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Predicting 1-year mortality among patients with decompensated cirrhosis: results of a multicentre evaluation of the Bristol Prognostic Score

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ABSTRACT

Objective Chronic liver disease continues to be a significant cause of morbidity and mortality yet remains challenging to prognosticate. This has been one of the barriers to implementing palliative care, particularly at an early stage. The Bristol Prognostic Score (BPS) was developed to identify patients with life expectancy less than 12 months and to act as a trigger for referral to palliative care services. This study retrospectively evaluated the BPS in a cohort of patients admitted to three Scottish hospitals.

Method Routinely collated healthcare data were used to obtain demographics, BPS and analyse 1-year mortality for patients with decompensated liver disease admitted to three gastroenterology units over two 90-day periods. Statistical analysis was undertaken to assess performance of BPS in predicting mortality.

Results 276 patients were included in the final analysis. Participants tended to be late middle-aged men, socioeconomically deprived and have alcohol-related liver disease. A similar proportion was BPS+ve (>3) in this study compared with the original Bristol cohort though had more hospital admissions, higher ongoing alcohol use and poorer performance status. BPS performed poorer in this non-Bristol group with sensitivity 54.9% (72.2% in original study), specificity 58% (83.8%) and positive predictive value (PPV) 43.4% (81.3%).

Conclusion BPS was unable to accurately predict mortality in this Scottish cohort. This highlights the ongoing challenge of prognostication in patients with chronic liver disease, furthering the call for more work in this field.

Summary box

What is already known about this subject?

- Despite patients with chronic liver disease having high rates of morbidity and mortality, few receive input from specialist palliative care.
- Multiple tools have been used to aid prognostication in chronic liver disease.
- The Bristol Prognostic Score (BPS) was developed to aid the identification of patients at risk of dying within 1 year and who may benefit from referral to specialist palliative care services.

What are the new findings?

- Although the BPS accurately predicted mortality in the original study, this was not replicated in this study of three Scottish hospitals.
- Key differences noted were in rates of hospital admission, ongoing alcohol use and lower performance status.

How might it impact on clinical practice in the foreseeable future?

- Further work is needed to identify better ways to predict both mortality and need for specialist palliative care in patients with chronic liver disease.
- Future directions may benefit from using patient-driven identification of need through symptom assessment and/or frailty assessment.

INTRODUCTION

Chronic liver disease, in particular at the cirrhotic stage, causes a significant burden of both morbidity and mortality, accounting for more than 1.32 million deaths globally each year.[1] While most other common malignant and non-malignant diseases have shown a declining mortality rate, deaths from liver disease in the UK have risen by over 400% since 1970.[2] Death rates from chronic liver disease are consistently highest for those aged under 65 years, making it a disease of working age. In the UK alone, deaths in this group accounts for 22 000 and 38 000 years of working life lost for women and men, respectively.[3 4] Cirrhosis is among the top five leading causes of death for people aged 20–34 years and is the leading cause of death for those aged 35–49.[2 4]

Patients with decompensated liver disease have high mortality rates, and a significant symptom burden. The prevalence of symptoms such as pain is comparable to those

dying of colon and lung cancer.[5] Despite this, such patients have low levels of referral to palliative care services.[6–8] There is growing recognition of the value that palliative care services bring to this group, with improved symptom control and patient satisfaction, lower hospital costs and reduced secondary care utilisation.[9–12]

Those living with and dying from decompensated liver disease experience a great deal of uncertainty with an often unpredictable disease trajectory.[13–15] Compared with those with decompensated liver disease alone, patients with a codiagnosis of hepatocellular carcinoma (HCC) or metastatic cancer have higher rates of referral to palliative care services,[7] suggesting this prognostic uncertainty is a major barrier to accessing specialist services. Other identified barriers include insufficient communication between clinicians and patients around goals of care as well as patient and clinician misperceptions about the role of palliative care.[16 17]

There are various laboratory and clinical markers of prognosis in cirrhotic liver disease, contributing to well-established prognostic models, including Child-Pugh Score and Model for End-stage Liver Disease (MELD).[18–20] However, these tools, widely used to predict prognosis and determine transplant priority, were initially designed to predict mortality in those undergoing surgical or radiological intervention for portal hypertension.[18–20] As such, they may not be best suited to identifying those for whom palliative care involvement is indicated. The Bristol Prognostic Score (BPS) was developed as a prognostic screening tool for inpatients with decompensated cirrhosis, to identify patients at high risk of dying within 12 months, for whom palliative care input should be considered.[21] The BPS comprises of five criteria: Child-Pugh C disease, >2 liver-related admissions in the last 6 months, ongoing alcohol use (in alcohol-related liver disease (ArLD)), unsuitable for transplant and WHO performance status 3–4. A score≥3 had a PPV for 1-year mortality of 81.3%, with a sensitivity of 72.2% and specificity of 83.8%. This threshold was suggested as a useful trigger for discussion in a supportive care multidisciplinary team meeting attended by gastroenterology and palliative care specialists.

Given existing evidence of under-referral to palliative care services, we sought to retrospectively evaluate the ability of BPS to identity those at risk of dying within 1 year following admission to one of three Scottish Hospitals.

METHODS

Sample selection

Patients over 18 years who were admitted with decompensated chronic liver disease during two 90-day periods and surviving to discharge were included. The first was from March to June 2017, chosen to coincide with existing data from an audit of symptom burden at one of the hospitals (Glasgow Royal Infirmary (GRI)).[22] Admissions from the other two hospitals (Forth Valley Royal Hospital (FVRH), Larbert and Ninewells Hospital (NW), Dundee) for this period were identified by screening discharges from gastroenterology units retrospectively. A similar audit of a further 3-month period from March to June 2019, was undertaken at all three sites, to increase numbers while ensuring 1 year of follow-up.

Patients were excluded if they were electively admitted for a procedure, did not have follow-up data at 1 year or died during their admission. Patients who died during admission were excluded in an attempt to standardise retrospective data collection, as parameters nearest discharge were used to give the most accurate reflection of liver function. All patients with HCC are discussed at a regional multidisciplinary team meeting (MDT) with advice for patients suitable for palliative treatment or best supportive care only to be added to the palliative care register. Our local experience reflects published data[7] that those with HCC are more likely to be referred to palliative care services, and as such we chose to focus on patients with liver disease without cancer, as an area of the highest unmet clinical need.

Data collection

All data were obtained from review of patients' electronic clinical records. Baseline demographic data were collected for each patient including gender, age at admission, date of admission, date of discharge and postcode. The latter was used to obtain Scottish Index for Multiple Deprivation (SIMD) 2016, a measure of socioeconomic deprivation which ranks postcode areas in Scotland.[23]

BPS was calculated using Child-Pugh Score (calculated based on parameters nearest patients' discharge); number of admissions in the preceding 6 months; ongoing alcohol consumption (if ArLD); suitability for transplant and performance status (using agreed proxy markers from clinic letters or allied healthcare professional assessment if performance status unavailable). For patients who did not undergo formal transplant assessment, the approach used in the BPS derivation cohort was adopted, wherein surrogates for unsuitability of transplant were used: ongoing alcohol misuse, age>75 and untreated extrahepatic malignancy.[21] The Scottish national Community Health Index (CHI) database records date of death provided this took place in Scotland, and date of death was recorded (where applicable) to identify deaths within 1 year post discharge. Further data were collected on aetiology of liver disease. Data not available from electronic records were obtained from paper notes (FVRH and NW) and discussion with the patients' main hepatologist, where required.

Statistics

IBM SPSS v27 Statistics Subscription was used for all statistical analysis. Descriptive statistics were presented for continuous data as mean (SD) or median (±IQR) according to normality. Categorical data were presented as percentages with frequencies. Chi-squared test was used to compare categorical variables between the combined Scottish cohort and the original Bristol cohort. A p value

Table 1 Demographic details of patients presenting with decompensated cirrhotic liver disease over a 90-day period from March to June 2017 and from March to June 2019, compared with Bristol cohort

	Scottish cohort	Bristol	P value
N	276	73	
Male, n (%)	187 (67.8)	58 (79.5)	0.052
Age	61 (51–68) Mean (SD)	54.5 (47–66.25) Median (IQR)	
BPS ≥3, n (%)	129 (46.7)	32 (43.8)	0.658
Child-Pugh C	112 (40.6)	36 (49.3)	0.179
ArLD n (%)	179 (64.9)	46 (63.0)	0.770
SIMD1 (%)	124/269 (46.1%)	NA	

ArLD, alcohol-related liver disease; SIMD, Scottish Index for Multiple Deprivation.

of ≤0.05 was considered statistically significant. Student's t-test or Mann-Whitney U test was used to compare continuous data as appropriate.

Receiver operating characteristic (ROC) curve analyses were performed for BPS as a continuous variable. Sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) were also calculated.

RESULTS

Baseline demographic data

Two hundred and ninety-five patients with decompensated liver disease surviving to discharge were identified during the audit period—13 patients were excluded as they died during admission. Of the 295 patients, 19 were excluded due to coexisting hepatocellular cancer diagnosis,[9] elective admission[5] and incomplete follow-up data,[5] giving a final cohort of 276 patients (120 GRI, 108 NW and 48 FVRH). Patients were typically male (187, 67.8%), in late middle age (median 61 years (±IQR) and predominantly suffering from ArLD (179, 64.9%). No significant differences were identified in comparison with the Bristol cohort (table 1). Likewise, a similar proportion of patients had Child's C cirrhosis (112 (40.6) vs 36 (49.3), p=0.179), and there was no difference in the proportion of patients with a BPS≥3 (129 (46.7%) vs 32 (43.8%), p=0.658). Among 269 patients for whom SIMD could be calculated, almost half (124, 46.1%) lived in the most deprived quintile (SIMD1).

Bristol Prognostic Score

One hundred and twenty-nine (46.7%) patients had a BPS of ≥3. The majority of patients scored points for being unsuitable for liver transplant (81.9%) and having ongoing alcohol use in the context of ArLD (74.9%). Compared with the BPS cohort, there was a statistically significant difference in patients with >2 liver-related admissions in the previous 6 months (23.6% vs 9.6%, p=0.009), ongoing alcohol use among those with ArLD (74.9% vs 60.3%, p=0.002), as well as a higher prevalence of patients with PS3/4 (34.1% vs 19.2%, p=0.014) between this Scottish cohort and the original Bristol cohort, respectively, (table 2).

Outcomes and BPS performance

One hundred and three patients (37.3%) died at 1-year follow, compared with thirty-six (49.3%) in the BPS cohort (p=0.063). Of the 103 patients who died, 56 (54.4%) had a BPS of ≥3 and 47 (45.6%) BPS<3. The performance characteristics of the BPS in this cohort were hence suboptimal with a sensitivity of 54.9% (95% CI: 45.2% to 64.6%), and specificity of 58.0% (50.7%–65.4%). AUROC for BPS as a continuous variable (figure 1) was 0.619 (95% CI: 0.552 to 0.686).

The PPV of a BPS≥3 was 43.4% (95% CI: 34.9% to 52.0%) while the NPV of 68.7% (95% CI: 61.2% to 76.2%). Among the 112 patients with Child-Pugh C stage disease, 44 died within 1 year of follow-up—PPV 44.6% (95% CI: 37.8% to 51.7%).

DISCUSSION

Involvement of palliative care teams as part of the wider multidisciplinary service has a number of demonstrable benefits for patients dying with advanced liver disease: shorter length of inpatient hospital stay; fewer invasive procedures; fewer in-hospital deaths; lower cost of care during terminal hospitalisation.[24] Patients referred to palliative care have also been shown to have comparable survival to those without referral, showing that often invasive, prolonged admissions may be futile in those with life-threatening advanced liver disease.[25] Hepatologists describe having limited time and feeling underprepared in having anticipatory care planning discussions with patients, thus adding to the drive for integrated collaborative approaches with palliative care playing a key role in the wider multidisciplinary service.[16]

Despite this demonstrable need and benefit for patients, access to specialist palliative care services for those with advanced liver disease is often limited and late. There is some hopeful evidence that palliative care consultation rates are improving, increasing from 0.97% in 2006 to 7.1% in 2012 for those with end-stage liver disease in the USA.[8] However, patients rarely receive referral to palliative care services outside of hospital, with one transplant centre in the USA reporting 90% of referrals occurred during a hospital admission.[26] There have been a number of identified barriers to accessing specialist palliative care, including poor patient and physician understanding of palliative care services; uncertain illness trajectories; physicians having insufficient time for discussions around anticipatory care planning and a lack of awareness that palliative care can complement rather than prohibit disease modifying treatments and transplantation for this group.[17] Furthermore, the difficulty in identifying those with specialist palliative care needs is an ongoing challenge.[27]

Table 2 Prevalence of individual criteria of BPS, compared with Bristol cohort

BPS domain	Scottish cohort	Bristol cohort	P value
Child-Pugh C disease n(%)	112 (40.6)	36 (49.3)	0.162
>2 liver-related admissions in previous 6 months, n (%)	65 (23.6)	7 (9.6)	0.009
Ongoing alcohol use in alcohol-related liver disease, n (%)	134 (74.9)	44 (60.3)	0.002
Unsuitable for transplant, n (%)	226 (81.9)	62 (84.9)	0.524
WHO performance status 3–4, n (%)	94 (34.1)	14 (19.2)	0.014

Familiar scoring systems, Child-Pugh and MELD, were originally designed to predict mortality post surgery and subsequently validated and adopted for prediction of overall mortality. By using a mixture of biochemical and clinical markers, these pre-established scoring systems ultimately fail to describe the individual patient, their symptom burden and comorbidities, which may be more indicative of palliative care need. By combining an established score (Child-Pugh) with global assessments of performance status, markers of disease trajectory (frequent admissions), social history (ongoing alcohol consumption) and lack of suitability for definitive treatment (liver transplantation), BPS sought to improve on existing scores to discriminate those likely to be in the last year of life.[21] This was true in the cohort from which it was derived, and it therefore appeared attractive as a trigger for consideration of palliative care involvement.

The original BPS study included 83 patients and showed that in those with a BPS of 3 or more, the test was highly discriminatory with sensitivity=72.2%, specificity=83.8% and the PPV=81.3%.[21] However, despite a similar frequency of BPS≥3 in our multicentre cohort of 276 patients, the performance of the BPS was poorer. In particular, given the goal of identifying patients entering the last year of life, the PPV for 1-year mortality was less than 50%. Among baseline characteristics of patients included, we were unable to identify any significant difference that would account for these discrepancies. On analysing the prevalence of each individual BPS domain between the two cohorts, it was identified that both ongoing alcohol use in ArLD and >2 liver-related admissions were higher among our population, as was the prevalence of poor (PS3/4) performance status. It may be that the predictive value of BPS is dependent on the rate of these underlying features within individual populations. The threshold for admission may vary between different locales based on features such as geographic distance from hospital, ease of accessing healthcare and differences in outpatient services. Ongoing alcohol may reflect societal attitudes, as well as available access to alcohol recovery services.

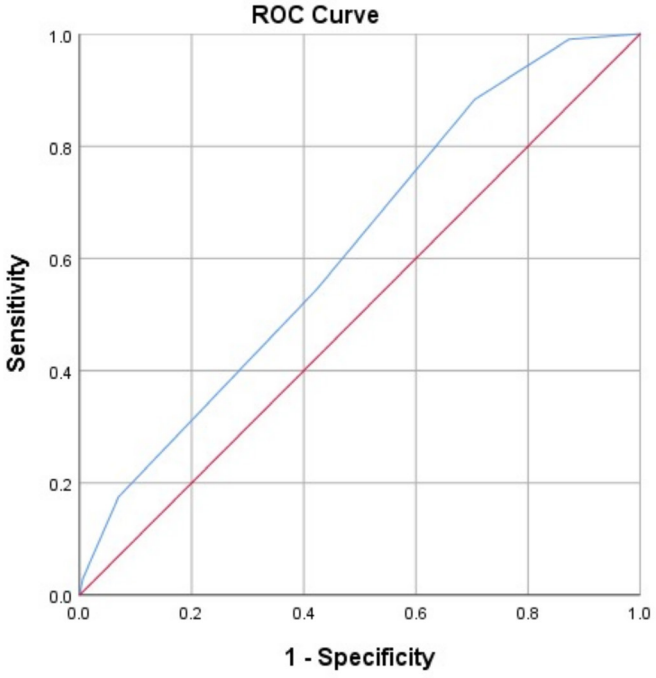

Figure 1 Receiver operating curve (ROC) for predicting 1-year mortality in a non-Bristol cohort using the Bristol Prognostic Score.

Although the performance status of patients is included in the BPS, this is as the 4-point Karnofsky Performance Status. More comprehensive evaluations of frailty have been developed, such as the Liver Frailty Index,[28] which can evaluate frailty in more detail and is known to globally reflect function and risk of mortality. Furthermore, given that the primary aim of the BPS was to highlight patients in need of palliative care review, it does not evaluate the symptom burden that these patients are experiencing. Indeed, there are yet to be well-established measures of symptom burden in this group. The Integrated Palliative care Outcome Scale (IPOS) is used in many palliative care settings and is often seen as a standardised way of assessing symptoms.[29] There are now many disease-specific IPOS assessments available including for dementia,[30] neurological conditions[31] and renal disease[32] but none have been validated for advanced liver disease. Symptom burden has been shown to escalate in the last month of life, with one study reporting an average of 14 physical symptoms per patient (identified by patient interview and case note review),[33] therefore integration of this into a prognosticating tool may help identify those at a higher risk of death but also those who would benefit most from specialist palliative care involvement. Furthermore, even in patients being considered for transplant there is known prognostic uncertainty with 7% dying each year while on the waitlist[34]; recent work has also demonstrated this group have

a significant symptom burden and can benefit from integrated specialist palliative care thus the design of the BPS that increases scores for patients who are not for transplant could potentially miss some of this symptomatic group.[26] The disproportionate contribution of patients with the highest levels of socioeconomic deprivation to this cohort is striking, and inadequate access to palliative care at the end of life further contributes to inequalities in healthcare experienced by those experiencing deprivation.[35 36]

Strengths and limitations

At inception, we were unaware of any external validation of the BPS. Subsequently, Low *et al*[27] have published their assessment of its utility. Like the original BPS study, this comprised a single-centre cohort of patients, and in addition was undertaken in a tertiary care centre. Although they judged it to be of potential benefit in their cohort with a similar PPV to the original study (79% vs 81%) for 1-year mortality, like us, they also noted a lower sensitivity for a BPS (59% vs 72%) than in the derivation cohort. To date, ours is the first multicentre evaluation of the BPS, the patients included reflecting unselected liver admissions in both urban and rural settings.

There are some differences in methodology used between this study and the original: patients were excluded if they died during the admission in an attempt to standardise data collection. Only 13 patients were excluded for this reason and this is unlikely to have significantly impacted on results in this large cohort. Furthermore, we excluded patients known to have HCC (nine in total) as there are data showing such patients are more likely to receive referral for palliative care,[7] and their prognosis is mainly influenced by the HCC rather than their liver disease.

This body of work was retrospective and suffers the known limitations of such studies. In particular, certain elements of Child-Pugh relied on researcher agreement and best estimates, for example, in assigning a score related to ascites. Retrospective calculation of WHO performance status was a further challenge, with attempts to overcome this by agreed criteria between data collectors; this was similar to the methodology of the original BPS study. Although not reaching statistical significance (p=0.06), 1-year mortality rates were higher in the Bristol cohort (49.3% vs 37.3%). Although rates of Child-Pugh C liver disease were similar, it may be that the original Bristol cohort was sicker, and better performance of a predictive score in a cohort may be explained by an increased likelihood of death within it. As thresholds for admission, specialisation of care (hepatology vs gastroenterology vs general medicine) and levels of support on discharge (eg, access to nurse specialists) vary between centres, it is important to ensure that any predictive score has adequate performance across a range of mortality rates.

CONCLUSION

In conclusion, although the BPS performed well in the original Bristol cohort, this could not be replicated in this larger multicentre population. Established prognosticating scores are potentially unreliable in different populations; perhaps due to the unpredictable nature of chronic liver disease, which is difficult to encapsulate based on biochemical/clinical parameters or varying contributions from different aetiologies. They also fail to consider the lived experience of individual patients. Thus, future predictors of both prognosis and palliative care need would benefit from integration of both clinician and patient-described parameters.

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Contributors SPB and SB were responsible for the study concept and design. SPB, KC, LH, KM, ES and AB-K were responsible for obtaining local Caldicott approval and the acquisition of data. SB, JFD and SPB undertook data analysis and interpretation of results. AA, JFD and SB provided supervision for each hospital site. SPB drafted the initial manuscript. KC, LH, AA, FF, JFD and SB critically revised the manuscript content. Consensus was reached between all contributors prior to data collection on standardised criteria for each variable to minimise interobserver variation. SB, ABK and LH collected data from Glasgow Royal Infirmary, SB and ES collected data from Ninewells Hospital and KC and KM collected data from Forth Valley Royal Hospital. All authors gave final approval of the manuscript for publication.

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Patient consent for publication Not applicable.

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Data availability statement Data are available upon reasonable request. Unidentifiable datasets are available which can be shared at the request of readers if there is a reasonable request.

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