

Postmeal Portal Flow Variations in HCV-related Chronic Hepatitis and Liver Cirrhosis with and without Hyperdynamic Syndrome

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Abstract. *Background:* Doppler ultrasonography (US) of portal blood flow and portal flow volume (PFV) are useful to define changes in portal hemodynamics of patients with chronic liver diseases. The meal test with postmeal PFV measurements is generally accepted as a reproducible noninvasive test to evaluate the severity of portal hypertension. The aim of this study was to evaluate whether monitoring PFV changes after ingestion of a standard meal would be useful to characterize patients with chronic hepatitis or liver cirrhosis in the presence or absence of hyperdynamic syndrome (HS) characterized by elevated PFV, splenomegaly, systemic hypotension and/or increased cardiac output. *Patients and Methods:* Thirty-seven patients (22 men and 15 women, median age 53 years) with hepatitis C virus infection and 20 healthy age- and sex-matched volunteers (Controls) were enrolled in the study. There were 19 (51.4%) patients with chronic hepatitis (Group A) and 18 (48.6%) with ultrasonographic evidence of liver cirrhosis (Child-Pugh class B), 9 of whom had an HS (Group B) while the remainder (Group C) did not. Each patient underwent liver color Doppler US and the test was repeated 30, 60 and 90 minutes after administration of a standard meal (300 kcal fluid meal containing 12 g of proteins, 11.6 g of lipids and 36.8 g of carbohydrates). *Results:* The baseline PFV did not differ ($p=NS$) between Controls and both Groups A and C, while the

PFV of Group B patients was significantly ($p<0.01$) higher. After 30 minutes, the PFV increased ($p<0.01$) both in Controls and Group A patients, while the differences were not significant in cirrhotic patients (Groups B and C). Our study confirmed that the postmeal PFV increases in both healthy individuals and in patients with chronic hepatitis, while in cirrhotic patients no significant changes occur. In conclusion, monitoring the portal blood flow in cirrhotic patients before and after administration of a standard meal might be a suitable test to evaluate potential disturbances of the flow itself. Moreover, the test could be useful to determine optimal pharmacological or surgical interventions aimed at restoring a better flow to the liver by reducing or favouring the occurrence of spontaneous mesenteric-systemic venous shunts.

Normal portal flow volume (PFV) is regulated by several factors, including hormonal secretion and splanchnic blood flow, which are in turn regulated by metabolic products, tissue osmolarity, local pO_2 , hydrogen ions, adenosine and nitric oxide (1). Moreover, it has been shown that PFV responds to functional stimulations (*i.e.* glucagon injection) and a poor PFV that increases during this test is associated with histological features of severe liver damage (2).

Unfortunately, the glucagon test is invasive and is not always tolerated by patients with liver cirrhosis, thus less invasive tests are required. Considering the hyperemia that develops in the intestinal mucosa during the postprandial period, some researchers have proposed the study of portal system hemodynamics during this period as a good tool for PFV evaluation, by observing an impaired response in cirrhotic patients compared to normal individuals (3-7). Currently, the meal test with postmeal PFV measurements is generally accepted as a reproducible

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noninvasive test to evaluate the severity of portal hypertension (5-8). However, it has never been utilized to test PFV changes in cirrhotic patients with and without hyperdynamic syndrome.

Doppler ultrasonography (US) of portal blood flow and PFV have proved to be useful to define changes in portal hemodynamics in chronic liver diseases (9, 10).

The aim of this study was to evaluate the ultrasonographic changes in portal system hemodynamics after a standard meal in patients affected by chronic liver diseases, with and without hyperdynamic syndrome.

Patients and Methods

Study population. Thirty-seven patients (22 men, and 15 women, median age 53 years) with hepatitis C virus infection, and 20 (Controls) healthy age-matched volunteers (12 men and 8 women, median age 49 years) were enrolled in this study. There were 19 (51.4%) patients (Group A) with chronic hepatitis (histological activity measured by the Knodell score ranging from 8 to 10), and 18 (48.6%) with ultrasonographic evidence of liver cirrhosis (Child-Pugh class B). Patients with diabetes mellitus or hyperthyroidism, as well as those treated with vasodilator and prokinetic drugs or with a history of gastroesophageal variceal hemorrhage were excluded from the study. No patients had spontaneous porto-systemic shunts at US evaluation.

Informed consent. Informed consent was obtained from all participants in accordance with institutional review board approval. The study protocol was approved by the Ethical Committee of the University of Campus Bio-Medico (Rome). There was no conflict of interest between authors.

According to Blendis *et al.* (11), 9 out of 18 patients with liver cirrhosis were considered as having a hyperdynamic syndrome (Group B), since they had elevated PFV at baseline splenomegaly, systemic hypotension and/or increased cardiac output. The other 9 patients with liver cirrhosis did not have any hyperdynamic syndrome (Group C).

Standard meal. All patients ingested a 200 ml fluid meal provided by our hospital of 1300 kJ (300 kcal) with the following composition: 12 g of proteins, 11.6 g lipids and 36.8 g of carbohydrates.

Color Doppler US evaluation. For each patient, liver examination by color Doppler US was performed by a single operator (MR) using Esaote AU 5 (Esaote, Genova, Italy) equipment and a convex 3.5 MHz probe. All patients were examined in the supine position after 12-hour fasting, before (basal observation) and 30, 60 and 90 minutes after the standard liquid meal ingestion. For each patient, the portal (PV) and splenic (SV) flow velocity (cm/s) was calculated by the Doppler system. PFV was obtained using the following formulas, as reported elsewhere (12):

Portal vein cross sectional area (cm²) = radius (r)² × π

Portal vein flow volume (PFV, mL/min) = cross sectional area × 60

Mean increase of PFV (mL/min) = (postmeal PFV) - (premeal PFV) / t
where t is the time after meal ingestion (30, 60, 90 min).

The vein cross sectional area and the PV and SV were measured using a subcostal approach at the crossing point of the portal vein with the hepatic artery, and at the splenic vein entrance into the portal vein stem, respectively. In order to reduce intraobservation variability and random error, both PV and SV were calculated as the mean of 3 Doppler sonography evaluations with the same angle of insonation in each patient. Patients with hepatofugal circulation, which could alter hepatic haemodynamics in our points of measurements, were excluded from the study.

Statistical analysis. All data are expressed as mean ± standard deviation (SD). Throughout this study, to determine whether there was a difference in PFV and its mean increase/min after meal in the same patient group or between different patient groups, the unpaired one-way analysis of variance (ANOVA) test and Student's *t*-test were used. Results with a *p*-value <0.01 were considered significant.

Results

Before the meal PFV did not differ (*p*=NS) between controls and both Groups A and C, while the PFV of Group B patients was significantly (*p*<0.01) higher. After 30 minutes, the PFV increased (*p*<0.01) both in controls and Group A patients, while the differences were not significant (*p*=NS) in cirrhotic patients (Groups B and C). No significant changes (*p*=NS) in mean PFV values were found at 60 and 90 minutes as compared to 30 and 60 minutes, respectively (Table I). The changes in PFV after 30, 60 and 90 minutes from the standard meal showed a linear decrease only in Controls and in patients with chronic hepatitis (Group A) (Figure 1).

Discussion

Portal hypertension is accompanied by intestinal microvascular alterations with arterial dilatation, decreased wall thickness and impaired blood flow. Norepinephrine, vasopressin and angiotensin-II seem to play a part in determining the altered microvascular response (3, 13). Studies in portal hypertensive rats have demonstrated increased blood flow velocity in intestinal first-order arterioles, together with a higher pressure and a greater diameter in intestinal third-order arterioles and substantial pressure elevation in first-order venules (14). Hyperdynamic circulation, characterized by (a) increased blood flow to the liver, (b) opening up or formation of venovenous shunts and (c) splenomegaly, is deemed as another modality of portal hypertension syndrome appearance in cirrhotic patients. Dilatation of the portal vein is associated with increased blood flow, as well as the opening up or formation of venovenous shunts and splenomegaly (11). Magnetic resonance imaging (MRI) studies confirmed that hepatic flow parameters correlate with the severity of cirrhosis and degree of portal hypertension (15). Doppler measurements give accurate noninvasive estimations of portal blood flow and

Table I. Portal flow volume (PFV, mL/min) measured by Doppler ultrasonography before a standard meal and at 30, 60 and 90 minutes after it. Mean±standard deviation. In each Group, the differences between PFV at 30 and 60 and between 60 and 90 minutes were not statistically significant (NS).

Groups	No. of patients	Before meal	30 min	<i>p</i>	60 min	<i>p</i>	90 min	<i>p</i>
Controls	20	891±122	1564±334	<0.01	1343±352	NS	1208±207	NS
A	19	986±141	1366±145	<0.01	1260±225	NS	1118±305	NS
B	9	1008±123	1123±121	NS	1158±135	NS	1121±124	NS
C	9	1981±131	2068±112	NS	2128±113	NS	2065±119	NS

Group A = chronic hepatitis patients, Group B = patients with liver cirrhosis with portal hyperdynamic syndrome, Group C = patients with liver cirrhosis without portal hyperdynamic syndrome.

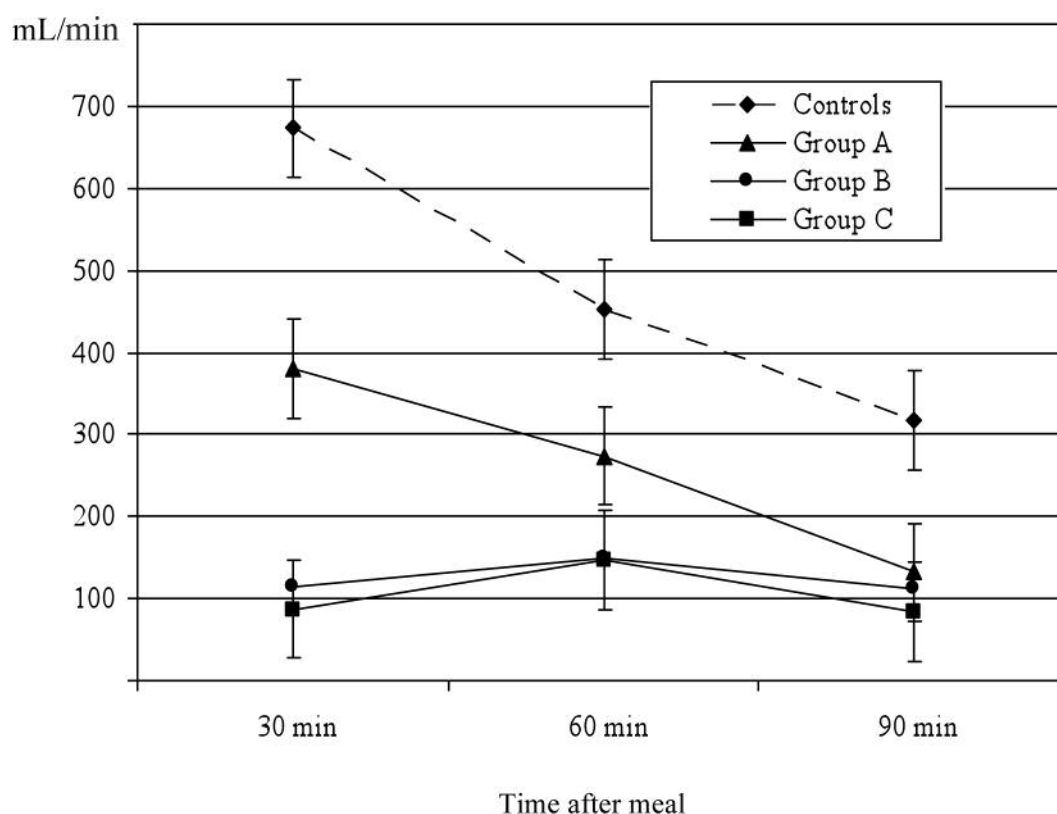


Figure 1. Changes in portal flow volume (mL/min) after 30, 60 and 90 minutes from the standard meal in Controls and in patients with chronic hepatitis (Group A) or liver cirrhosis with (Group B) and without (Group C) hyperdynamic syndrome.

are useful to detect hemodynamic changes in portal venous system after meal intake (16). Thus, this test may be used to monitor physiological stimuli in patients with portal hypertension (8, 9).

Our study confirmed that the postmeal PFV increases both in healthy individuals and in patients with chronic hepatitis, while in cirrhotic patients no significant changes occur (5, 7). In some studies, an altered portal blood flow was considered a new prognostic factor in patients with hepatitis, and this test

should be considered useful for patients with chronic hepatitis and those at risk of developing cirrhosis (17).

In conclusion, monitoring the PFV in cirrhotic patients before and after administration of a standard meal might be a suitable test to evaluate potential disturbances of the flow itself. Moreover, this test could be useful to determine optimal pharmacological or surgical interventions aimed at restoring a better flow to the liver by reducing or favouring the occurrence of spontaneous mesenteric-systemic venous shunts.

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