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Portal Blood Velocity and Flow in Aging Man[1]

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Abstract. The portal blood velocity and flow were measured by means of pulsed echo-Doppler in 60 normal subjects of 4 different age groups (≤ 40, 41–55, 56–70, ≥ 71 years). All subjects had normal routine liver function tests and no history of liver disease. Portal blood velocity decreased from 15.7 ± 3.2 cm/s in younger subjects to 12.4 ± 1.7 in subjects over 71 years (ANOVA: $p = 0.005$). Similarly portal blood flow decreased ($p = 0.025$). Both portal blood velocity and flow were inversely correlated with age ($r = -0.583$ and -0.505, respectively). No changes in portal vein diameter were observed. The age-related decline in portal flow may account for the decrease in hepatic blood flow previously documented in the elderly.

The progressive increase in the life span has produced an increasing interest in medical problems in the elderly. Aging itself might cause alterations in the function of several organs in the absence of any well-defined disease.

Previous studies showed that the liver decreases in weight and in volume from 50 years onwards [1, 2] and, in extreme old age, the liver may be very small (550 g) [3]. Also liver function, measured by several dynamic functional tests, appears to decrease progressively in relation to aging [4, 5]. Studies based on the hepatic extraction of drugs documented that total hepatic blood flow is decreased in the elderly [6], but no data are available on portal flow. In the last few years technological developments in pulsed Doppler equipment made it possible to obtain a noninvasive measurement of blood velocity and flow in deep abdominal vessels [7]. We measured the portal flow in a series of normal subjects of different age groups to study portal vein hemodynamics in the course of aging.

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Table 1. Portal caliber and flow in aging man (mean ± SD)

Age years	Body surface m^2	Portal caliber cm	Portal blood velocity cm/s	Portal blood flow		Congestion index cm·s
				ml/min	ml/(min·m^2)	
≤40	1.64±0.13	1.00±0.09	15.7±3.2	740±147	454±84	0.053±0.016
41–55	1.70±0.17	1.02±0.12	15.5±2.6	760±166	451±104	0.055±0.019
56–70	1.67±0.11	1.00±0.10	13.9±2.4	656±175	394±101	0.058±0.016
≥71	1.64±0.14	1.01±0.10	12.4±1.7	595±106	361±53	0.066±0.019
ANOVA p =	0.619	0.269	0.005	0.025	0.023	0.260

Materials and Methods

Subjects

Sixty subjects belonging to 4 age groups (≤40, 41–55, 56–70, ≥71 years) were studied. Each group consisted of 15 subjects, with no history or biochemical data consistent with previous or active liver disease. Thirty-two subjects were members or relatives of the medical staff and were examined as outpatients. Twenty-eight subjects were hospitalized for mild gastrointestinal diseases, osteoarthritis or chronic bronchitis. Data regarding their body surface are reported in table 1. The body weight was within ± 10% of the ideal body weight. All subjects had normal routine liver function tests (albumin, cholesterol, prothrombin activity, bilirubin, alkaline phosphatase, aspartate and alanine transaminases). At the time of the study no subject was taking drugs known to affect the liver function or the cardiovascular system.

All subjects gave their informed consent to take part in the study. The protocol was approved by the steering committee of the National Research Council (CNR), Rome, Italy; Target Project 'Preventive Medicine and Rehabilitation'; Subproject SP2 'Mechanism of Aging'.

Methods

Portal venous blood flow was evaluated by means of an equipment which combines a mechanical sector scanner (3.5 MHz transducer) and a pulsed Doppler (Aloka SSD-280; UGR 23). All subjects were examined in the morning, after an overnight fast, in the supine position. The fasting state was chosen to permit a better visualization of the portal vein and to avoid changes in the blood flow caused by the absorption of nutrients. Two independent, equally skilled investigators evaluated the portal caliber and the portal blood velocity during two consecutive mornings. The portal blood flow was obtained by multiplying the blood velocity by the cross-sectional area of the vessel, calculated on the basis of the inner diameter, assuming circular geometry. More details on technical problems of Doppler analysis were previously described and the method was validated in an in vitro study [8].

In the same subjects we calculated the congestion index using the equation proposed by Moriyasu [9]:

$$\text{Congestion index} = \frac{\text{cross-sectional area of portal vein}}{\text{blood flow velocity of portal vein}}$$

Interobserver variations in the estimated portal blood velocity were lower than 10%. The average estimated portal blood flow rate varied within ± 10%.

Data in the text and in the table are the mean ± SD of the mean values of individual subjects calculated by the independent operators during the 2 days of investigations.

Differences between the mean values of the different parameters, in the various age groups, were tested for significance by means of one-way analysis of variance (ANOVA). The r coefficients of correlation were assessed by linear correlation analysis.

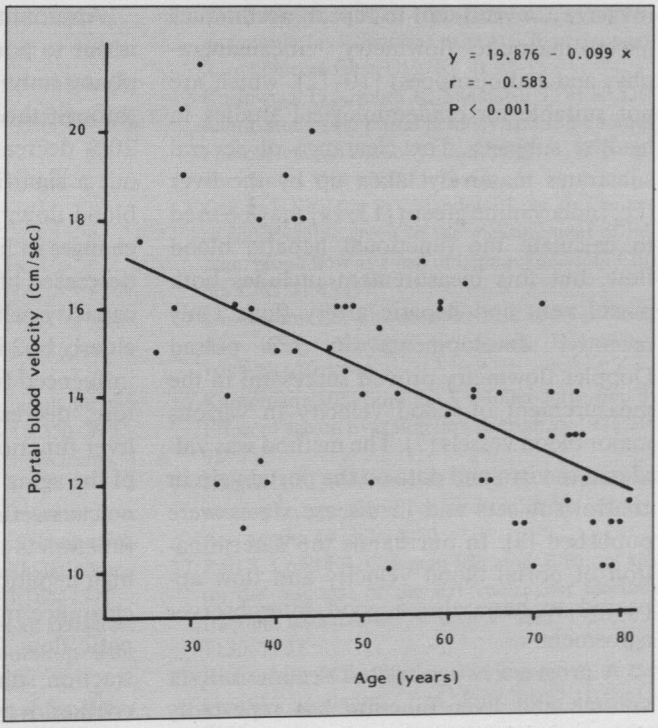

Fig. 1. Correlation between age and portal blood velocity in subjects of different age groups.

Results

The results are reported in table 1. No changes in the mean portal vein caliber were observed in the course of aging, while portal blood velocity and flow progressively declined from 55 years onwards. Portal blood velocity ranged from 11 to 22 cm/s (median 16) in subjects under 40 years, while in subjects aged 71 or more it ranged from 10 to 16 cm/s (median 12). Consequently, the mean portal flow ranged from 340 to 664 ml/(min·m^2) (median 439) in the youngest age group and from 274 to 469 (median 361) in subjects aged 71 or more. The congestion index increased slightly in the older subjects, but the difference was not statistically significant. The highest values (>0.100 cm·s) were observed in the older age group, while in subjects under 40 years it never exceeded 0.086.

A negative correlation was observed between age and portal blood velocity ($r = -0.583$; $p < 0.001$) (fig. 1) or flow ($r = -0.505$; $p < 0.001$).

Discussion

This study shows that portal blood flow, measured by ultrasonography, progressively diminishes in normal subjects in the course of the aging process. The measurement of portal blood flow has so far been based on

invasive or difficult-to-repeat techniques (electromagnetic flowmetry, cineangiography, and radioisotopes) [10–12], which are not suitable for epidemiological studies in healthy subjects. The clearance of several substrates massively taken up by the liver (i.e. indocyanine green) [13, 14] may be used to calculate the functional hepatic blood flow, but this measurement includes both portal vein and hepatic artery flow. Only recently, developments in US pulsed Doppler flowmetry proved successful in the measurement of blood velocity in various major blood vessels [7]. The method was validated in vitro and data on the portal vein in control subjects and in disease states were published [8]. In our hands the determination of portal blood velocity and flow appeared to have also a good interobserver agreement.

A progressive age-related decline in liver volume and liver function has repeatedly been documented, in relation to aging [1–5]. Changes in liver function do not seem to affect the synthesis or metabolism of endogenous products or substrates, which are maintained at nearly normal values also in extremely old subjects [15, 16]. However, when the reserve capacity of the liver is challenged by means of exogenous substrates, a decreased capacity of the liver is clearly found in aging [4, 5].

Changes in total hepatic flow in the elderly had previously been reported in studies aimed to determine drug disposition in the course of aging [6]. The present paper shows that the fasting, postabsorptive splanchnic flow across the liver is reduced. In the presence of a normal resting cardiac output [17], decreased portal flow may result from a reduced mesenteric artery flow, possibly due to atherosclerosis.

Approximately 80% of hepatic blood flow is due to portal flow, the hepatic artery supplying only 20% of the total blood flowing through the liver in the basal state [18]. A 20% decrease in portal blood flow carries out a significant reduction in total hepatic blood flow; this raises the question whether changes in liver function may be related to a decreased blood flow. Galactose elimination capacity, which proved to be reduced in the elderly in 2 independent studies [4, 5], is not influenced by the hepatic blood flow. Therefore, decreased portal flow and decreased liver function are probably different aspects of the aging process, which interact but have no cause-effect relationship. Only when liver function is measured using compounds with high hepatic extraction [13, 14], a decreased clearance may be related to the reduced hepatic flow. This is the reason why high extraction substances have different pharmacokinetics in the elderly, with precise clinical implications.

In the present paper we showed that the portal vein caliber does not change in the course of aging. An increased caliber of the portal, splenic and mesenteric veins, particularly if corrected for the body surface, is a sensitive and specific marker of portal hypertension [19]. Moriyasu et al. [9] proposed that also the 'congestion index', i.e. the ratio between the cross-sectional area and the blood velocity in the portal vein, measured by pulsed echo-Doppler, might reflect the portal vein pressure. In our series the 'congestion index' was always within normal limits, and the slight increase observed in the oldest age group might be explained both by a decrease in liver volume [1, 2] and by an increase in liver fibrosis [20], which justify an increased liver resistance. Only invasive, direct measurements of the portal pressure

might confirm this hypothesis. Alternatively, echo-Doppler provides a noninvasive method suitable for longitudinal, epidemiologic studies, which are needed to confirm the present cross-sectional results.

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