Pressure of intraoesophageal varices assessed by fine needle puncture: its relation to endoscopic signs and severity of liver disease in patients with cirrhosis

G KLEBER, T SAUERBRUCH, G FISCHER, AND G PAUMGARTNER

From the Department of Medicine II, University of Munich, FRG

SUMMARY In 40 patients with cirrhosis and oesophageal varices transmural variceal pressure was assessed endoscopically by fine needle puncture and related to endoscopic signs as well as to the severity of liver disease. Transmural pressure was significantly ($p < 0.01$) higher in the presence of a red colour sign (26.7 (7.8) cm H₂O) than in its absence (19.1 (6.6) cm H₂O). Transmural pressure, however, was not significantly related to diameter or number of varices (diameter > 5 mm: 23.7 (8.4), diameter ≤ 5 mm: 22.2 (7.9) cm H₂O; number > 3 : 23.2 (8.0), number ≤ 3 : 22.2 (7.8) cm H₂O). The Child status (Child A: 23.9 (8.0), Child B/C: 21.3 (8.1) cm H₂O) and individual Child-Pugh parameters including ascites (ascites present: 23.2 (8.3) cm H₂O, ascites absent: 22.8 (8.1) cm H₂O) were not significantly related to transmural variceal pressure. We conclude that the endoscopic visibility of a red colour sign on the varices is associated with a high transmural oesophageal variceal pressure. Our results favour the hypothesis that variceal pressure may be of major importance for the development of the red colour sign.

Cherry red or haematocystic spots on the variceal surface (red colour sign¹), have been supposed to be risk factors for oesophageal variceal haemorrhage in patients with portal hypertension.² It has been suggested that this endoscopic sign corresponds histologically to dilated intraepithelial blood filled channels communicating with subepithelial capillaries.^{3,4} The pathogenesis of the red colour sign is unknown and its relationship to haemodynamic parameters in patients with cirrhosis has as yet not been evaluated. Only recently, measurement of variceal blood pressure has become a new approach in the evaluation of portal hypertension.^{5,6} We hypothesised that an increase in blood pressure may be associated with the development of the red colour sign. We therefore measured transmural oesophageal variceal blood pressure in cirrhotic patients with and without the red colour sign on the varices. In addition the relation of transmural oesophageal

variceal pressure to various other clinical, laboratory and endoscopic parameters was investigated.

Methods

PATIENTS

Between July 1985 and November 1987 transmural oesophageal variceal pressure was assessed endoscopically immediately before the first sclerotherapy session in 40 patients with liver cirrhosis and medium or large sized (diameter > 2 mm) oesophageal varices. Patients characteristics are given in Table 1.

At the time of pressure measurement various clinical and laboratory parameters were assessed (Table 1). From these the patients were grouped according to a modified Child classification.⁷ None of the patients were on prophylactic medical treatment for bleeding or on drugs known to reduce variceal or portal blood pressure. All ascitic and 12 of 29 nonascitic patients were on diuretic treatment.

After premedication with 10 mg diazepam and 40 mg n-butylscopolamin an Olympus GIF K 10 endoscope was introduced with the patient in his left

Address for correspondence: Dr G Kleber, Department of Medicine II, Klinikum Grosshadern, University of Munich, Marchioninstr. 15, D 8000 Munich 70, West Germany.

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Table 1 Clinical, laboratory and endoscopic characteristics in cirrhotic patients at the time of assessment of transmural oesophageal variceal blood pressure

Patients (n)	40
Age (yr)	61 (10)
Sex: male/female (n)	27/13
Aetiology of cirrhosis: alcoholic/non-alcohol. (n)	22/18
Bleeding history: positive/negative (n)	16/24
Severity of liver disease:	
Child A/B/C (n)	25/11/4
Bilirubin ($\mu\text{mol/l}$)	46 (62)
Albumin (g/l)	4.0 (0.6)
Prothrombin time (%)	73 (14)
Encephalopathy: present/absent (n)	13/27
Ascites (n)	
Absent	29
Moderate	7
Tense	4
Endoscopic parameters:	
Variceal diameter: $>5/\leq 5$ mm (n)	19/21
Variceal number: $>3/\leq 3$ (n)	27/13
Red colour sign: present/absent (n)	20/20
Oesophagitis present (n)	3

lateral position. During endoscopy the diameter (measured with an open biopsy forceps which had a span of 5 mm) and number of varices were assessed. In addition, the presence or absence of the red colour sign¹ was recorded by the same investigator immediately before determination of the pressure. The presence of the red colour sign was defined by the visibility of at least one typical red colour sign on the distal part of the varix punctured. In few patients there was only one typical red colour sign visible. The vast majority of the patients, however, exhibited multiple red colour signs on several variceal columns.

Determination of transmural oesophageal variceal pressure was achieved by simultaneous recording of intravariceal and oesophageal luminal pressures. The pressure curves were read by two independent

observers who were not involved in assessment of the endoscopic aspect of the varices. For measurement of oesophageal luminal pressure a Teflon tube (od 1.5 mm) with an outlet of 0.7 mm at its tip was attached to the outer surface of the endoscope, with the tip of this tube placed at the end of the endoscope. For measurement of intravariceal pressure a second Teflon tube of the same size, which was connected to a sclerotherapy needle (id 0.4 mm, od 0.6 mm), was used. Both tubes were perfused with 0.6 ml $\text{H}_2\text{O}/\text{min}$ using a high pressure low compliance capillary perfusion system (Mui Scientific, Canada). The tubes were connected to electromechanical transducers and pressures were recorded using a Beckman R 611 dynograph. Calibrations were done before each measurement by rising the needle to varying heights between 0 and 40 cm H_2O . The sclerotherapy needle was introduced through the biopsy channel of the endoscope and the needle's tip placed outside the endoscope within 1 to 2 cm from its distal end. After recording of intraoesophageal luminal pressure with both tubes simultaneously (A-B, Fig. 1), the largest variceal column 5 cm above the gastrooesophageal junction was punctured and the sclerotherapy needle was placed into an intravariceal position in the same way as this is done during routine sclerotherapy. An intramural position of the tip of the needle could be easily detected by an immediate increase of pressure to high values resulting from the tissue resistance to the perfusion (B-C, Fig. 1). The needle then was gently advanced or withdrawn until the tip of the needle was placed in the lumen of the varix. This position was identified by the typical respiration dependent pressure fluctuations (C-D, Fig. 1). With the other tube oesophageal luminal pressure was continuously recorded during measurement of intravariceal pressure. After 30 to 360 seconds of measurement, the sclerotherapy needle was gently withdrawn into the oesophageal

Fig. 1 Simultaneous recording of intravariceal blood pressure and oesophageal luminal pressure. Two measurements were performed consecutively in this patient. Lower line: Continuous oesophageal luminal pressure recording with a tube attached to the outer surface of the endoscope. Upper line: Pressure recording obtained via the sclerotherapy needle: A-B=recording of oesophageal luminal pressure, B=needle punctures variceal wall, the tip of the needle is not yet placed in the variceal lumen, C-D=correct intravariceal position of the needle's tip, which is identified by the typical respiration dependent pressure fluctuations, D=needle is withdrawn from varix. Transmural oesophageal variceal pressure was calculated as the difference between upper and lower line.

lumen (D, Fig. 1), resulting in a typical oesophageal luminal pressure recording (A-B, Fig. 1). Thereafter, the varix was compressed with the endoscope for three minutes to prevent potential bleeding from the puncture site. No serious complications were observed. We have shown previously that no significant intraindividual pressure changes are observed when repeated measurements are performed before and within 30 minutes after administration of a placebo.⁹ The study was approved by the Ethical Committee of the Faculty of Medicine, University of Munich.

STATISTICAL ANALYSIS

Results are given as means $\pm$ standard deviation (SD). The relationship between the degree of variceal pressure and the individual clinical, laboratory or endoscopic parameters was performed by the Mann-Whitney or Fisher's exact test or by linear regression analysis where appropriate.

Results

In this series of patients with cirrhosis transmural oesophageal variceal pressures ranged from 8.6 to 42.5 (22.9 (8.1)) cm H₂O.

Transmural pressure was not significantly related to age ($r = -0.05$), sex (men: 22.4 (8.7), women: 23.9 (6.7) cm H₂O) or etiology of cirrhosis (alcoholic: 22.9 (8.2), non-alcoholic: 22.9 (8.1) cm H₂O).

No relationship was found between transmural pressure and diameter or number of varices (Table 2). The transmural pressure was significantly higher, however, in patients in whom the red colour sign was seen on the varices than in the other patients (26.7 (7.8) cm H₂O v 19.1 (6.6) cm H₂O, $p < 0.01$, Table 2, Fig. 2).

The red colour sign was observed significantly ($p < 0.05$) more frequently in patients in whom the number of varices exceeded three compared with patients with a smaller number of varices. It was not

Fig. 2 Transmural oesophageal variceal blood pressure in patients with liver cirrhosis with and without the red colour sign.

Table 2 Transmural oesophageal variceal blood pressure (cm H₂O) in relation to endoscopic signs and liver function

Variceal diameter		
≤5 mm	22.2 (7.9)	ns
>5 mm	23.7 (8.4)	
Variceal number		
≤3	22.2 (7.8)	ns
>3	23.2 (8.3)	
Red colour sign		
Present	26.7 (7.8)	$p < 0.01$
Absent	19.1 (6.6)	
Severity of liver disease		
Child A	23.9 (8.0)	ns
Child B/C	21.3 (8.1)	

related, however, to the variceal diameter (Table 3). None of the endoscopic criteria including the red colour sign (Table 3) was significantly related to the clinical or laboratory parameters of the Child-Pugh classification.

Transmural variceal pressure was not significantly related to the Child status (Child A: 23.9 (8.0), Child B/C: 21.3 (8.1) cm H₂O, Table 2) nor to serum bilirubin ($r = -0.26$) or albumin ($r = -0.13$) nor to the prothrombin time ($r = 0.12$). No significant association was found between the degree of variceal pressure and the presence of ascites (present: 23.2 (8.3), absent: 22.8 (8.1) cm H₂O). Transmural variceal pressure was similar in patients treated with diuretics (22.3 (7.2) cm H₂O) and in untreated patients (23.1 (8.8) cm H₂O).

Table 3 Prevalence of the red colour sign in relation to endoscopic signs and liver function

	Red colour sign	
	Present	Absent
Patients (n)	20	20
Oesophagitis		
Present	2	1
Absent	18	19*
Variceal diameter		
≤5 mm	9	12*
>5 mm	11	8
Variceal number		
≤3	5	11
>3	15	9†
Bilirubin		
<34 µmol/l	15	13
≥34 µmol/l	5	7*
Albumin		
≤4 g/l	12	13
>4 g/l	8	7*
Ascites		
Present	4	6
Absent	16	14*
Child		
A	14	11
B/C	6	9*

* = ns; † = p < 0.05.

Discussion

Improved methods for measurement of intravariceal pressure⁶ have led to renewed interest in this important haemodynamic parameter in patients with oesophageal varices and have made clinical studies feasible. Transmural oesophageal variceal pressures in the present study were obtained by simultaneous recording of intravariceal and oesophageal luminal pressures and were found in a similar range (8.6–42.5 cm H₂O) as those previously reported by others in smaller series.^{6,10} We report the relation of this pressure to various endoscopic signs and to the severity of liver disease in 40 patients with cirrhosis. This study group (Table 1) comprised only few Child C patients and did not include patients with very small varices because we feel that exact puncture of these vessels is difficult. Many patients with large varices and no previous bleeding were included because of the relatively large number of patients referred to our endoscopy unit for prophylactic sclerotherapy during the study period.

Evidence has been presented that the red colour sign¹ is a bleeding risk indicator in patients with oesophageal varices.² This endoscopic sign corresponds to dilated blood filled channels lying within and beneath the squamous epithelium and communicating with subepithelial capillaries.^{3,4} Interobserver variability in rating of the presence or absence of the

red colour sign has been shown to be low.¹¹ Thus, the influence on our results by an observation bias is probably minor. Chronic variceal hypertension might cause impairment of variceal tissue structure by 'erosion from within'¹³ and lead to the development of these lesions. This has been suggested earlier¹ and is supported by the present study: Transmural oesophageal variceal pressure was nearly 40% higher in the presence than in the absence of the red colour sign. The finding of a significant correlation between variceal blood pressure and the presence of the red colour sign seemed to be independent from other factors, since neither variceal pressure nor the red colour sign were significantly related to any of the various endoscopic, clinical and laboratory parameters assessed in the present study. The only exception was that the red colour sign was observed in significantly more patients in whom the number of varices exceeded three. This may be the result of the larger variceal surface in these patients. On the other hand, small pressure differences between patient groups with and without the criteria listed in Table 3 may have been missed due to a rather small number of patients in the present study (type II error).

Oesophagitis¹² – that is, 'erosion from without'¹³ has been suggested⁴ to be unlikely to play a major role in the development of the red colour sign and was only occasionally associated with the red colour sign in our patients (Table 1).

Although in contradiction to the results of some,^{6,10} but not all¹⁴ authors the absence of a significant correlation between variceal pressure and diameter or number of varices is not a surprise. An increase in portal pressure might well be counterbalanced by a consecutive increase in variceal diameter leading to decreased resistance and increased flow¹⁵ without a rise in variceal pressure. Small varices, however, were not included in the present study because of the difficulty of pressure measurement. It might well be that these small vessels do have low pressures.

No reports are available on the relationship between variceal pressure and the severity of liver disease. Portal pressure has been found to be slightly higher in patients with severe liver disease as compared with patients with mild liver disease.¹⁶ We did not find a significant relation between the variceal pressure and the Child status or individual clinical or laboratory tests reflecting the severity of liver disease. This may have been because of the low number of Child C patients included in the study.

It is of particular interest that the presence of ascites was not associated with an increased transmural variceal pressure. Ascites has been suggested^{17,18} to be an important indicator of the risk of variceal bleeding. Most authors^{8,19–21} have found a rise in portal pressure in ascitic patients. A pre-

liminary report²² suggests that acute experimentally induced intra-abdominal pressure rises cause increments in oesophageal variceal pressure. The effects of chronic portal hypertension on variceal pressure might be different, however: our study shows that transmural oesophageal variceal blood pressure is not higher in patients with ascites than in those without ascites. The results could be interpreted in the sense that a potential increase in portal pressure caused by ascites is counterbalanced by an increased resistance to upper portosystemic collateral flow²³ or by an increased intrathoracic pressure²⁴ as a result of ascites. Both mechanisms would act to reduce transmural variceal pressure either by not allowing portal pressure to be fully transmitted to oesophageal varices or by counterbalancing the intravariceal by a raised extravariceal pressure. It is not clear how portal pressure correlates to variceal pressure because no simultaneous measurements¹⁰ using the same reference pressure have been reported in the literature.

In conclusion, this study suggests that the red colour sign is an indicator of high variceal pressure. No other endoscopic, clinical or laboratory test including ascites was associated with the degree of variceal pressure rise.

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