |
| Intestinal                                          | 88 (45.1)        | 34 (41.5)    | 37 (46.8) | 17 (50.0) | 0.602 |
| Diffuse                                             | 27 (13.8)        | 14 (17.1)    | 11 (13.9) | 2 (5.9)   |
A univariate analysis (Table 3) indicated that tumour size, open surgery, advanced pathological stage, presence of lymphatic permeation, venous invasion and perineural invasion and higher score of COA-NLR were significantly associated with DFS. However, a multivariate analysis (Table 3) identifies only pathological stage as an independent prognostic factor for DFS.

Analysis according to the proposed cut-off in literature

Using the proposed NLR cut-off of 4.5 in the literature [25], our population is categorized according to the COA-NLR score—139 (68.5%) to score 0, 49 (24.1%) to score 1 and 15 (7.4%) to score 2.

Regarding survival analysis, OS and DFS remain associated with COA-NLR score, with patients with score 0 and 1 having a better OS and DFS than patients with score 2 (Supplementary Fig. 1). COA-NLR remains significantly associated with OS in univariate analysis but loses its statistically significance in multivariate analysis when adjusted to other prognostic factors (Supplementary Table 1). Regarding DFS, both pathological stage and COA-NLR were independent prognostic factors in multivariate analysis (Supplementary Table 1).
Discussion

We intended to evaluate the impact of COA-NLR score on the prognosis of GC patients, submitted to curative-intent resectional surgery.

Gastric cancer is an inflammation-driven cancer where inflammatory responses act as an important role on tumour development and progression [27]. Patient’s outcomes depend on tumour-related factor, therapy approach features and, also, on host-related factors, such as patient’s immunological and nutritional status and SIR [6–10].

Malnutrition is known to be prevalent among cancer patients and it is associated with higher risk of postoperative complications and poor prognosis. Nutrition status evaluation is an important step of cancer care management and treatment decisions [28]. On a daily practice, the serum

![Fig. 4 Survival analysis, with Kaplan–Meier curves for OS (a) and DFS (b). Kaplan–Meier curves for OS, adjusted do pStage I (c), II (d) and III (e). KM, Kaplan–Meier; OS, overall survival; DFS, disease-free survival; pStage, pathological stage](image-url)
protein albumin has been used as a simple and reproducible parameter to assess nutrition status. Prior studies described serum albumin as an independent predictor of survival outcome in several types of cancer, such as on GC where lower COA was associated with worse GC patient’s prognosis [20–23, 29]. SIR, as an important role in the progressive nutritional and functional decline, has been displayed as a plausible confounding factor to the impact of serum albumin concentration on cancer patient’s survival [20, 21, 30]. Considering this, measurement of SIR has been included in the definition of cancer cachexia alongside with weight loss and sarcopenia [31]. It is widely accepted the relationship between inflammation and cancer development [32]. NLR has been widely presented as an index of SIR and studied in diverse clinical disorders, such as critically ill and cancer patients [9, 11–13, 33–37]. NLR proposes to evaluate the inverse relationship between neutrophils and lymphocytes, based on the SIR and on cancer patient’s immunological status. Recent studies have suggested that NLR could be used as a prognostic marker in malignance disorder, with a meta-analysis showing an association between higher NLR and worse GC patients’ prognosis [13].

Host-related factor assessment, such as nutrition, inflammatory and immune status, is essential on management and treatment strategy decisions of cancer patients. Preoperative nutritional care on moderately or severely malnourished gastrointestinal cancer patients showed to reduce postoperative morbidity and mortality [38]. Thereby, COA-NLR score, as a simple and reproducible parameter, could be used to facilitate a more practical assessment and then address a more appropriate and individualized therapy approach. Higher COA-NLR score aims to define GC patients with higher risk of poor prognosis, based on their malnutrition and inflammatory status. This score was first described by Sun et al. and was displayed as a predictor of OS, independent of TNM stage. In their study, COA-NLR score was significantly associated with poor prognosis and was able to classify GC patients into three independent groups, before curative-intent surgery [24].

In our study, patients with higher COA-NLR score were significantly characterized by higher age and higher ASA score, acknowledged predictors of poor tolerance to an illness status. Patients classified as COA-NLR 2 were also significantly associated with worse clinicopathological features such as higher tumour size, advanced pathological stage and with more lymphatic permeation and perineural invasions. Likewise, COA-NLR score 2 patients had significantly higher CRP concentration, an acute-phase protein also used to evaluate the inflammatory status. In this way, our analysis showed a significantly association between higher COA-NLR score and poor prognosis features. For our studied population, higher COA-NLR scores were significantly associated with lower OS and lower DFS. Concerning adjustment to pathological stage, survival analysis showed that, independent of pathological stage, higher COA-NLR scores were still significantly associated with lower OS. We performed a multivariate analysis that exposed age, type of surgery approach, pathological stage and COA-NLR score 2 as independent prognostic factors for OS and only pathological stage as an independent prognostic factor for DFS. In this manner, our findings support Sun et al. findings and picture COA-NLR score as a conceivable and valuable predictor of OS in GC patients.

The use of clinical biomarkers such as COA-NLR implies to dichotomize an originally continuous variable. Defining different cut-offs may have different clinical implications. We used a statistical method to determine the optimal NLR cut-off in our population, in order to have the most well-defined value for our reality. Several other cut-offs have been proposed in literature. Nevertheless, in a recent systematic review, a NLR cut-off of 4.5 is proposed as the optimal value to be used in clinical practice and research purposes [25]. In order to assess the value of this cut-off in our population, we performed the analysis in our cohort using the proposed value with similar results. Using this cut-off, COA-NLR did not show to be an independent prognostic factor for OS in our population. We believe...
### Prognostic factors for OS and DFS, univariate and multivariate analysis (Cox regression)

| Prognostic factors for OS | Prognostic factors for DFS |
|---------------------------|-----------------------------|
| **Univariate analysis**   | **Multivariate analysis**   | **Univariate analysis**   | **Multivariate analysis**   |
| **HR** | **CI 95%** | **p value** | **HR** | **CI 95%** | **p value** | **HR** | **CI 95%** | **p value** |
| Age | 1.037 | 1.022-1.052 | <0.001 | 1.028 | 1.005-1.050 | **0.015** | 1.009 | 0.991-1.027 | 0.348 |
| Tumour size | 1.130 | 1.084-1.178 | <0.001 | 1.203 | 1.142-1.268 | **<0.001** | 1.203 | 1.142-1.268 | **<0.001** |
| Type of surgery approach | | | | | | | | | |
| Laparoscopic | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Open | 1.953 | 1.422-2.682 | <0.001 | 1.686 | 1.030-2.755 | **0.038** | 1.539 | 1.009-2.349 | **0.046** |
| Type of lymphadenectomy | | | | | | | | | |
| D1 | 2.540 | 1.659-3.890 | <0.001 | 2.382 | 1.321-4.294 | **0.004** | 1.289 | 0.708-2.163 | 0.338 |
| D1+ | 4.439 | 3.043-6.474 | <0.001 | 2.923 | 1.675-5.101 | **<0.001** | 0.408 | 0.790-0.453 | 0.408 |
| D2+ | 0.570 | 0.381-0.851 | **0.006** | 1 | 1 | 1 | 1 | 1 | 1 |
| Pathologic stage | | | | | | | | | |
| I | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| II | 2.699 | 1.924-3.785 | <0.001 | 3.338 | 2.154-5.172 | **<0.001** | 3.338 | 2.154-5.172 | **<0.001** |
| III | 4.354 | 2.794-6.783 | **<0.001** | 4.354 | 2.794-6.783 | **<0.001** | 4.354 | 2.794-6.783 | **<0.001** |
| Lymphatic permeation | | | | | | | | | |
| Absence | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Presence | 2.699 | 1.924-3.785 | <0.001 | 3.338 | 2.154-5.172 | **<0.001** | 3.338 | 2.154-5.172 | **<0.001** |
| Venous invasion | | | | | | | | | |
| Absence | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Presence | 2.699 | 1.924-3.785 | <0.001 | 3.338 | 2.154-5.172 | **<0.001** | 3.338 | 2.154-5.172 | **<0.001** |
| Perineural invasion | | | | | | | | | |
| Absence | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Presence | 2.186 | 1.612-2.966 | <0.001 | 1.540 | 0.793-2.989 | 0.202 | 1.540 | 0.793-2.989 | 0.202 |
| COA-NLR | | | | | | | | | |
| COA-NLR 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| COA-NLR 1 | 1.355 | 0.800-2.296 | 0.259 | 1.209 | 0.706-2.068 | 0.489 | 1.209 | 0.706-2.068 | 0.489 |
| COA-NLR 2 | 4.205 | 2.417-7.316 | **<0.001** | 2.263 | 1.251-4.093 | **0.007** | 2.263 | 1.251-4.093 | **0.007** |

HR, hazard ratio; CI 95%, confidence interval 95%; OS, overall survival. Significant p values (<0.05) are highlighted in bold.
that this difference is more related to cohort features and sample size than to the cut-off value itself.

Multidisciplinary assessment of GC patients would benefit on easy and simple score capable of predict prognosis. A prospective study regarding the effect of preoperative nutrition on patients with GC showed a lower 3-year OS and DFS in malnourished patients than in those receiving adequate nutrition [39]. Another study, besides showing that 3-year OS and DFS rates were significantly lower in malnourished GC patient, also showed that preoperative correction of hypoalbuminemia was significantly associated with higher OS and DFS, for pStage II and III [40]. These results suggest that preoperative status in GC patients should be optimized. Despite the several prognostic predictors describe on the literature, COA-NLR might be a reproducible score able to identify patients at risk of poor prognosis after curative-intent surgery.

The limitations of the present study include its retrospective nature; analysis of a limited number of patients; and being a single-centre study; nonetheless, this assures homogeneity in the treatment plan because all patients were evaluated and treated by the same multidisciplinary team; the selected hospital is a tertiary centre receiving patients in poorer health conditions and may not be representative of the general population; only patients submitted to curative-intent surgery were included in the study.

Despite the necessity for a standardized value to be used in clinical practice, more prospective larger trials are needed to define the optimal cut-off value. Nevertheless, using the already proposed cut-off value or a calculated value for each specific population may be a way to help multidisciplinary teams on the decision making regarding personalized preoperative optimization of patient’s status.

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Data availability Yes.

Code availability Not applicable.

Declarations

Competing interests The authors declare no competing interests.

Ethics approval Ethics approval by the ethics committee.

Consent to participate Not applicable.

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Conflict of interest The authors declare no competing interests.

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