**Prognostic importance of the inflammation-based Glasgow prognostic score in patients with gastric cancer**

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**BACKGROUND:** The inflammation-based Glasgow prognostic score (GPS) has been shown to be a prognostic factor for a variety of tumours. This study investigates the significance of the modified GPS (mGPS) for the prognosis of patients with gastric cancer.

**METHODS:** The mGPS (\( \text{mGPS} = 0 \) = C-reactive protein (CRP) \( \leq 10 \text{ mg l}^{-1} \), \( 1 = \text{CRP} > 10 \text{ mg l}^{-1} \) and \( 2 = \text{CRP} > 10 \text{ mg l}^{-1} \) and albumin \( < 35 \text{ g l}^{-1} \) ) was calculated on the basis of preoperative data for 1710 patients with gastric cancer who underwent surgery between January 2000 and December 2007. Patients were given an mGPS of 0, 1 or 2. The prognostic significance was analysed by univariate and multivariate analyses.

**RESULTS:** Increased mGPS was associated with male patient, old age, low body mass index, increased white cell count and neutrophils, elevated carcinoembryonic antigen and CA19-9 and advanced tumour stage. Kaplan–Meier analysis and log-rank test revealed that a higher mGPS predicted a higher risk of postoperative mortality in both relative early-stage (stage I; \( P < 0.001 \)) and advanced-stage cancer (stage II, III and IV; \( P < 0.001 \)). Multivariate analysis demonstrated the mGPS to be a risk factor for postoperative mortality (odds ratio 1.845; 95% confidence interval 1.184–2.875; \( P = 0.007 \)).

**CONCLUSION:** The preoperative mGPS is a simple and useful prognostic factor for postoperative survival in patients with gastric cancer.

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**Keywords:** gastric cancer; C-reactive protein; albumin; prognostic score; survival

Gastric cancer is the fourth most common cancer worldwide, and the second most frequent cause of mortality (Crew and Neugut, 2006; Kamangar et al, 2006). In Japan, although the incidence of gastric cancer has decreased, gastric cancer remains the most frequent cause of morbidity among patients with malignant tumours (Inoue and Tsugane, 2005). Although recent years have seen improvements in surgical techniques and adjuvant chemotherapy, the long-term survival of patients with advanced-stage gastric cancer remains unsatisfactory (Sasako et al, 2008).

There is increasing evidence that, in addition to tumour stage and the proliferative activity of tumour cells, the systemic inflammatory response is associated with malignancy (Roxburgh et al, 2009; McArdle et al, 2010; Richards et al, 2010). C-reactive protein (CRP), an acute-phase response protein, has been proven to be an independent prognostic factor for survival in many malignancies, including gastric cancer (Jagdev et al, 2010; Roxburgh and McMillan, 2010). In addition, hypoalbuminemia, a typical index of malnutrition, has been reported to be associated with poor survival in advanced cancer (Crumley et al, 2010; Lai et al, 2010). Recently, the Glasgow prognostic score (GPS), based on serum CRP and albumin levels, was developed to aid in the assessment of cancer prognosis (Ishizuka et al, 2009; Richards et al, 2010). An elevated GPS has been shown to be associated with worse prognosis for a number of different tumours (McMillan, 2009). Thus, the GPS may be a prognostic marker in cancer, independent of stage and biochemical tumour markers (McMillan, 2009; Roxburgh et al, 2009).

The GPS has also been shown to be a prognostic factor in advanced gastrointestinal cancers, including oesophageal and colorectal cancer (Kobayashi et al, 2008; Ishizuka et al, 2009). However, only few studies have used the GPS for postoperative prognostication of patients with gastric cancer. Thus, in the present study, we collected data retrospectively from 1710 patients with operable gastric cancer and investigated the significance of the preoperative GPS for postoperative survival in these patients.

**MATERIALS AND METHODS**

The gastric cancer database from the Department of Gastroenterological Surgery at The Cancer Institute Hospital, Tokyo, Japan, was reviewed retrospectively. Patients with gastric adenocarcinoma who had undergone curative (R0 resection) or palliative gastrectomy between January 2000 and December 2007 and for whom preoperative laboratory data for CRP and albumin were available were enrolled into the study. Palliative surgery is defined as the presence of any gross or microscopic residual tumours remaining postoperatively regardless of whether the surgical attempt was originally palliative or curative. Patients who died within 30 days after surgery, or those who died of non-cancer-related causes were excluded from the study. Patients who had other malignancies or who had inflammatory diseases that might have increased CRP levels were also excluded from the study. To remove any influence of neoadjuvant chemo/radiotherapy on survival or GPS, patients who received neoadjuvant chemotherapy...
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RESULTS

During 2000–07, 2601 patients underwent gastric cancer surgery. Of these, 845 were excluded from analysis because data on their CRP and albumin levels were not available, and 46 were excluded because of neoadjuvant chemotherapy, postoperative death or non-cancer death. Of the 1710 included patients with gastric cancer (1157 men; 553 women), 240 (14.0%) had elevated CRP because of neoadjuvant chemotherapy, postoperative death or non-cancer death. Of the 1710 included patients with gastric cancer, 1078 (63.6%) had elevated CRP (0.05 was considered significant. All statistical analyses were performed using SPSS version 13.0 (SPSS, Chicago, IL, USA).

Table I  Clinical and laboratory characteristics associated with overall survival

| No. of patients | Overall survival (months), mean (95% CI) | P-value* |
|-----------------|------------------------------------------|----------|
| Sex             |                                          |          |
| Male            | 1157                                     | 90.0 (87.0–93.0) | 0.185 |
| Female          | 553                                      | 96.2 (91.9–100.5) |          |
| Age (years)     |                                          |          |
| <65             | 885                                      | 98.1 (94.7–101.4) | <0.001 |
| ≥65             | 813                                      | 85.9 (82.1–89.8) |          |
| Body mass index (kg m−2) |                                    |          |
| <18.5           | 261                                      | 61.4 (55.8–67.0) | <0.001 |
| 18.5–25         | 1138                                     | 96.1 (93.0–99.2) |          |
| ≥25             | 233                                      | 96.1 (91.4–100.9) |          |
| Tumour location |                                          |          |
| Upper third     | 460                                      | 79.2 (74.6–83.8) | <0.001 |
| Middle third    | 772                                      | 100.5 (96.9–104.2) |          |
| Lower third     | 470                                      | 88.2 (83.1–93.3) |          |
| White cell count (× 109/l−1) |                          |          |
| <1.1            | 1682                                     | 93.3 (90.7–96.0) | 0.156 |
| ≥1.1            | 27                                       | 60.4 (48.7–72.2) |          |
| Neutrophils (× 109/l−1) |                              |          |
| <7.5            | 1605                                     | 94.0 (91.4–96.7) | <0.001 |
| ≥7.5            | 50                                       | 59.2 (46.1–72.3) |          |
| Lymphocytes (× 109/l−1) |                                  |          |
| <3              | 1592                                     | 92.9 (90.2–95.6) | 0.208 |
| ≥3              | 63                                       | 95.0 (85.4–104.6) |          |
| CEA (ng ml−1)   |                                          |          |
| ≤5              | 1433                                     | 95.4 (92.7–98.1) | <0.001 |
| >5              | 233                                      | 55.9 (49.9–61.8) |          |
| CA19-9 (ng ml−1) |                                          |          |
| ≤37             | 1406                                     | 94.1 (91.4–96.8) | <0.001 |
| >37             | 151                                      | 48.5 (40.4–56.3) |          |
| CRP (mg l−1)    |                                          |          |
| ≤10             | 1565                                     | 95.8 (93.2–98.5) | <0.001 |
| >10             | 145                                      | 51.4 (44.5–58.2) |          |
| Albumin (g l−1) |                                          |          |
| ≤35             | 162                                      | 38.8 (33.0–44.5) | <0.001 |
| >35             | 1548                                     | 97.8 (95.2–100.4) |          |
| Tumour stage (pTNM) |                                        |          |
| I               | 997                                      | 113.5 (111.0–116.0) | <0.001 |
| II              | 200                                      | 82.6 (77.2–87.9) |          |
| III             | 245                                      | 68.1 (62.0–74.1) |          |
| IV              | 268                                      | 28.7 (23.9–33.5) |          |
| mGPS             |                                          |          |
| 0               | 1565                                     | 95.8 (93.2–98.5) | <0.001 |
| 1               | 78                                       | 62.2 (53.4–71.1) |          |
| 2               | 67                                       | 35.9 (27.0–44.8) |          |

Abbreviations: CEA = carcinoembryonic antigen; CRP = C-reactive protein; mGPS = modified Glasgow prognostic score; pTNM = pathological tumour-node-metastasis staging. "Kaplan–Meier survival analysis."
To clarify whether the mGPS has different prognostic value depending on tumour stage, patients were divided into two groups, namely those with relatively early-stage tumours (stage I; \( n = 997 \)) and those with advanced-stage tumours (stage II, III and IV; \( n = 713 \)). Significant differences in survival were found for patients with mGPS of 0, 1 and 2 in both groups (both \( P < 0.001 \)) (Figures 2 and 3).

**DISCUSSION**

The present retrospective study analysed individual clinical data for 1710 patients who underwent surgery for a pure cohort of gastric cancer in a high-volume center in Japan. The results demonstrate the prognostic value of the mGPS for gastric cancer. Although the GPS has been reported to have prognostic significance in a variety of cancers, its value in gastric cancer has not been fully investigated (Elahi et al, 2004; Crumley et al, 1993).

**Table 2** Relationships between clinicolaboratory characteristics and mGPS

| mGPS 0 | mGPS 1 | mGPS 2 |
|--------|--------|--------|
| n (%)  | n (%)  | n (%)  |

| Sex     | Male    | 1045 (90.3) | 60 (5.2) | 52 (4.5) | 0.036 |
|---------|---------|-------------|----------|----------|-------|
| Female  | 520 (94.0) | 18 (3.3) | 15 (2.7) |        |       |

| Age (years) | <65 | 831 (93.9) | 29 (3.3) | 25 (2.8) | 0.001 |
|-------------|-----|-----------|----------|----------|-------|
|            | ≥65 | 723 (88.9) | 48 (5.9) | 42 (5.2) |       |

| Body mass index (kg m\(^{-2}\)) | <18.5 | 212 (81.2) | 17 (6.5) | 32 (12.3) | <0.001 |
|---------------------------------|-------|-----------|----------|-----------|--------|
|                                 | ≥18.5 | 1059 (93.1) | 47 (4.1) | 32 (2.8) |        |

| Tumour location | Upper third | 414 (90.0) | 22 (4.8) | 24 (5.2) | 0.069 |
|-----------------|-------------|-----------|----------|----------|-------|
|                 | Middle third | 722 (93.5) | 29 (3.8) | 21 (2.7) |       |
|                 | Lower third  | 421 (89.6) | 27 (5.7) | 22 (4.7) |       |

| White cell count (×10\(^9\) l\(^{-1}\)) | <11 | 1556 (92.5) | 70 (4.2) | 56 (3.3) | <0.001 |
|-----------------------------------------|-----|-------------|----------|----------|--------|
|                                         | ≥11 | 8 (29.6) | 8 (29.6) | 11 (40.7) |       |

| Neutrophils (×10\(^9\) l\(^{-1}\)) | <7.5 | 1498 (93.3) | 65 (4.0) | 42 (2.6) | <0.001 |
|-----------------------------------|-----|------------|----------|----------|--------|
|                                    | ≥7.5 | 19 (38.0) | 12 (24.0) | 19 (38.0) |       |

| Lymphocytes (×10\(^9\) l\(^{-1}\)) | <3 | 1458 (91.6) | 75 (4.7) | 59 (3.7) | 0.633 |
|-----------------------------------|---|-------------|----------|----------|-------|
|                                    | ≥3 | 59 (93.7) | 2 (3.2) | 2 (3.2) |       |

| CEA (ng ml\(^{-1}\)) | ≤5 | 1342 (93.6) | 56 (3.9) | 25 (2.4) | <0.001 |
|-----------------------|---|------------|----------|----------|--------|
|                       | >5 | 184 (79.0) | 20 (86.6) | 29 (12.4) |       |

| CA19-9 (ng ml\(^{-1}\)) | ≤37 | 1299 (92.4) | 57 (4.1) | 50 (3.6) | 0.006 |
|-------------------------|---|------------|----------|----------|-------|
|                         | >37 | 128 (84.8) | 12 (79.9) | 11 (73) |       |

| Tumour stage | I | 961 (96.4) | 30 (3.0) | 6 (0.6) | <0.001 |
|--------------|---|------------|----------|----------|-------|
|              | II | 177 (88.5) | 9 (4.5) | 14 (70) |       |
|              | III | 219 (89.4) | 13 (5.3) | 13 (5.3) |       |
|              | IV | 208 (77.6) | 26 (9.7) | 34 (12.7) |       |

**Table 3** Univariate and multivariate analyses of overall survival

| Univariate analysis | Multivariate analysis |
|---------------------|-----------------------|
| Sex                 |                       |
| Age                 |                       |
| Body mass index     |                       |
| Tumour location     |                       |
| White cell count    |                       |
| Neutrophils         |                       |
| Lymphocytes         |                       |
| CEA                 |                       |
| CA19-9              |                       |
| Tumour stage        |                       |
| mGPS (0, 1, and 2) |                       |

| Abbreviations: CEA = carcinoembryonic antigen; mGPS = modified Glasgow prognostic score. aFactors \( P < 0.10 \) in univariate analysis were included in the multivariate analysis. |

To clarify whether the mGPS has different prognostic value depending on tumour stage, patients were divided into two groups, namely those with relatively early-stage tumours (stage I; \( n = 997 \)) and those with advanced-stage tumours (stage II, III and IV; \( n = 713 \)). Significant differences in survival were found for patients with mGPS of 0, 1 and 2 in both groups (both \( P < 0.001 \)) (Figures 2 and 3).

**Figure 1** Relationship between the mGPS (mGPS 0, 1, 2 from top to bottom) and overall survival in patients with gastric cancer.

**Figure 2** Relationship between the mGPS (mGPS 0, 1, 2 from top to bottom) and overall survival in patients with relatively early gastric cancer (stage I).
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The authors declare no conflict of interest.
REFERENCES

Al-Shaiba R, McMillan DC, Angerson WJ, Leen E, McArdle CS, Horgan P (2004) The relationship between hypoaobuminaemia, tumour volume and the systemic inflammatory response in patients with colorectal liver metastases. Br J Cancer 91: 205–207

Crew KD, Neugut AI (2006) Epidemiology of gastric cancer. World J Gastroenterol 12: 354–362

Crumley AB, McMillan DC, McKernan M, McDonald AC, Stuart RC (2006) Evaluation of an inflammation-based prognostic score in patients with inoperable gastro-oesophageal cancer. Br J Cancer 94: 637–641

Crumley AB, Stuart RC, McKernan M, McMillan DC (2010) Is hypoaobuminaemia an independent prognostic factor in patients with gastric cancer? World J Surg 34: 2393–2398

Elahi MM, McMillan DC, McArdle CS, Angerson WJ, Sattar N (2004) Score based on hypoaobuminaemia and elevated C-reactive protein predicts survival in patients with advanced gastrointestinal cancer. Nutr Cancer 48: 171–173

Fearon KC, Voss AC, Hustead DS (2006) Definition of cancer cachexia: effect of weight loss, reduced food intake, and systemic inflammation on functional status and prognosis. Am J Clin Nutr 83: 1345–1350

Inoue M, Tsugane S (2003) Epidemiology of gastric cancer in Japan. Postgrad Med J 81: 419–424

Ishizuka M, Nagata H, Takagi K, Kubota K (2009) Influence of inflammation-based prognostic score on mortality of patients undergoing chemotherapy for far advanced or recurrent unresectable colorectal cancer. Ann Surg 250: 268–272

Jagdev SP, Gregory W, Vasudev NS, Harnden P, Sim S, Thompson D, Cartledge J, Selby PJ, Banks RE (2010) Improving the accuracy of preoperative survival prediction in renal cell carcinoma with C-reactive protein. Br J Cancer 103: 1649–1656

Kamangar F, Dores GM, Anderson WF (2006) Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. J Clin Oncol 24: 2137–2150

Kim DX, Oh SY, Kwon HC, Lee S, Kwon KA, Kim BG, Kim SG, Kim SH, Jung JS, Kim MC, Kim KH, Han JY, Kim HJ (2009) Clinical significances of preoperative serum interleukin-6 and C-reactive protein level in operable gastric cancer. BMC Cancer 9: 155

Kobayashi T, Teruya M, Kishiki T, Endo D, Takenaka Y, Tanaka H, Miki K, Kobayashi K, Morita K (2008) Inflammation-based prognostic score, prior to neoadjuvant chemoradiotherapy, predicts postoperative outcome in patients with esophageal squamous cell carcinoma. Surgery 144: 729–735

Kodera Y, Ishiyama A, Yoshikawa T, Kinoshita T, Ito S, Yokoyama H, Mochizuki Y, Ito H, Tsuburaya A, Sakamoto J, Nakao A (2010) A feasibility study of postoperative chemotherapy with S-1 and cisplatin (CDDP) for gastric carcinoma (CCOG0703). Gastric Cancer 13: 197–203

Koike Y, Miki C, Okugawa Y, Yokoe T, Toiyama Y, Tanaka K, Inoue Y, Kusunoki M (2008) Preoperative C-reactive protein as a prognostic and therapeutic marker for colorectal cancer. J Surg Oncol 98: 540–544

Lai CC, You JF, Yeh CY, Chen JS, Tang R, Wang JY, Chin CC (2010) Low preoperative serum albumin in colon cancer: a risk factor for poor outcome. Int J Colorectal Dis 26(4): 473–481

Leitch EF, Chakrabarti M, Crozier JE, McKee RF, Anderson JH, Horgan PG, McMillan DC (2007) Comparison of the prognostic value of selected markers of the systemic inflammatory response in patients with colorectal cancer. Br J Cancer 97: 1266–1270

Lien YC, Hsieh CC, Wu YC, Hsu HS, Hsu WH, Wang LS, Huang MH, Huang BS (2004) Preoperative serum albumin level is a prognostic indicator for adenocarcinoma of the gastric cardia. J Gastrointest Surg 8: 1041–1048

McArdle PA, Qayyum T, McMillan DC (2010) Systemic inflammatory response and survival in patients with localised prostate cancer: 10-year follow-up. Urol Int 84: 430–435

McMillan DC (2009) Systemic inflammation, nutritional status and survival in patients with cancer. Curr Opin Clin Nutr Metab Care 12: 223–226

Nozoe T, Iguchi T, Egashira A, Adachi E, Matsukuma A, Ezaki T (2011) Significance of modified Glasgow prognostic score as a useful indicator for prognosis of patients with gastric carcinoma. Am J Surg 201: 186–191

Nozoe T, Saeki H, Sugimachi K (2001) Significance of preoperative elevation of serum C-reactive protein as an indicator of prognosis in esophageal carcinoma. Am J Surg 182: 197–201

Richards CH, Leitch EF, Horgan PG, Anderson JH, McKee RF, McMillan DC (2010) The relationship between patient physiology, the systemic inflammatory response and survival in patients undergoing curative resection of colorectal cancer. Br J Cancer 103: 1356–1361

Roxburgh CS, McMillan DC (2010) Role of systemic inflammatory response in predicting survival in patients with primary operable cancer. Future Oncol 6: 149–163

Roxburgh CS, Salmon JM, Horgan PG, Oien KA, McMillan DC (2009) Comparison of the prognostic value of inflammation-based pathologic and biochemical criteria in patients undergoing potentially curative resection for colorectal cancer. Ann Surg 249: 788–793

Sasako M, Sano T, Yamamoto S, Kurokawa Y, Hashimoto A, Kurita A, Hiratsuka M, Tsujinaka T, Kinoshita T, Arakai Y, Yamamura Y, Okajima K (2008) D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer. N Engl J Med 359: 453–462

Shimoda M, Katoh M, Kita J, Sawada T, Kubota K (2010) The Glasgow prognostic score in gastric cancer. Br J Cancer 102: 279

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