The Predictive Value of the Modified Glasgow Prognostic Score (Mgps) in Determining Outcome Following Elective Colorectal Cancer Surgery

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Abstract

Background: The mGPS (modified Glasgow Prognostic Score) provides a measure of systemic inflammation in patients with cancer, based on C-reactive protein (CRP) and Albumin. The aim of this study was to determine the role of mGPS in predicting outcome following elective curative colorectal cancer resections; in terms of survival, stage of disease, likelihood and interval of cancer recurrence.

Methods: We in Raigmore Hospital, Inverness have a prospective database of patients undergoing colorectal cancer resections. This database was reviewed between January 2008 and January 2012, yielding 986 patients. Data on pre-operative CRP and Albumin, survival, pathology, and recurrence was collected retrospectively, with patients followed up to 1st February 2015. Patients were classified according to their mGPS score. The mGPS was calculated as follows: CRP< 10mg/L=mGPS 0; CRP >10mg/L or Albumin≤ 35g/L=mGPS 1; CRP >10mg/L and Albumin≤ 35g/L=mGPS 2. Data was found to be parametric and comparisons between mGPS groups were done using the ANOVA test. A p-value of < 0.05 was deemed significant.

Results: 387 patients were eligible for inclusion (having had elective curative resections with a calculable mGPS). Survival was significantly different at 45.7, 39.9 and 35.9 months for mGPS groups of 0-2 respectively (p=0.0012). Although there was a trend towards higher TNM staging with rising mGPS, this was not significant (p=0.054). Higher mGPS predicted an increased chance of disease recurrence, with a 17.6% vs. 31.6% vs. 37.1% recurrence rate for mGPS groups of 0-2 respectively. Higher mGPS scores were also associated with a significantly shorter time to recurrence, at 42.3 vs. 34.9 vs. 28.9 months (p=0.0008).

Conclusion: The mGPS has value in predicting survival, disease recurrence and time to recurrence in colorectal cancer. The score may be helpful as a decision making tool for the multidisciplinary team.

Introduction

Colorectal cancer (CRC) is the most common cancer of the GI tract and the third most common cause of cancer death in western countries [1]. There are 41,000 new cases of CRC recorded each year in the UK with 15900 deaths per year [2]. Despite the improvement and advances in treatment, approximately half of those undergoing surgery with curative intent subsequently die from the disease [3].

Currently we rely on accurate staging of the tumour to determine its prognosis. There are other patient related factors like nutritional status and functional decline that is associated with poorer outcome independent of tumour stage. These factors are subjective, and therefore not very reliable [4]. Survival rates vary in CRC patients, even in those with the same tumour node metastasis [5]. It is therefore important to identify a preoperative indicator of poor postoperative outcome to help guide treatment of such patients.

There is good evidence that the presence of a systemic inflammatory response is a key factor in the determination of a poor prognosis [4]. Cancer can induce local or systemic inflammation, the cascade is mediated by the activation of transcription factors and the production of major inflammatory cytokines which can influence cell proliferation, cell survival, angiogenesis, tumour cell migration, invasion, metastasis and inhibition of adaptive immunity [6]. CRC has a close
relationship with inflammation – this is typified by inflammatory bowel diseases which have premalignant lesion that can lead to the development of CRC [7]. Cyclooxygenase-2 inhibitors and non-steroidal anti-inflammatory drugs have been found to decrease the incidence of colorectal adenoma and CRC [8].

The modified Glasgow Prognostic Score (mGPS) provides a measure of systemic inflammation in patients with cancer, based on C-reactive protein (CRP) and albumin measurements. The mGPS provides a score which ranges between 0 and 2. The mGPS is one of a group of inflammatory marker-based predictive scores which has been shown to have prognostic utility in oesophageal, non-small cell lung and prostate cancers [9-11].

A rise in CRP concentrations is often associated with a corresponding fall in albumin - this inverse relationship was noted across different tumour types [4]. Albumin concentrations reflect both systemic inflammation and the amount of lean tissue, and it would be important to determine the prognostic value of both combined [12]. The GPS was recently modified on the basis that hypoalbuminemia in patients without an elevated CRP concentration had no significant association with cancer-specific survival [13]. The modified score is simple to measure and can be standardised worldwide. There have been a few studies to show the prognostic value of mGPS in colorectal cancer [14-18], hitherto, this is the first study which examined the role of mGPS in the prediction of more commonly examined variables after curative surgery. The aim of this study was to determine the role of mGPS in predicting outcome after elective curative colorectal surgery with attention to survival, disease stage, and likelihood of recurrence.

**Methods**

Raigmore Hospital in Inverness is a large district general hospital. Patients who met the inclusion criteria, namely those with non metastatic colorectal cancer who underwent an elective colonic resection as part of the treatment programme were included in the study. All patients with colonic cancers would have had staging CT scans of their chest, abdomen and pelvis. Those with rectal cancers would have had an MRI scan for local staging in addition to the above mentioned CT scans. Patient would have had their diagnosis confirmed with preoperative biopsies at time of colonoscopy.

After identification of this cohort of patients, all demographic data and pre-operative CRP and Albumin data were collected retrospectively. This involved examination of casenotes electronically and when necessary, hard copies of medical records. CRP and albumin levels were usually (but not always) measured as part of anaesthetic work-up prior to surgery. This enabled a calculation of a mGPS score for the majority of patients. Patients were grouped into one of three mGPS categories depending on their CRP and albumin measurement. Table 1 details the calculation of the mGPS score. Unfortunately patient who did not have a CRP or albumin measured preoperatively had to be excluded from the study. Likewise, patients who presented as emergencies and/or had other obvious adverse conditions at the time of blood collection were excluded from the study as their CRP and/or albumin measurement would have been predictably abnormal. Patients unfit for surgery and patients who had non-curative resections, largely for purposes of palliation were excluded from the study. As this was a longitudinal study to examine the role of the mGPS, patients who died prior to their surgery or within 30 days of their operation were also excluded.

Surgery was performed by one of 4 fully accredited colorectal surgeons within the department of general surgery. All postoperative histopathology was recorded using a standard proforma. Follow-up data for the above cohort of patients was collected until 1st February 2015. Patients who had potentially curative surgery were then followed up in our nurse led clinic. Our follow up programme consists of regularly consultations at 3 monthly intervals for the first year. Thereafter consultations are conducted at 6 monthly intervals for another 4 years. Cross sectional imaging in the form of CT scans (chest, abdomen and pelvis) are routinely performed 6 monthly for the first 3 years. Endoluminal surveillance in the form of colonoscopy to exclude metachronous lesions and disease recurrence are done at one and 5 years after index surgery.

All recorded data was found to be parametric. Chi-Square analysis and ANOVA analysis was performed for categorical and continuous data respectively. A p-value of < 0.05 was deemed significant.

**Results**

There were three hundred and eighty seven patients that were...
appropriate for analysis. These patients had complete data (with a calculable mGPS) and were therefore included in the final analysis. The remaining 587 were excluded. Table 2 provides further details and reasons for their exclusion.

There were 214 (55%) males. Mean age at time of surgery was 69.4 years. The most common site for cancer in our study population was within the rectum. Further details for our study population are provided in Table 3. More than 40 percent of our patients had lymph node positive disease on postoperative histology. Despite excluding patients with known metastatic disease (after preoperative staging) from our study, a further 1.8% of patients were found to have features of metastatic disease within their postoperative histology. Further details of postoperative histopathology are provided in Table 4.

Neoadjuvant therapy was utilised in approximately 10.6% of patients, this was utilised predominantly for patients with margin threatened rectal cancers. Patients with lymph node positive disease were offered adjuvant chemotherapy if fit. This was offered to 27.4% of patients in our study population.

The vast majority of patients in the study had a mGPS score of 0 (57.4%). Less than a quarter had a mGPS of 1 (24.5%) and finally only 18.1% had an mGPS of 2. Survival was significantly poorer for patients with a higher mGPS score. As shown in Figure 1, mean survival was 45.7, 39.9 and 35.9 months for mGPS groups of 0-2 respectively, with standard deviations of 18.7, 22 and 24.5 months. The difference between groups was significant on ANOVA testing (p=0.0012).

Disease stage was more advanced in patient with a higher mGPS score although this did not reach statistical significance. (p=0.054). The stage of disease according to mGPS score is detailed in Table 5.

On long term follow-up, 95 out of 387 patients (24.5%) developed recurrent cancer. As shown in Figure 2, a higher mGPS was associated with a greater likelihood of disease recurrence. Disease recurrence had developed in 17.6% vs. 31.6% vs. 37.1% of patients with mGPS scores of 0-2 respectively (p=0.0007). Figure 3 illustrates that a higher mGPS was also associated with a significantly shorter interval to disease recurrence, at 42.3 vs. 34.9 vs. 28.9 months for mGPS groups.
of 0-2 respectively (p=0.0008), with standard deviations of 21.1, 22.6 and 26.4 months.

**Discussion**

The purpose of this study was to assess the prognostic utility of the mGPS score in a cohort of patient with colorectal cancer who underwent potentially curative surgery. We have demonstrated that patients with higher mGPS scores have a greater likelihood of disease recurrence and poorer survival on long term follow-up. Currently, postoperative pathological examination is the gold standard for predicting postoperative outcome; of course this is only possible after surgical resection. Even with such information available to clinicians, it has been shown that patients can have very different outcomes despite having very similar diseases stages [17]. Thus, there remains a need for a preoperative predictive marker.

Studies have shown that elevated CRP may be associated with tumour size, distant metastasis, vascular invasion, lymph node metastasis, and tumour recurrence, resulting in poor prognosis [19]. The GPS, an inflammation based prognostic score involving CRP and albumin was designed by Forrest et al. [20]. CRP and albumin are acute phase proteins, which are produced in the liver in response to inflammatory cytokines, mainly IL-6 and IL-1β [21]. CRP elevates in response to an inflammatory stimulus, but albumin is known to decrease in cancer patients due to malnutrition and systemic inflammation [12].

The utility of simple markers such as CRP and albumin is interesting. Links between cancer and inflammation have been postulated since the 19th century – these have been based on observations that tumours often arise at sites of chronic inflammation and that inflammatory cells are often present in biopsy specimens collected from tumour tissue [7,14]. In colitis associated colon cancer, chronic inflammation causes oxidative damage to the DNA, leading to p53 mutations in tumour cells, and the inflamed epithelium and the inflammatory microenvironment at the tumour border can influence several key stages of invasion and metastasis [22]. In general, inflammation is known to affect all phases of carcinogenesis and may be responsible for the initiation of genetic mutation. Inflammation may modify the tissue microenvironment directly, which permits cancer cells to progress and metastasize. Alternatively, inflammation may allow tumour progression by indirect suppression of the immune response to tumour cells [23].

We are conscious that this paper has several weaknesses. First, this study has been done retrospectively, so it was not possible to ensure CRP and albumin measurements in all suitable patients. There was also a subset of patients that had to be excluded due to missing data. We limited our dataset because we were strict with our exclusion criteria. In order to exclude potential confounders, we were careful not to include patients who may have had artificially raised CRPs from concomitant pathology or obstruction at time of emergency presentation. However, if such patients (i.e. patients with emergency presentation and tumour perforations) were to be included in the overall analysis, we would have detected an even stronger relationship between high mGPS scores and poorer outcomes. This would have led to positive bias in the study.

The mGPS should not replace gold standard assessments for disease staging or follow-up nor should it replace the time honoured surgical judgement about appropriateness for surgery. However, the mGPS may be used to help aid decision making. We believe that it is particularly useful in the aging octogenarian with borderline mental, physical and social function, where the ‘time to benefit’ from surgery for their colorectal cancer is severely curtailed because of advance age and concurrent co-morbidity. If elderly patients have technically operable disease, but are marginally fit or unsure about an operation, a poor mGPS score preoperatively may provide reassurance to the clinician that surgery is less likely to be in the interest of the patient.

**Conclusion**

The mGPS has prognostic value in patients with colorectal cancer for the prediction of survival, likelihood of disease recurrence and interval to such an occurrence. In frail patients where surgery can be fraught with risk, the use of the mGPS may help the multidisciplinary team to make the right decision.

**References**


