An Analysis of Prognostic Biomarkers of the Systemic Inflammatory Response in Cancers of Unknown Primary

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Background

Cancers of unknown primary represent between **3 and 5%** of all malignancies worldwide.[1] Survival in favourable clinico-pathological subsets (20%) is a median of 24 months.[2] In the remainder of 'poor prognosis' patients survival can be as little as **1-3 months**.[3] In order to rationalise treatment and investigation it is essential to provide accurate prognostic data to help patients.

Aims

It is firmly established that biomarkers of the systemic inflammatory response (albumin and CRP combined in the modified Glasgow prognostic score (mGPS)) predict survival in cancers with established primary site. The aim of this study was to establish their utility in prognosis in CUP. [4,5]

mGPS

Modified Glasgow Prognostic Score (mGPS)	CRP (mg/l)	Albumin (g/dl)
0	≤ 10	Any
1	≥ 10	Any
2	> 10	< 35

Table 1: Modified Glasgow Prognostic score (mGPS)

Methods

A prospective data collection was undertaken of patient referrals to the CUP service at the Edinburgh Cancer Centre between 2010–2019. Eligible patients were 18 years or over and had confirmed or provisional CUP.[6] Patients with favourable clinico-pathological subgroups were largely excluded. Patients were referred from a range of clinical settings and were not all fit to attend oncology clinic. The survival time, defined as date of biopsy until death, or censored if alive at follow-up date, was calculated. Survival curves were plotted using Kaplan-Meier methods and the log rank test applied. Survival analysis was carried out using Cox's proportional-hazards model and hazard ratios were calculated.

Results

Patient characteristics	n=190	
	n (%)	Median (IQR)
Age years (≤65, 66-74, ≥75)	71 (37), 55 (29), 64 (34)	69 (60-76)
Female	102 (54)	
Survival months (<1, 1-3, >3)	49 (26), 66 (35), 75(39)	2.1 (1-5.3)
mGPS (0, 1, 2)	20 (11), 53 (28), 117 (61)	

Table 2: Clinico-pathological characteristics of patients with cancer of unknown primary

mGPS is predictive of survival

- Median survival was **2.1** months in this patient cohort.
- 89% of patients had a CRP >10mg/l at diagnosis.
- **mGPS** stratified median survival from **9.6 months** with **mGPS of 0** to **1.5 months** with **mGPS of 2** (**p=0.001**).
- **71%** of those patients with mGPS of 2 were dead at three months compared to **21%** those patients with mGPS of 0.

Survival

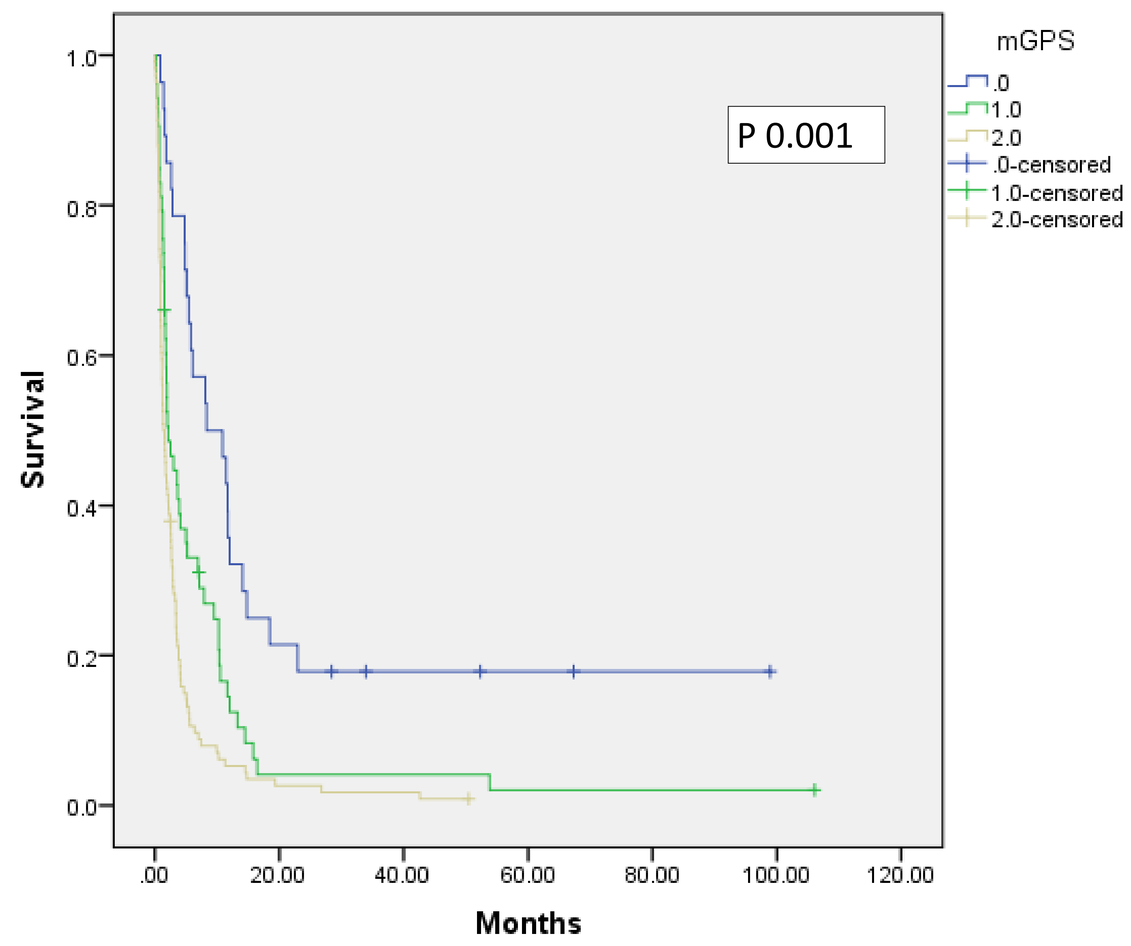

Fig 1: Kaplan-Meier curve showing the relationship between mGPS and survival in patients with CUP

	Number alive at one month (%)	Number alive at three months (%)	Median survival (months)
mGPS			
0	28 (96)	24 (79)	9.6 (4.8-17.5)
1	53 (81)	27 (47)	2.1 (1.3-8.7)
2	117(64)	49(29)	1.5 (0.7–2.4)

Table 3: The relationship between mGPS and absolute (percentage) survival at one month and three months, and median survival in patients with CUP

Conclusions

This analysis of 190 CUP patients has shown that mGPS, a biomarker of the systemic inflammatory response, is a strong prognostic factor in patients with 'poor prognosis' CUP. This simple score is derived from commonly used blood tests. When used alongside clinical assessment, standardised investigation and performance status it can provide additional objective information regarding prognosis. This may facilitate discussions with patients and help with decisions regarding the investigation and treatment of patients with CUP.

In patients with mGPS of 2 it can help support early conversations about advanced care planning.

We would advocate future work incorporating independent validation in other cohorts of CUP patients and, if supported, incorporating these biomarkers of the systemic inflammatory response into CUP clinical pathways and trials.

References

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