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New abdominal collaterals at ultrasound: A clue of progression of portal hypertension

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Abstract

Background. Abdominal ultrasound can detect non-invasively the presence of abdominal portal-systemic collaterals in patients with liver cirrhosis. Abdominal portal-systemic collaterals may be protective from the formation and growth of oesophageal varices, but available data are inconclusive.

Aim. We aimed at investigating the relationship between abdominal portal-systemic collaterals and variceal formation and growth.

Methods. We studied 126 cirrhotic patients without ($n=43$) or with small ($n=83$) oesophageal varices who entered a protocol of serial ultrasonographic and endoscopic examinations for a median of 55 months. Presence and kind of abdominal portal-systemic collaterals was recorded on first ultrasonography and on each control thereafter.

Results. At inclusion, abdominal portal-systemic collaterals were found in 19/43 patients without varices and in 23/83 patients with small varices (NS). There was no difference in variceal formation and growth between patients with and without abdominal portal-systemic collaterals at inclusion. However, patients developing new abdominal portal-systemic collaterals during follow-up had a significantly higher rate of variceal formation (56.2% vs. 22.2%; $p=0.024$) and growth (52.9% vs. 30.6%; $p=0.041$) compared with patients with unchanged ultrasonography.

Conclusions. Abdominal collaterals are not protective from the formation or growth of oesophageal varices. Conversely, new abdominal portal-systemic collaterals emergence is a non-invasive clue of formation and progression of varices. Therefore, endoscopy is probably indicated whenever new abdominal portal-systemic collaterals are detected in cirrhotic patients.

Keywords: Collateral circulation; Oesophageal varices; Portal hypertension; Ultrasonography

1. Introduction

Portal hypertension is the most common complication of liver cirrhosis. Its most frequent consequence is the formation of a collateral portal-systemic circulation that develops in an attempt to decompress the portal system [1]. The clinical significance of the development of collateral vessels such as gastro-oesophageal varices is related to their progressive enlargement and rupture, which carries a 15–35% risk of short-term death for patients undergoing a first episode of bleeding [2]. When medium–large size (F2–F3 according to Beppu classification) [3] oesophageal varices are observed, a medical or endoscopic treatment should be performed to reduce the risk of variceal rupture [4]. Therefore, it has been suggested that patients should undergo periodic surveillance endoscopies until the diagnosis of F2–F3 varices is made, since non-invasive techniques cannot accurately predict this occurrence [4]. Ultrasound-Doppler (US) can diagnose abdominal collateral vessels, which are a specific clue of portal hypertension [5,6]: they have been reported in 38% of unselected cirrhotic patients

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[7], and some of them, such as ectasic left gastric vein or spontaneous spleno-renal shunts, are pathophysiologically linked to the formation of gastro-oesophageal varices. Patent paraumbilical vein (PUV), which connects the portal venous system to the external iliac venous district via the veins of the ventral abdominal wall and the inferior epigastric vein [8], is the collateral circulation on which most data have been accumulated. It is present in 9–26% of unselected cirrhotic patients [9], and it is more frequently seen in patients with decompensated disease [10], and in alcoholic patients [11]. Due to its anatomical connection, PUV does not feed oesophageal venous district, and some Authors claim that it bears a protective role on variceal rupture [12]. Abdominal collateral circulation has also been correlated to the presence of oesophageal varices [7]. At this time there is no study investigating the clinical meaning of ultrasonographic finding of a patent PUV or of other abdominal collateral vessels in the subset of patients without varices or with small varices; specifically, it is not known whether abdominal collaterals represent a hint of a more advanced step in the natural history of the disease or a protection from the de novo development or growth of gastro-oesophageal varices. The aim of this study was to examine these aspects.

2. Materials and methods

2.1. Patients

This study was approved by the Senior Staff Committee of University Hospital, a board that regulates non-interventional studies and is comparable to an Institutional Review Board. Patients were recruited among the cirrhotic population followed up at the ultrasonography and endoscopy laboratories of the two units participating in the study between 1992 and 2004. In agreement with the international consensus, we usually follow-up cirrhotic patients with endoscopy at 2–3 years intervals when they have no varices and at 1–2 years intervals when they show small varices at the first examination. Patients also routinely underwent abdominal US every 6 months for screening and surveillance of the occurrence of hepatocellular carcinoma.

In the present analysis we enrolled all the patients with cirrhosis diagnosed by biopsy, laboratory or clinical features, with at least two endoscopic controls and paired (±1 month) US examinations, showing no varices or small (F1 in Beppu's classification) varices at first endoscopy. Clinical and laboratory data at entrance were collected. We excluded patients with portal vein thrombosis (PVT), multifocal hepatocarcinoma (HCC), previous endoscopic treatment for variceal eradication and previous or current treatment with beta-blockers. Overall, 157 files of patients without varices or with small varices at first endoscopy were analysed; 31 cases were excluded due to the presence of PVT ($n = 8$), multifocal HCC ($n = 6$), previous endoscopic treatment of oesophageal varices ($n = 4$) or inadequate endoscopic and/or ultrasonographic follow-up ($n = 13$).

The study cohort consisted of 126 cirrhotic patients (age 57 ± 10 years; males 58.7%), 43 (34.1%) without varices and 83 (65.9%) with small varices at first observation. Aetiology of cirrhosis was related to HCV in 52 cases (41.3%), alcohol related in 46 cases (36.5%), HCV and alcohol related in 13 cases (10.3%), HBV related in 6 cases (4.8%), HBV and HCV related in 3 cases (2.4%) and in 6 cases (4.7%), patients' cirrhosis was caused by other aetiologic factors.

Child–Pugh score was in mean 6.3 ± 1.5 points; 73 patients (57.9%) belonged to Child class A, 47 patients (37.3%) to class B and 6 patients (4.7%) to class C.

The endoscopic endpoints evaluated were the first appearance of gastro-oesophageal varices in patients without varices at entrance and the progression to medium–large size varices in patients with small varices at entrance. The ultrasonographic endpoint was defined as the de novo appearance of one or more abdominal portal-systemic collateral (APC), without taking into account possible changes in their size or blood flow. Mean follow up was 55 ± 36 months (range 12–159). Table 1 summarizes the clinical, endoscopic and ultrasonographic data of the population studied.

2.2. Ultrasonographic evaluation

In our centres the presence and the site of spontaneous portal-systemic collaterals (APC) are routinely investigated in cirrhotic patients; these data were collected at first observation and at each following evaluation from the US files of the patients. Echo-Doppler evaluation were obtained by a small number of experienced operators, using two different ultrasonographic equipments (Esaote Ansaldo AU5 and Esaote Technos, Genoa, Italy) with a 4.5–7 MHz convex probe provided by a colour- and pulsed Doppler device. APC were identified by the finding of convoluted anechoic channels with venous flow confirmed by colour-Doppler. Collateral vessels were categorized as follows: PUV was diagnosed when a vessel directing to the abdominal wall with hepatofugal flow was seen in connection with the left branch of portal vein; collaterals supplied by left gastric vein (LG) when collateral vessels posterior to the left hepatic lobe with hepatofugal flow were seen; spleno-renal shunt (SR) when tortuous, collateral vessels were seen between spleen and left kidney; other vessels were noted as "other" collaterals. Photographic records were available in all the included cases.

2.2.1. Statistical analysis

Statistical analysis was performed by SPSS statistical package (SPSS Inc., Chicago, IL, USA). All results are expressed as mean ± standard deviation (S.D.). Comparisons between groups were done by Student's *t*-test for unpaired data. Comparisons within each group were tested using Student's *t*-test for paired data for parametric variables and by Chi-square test for frequencies. Correlations between con-

Table 1
Main baseline clinical, biochemical and ultrasonographic characteristics of the patients included in the study

	Overall ($n=126$)	No varices ($n=43$)	Small varices ($n=83$)	p	No APC ($n=84$)	APC ($n=42$)	p
Age (years)	57 ± 10	56 ± 11	57 ± 11	0.66	58 ± 10	54 ± 11	0.07
Gender (M/F)	74/52	22/21	52/31	0.21	48/36	26/16	0.68
Child–Pugh score	6.3 ± 1.5	6.7 ± 1.7	6.4 ± 1.6	0.31	6.0 ± 1.3	7.6 ± 1.8	<0.001
Ascites (none/slight/severe)	99/25/2	31/10/1	68/15/1	0.55	72/12/0	27/13/2	0.006
Encephalopathy (n)	3	1	2	0.62	0	3	0.04
No/F1 varices (n)	43/83				24/60	19/23	0.10
Gastric varices (n)	1	0	1	0.47	0	1	0.15
Gastropathy (n)	18	5	13	0.82	7	11	0.02
Bilirubin (mg/dl) (n.v. 0.2–1.1)	1.8 ± 1.5	1.7 ± 1.6	1.9 ± 1.4	0.65	1.4 ± 1.1	2.7 ± 1.8	<0.001
INR (n.v. 0.90–1.20)	1.39 ± 0.28	1.34 ± 0.26	1.43 ± 0.29	0.26	1.31 ± 0.26	1.51 ± 0.28	0.001
Albumin (g/dl) (n.v. 3.5–5.0)	3.5 ± 0.6	3.6 ± 0.5	3.4 ± 0.7	0.22	3.7 ± 0.7	3.2 ± 0.5	0.01
APC at US (%)	38.0	44.1	27.7	0.42			
PUV at US (%)	18.2	25.6	14.5	0.19			

p values refer to the comparison between patients with and without varices (first column) and to the comparison between patients with and without APC (second column).

tinuous variables were made by Pearson's test. A p value of <0.05 was considered statistically significant.

3. Results

3.1. Presence and progression of abdominal collaterals at US (Table 2; Fig. 1)

Forty-two patients (33.3%) showed APC at baseline; among these 23 showed PUV. In patients with PUV, other abdominal collaterals were observed significantly more frequently than in patients without PUV (43.4% vs. 18.4%; $p<0.01$). Patients with APC at baseline had a higher Child–Pugh score, a higher rate of ascites and hypertensive gastropathy, and they showed a trend towards a lower rate of presence of oesophageal varices compared with patients without APC (Table 1).

During follow-up 50/126 patients (39.7%) developed new abdominal APC at US, with a mean incidence of 7% per year. No patient experienced disappearance of APC. No difference in the rate of appearance of new APC was observed between patients without varices (16 out of 43) and patients with small varices (34 out of 83; $p=0.545$) at enrolment. A de novo PUV was observed in 18 out of 50 cases (8 out of 16 patients without varices at enrolment and progression of US and 10/34 with small varices at enrolment).

No difference in the rate of de novo formation of APC was observed between patients who at baseline had no varices and no APC (10/24) and patients who at baseline had F1 varices and no APC (26/60; $p=0.826$). Similarly, no difference was observed in the rate of aggravation of APC between patients who at baseline had no varices and at least one APC (6/19) and patients who at baseline had both F1 varices and APC (8/23; $p=0.889$).

Table 2
Distribution of abdominal portal-systemic collaterals studied at US in the studied population observed at baseline ($n=126$)

PUV	23 (18.2%)
LG	11 (8.7%)
SR	13 (10.3%)
Other	5 (3.9%)

The 52 collaterals were observed in 42 patients. PUV: paraumbilical vein; LG: left gastric vein; SR: spleno-renal shunt.

3.2. Progression of endoscopic signs of portal hypertension according to US findings

The worsening of portal hypertension at endoscopy was associated with the de novo appearance or aggravation of APC at US (Chi square $p=0.003$; Table 3). Overall, among patients with new APC, varices appeared or increased in size in 54.0% while in patients with stable US this occurred in 27.6% of the cases ($p=0.003$). The same was observed independently whether the patients had or not APC at first observation (Tables 3 and 4).

3.2.1. Formation of oesophageal varices in patients with and without APC

During follow-up 15/43 (34.9%) of the patients without endoscopic signs of portal hypertension at enrolment developed oesophageal varices, with a mean incidence of 6.5% per year. At first observation 19 (44.1%) patients without varices had APC at US; among these, 11 (25.6%) had a

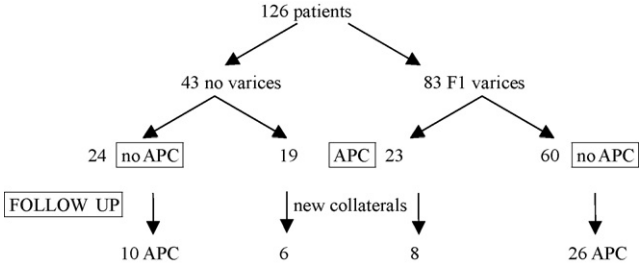

Fig. 1. Formation and growth of APC according to the presence or absence of oesophageal varices at inclusion. As shown, no difference was observed between the two groups.

Table 3
Parallelism between endoscopic and ultrasonographic signs of portal hypertension in the whole population studied

	Stable endoscopic signs of portal hypertension ($n=78$)	Worsening of endoscopic signs of portal hypertension ($n=48$)
Stable ultrasonographic signs of portal hypertension ($n=76$)	55	21
Worsening of ultrasonographic signs of portal hypertension ($n=50$)	23	27

Chi square 8.89; $p=0.003$.

Table 4
Parallelism between endoscopic and ultrasonographic signs of portal hypertension in the studied population without APC at entrance ($n=84$)

	Stable endoscopic signs of portal hypertension ($n=49$)	Worsening of endoscopic signs of portal hypertension ($n=35$)
Stable ultrasonographic signs of portal hypertension ($n=48$)	34	14
Worsening of ultrasonographic signs of portal hypertension ($n=36$)	15	21

Chi square 7.2; $p<0.01$.

patent PUV. No difference in the rate of appearance of varices was observed between patients with APC (6 out of 19) and patients without APC (9 out of 24; $p=0.686$) at baseline examination (Fig. 2). Similarly, no difference in the rate of formation of varices was found between patients with and without PUV at baseline examination (2 out of 11 vs. 13 out of 32, respectively; $p=0.276$).

The rate of formation of varices was significantly higher in patients with new abdominal collaterals formed on follow-up versus patients with stable US: 56.2% versus 22.2%, $p=0.024$. In 33.3% of these patients, the worsening of US was noted several months before variceal appearance (in mean 23.8 ± 13.0 months before), while in 66.7% it was detected on the US examination paired to endoscopic control. The diagnostic value of the finding of new APC in the setting of variceal appearance was as follows: sensitivity 60%, specificity 75%, positive likelihood ratio 2.40, negative likelihood ratio 0.53.

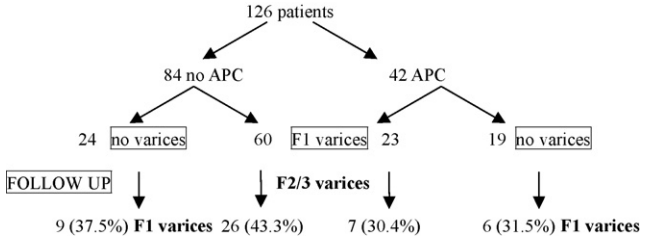

Fig. 2. Formation and growth of oesophageal varices according to the presence or absence of APC at inclusion. As shown, no difference was observed between the two groups.

The appearance of oesophageal varices in patients with a de novo PUV versus those presenting with other kind of new abdominal collaterals was not statistically different (75.0% vs. 37.5%; $p=0.131$).

3.2.2. *Progression of oesophageal varices in patients with and without APC*

In 33/83 patients (39.8%) with small varices at entrance we observed a progression of the varices, with a mean incidence of growth of 9% per year. No patient showed regression of oesophageal varices. Patients with small varices at baseline were not significantly different from those without varices for severity of liver dysfunction (Table 1). At first observation 23 (27.7%) patients with small varices had APC at US; among these, 12 (14.5%) had a patent PUV. No difference in the rate of progression of varices was observed between patients with APC (7 out of 23) and patients without APC (26 out of 60; $p=0.283$) at baseline examination (Fig. 2). In addition, no difference in the rate of growth of varices was found between patients with and without PUV at baseline examination (3 out of 12 vs. 30 out of 71, respectively; $p=0.347$).

Variceal progression occurred significantly more in patients with new abdominal collaterals on follow-up versus patients with stable US: 52.9% versus 30.6%, $p=0.041$. In 44.4% of these patients the worsening of US was noted some months before variceal appearance (in mean 12.6 ± 6.7 months before), while in 55.6% it was detected on the US examination paired to endoscopic control. The diagnostic value of the finding of new APC in the setting of variceal progression was as follows: sensitivity 54.5%, specificity 68%, positive likelihood ratio 1.78, negative likelihood ratio 0.65.

Variceal progression rate did not differ in patients with de novo PUV versus patients with appearance of other abdominal collaterals (60.0% vs. 45.8%; $p=0.753$).

4. Discussion

Previous studies have shown that the presence of collaterals at US had a sensitivity of 80% in detecting portal hypertension and that a higher number of collaterals correlate with a higher HVPG [13]. Also, PUV and APC in general are more often seen in patients with decompensated disease [10,14] and with alcoholic cirrhosis [11], who as well more often show large oesophageal varices, leading to the commonly held concept that abdominal collateral circulation is an indirect sign of severe portal hypertension. While some Authors found a very high rate of large oesophageal varices in patients with PUV supporting this hypothesis [15,16], other Authors claimed a protective role of PUV on the development of large oesophageal varices [17] and on the risk of variceal bleeding [12].

Whether abdominal collaterals, and particularly PUV, should or should not be viewed as a sign of more severe portal hypertension or as a protective factor on the progression of endoscopic signs of portal hypertension is an open question, since there is no study including data on the time course of endoscopic and ultrasonographic signs of portal hypertension to verify which of these hypotheses is correct. This study was designed to clarify this issue.

We found that collaterals at ultrasound are already present in about one third of the patients without varices or with small ones, and that in this population they are more frequent in Child B–C patients, thus confirming a previous report that it is an indirect sign of advanced disease [7]. Also, patients with APC had a higher prevalence of ascites, confirming previous data [14].

Comparing patients with and without APC at baseline, we found a trend toward a lower prevalence of varices in the group with US collaterals at enrolment (Table 1). This result, together with the finding that in some cases APC appeared several months before oesophageal varices, suggests that in some cases abdominal collaterals at US are the first picture of portal hypertension. Probably depending from a different anatomy, in some cases portal hypertension seems to lead first to the opening of APC and later to that of oesophageal varices, while in other cases, oesophageal varices may open before the opening of APC; along time, as portal hypertension progresses, both US and endoscopic signs of portal hypertension simultaneously progress as demonstrated by the present study.

Due to the inclusion criteria of this study, we could not test the hypothesis that US collaterals are more frequently found in patients with larger oesophageal varices; yet, in a prospective study recently performed by our group on cirrhotic patients with medium–large oesophageal varices [18], we found that one or more collateral vessels were visible at US in 66.7% of patients, a prevalence about two-fold that we report in the present study in patients with milder endoscopic signs of portal hypertension.

As for the rate of appearance and growth of oesophageal varices, our data confirm previous observations by our group [19] and by other authors [20–22], but more importantly, the presence of abdominal collaterals at the first US examination was not correlated to a higher rate of development or worsening of endoscopic signs of portal hypertension. Specifically, a patent PUV did not seem to be protective on the formation or growth of oesophageal varices, since the rate of appearance or growth of oesophageal varices were nearly identical in patients with or without PUV at baseline examination (Fig. 2); furthermore, similarly to what observed in the whole population, the appearance of a new PUV correlated with a higher rate of appearance of varices.

We recognize some limitations of the present study. Due to the lack of a predefined sample size, underestimation of a possible protective effect of abdominal collaterals on the formation and growth of varices cannot be excluded. However, previous observations by other Authors support our results. It has been suggested in fact that abdominal collaterals are not protective on large varices formation and on variceal rupture [17,12], and as variceal formation, growth and rupture are a continuum of events, these data are in agreement with our findings.

As for the ultrasonographic studies, there might have been a possible underrating of abdominal collaterals due to abdominal gas or obesity. However, this possible bias would have been constant in all the examinations, and patients with insufficient visualization at US were excluded from the present analysis; moreover, US operators were skilled in the examination of cirrhotic patients.

Nonetheless, the main finding of this study is that the formation of new APC and the progression of portal hypertension on endoscopy had a parallel course: in the follow-up, about 40% of cirrhotic patients showed one or more new APC at US examinations; this subgroup of patients showed a worsening of endoscopic signs of portal hypertension more often than patients with unchanged US findings.

Therefore, our data suggest that the observation at US of new APC might be considered a non-invasive clue of worsening of portal hypertension. In consideration of the fact that as much as 10% of acute variceal bleeding episodes (which still carry a 15–20% mortality in cirrhotic patients) occur in the interval between two scheduled control endoscopies, our finding may be relevant in clinical practice, as it suggests to perform an earlier surveillance endoscopy in the subgroup of patients showing aggravation of APC at US examination, thus potentially avoiding significant morbid-mortality due to variceal rupture.

In conclusion, abdominal collaterals are a frequent finding at US examination in cirrhotic patients without oesophageal varices or with small varices and are not protective from the development or growth of oesophageal varices. Patients with worsening of US signs of portal hypertension, in terms of new APC, present worsening of the endoscopic picture significantly more frequently than patients with stable APC. APC can therefore be considered a non-invasive clue of ongoing worsening of portal hypertension, and it may be suggested that this could represent an indication to shorten the interval between endoscopic controls in cirrhotic patients.

Practice points

- Abdominal collaterals at ultrasound are a frequent finding in cirrhosis.
- Collaterals are more frequently observed in decompensated patients.
- They are not protective from the development or growth of oesophageal varices.
- Conversely, variceal formation and growth are more frequent in patients with increasing collaterals at ultrasound.

Research agenda

- The observation of new abdominal portal-systemic collaterals may represent an indication to shorten the interval between endoscopic controls in cirrhotic patients.
- The usefulness of this approach needs to be prospectively confirmed.

Conflict of interest statement
None declared.

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