Original Article
Modified Glasgow prognostic score as a prognostic factor in gastric cancer patients: a systematic review and meta-analysis

Xinwu Zhang, Xi Chen, Tao Wu, Yan Zhang, Kun Yan, Xiaoli Sun

Department of General Surgery, The Second Affiliated Hospital, College of Medicine, Xi’an Jiaotong University, Xi’an, China

Received June 30, 2015; Accepted September 14, 2015; Epub September 15, 2015; Published September 30, 2015

Abstract: Objective: Modified Glasgow prognostic score (mGPS) had been reported to associate with the prognosis of gastric cancer (GC), but its significance in gastric cancer patients has not been studied fully. Methods: PubMed; EMBASE; Web of Science and CNKI data base were searched to identify studies using the mGPS in gastric cancer patients. Outcome measures that were evaluated included overall survival (OS), lymphatic invasion and venous invasion in patients with gastric cancer. Results: A total of seven studies comprising 3206 patients were included in the meta-analysis of which all used OS as an outcome measure, three studies reported lymphatic invasion and three evaluated venous invasion. The results show that OS was worse in patients with an mGPS=1 and 2 (odds ratio [OR]=2.54, 95% [CI]: 1.62-3.98 and OR=12.02, 95% [CI]: 6.79-21.28, respectively) compared with those with a score of 0 (both \( P < 0.01 \)). Furthermore, gastric cancer patients with mGPS≥1 have higher rates of lymphatic and venous invasion with ORs of 2.51 (95% CI: 1.80-3.51) and 2.63 (95% CI: 1.35-5.11) respectively (both \( P < 0.01 \)). Conclusions: The mGPS could be used as a prognosis predictor for gastric cancer patients and associated lymphatic and venous invasion.

Keywords: mGPS, gastric cancer, prognostic factor, meta-analysis

Introduction

Gastric cancer (GC) is the fourth most common cancer and second leading cause of cancer-related mortality in the world [1, 2]. Although surgery and chemotherapy have improved treatment outcome, the survival rate of patients with GC remains unsatisfactory [3]. As treatment plans are becoming more individualized for each patient, it is important to assess disease progression in a timely manner and accurately evaluate the prognosis [4, 5]. Tumor inflammatory markers are useful indicators of disease development as the inflammatory response is known to promote tumor growth, invasion, angiogenesis and metastasis [6]. Indeed, a close relationship between tumor prognosis and systemic inflammation has been established using markers detected in peripheral blood [7]. Chronic inflammation has also been associated with the progression of GC [8-10], though the exact mechanism for this requires further study.

The modified Glasgow Prognostic Scores (mGPS) provides an inflammation-based prognostic assessment of various tumor type [11, 12]. Despite some studies that have reported the association between mGPS and GC patients, due to differences in inclusion criteria and limited sample sizes limiting its role. Its significance in patients with gastric cancer has not been studied fully. So, it is reasonable to hypothesize that mGPS is a good candidate for predicting the prognosis of GC. In order to more clearly evaluate this, a meta-analysis was conducted to determine whether the mGPS is a useful prognostic factor in GC patients and to assess the relationship between mGPS and clinicopathologic parameters.

Materials and methods

Data sources and searches

The following databases were searched for relevant articles published up until December
Modified glasgow prognostic score for gastric cancer

2014: PubMed; EMBASE; Web of Science and the China National Knowledge Infrastructure. Search terms included “gastriccancer”, “prog-nostic”, “mGPS” and “modified Glasgow Prog-nostic Score”. Two reviewers manually search ed the reference lists of identified studies for potential related articles. Only literature published in peer-reviewed journals was included.

Inclusion and exclusion criteria

For inclusion in the meta-analysis, relevant studies were required to include: 1) pathologic examination for diagnosis of GC; 2) pretreat-ment C-reactive protein (CRP) and albuminlev-els measured from peripheral blood samples, mGPS evaluation criteria are formulated by their own laboratories; 3) multivariate analysis for estimation of the hazard ratio (HR). Patients who had other inflammatory diseases causing serum elevations of CRP and albumin were excluded from the study. Nonhuman GC studies, duplicatearticles, abstracts and letters were excluded from the analysis. Two reviewers evaluated all candidate literature and resolved any disagreement by discussion.

Data extraction

The following data were extracted from relevant identified: author’s first name, year of publication, country and size of the population studied, Tumor-node metasta-sis stage of GC; treatment, the number of patients with mGPS=0, 1 or 2; follow-up period, lymphatic and venous invasion, and overall survival (OS) rate. Some studies do not provide exhaustive OS, we calculate the number of overall survival patients based on overall survival figure in the studies.

Statistical analysis

Analysis was conducted using RevMan 5.2 analysis software (Cochrane Collaboration, Copenhagen, Denmark). Associations between mGPS and clinical or pathologic parameters were performed using odds ratios (OR) and 95% confidence intervals (CI). If several estimates were reported with in the same article, the strongest value was selected. The estimates of ORs were weighted and pooled using the Mantel-Haenszel fixe deffects model. If \( P \geq 50\% \), the random-effects model was applied to calculate the pooled OR and 95% CI. Statistical heterogeneity was assessed using the Cochran’s Q and \( I^2 \) statistics, Publication bias was assessed by visual inspection of the funnel plot. All statistical tests were two-sided, and statistical significance was defined as \( P \leq 0.05 \).

Results

Study selection

A flow chart depicting the search and study selectionis showed in Figure 1. The initial search identified 84 studies, of which seven studies comprising 3206 patients that were published between 2011 and 2014 were finally included for the meta-analysis [12-18]. Study characteristics are presented in Table 1.

OS

There was significant heterogeneity (\( P \geq 50\% \)) among these studies with regard to mGPS and
## Modified glasgow prognostic score for gastric cancer

Table 1. Baseline characteristics of the studies included in the meta-analysis

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Study region</th>
<th>Samples (n)</th>
<th>Treatment</th>
<th>Outcome</th>
<th>Clinical stage</th>
<th>Survival analysis</th>
<th>Number of mGPS=0/1/2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tadahiro et al., 2011</td>
<td>Japan</td>
<td>232</td>
<td>Gastrectomy and lymph node dissection, no neoadjuvant therapy</td>
<td>OS</td>
<td>GC</td>
<td>Multivariate analysis</td>
<td>140/64/28</td>
</tr>
<tr>
<td>Jae-Heon et al., 2012</td>
<td>Korea</td>
<td>104</td>
<td>Palliative chemotherapy</td>
<td>OS</td>
<td>Advanced GC</td>
<td>Multivariate analysis</td>
<td>58/29/17</td>
</tr>
<tr>
<td>Shinsuke et al., 2014</td>
<td>Japan</td>
<td>552</td>
<td>Curative gastrectomy with lymph node dissection, adjuvant chemotherapy</td>
<td>OS</td>
<td>GC</td>
<td>Multivariate analysis</td>
<td>494/24/34</td>
</tr>
<tr>
<td>Kotaro et al., 2014</td>
<td>Japan</td>
<td>294</td>
<td>Gastrectomy and lymph node dissection</td>
<td>OS</td>
<td>GC</td>
<td>Multivariate analysis</td>
<td>174/84/36</td>
</tr>
<tr>
<td>Aurello et al., 2014</td>
<td>Italy</td>
<td>102</td>
<td>Gastrectomy and lymph node dissection</td>
<td>OS</td>
<td>GC</td>
<td>Multivariate analysis</td>
<td>49/25/28</td>
</tr>
<tr>
<td>Jiang et al., 2012</td>
<td>Japan</td>
<td>1710</td>
<td>Curative or palliative gastrectomy</td>
<td>OS</td>
<td>GC</td>
<td>Multivariate analysis</td>
<td>1565/78/67</td>
</tr>
<tr>
<td>Zhang et al., 2014</td>
<td>China</td>
<td>212</td>
<td>Curative or palliative gastrectomy, chemotherapy</td>
<td>OS</td>
<td>Stage III-IV GC</td>
<td>Multivariate analysis</td>
<td>136/45/31</td>
</tr>
</tbody>
</table>

GC: gastric cancer; OS: overall survival; DFS: disease-free survival; PFS: progression-free survival.
Modified glasgow prognostic score for gastric cancer

OS, and thus a random-effects model was applied to calculate the pooled OR and 95% CI (Figure 2). The results show that patients with a mGPS=1 or 2 have a shorter OS than those with a score of 0 (both P=0.02).

mGPS and lymphatic invasion

Three studies compared mGPS and lymphatic invasion in GC patients. The analysis show that patients with an mGPS≥1 have a significantly higher positive lymphatic invasion rate (P<0.01) (Figure 3).

mGPS and venous invasion

Three studies compared mGPS and venous invasion in GC patients. A random-effects model was applied to deal with heterogeneity in this section. The results show that patients with a mGPS≥1 have a significantly higher positive venous invasion rate (P<0.01) (Figure 4).
Modified glasgow prognostic score for gastric cancer

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>mGPS 1,2</th>
<th>mGPS 0</th>
<th>Odds Ratio</th>
<th>M.H. Random</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kotoh 2014</td>
<td>63</td>
<td>120</td>
<td>72</td>
<td>174</td>
<td>36.3%</td>
</tr>
<tr>
<td>Shinsuke 2014</td>
<td>42</td>
<td>58</td>
<td>251</td>
<td>494</td>
<td>32.5%</td>
</tr>
<tr>
<td>Total events</td>
<td>144</td>
<td>341</td>
<td>270</td>
<td>808</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Publication bias

A funnel plot was used to assess the included studies for overall publication bias showed symmetry for OS rate (Figure 5).

Discussion

The host inflammatory response influences the progression of cancer and recent studies indicate that these responses and cancer immune-editing play important roles in promoting the response and immunity of tumors [19-21]. Inflammatory cells provide tumors with nutritional factors, as well as adhesion molecules and chemokines which aid in metastasis [22]. Some inflammatory cytokine increase vascular permeability and promotes tumor metastasis [23].

There are several markers that can be used to assess the systemic inflammatory response, including serum CRP levels and hypoalbuminemia. Hypoalbuminemia is thought to be a consequence of the inflammatory response associated with elevated CRP levels [24] and has been considered as a prognostic indicator for gastrointestinal tumors [25, 26], colorectal [27, 28], esophageal [29], and pancreatic cancers [30]. The mGPS is based on evaluation of CRP levels and hypoalbuminemia, and has recently been associated with the prognosis of patients with digestive tract cancer [31, 32].

Figure 4. Forest plots of studies evaluating venous invasion and modified Glasgow Prognostic Score (mGPS). Venous invasion in gastric cancer patients with a mGPS score ≥1 compared with patients with a mGPS score of 0. CI: confidence interval.

Figure 5. Funnel plot for evaluation OS of publication bias. mGPS 0 and mGPS1 (A) and mGPS 0 and mGPS2 (B). OR: odds ratio.
Interleukin 1, interleukin 6, tumor necrosis factor and other proinflammatory cytokines can cause serum C-reactive protein elevated in patients with gastric cancer. These cytokines can promote gastric cancer cell proliferation, anti-apoptosis and angiogenesis by activating the downstream transcription factor, such as STAT3 and so on, which is significantly associated with inflammation, immunity, and oncogenesis [33, 34] and promotes lymph node metastasis and vascular metastasis [35, 36]. So constitutive activation of STAT3 have a poor prognosis in gastric cancer patients associated with mGPS [37-39]. Thus, mGPS have a close relationship with tumor metastasis in gastric cancer patients. The results of this meta-analysis show that the mGPS can also be used as a prognostic indicator for GC.

In addition to a reduced OS, GC patients with a higher mGPS are more likely to show lymphatic and venous invasion have a worse prognosis. These findings are consistent with previous studies showing that node metastasis and angiogenic metastasis which affect the prognosis of GC [40, 41].

In summary, the results of this meta-analysis indicate that GC patients with a mGPS≥1 have a worse prognosis than patients with a mGPS=0, thus the preoperative mGPS could serve as a prognostic factor to evaluate the survival of these patients. However, the limited number of eligible studies and different laboratories has different evaluation criteria about mGPS included in the meta-analysis necessitates further verification to confirm these results.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Xiaoli Sun, Department of General Surgery, The Second Affiliated Hospital, College of Medicine, Xi’an Jiaotong University, 157 Xi Wu Road, Xi’an 710004, Shaanxi Province, P. R. China. Tel: +86-29 87679278; Fax: +86-29 87679278; E-mail: doctorsunxiaoli@163.com

References


Modified glasgow prognostic score for gastric cancer


Modified glasgow prognostic score for gastric cancer


