Non-invasive Diagnosis of Oesophageal Varices Using Systemic Haemodynamic Measurements by Finometry: Comparison with Other Non-invasive Predictive Scores

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Background/Aims: **Cirrhosis and portal hypertension are characterised by a hyperdynamic circulation, which is independently associated with variceal size. Non-invasive techniques for measurement of systemic haemodynamics are now available. The aim of the study was to prospectively assess the accuracy of systemic haemodynamics measured non-invasively for the detection of oesophageal varices in cirrhotic patients as compared to other currently available non-invasive methods.** ***Methods:*** **In a study of 29 cirrhotic patients, systemic haemodynamics were studied non-invasively using the Finometer® (mean arterial pressure (MAP), cardiac output (CO)/index, heart rate (HR), peripheral vascular resistance) and portal pressure was assessed by hepatic venous pressure gradient. Sensitivity, specificity, predictive values and area under the receiver operating characteristic (ROC) curves were assessed for predicting presence of varices and large oesophageal varices. Results were compared to child's classification, platelet/spleen ratio and ALT/AST ratios as predictors of the presence of large varices.** ***Results:*** **Using finometry large oesophageal varices were correctly predicted in 83% of patients compared to other non-invasive techniques (range 66–76%).** ***Conclusions:*** **Non-invasive assessment of systemic haemodynamics using finometry could aid the identification of patients who do not immediately require variceal surveillance reducing the numbers of endoscopies and ensuring services are provided to those most likely to benefit. (J Clin Exp Hepatol 2016;6:195–202)**

INTRODUCTION

Although mortality from a variceal bleeding episode has decreased with improved endoscopic and radiological techniques together with new pharmacologic therapies, a 15–20% mortality[1–4] means that bleeding from oesophageal varices remains of significant clinical importance. Early diagnosis of varices before the first bleed is essential as studies of primary prophylaxis clearly show that the risk of variceal haemorrhage can be reduced by 50% to about 15% for large oesophageal varices.[5,6] Current guidelines therefore recommend that all cirrhotic patients should be screened for varices at diagnosis, with follow-up every 2–3 years for patients without varices (depending upon liver disease severity) and 1–2 yearly for patients with small varices, to assess for enlargement of varices and need for prophylactic treatment.[7] Upper GI endoscopy remains the gold standard for screening, but this test is not without its own limitations. The current guidelines cause a significant burden and cost to endoscopy units, and necessitate patients having repeated unpleasant procedures even when up to 50% may still not have developed oesophageal varices 10 years after the initial diagnosis.[8] If it were possible to predict oesophageal varices by non-invasive means, this restricts testing to the population deemed to be at most risk and reduce the number of endoscopies required. Such a screening test should be simple, quick, reproducible and cost-effective.

Numerous surrogate markers have been evaluated to non-invasively predict the presence of oesophageal varices. These include platelet count (9–12), platelet count/spleen diameter ratio (13–19) and AST/ALT ratio (20). To date, none of these have proved accurate enough to be used routinely and avoid endoscopy.

Portal hypertension is characterised by an increased cardiac output (CO), heart rate (HR) and stroke volume (SV) and reduced peripheral vascular resistance.[21] The

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Abbreviations: MELD: model of end stage liver disease; LOV: large oesophageal varices; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; HR: heart rate; SV: stroke volume; CO: cardiac output; CI: cardiac index; PVR: peripheral resistance; NIEC: North Italian Endoscopy Club; HVPG: hepatic venous pressure gradient; PT: prothrombin time; AAR: AST/ALT ratio; PSDR: platelet count-to spleen diameter ratio; IQR: interquartile range; ROC: receiver operating characteristic; Se: sensitivity; Sp: specificity; PPV: positive predictive value; NPV: negative predictive value; LR+: positive likelihood ratio; LR−: negative likelihood ratio
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Finometer® (Finapres Medical Systems, Amsterdam, The Netherlands) is a non-invasive device that allows continuous beat-to-beat blood pressure and haemodynamic monitoring over a number of hours. Utilising a volume-clamp method to provide a continuous measure of finger pressure with subsequent reconstruction of brachial pressure, it allows the computation of an aortic flow wave form and impedance from which HR, SV, peripheral vascular resistance and cardiac output can be derived. The Finometer therefore provides a non-invasive method of continuous beat-to-beat measurement of systemic haemodynamic variables with good positive correlation to portal pressure.[22]

The aim of this prospective study was to assess the predictive value of systemic haemodynamics assessed non-invasively using finometry for the diagnosis of oesophageal varices in cirrhotic patients, and to compare it with other currently available non-invasive predictors.

METHODOLOGY

29 patients with proven cirrhosis (irrespective of aetiology) were studied. All patients were known to have endoscopically proven oesophageal varices or to require an endoscopy for suspected oesophageal varices. Exclusions included a prior history of variceal bleeding requiring therapeutic variceal intervention or known portal vein thrombosis or a history of cardiac complications due to cirrhosis. Non-portal hypertension exclusions included a documented history of cardiac disease or hypertension. Patients with known oesophageal varices taking β-blockers had their drugs discontinued 14 days prior to any haemodynamic measurements. Written consent was obtained and our local research ethics committee approved the study.

The study protocol entailed two separate visits. At the initial visit, endoscopic and non-invasive haemodynamic (fasting) assessments were performed following a detailed clinical and alcohol assessments. Laboratory assessment including bilirubin, albumin, platelet count, prothrombin time (PT), AST, ALT and sodium were undertaken to allow the calculation of the Child–Pugh and MELD scores. At the second visit, a non-fasting non-invasive haemodynamic study was repeated to verify the initial results together with an ultrasound to assess bipolar spleen size.

Evaluation of beat-to-beat blood pressure using the Finometer® was carried out as previously described.[22] Readings were taken on different days and at different times by a single operator trained in the technique. The results of the recordings were not known prior to endoscopy. The following haemodynamic variables were calculated: systolic and diastolic blood pressure (SBP, DBP), mean arterial pressure (MAP), HR, SV, CO, cardiac index (CI), and peripheral resistance (PVR).

An experienced endoscopist performed gastroscopy with oesophageal varices being classified according to the Japanese Research Society for Portal Hypertension and the Japanese score, NIEC index and 1 year probability of bleeding calculated.[23–25] Patients were separated into two groups, Group 1 – absent or small varices; Group 2 – medium or large varices, or gastric varices (LOV). The findings were agreed between the endoscopist and a second clinician observing the procedure.

Portal pressure was assessed by measurement of the hepatic venous pressure gradient (HVPG) as described by Groszmann and Wongcharatrawee.[26] HVPG was calculated as the difference between the occluded and the free hepatic venous pressure (mmHg). Three consecutive measurements were taken and the results averaged.

To facilitate the calculation of non-invasive predictive scores, the following laboratory parameters were recorded: serum bilirubin, albumin, PT, platelet count, aspartate transaminase (AST), alanine transaminase (ALT) and creatinine, together with the ultrasound derived bipolar spleen diameter, grade of ascites and encephalopathy. This facilitated calculation of Child–Pugh score and class, MELD, AST/ALT ratio (AAR) and the platelet count-to spleen diameter ratio (PSDR).

STATISTICAL ANALYSIS

Results are expressed as median (interquartile range, IQR). Differences between groups were compared using the Mann–Whitney test and the association between two variables was assessed by the Spearman correlation co-efficient. Analyse-It for Microsoft Excel (Version 2.21) was used for statistical analysis. P values <0.05 were considered statistically significant.

Receiver operating characteristic (ROC) curves were constructed and sensitivity (Se), specificity (Sp), positive and negative predictive values (PPV and NPV), positive likelihood ratio (LR+) and negative likelihood ratio (LR−) were calculated. ROC curves were used to establish the optimal cut-offs for each predictor, as they were not specifically designed to detect oesophageal varices.

RESULTS

The characteristics of the 29 patients (20 men and 9 women) are shown in Table 1. The median age was 47 years (42–55 years). Aetiology of the cirrhotic cohort included alcohol abuse (n = 18; [62%]), alcohol abuse and hepatitis C (n = 5; [17%]), alcohol abuse and autoimmune hepatitis (n = 3; [10%]), autoimmune hepatitis (n = 2; [7%]) and hepatitis C (n = 1; [4%]). 19 patients (66%) were abstinent from alcohol. Child–Pugh stratification was class A (62%), Class B (34%) and Class C (4%). Oesophageal varices were present in 23 patients (79%), classified as small in 12 patients, medium in 8 patients and large in 3 patients. None of the included patients had evidence of gastric varices at endoscopy. As a