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Prevalence and clinical outcome of hepatic haemangioma with specific reference to the risk of rupture: a large retrospective cross-sectional study.

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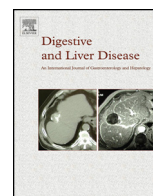
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Liver, Pancreas and Biliary Tract

Prevalence and clinical outcome of hepatic haemangioma with specific reference to the risk of rupture: A large retrospective cross-sectional study

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ABSTRACT

Background: Prevalence and incidence of hepatic haemangioma are estimated from autopsy series only. Although benign and generally asymptomatic, hepatic haemangioma can cause serious complications. **Aims:** The aim of the study was to assess the prevalence of hepatic haemangioma and to attempt to quantify the risk of major complications such as spontaneous rupture.

Methods: We retrospectively analyzed the radiology database of a Regional University Hospital over a 7-year period: the radiological records of 83,181 patients who had an abdominal computed tomography or magnetic resonance scan were reviewed. Diagnoses made at imaging were reviewed and related to clinical course.

Results: Hepatic haemangioma was diagnosed in 2071 patients (2.5% prevalence). In 226 patients (10.9%), haemangioma had diameter of 4 cm or more (giant haemangioma). The risk of bleeding was assessed on patients without concomitant malignancies. Spontaneous bleeding occurred in 5/1067 patients (0.47%). All 5 patients had giant haemangioma: 4 had exophytic lesions and presented with haemoperitoneum; 1 with centrally located tumour experienced intrahepatic bleeding.

Conclusion: Giant haemangiomas have a low but relevant risk of rupture (3.2% in this series), particularly when peripherally located and exophytic. Surgery might be considered in these cases.

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1. Introduction

Haemangioma is considered the most common benign tumour of the liver; however, little epidemiological data are available on its prevalence, which is estimated from autopsy series only: in these

series, prevalence ranges from 0.4% to 7.3% [1–3]. The female to male ratio of the incidence of haemangiomas is 5:1, and they are identified more frequently in middle-aged women [4]. Although its pathogenesis is not well understood, hepatic haemangioma (HH) is considered as a congenital vascular malformation that enlarges by ectasia rather than by neoplastic growth. Macroscopically, HHs are well-circumscribed, hypervascular lesions that microscopically arise from the endothelial cells that line blood vessels and consist of multiple, large vascular channels lined by a single layer of endothelial cells and supported by collagenous walls [5]. Their blood supply arises from the hepatic artery. HHs are typically diagnosed incidentally during a routine abdominal ultrasound and generally present as small-sized, asymptomatic nodules, although they may grow in size. In most cases, HHs are of little, if any, clinical relevance however, some cases of bleeding or rupture have been reported, thus

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raising concerns regarding the possible evolution of the disease [6]. Other possible complications of HH are severe abdominal pain not responsive to medical therapy, symptoms related to the compression of adjacent organs, uncertainty regarding the diagnosis with a suspicion of malignancy, increasing size during follow-up and incidence of Kasabach–Merrit syndrome [7]. Some studies reported that giant haemangiomas (main diameter ≥ 4 cm) [8] are more frequently symptomatic and carry a higher risk of rupture [9–14].

The aim of this study is to assess the prevalence and the incidence of the disease and to quantify the risk of major complications, with particular reference to spontaneous HH rupture. For this purpose, all the HH cases observed at a regional hospital over a 7-year period were reviewed.

2. Materials and methods

The University Hospital of Ancona is a regional hospital that serves a population of 150,000. The hospital Department of Radiology has a centralized picture archiving and communication system (PACS), in which the reports and images of computed tomography (CT) and magnetic resonance imaging (MRI) investigations are stored; the system is electronically accessible and is searchable for specific information.

PACS was retrospectively analyzed, focusing on a 7-year period (January 2005–December 2011); all radiological reports of CT and MRI scans of the abdomen containing the following key words: haemangioma, haemangiomas, hemangiomatous and haemangiomatosis, were reviewed by two trained radiologists.

Liver CT scans were performed with a 64-row CT scanner (Light-Speed VCT, GE). All acquisitions were performed at 120 kV with automatic mA, reconstructing contiguous axial slices of 2.5 mm, completed with coronal and sagittal reconstructions. All baseline CT exams were conducted with a pre-contrast scan and a triphasic study, administering iodine contrast media at 350–370 mgI/ml with a dose of 1.5–1.8 ml/kg of body weight with an injection rate of 3–4 ml/s, followed by a saline bolus. Arterial phase was obtained with bolus tracking technique with an aortic threshold of 150 HU and 7 s of scan delay or, alternatively, with 25–30 s fixed delay from bolus injection. Portal venous phase was obtained with a 60–70 s fixed delay or a 40 s delay from bolus tracking threshold. Equilibrium phase was obtained at 120–180 s, sometimes completed with an ultra-delayed phase to demonstrate the fill-in pattern.

MRI examinations were performed with 1.5T superconductive scanners (GE Signa Hdx; Philips Achieva) with T2-weighted images: axial FSE, coronal SSFSE axial fat saturated SSFSE (slice thickness 5 mm, slice spacing 5 mm). T1-weighted axial images were obtained with GRE sequences in and out of phase (slice thickness 5 mm, slice spacing 5 mm), ad with fat saturation. Triphasic study was performed after administration of Gd-Chelates (Gd-DOTA: 0.1 mmol/kg body weight@2 ml/s) followed by a saline bolus. Images were obtained with T1-weighted 3D GRE fat saturated pulse sequences (slice thickness 4 mm, and slice spacing 2 mm) within the maximum k-space contrast resolution at approximately 25–35 s after bolus injection for the arterial phase, 45–65 for the portal venous phase and 120–180 s for the equilibrium phase. Sometimes the study was completed with ultra-delayed acquisitions.

A diagnosis of liver haemangioma was made when the following features were present on CT or MRI [15]: a sharply defined and hypodense nodule on a non-contrast CT scan or the presence of an hypointense nodule on T1-weighted images and an intensely hyperintense nodule on T2-weighted images at the MRI; a contrast-enhancement pattern characterized by peripheral nodular enhancement followed by a progressive centripetal filling on scans of both imaging techniques.

Table 1

Aetiology of malignancy in 1004 patients with incidental haemangioma.

Colon-rectum	225 (22.4%)
Lung	157 (15.6%)
Female genital tract	93 (9.2%)
Male urinary tract	85 (8.5%)
Breast	80 (8.0%)
Kidney	71 (7.1%)
Pancreas	55 (5.5%)
Liver (primary and secondary neoplasm)	48 (4.8%)
Haematological System	42 (4.2%)
Esophageal-gastric tract	38 (3.8%)
Neuroendocrine System	18 (1.7%)
Other	92 (9.2%)

Overall, 83,181 patients were reviewed, of whom 70,163 (84.3%) had undergone abdominal CT scan only, 8678 (10.5%) had undergone abdominal MRI only and 4340 (5.2%) had undergone both CT and MRI.

The overall prevalence and incidence of HH, as well as prevalence and incidence at CT scan and MRI were calculated on this population.

The study on the clinical features of HH was performed on all those patients who had a radiological diagnosis of the disease, while the risk of bleeding over time was assessed only in those HH patients who did not have concomitant malignant disease, in order to prevent any influence of the malignancy on follow-up.

In this latter group (HH carriers without malignant disease), we completed follow-up by reviewing PACS and by collecting clinical information through an interview performed by a single physician assessing three specific features, namely: symptoms or complications related to the haemangioma, need for hospitalization, follow-up that was carried out after the diagnosis of HH. In addition, the patients were asked to inform us whenever a new event took place and were advised to undergo abdominal ultrasound examination yearly. In the presence of symptoms, complications or hospitalizations, clinical reports were collected and accurately examined to correlate the clinical picture with the benign liver tumour. This accurate review of data allowed us to evaluate the rate of symptoms, complications, rupture, morbidity and mortality related to HH. Descriptive statistics were reported as percentage, mean \pm standard deviation (SD) or median and range. Duration of the follow up was defined as the time interval between the diagnosis of HH and the time of the survey.

3. Results

Of the patients reviewed, 2071 met the radiological criteria for the diagnosis of HH. In 1767 of these 2071 patients (85.3%), the diagnosis of liver haemangioma was incidental and in 214 (10.3%) of these patients it resulted from the diagnostic CT or MRI characterization of a liver lesion identified using ultrasonography; in additional 90 of these patients (4.4%), HH was known and imaging was part of a regular follow-up. Incidental diagnosis was made during the evaluation or the follow-up of a malignancy in 1004 (48.5%) patients, during the assessment of a benign disease in 759 (36.6%) patients and at the time of the spontaneous rupture of a previously unknown haemangioma in 4 (0.2%) patients (Tables 1 and 2).

Data of the 90 patients with a regular follow-up for a previously diagnosed HH were updated, imaging was reviewed to assess possible morphological and clinical changes over time. The records of the 4 patients who presented with spontaneous bleeding were reviewed.

The overall prevalence of haemangioma at the radiological imaging during the study period was 2.5% (2071 patients with a diagnosis of HH in the entire study population). The prevalence of haemangioma at the CT scan was 2.4% (1660 patients with HH

Table 2
Types of benign conditions in 759 patients with incidental haemangioma.

Acute and chronic lung disease	133 (17.5%)
Vascular disease	118 (15.6%)
Trauma	98 (12.9%)
Chronic liver disease	83 (10.9%)
Benign neoplasm	82 (10.8%)
Acute abdominal pain	55 (7.3%)
Inflammatory bowel disease	48 (6.3%)
Benign prostate hyperplasia	47 (6.2%)
Cholelithiasis	46 (6.0%)
Female genital tract disease	21 (2.8%)
Other	28 (3.7%)

of 70,163 who underwent CT scan), and the prevalence of haemangioma at the MRI was 8% (701 patients with HH of 8678 who underwent MRI).

The overall incidence of haemangioma assessed with radiologic imaging ranged between 2.5% and 3.4% (the number of new diagnoses of liver haemangioma per year, considering both CT and MRI scans). The incidence of new cases of diagnosed HH ranged between 2.2% and 2.7% with the CT scan and between 5.5% and 11.5% at the MRI scan.

The mean age of the HH carriers was 59 ± 15 years. Overall, there were 988 women (47.7%) and 1083 men (52.3%) in the study; 61.3% of the haemangiomas were located in the right liver, 21.5% in the left liver and 17.2% occupied portions of both lobes. The mean size was 19.7 ± 19.4 mm, and the largest haemangioma was 23 cm in diameter; 281 (13.5%) patients had three or more HHs. In 1845 patients (89.1%), the diameter of the HH was less than 4 cm, whereas in 226 patients (10.9%) the diameter was equal to or greater than 4 cm (the size of a giant haemangioma).

The clinical outcome with particular regard to spontaneous rupture, was assessed on those 1067 patients who did not carry malignancies. The follow-up of these 1067 patients ranged between 27 and 112 months (mean of 72.6 ± 24.2 months). Only 25 patients whose diagnosis of HH was made in December 2011, had a follow-up shorter than 3 years; follow-up of these latter 25 patients was of 27 months.

3.1. Giant haemangioma

One hundred fifty seven patients had a giant HH (14.7%). In this group, mean age was 55 ± 15 years, females were 57.9%; 42.7% of the haemangiomas were located in the right liver, 17.2% in the left liver and 40.1% occupied portions of both lobes. The mean size was 68.7 ± 20.3 mm, and the largest haemangioma had a diameter of 23 cm; 58 (36.9%) patients had three or more HHs. In 77 patients (49%) the HHs were peripherally located: in 37 of these patients, the HHs had an exophytic growth pattern; in the remaining 80 patients (51%), the HHs were centrally located.

Five of 157 patients (3.2%) with giant HH had symptoms related to the tumour in the absence of rupture: persistent abdominal pain (3 cases) and nausea and vomiting resulting from gastric compression (2 cases). Those 5 patients only within all the study group (1067) manifested clinical symptoms (0.47%).

Five of 157 patients (3.2%) developed spontaneous haemangioma rupture and required surgery and/or emergency transcatheter arterial embolization (Table 3). The HH rupture caused haemoperitoneum in 4 patients, who had peripherally located exophytic HHs. One patient with a centrally located non-exophytic HH developed intrahepatic haemorrhaging. Overall, rupture occurred in 4 of 37 (10.8%) patients who carried a peripherally located exophytic HH and in 1 of 80 (1.3%) patients who carried a centrally located HH. No case of rupture was observed in those 40 patients who had a peripherally located non-exophytic HH. The other 147 giant HH patients remained asymptomatic.

In 8 giant HHs (5.1%), the size of the tumour and the risk of rupture were considered as an indication for elective treatment, whereas an increase in the size of the HH during a regular follow-up was an indication for treatment in 9 patients (5.7%). In one (0.6%) case, liver resection was performed for the doubt of a possible malignancy, specifically a cholangiocellular carcinoma.

Forty-two patients in this group (26.7%) had regular follow-up of their giant HH following initial diagnosis: in 32 (76.2%) the HH remained stable in size, whereas an increase in the diameter was observed in 8 (19%) patients (mean 19.8 ± 15.5 mm) and a reduction in size was observed in 2 (4.7%) patients (15 mm and 70 mm, respectively) during a mean follow-up of 76 ± 24.1 months (range 27–112 months). One of these patients underwent intrahepatic rupture and received emergency treatment 2.92 months after the initial diagnosis.

3.2. Haemangioma <4 cm

In this group of 910 patients (85.3%), mean age was 57 ± 15 years, females were 46.4%; 60.7% of the HHs were located in the right liver, 21.9% in the left liver, and 17.4% were bilateral; 118 patients (13%) had three or more haemangiomas. The mean size was 19.8 ± 14.9 mm.

All the patients in this group remained asymptomatic and no haemorrhagic complications were recorded.

In 1 case (0.1%), a transarterial embolization was performed at the specific request of patient, who experienced psychological discomfort from the knowledge of having a tumour.

3.3. Evolution of HH in during follow-up

Among the 90 patients who instituted regular follow-up after the diagnosis of haemangioma, mean age was 50 ± 15 years; females were 68.9%; 33.7% of the HHs were located in the right liver, 11.2% in the left liver and 55.1% were bilateral; 42 (46.6%) patients had 3 or more HHs. The mean size was 67.3 ± 20.3 mm, and the largest haemangioma was 23 cm in size. The mean follow-up was 76.6 ± 23.8 months (range 27–112 months).

In 68 of these patients (75.6%), HH remained stable in size whereas an increase in the diameter (mean 23.5 ± 16.4 mm) was observed in 20 patients (22.2%), and a reduction in size (of 70 and 15 mm, respectively) was observed only in 2 patients (2.2%). Forty two patients carried giant HH as previously discussed.

Intrahepatic rupture developed in one case (1.1%) who received emergency treatment and five patients (5.5%) had symptoms that indicated an elective treatment.

3.4. Patients who required treatment

Treatment for HH was performed in 29/1067 patients (2.7%): 23 patients underwent liver resection and 8 underwent transcatheter arterial embolization (TAE); in 2 patients TAE was performed as a bridge technique before surgical resection.

Of these 29 patients, 5 required emergency treatment because of haemorrhagic complications from tumour rupture, and 4 of them presented with haemoperitoneum whereas one experienced intrahepatic haemorrhage. The 4 patients who presented with haemoperitoneum underwent emergency surgery as follows: a right hepatic artery ligation with packing followed by a right lobectomy was performed in two patients, of whom one died of irreversible liver failure and the other developed bilateral pleural effusion that required a thoracic drain. In the other 2 patients with haemoperitoneum, arterial embolization was performed in the first instance to haemodynamically stabilize the patient, which was followed by surgical resection (left lobectomy). In the latter two cases, the postoperative course was uneventful. The mean length of stay

Table 3
Spontaneous haemangioma rupture cases: patient characteristics, treatment and outcome.

Patient No. (year)	Age (years) (Sex)	Diameter ^a (Location ^b)	Exophytic	Clinical presentation	Treatment	Outcome	Other lesions: n° (Segment)
1 (2005)	27 (M)	8 (II–III)	Yes	Free rupture, haemoperitoneum	First: emergency arterial embolization Second: elective left lobectomy	Uncomplicated postoperative course; remains symptom-free	Yes, 1 (VI)
2 (2007)	29 (F)	10 V–VI–VII–VIII	Yes	Free rupture, haemoperitoneum	First: emergency right hepatic artery ligation & packing Second: urgent right hepatectomy	Postoperative bilateral pleural effusion; remains symptom-free	No
3 (2007)	57 (F)	6 VII–VIII	No	Intrahepatic haemorrhage	Emergency arterial embolization	Uncomplicated course; remains symptom-free	No
4 (2009)	39 (F)	9 III	Yes	Free rupture, haemoperitoneum	First: emergency arterial embolization Second: urgent left lobectomy	Uncomplicated postoperative course; remains symptom-free	No
5 (2010)	38 (F)	18 V–VI–VII–VIII	Yes	Free rupture, haemoperitoneum	First: emergency right hepatic artery ligation & packing Second: urgent right hepatectomy	Postoperative acute liver failure and death	Yes, 6 (II–III–IV–VI)

M, male; F, female.

^a Centimetres.^b Segment.**Table 4**
Elective liver resection: patient and haemangioma characteristics and indications.

N	19
Median age, years (range)	49 (34–68)
Female gender (%)	14 (73.6)
Largest HH location	
Right lobe (%)	7 (31.6)
Left lobe (%)	5 (15.8)
Bilobar (%)	12 (52.6)
Median size in centimetres (range)	10.2 (6–17)
Giant Haemangioma ≥ 4 cm (%)	19 (100)
More than three HH (%)	8 (42.1)
Median number of additional HH (range)	5.5 (1–9)
Indication for surgery	
Increasing size on serial imaging (%)	9 (47.3)
Size alone (%)	5 (26.3)
Inability to exclude malignancy (%)	1 (5.3)
Symptoms (%)	4 (21.1)

HH, hepatic haemangioma.

was 9.33 ± 6.8 days (range 4–17 days). The only patient who presented with intrahepatic haemorrhage underwent emergency TAE, which led to a complete devascularization of the lesion; no further treatment was required for this patient, and no complications were recorded. In the latter patient, HH was known before the rupture.

Of the 24 patients treated in an elective setting, 19 underwent surgical resection and five underwent TAE (Tables 4 and 5).

The increase in size of HH during a regular follow-up represented an indication for elective surgical treatment in 9 patients with giant HH. In these patients, whose median HH size was initially of 55 mm (range 30–100 mm), a median increase in size of 45 mm (16–70 mm) was observed over a median follow-up of 55 months (range 3–240).

There were no perioperative deaths after surgery, and only two postoperative complications were recorded (intraabdominal haematic collection treated with percutaneous drainage, and right pleural effusion treated with a thoracic drain). The mean hospitalization period was of 7 ± 5 days (range 3–25 days).

The diagnosis of haemangioma was histologically confirmed in all resected specimens.

Table 5
Elective arterial embolization: patient and haemangioma characteristics and indications.

N	5
Median age, years (range)	49 (35–66)
Female gender (%)	3 (60)
Largest HH location	
Right lobe (%)	1 (20)
Left lobe (%)	2 (40)
Bilobar (%)	2 (40)
Median size cm (range)	7.5 (2.5–10)
Giant haemangioma ≥ 4 cm (%)	4 (80)
More than three HH (%)	2 (40)
Median number of additional HH (range)	0
Indication for embolization	
Size alone (%)	3 (60)
Symptoms (%)	1 (20)
Patient's choice (%)	1 (20)

HH, hepatic haemangioma.

Of the 5 patients who underwent TAE, 60% were women; mean age was 49 ± 15 years (range 35–66 years).

There was no significant complication following TAE; however, treatment was completely successful in achieving complete devascularization of the lesion only in two patients (40%).

4. Discussion

In our large series of more than 83,000 patients who underwent abdominal CT and/or MRI scan over a seven-year period, the prevalence of HH was 2.5%; to our knowledge this figure represents the only one available that is not drawn from autopsy series.

The prevalence of HH in those 8678 patients who underwent MRI as a first instance imaging was significantly higher (8%); it has been proved that MRI has higher sensibility and specificity in detecting small hepatic lesions (<20 mm) in comparison with other imaging techniques [16–18] and that it can identify small haemangiomas that can go undetected at CT scan. The real prevalence of HH could therefore be higher than the overall 2.5% recorded in the entire population of our study which included 70,163 patients who had CT scan only.

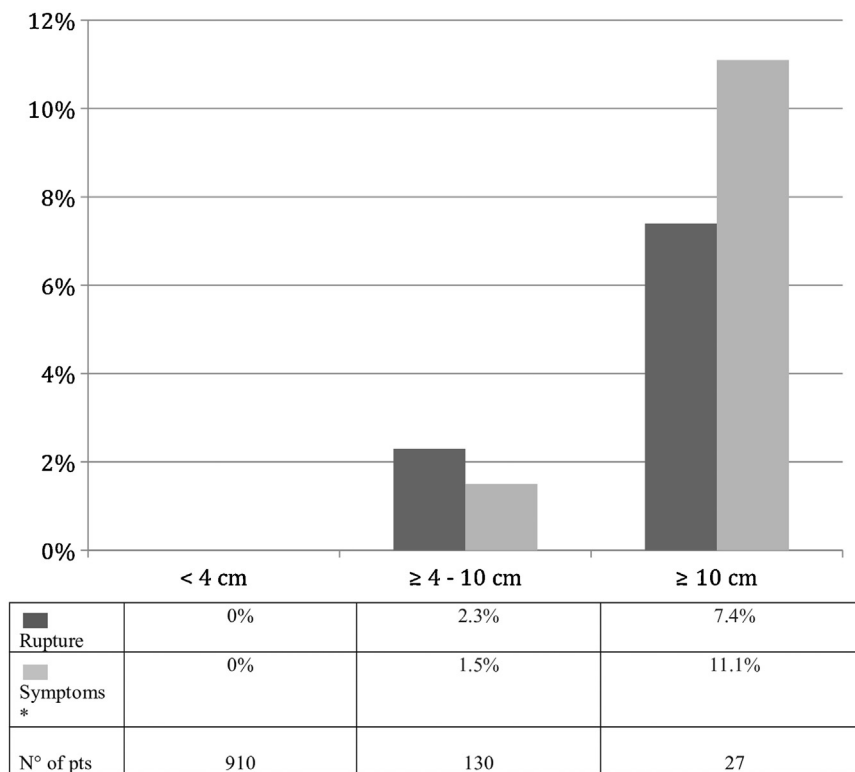


Fig. 1. Risk of rupture and symptoms related to the size of haemangioma. *Symptoms: Abdominal pain not responsive to medical therapy; nausea, vomiting, early satiety related to gastric compression.

Differing from the data drawn from autopsy series [1–3], in our analysis, HH was found more frequently in men over 50 years of age, most likely because the most frequent circumstance of diagnosis was during the staging or follow-up of malignancies.

It is generally thought that the natural history of HH is mostly uncomplicated and that the risk of its most serious complication, spontaneous rupture, is extremely low [9,13,19–23]; however, no study has quantified the rate of rupture in a population of HH carriers. The literature is predominantly based on case reports [9,24–35]. Donati et al. [6] recently reviewed the literature published between 1898 and 2010 on HH rupture, and 83 articles were found, of which 9 reported more than 1 case of HH rupture including post traumatic cases. The maximum number of cases ($n=3$) of spontaneous rupture was reported by Farges et al. in 1995 [9]. These reports were from surgical series and focused on the treatment of the condition; the only clear message that could be taken from these reports is that the mortality associated with HH rupture is remarkably high (35%).

In this series, we report five cases of spontaneous rupture of HH, 4 of which presented with haemoperitoneum. By relating this figure to the number of HHs diagnosed at a regional hospital in a 7-year period, we quantified the rate of rupture as 0.47%. This study confirms that HH rupture has a heavy mortality (20% in this series).

In contrast to the findings from Donati [6], in our study the size of the HH was linked with the risk of rupture as reported in Fig. 1. All the cases of rupture that we observed occurred in carriers of giant HHs, whereas no case of rupture was recorded among 910 carriers of HHs of less than 4 cm in diameter. Whereas in 4 of the 5 patients who carried giant HH and experienced HH rupture the disease was previously unknown, rupture also occurred in 1 patient who was under regular follow-up. Of the 42 carriers of giant HH who were under regular follow-up, 1 (2.4%) eventually underwent rupture; these findings might suggest that the risk of bleeding of giant HH, although low, is not as remote as has been hypothesized. Rupture

was more frequent in peripherally located and exophytic giant HHs: rupture was observed in 4/37 patients (10.8%) who carried an HH with these features.

No bleeding was observed in carriers of peripherally located, non-exophytic HHs whereas 1 case of rupture was recorded in 80 carriers (1.25%) of centrally located HHs; in this latter case the clinical course was less severe because the bleeding remained intra-hepatic.

The optimum management of giant HHs that do not fulfil the classical triad of criteria for treatment (symptoms not responsive to medical therapy, rapid tumour enlargement, diagnostic doubt with a suspicion of malignancy) remains an open issue. Besides, with regard to the “rapid enlargement” of the tumour, rapidity and rate of tumour enlargement warranting treatment are not clearly defined.

Our data seem to indicate that treatment should be considered in cases of peripherally located giant HHs with an exophytic growth pattern, which carry a higher risk of rupture.

Haemangiomas of less than 4 cm in diameter or centrally located giant HHs should be followed up with US; we recommend our patients to undergo US one year after the initial diagnosis and, if the lesion remains stable in the first year of follow-up, to repeat US every other year.

For those HHs that require treatment, transarterial embolization is an appealing option as it is safe and minimally invasive; a reduction in size or a change in the radiological appearance of HH secondary to the devascularization of the treated lesion has been reported following TAE [36–42].

However, there are no data available to establish whether the size reduction obtained with TAE is then maintained over time; long-term follow-up is required to judge on the real efficacy of TAE while surgery undoubtedly provides a definitive treatment.

In our series, when TAE was performed on the basis of size alone, it was partially effective in one case and completely ineffective in

the remaining two cases; surgery, performed laparoscopically in most cases, was always successful. Therefore, in the absence of clear guidelines and data on the long-term results of TAE, we preferred to offer surgery in selected cases.

Because HH is a benign tumour, the liver resection must have a minimal mortality and a low morbidity [11,43,44]. Among our patients, we had no perioperative deaths in the elective setting, and only two patients developed major postoperative complications classified as grade IIIa according to the Clavien-Dindo classification [45].

Successful use of TAE before surgical resection in the urgent setting of HH rupture with haemoperitoneum was first reported by Yamamoto et al. in 1991 [31]. The usefulness of TAE as a bridge treatment to surgery in these circumstances has been confirmed by other authors [26,34,38,41]. In the presence of ruptured HH, TAE can control the bleeding, stabilize the patient and allow a safer surgical excision. The aim of TAE is to decrease the size of the HH, especially when large, producing a shrinkage of the tumour by blocking its arterial supply. Therefore, surgical resection can be changed from an emergency to an elective procedure with a lower risk of intraoperative bleeding, as shown by our data.

Symptoms linked to the presence of the HH were uncommon in our series, and, overall, only 5/1067 HH carriers complained of symptoms (0.47%). These 5 patients had giant HH (Fig. 1).

Whereas several studies [6,9,19,20,22,44,46] have reported that an increase in size from the initial diagnosis is observed in less than 5% of cases, in our series, 20/90 patients who were followed with imaging at regular intervals showed tumour enlargement (22.2%).

In only one case in this series, surgery was indicated because of the failure to exclude malignancy on imaging; this finding confirms the high specificity of the available diagnostic tools, particularly MRI [16–18].

In conclusion, this report provides data on the prevalence of HH in the general population and offers an insight on its possible evolution. Based on our findings, giant HH, when peripherally located and exophytic, should most likely be considered for treatment because of its risk of rupture.

Conflict of interest

None declared.

References

- [1] Ishak KG, Rabin L. Benign tumors of the liver. *Medical Clinics of North America* 1975;59:995–1013.
- [2] Choy BY, Nguyen MH. The diagnosis and management of benign hepatic tumors. *Journal of Clinical Gastroenterology* 2005;39:401–12.
- [3] Brouwers MAM, Peeters PMJG, De Jong KP, et al. Surgical treatment of giant haemangioma of the liver. *British Journal of Surgery* 1997;83:314–6.
- [4] Trotter JF, Everson GT. Benign focal lesions of the liver. *Clinics in Liver Disease* 2001;5:17–42.
- [5] Hugh TJ, Poston GJ. Benign liver tumors and masses. In: Blumgart L, Fong Y, editors. *Surgery of the liver and biliary tract*. Edinburgh: Churchill Livingstone; 2001. p. 1397–422.
- [6] Donati M, Stavrou GA, Donati A, et al. The risk of spontaneous rupture of liver hemangiomas: a critical review of the literature. *Journal of Hepato-Biliary-Pancreatic Surgery* 2011;18:797–805.
- [7] Hall GW. Kasabach–Merritt syndrome: pathogenesis and management. *British Journal of Haematology* 2001;112:851–62.
- [8] Hamaloglu E, Altun H, Ozdemir A, et al. Giant liver haemangioma: therapy by enucleation or liver resection. *World Journal of Surgery* 2005;29:890–3.
- [9] Farges O, Daradkeh S, Bismuth H. Cavernous hemangiomas of the liver: are there any indications for resection. *World Journal of Surgery* 1995;19:19–24.
- [10] Belli L, De Carlis L, Beati C, et al. Surgical treatment of symptomatic giant hemangiomas of the liver. *Surgery, Gynecology and Obstetrics* 1992;174:474–8.
- [11] Iwatsuki S, Starzl TE. Personal experience with 411 hepatic resections. *Annals of Surgery* 1988;208:412–34.
- [12] Lerner SM, Hiatt JR, Salamandra J, et al. Giant cavernous liver hemangiomas: effect of operative approach on outcome. *Archives of Surgery* 2004;139:818–21.
- [13] Schnelltdorfer T, Ware AL, Smoot R, et al. Management of giant haemangioma of the liver: resection versus observation. *Journal of the American College of Surgeons* 2010;211:724–30.

- [14] Demircan O, Demiryurek H, Yagmur O. Surgical approach to symptomatic giant cavernous haemangioma of the liver. *Hepato-Gastroenterology* 2005;52:183–6.
- [15] Caseiro-Alves F, Brito J, Araujo AE, et al. Liver haemangioma: common and uncommon findings and how to improve the differential diagnosis. *European Radiology* 2007;17:1544–59.
- [16] Unal O, Sakarya ME, Arslan H, et al. Hepatic cavernous hemangiomas: patterns of contrast enhancement on MR fluoroscopy imaging. *Clinical Imaging* 2002;26:39–42.
- [17] Semelka RC, Martin DR, Balci C, et al. Focal liver lesions: comparison of dual-phase CT and multisequence multiplanar MR imaging including dynamic gadolinium enhancement. *Journal of Magnetic Resonance Imaging* 2001;13:397–401.
- [18] Tello R, Fenlon HM, Gagliano T, et al. Prediction rule for characterization of hepatic lesions revealed on MR imaging: estimation of malignancy. *American Journal of Roentgenology* 2001;176:879–84.
- [19] Okano H, Shiraki K, Inoue H, et al. Natural course of cavernous hepatic haemangioma. *Oncology Reports* 2001;8:411–4.
- [20] Pietrabissa A, Giulianotti P, Campatelli A, et al. Management and follow-up of 78 giant haemangiomas of the liver. *British Journal of Surgery* 1996;83:915–8.
- [21] Tait N, Richardson AJ, Muguti G, et al. Hepatic cavernous haemangioma: a 10 year review. *Australian and New Zealand Journal of Surgery* 1992;62:521–4.
- [22] Gandolfi L, Leo P, Solmi L, et al. Natural history of hepatic haemangiomas: clinical and ultrasound study. *Gut* 1991;32:677–80.
- [23] Lise M, Feltrin G, Da Pian PP, et al. Giant cavernous hemangiomas: diagnosis and surgical strategies. *World Journal of Surgery* 1992;16:516–20.
- [24] Santos Rodrigues AL, Silva Santana AC, Carvalho Araújo K, et al. Spontaneous rupture of giant hepatic haemangioma: a rare source of hemoperitoneum. *Case report. Il Giornale di chirurgia* 2010;31:83–5.
- [25] Jain V, Ramachandran V, Garg R, et al. Spontaneous rupture of a giant hepatic haemangioma: sequential management with transcatheter arterial embolization and resection. *Saudi Journal of Gastroenterology* 2010;16:116–9.
- [26] Corigliano N, Mercantini P, Amodio PM, et al. Hemoperitoneum from a spontaneous rupture of a giant haemangioma of the liver: report of a case. *Surgery Today* 2003;33:459–63.
- [27] Chen ZY, Qi QH, Dong ZL. Etiology and management of hemorrhage in spontaneous liver rupture: a report of 70 cases. *World Journal of Gastroenterology* 2002;8:1063–6.
- [28] Cappellani A, Zanghi A, Di Vita M, et al. Spontaneous rupture of a giant haemangioma of the liver. *Annali Italiani di Chirurgia* 2000;71:379–83.
- [29] Scribano E, Loria G, Ascenti G, et al. Spontaneous hemoperitoneum from giant multicystic haemangioma of the liver: a case report. *Abdominal Imaging* 1996;21:418–9.
- [30] Aiura K, Ohshima R, Matsumoto K, et al. Spontaneous rupture of liver haemangioma: risk factors of rupture. *Journal of Hepato-Biliary-Pancreatic Surgery* 1996;3:308–12.
- [31] Yamamoto T, Kawarada Y, Yano T, et al. Spontaneous rupture of haemangioma of the liver: treatment with transcatheter hepatic arterial embolization. *American Journal of Gastroenterology* 1991;86:1645–9.
- [32] Stayman Jr JW, Polsky HS, Blaum L. Ruptured cavernous haemangioma of the liver. *Pennsylvania Medicine* 1976;79:62–3.
- [33] Sewell JH, Weiss K. Spontaneous rupture of haemangioma of the liver. *Archives of Surgery* 1961;83:105–9.
- [34] Mazziotti A, Jovine E, Grazi GL, et al. Spontaneous sub capsular rupture of hepatic haemangioma. *European Journal of Surgery* 1995;161:687–9.
- [35] Andersson R, Tranberg K-G, Bengmark S. Hemoperitoneum after spontaneous rupture of liver tumor: results of surgical treatment. *HPB Surgery* 1988;1:81–3.
- [36] Althaus S, Ashdown B, Coldwell D, et al. Transcatheter arterial embolization of two symptomatic giant cavernous hemangiomas of the liver. *Cardiovascular and Interventional Radiology* 1996;19:364–7.
- [37] Jesic R, Radjokovic S, Tomic D, et al. Personal experience in embolization of liver hemangiomas. *Srpski Arhiv Za Celokupno Lekarstvo* 1998;126:349–54.
- [38] Srivastava DN, Gandhi D, Seith A, et al. Transcatheter arterial embolization in the treatment of symptomatic cavernous hemangiomas of the liver: a prospective study. *Abdominal Imaging* 2001;26:510–4.
- [39] Deutsch GS, Yeh KA, Bates 3rd WB, et al. Embolization for management of hepatic hemangiomas. *American Surgeon* 2001;67:159–64.
- [40] Cao X, He N, Sun J, et al. Interventional treatment of huge hepatic cavernous haemangioma. *Chinese Medical Journal* 2000;113:927–9.
- [41] Giavroglou C, Economou H, Ioannidis I. Arterial embolization of giant hepatic hemangiomas. *Cardiovascular and Interventional Radiology* 2003;26:92–6.
- [42] Zeng Q, Li Y, Chen Y, et al. Gigantic cavernous haemangioma of the liver treated by intra-arterial embolization with pingyangmycin-lipiodol emulsion: a multicenter study. *Cardiovascular and Interventional Radiology* 2004;27:481–5.
- [43] Yoon SS, Charny CK, Fong Y, et al. Diagnosis, management and outcomes of 115 patients with hepatic haemangioma. *Journal of the American College of Surgeons* 2003;197:392–402.
- [44] Herman P, Costa MLV, Machado MA, et al. Management of hepatic hemangiomas: a 14-year experience. *Journal of Gastrointestinal Surgery* 2005;9:853–9.
- [45] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Annals of Surgery* 2004;240:205–13.
- [46] Yamagata M, Kanematsu T, Matsumata T, et al. Management of haemangioma of the liver: comparison of results between surgery and observation. *British Journal of Surgery* 1991;78:1223.