Imaging of hepatic hypervascular tumors & clinical implications
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Download date: 07 Jan 2019
Grading and management of bleeding in hepatocellular adenoma.

Analysis in a prospective series of 45 patients.

Chapter 5
OBJECTIVE

Hepatocellular adenoma (HCA) is a benign hepatic lesion with risk of spontaneous bleeding. In a prospective series of patients with HCA, bleeding was assessed in conjunction with a grading system. Outcomes of management were evaluated.

SUBJECTS AND METHODS

Consecutive patients from 2008-2012 diagnosed with HCA were included. Reference standard was histopathology, MR and/or CT imaging. Patient characteristics were noted. Bleeding was scored and graded on imaging: intratumoral (Grade I), intrahepatic (Grade II), and extrhepatic (Grade III). Treatment of bleeding consisted of observation in hemodynamically stable patients and selective transarterial embolization (TAE) in patients requiring blood transfusion. Elective resection was performed in HCA>5cm.

RESULTS

HCA was confirmed in 45 patients with a total of 195 adenomas. Bleeding was found in 29/45 (64%) patients and in 42/195 (22%) adenomas, graded as Grade I: 29/42, Grade II: 9/42, and Grade III: 4/42. Two patients with Grade I bleeding, 2 with Grade II, and 3 with Grade III required TAE. Size of bleeding-area was larger in patients undergoing TAE regardless of grading (P=0.011; cut-off 60mm. Relation to the liver capsule was significant for bleeding (P <0.001): intrahepatic adenomas 10/85, subcapsular 17/89, and exophytic 16/24).

CONCLUSION

We propose a grading system of bleeding HCA in which Grade I and II with bleeding-area larger than 6cm, and all Grade III bleeding are preferably treated with TAE. Additional care, with follow-up or preventive treatment is advised in patients with exophytic adenomas.

INTRODUCTION

Hepatocellular adenoma (HCA) is a benign lesion although not without risk of complications. Besides an estimated risk of 4.3% of malignant transformation in adenomas larger than 5cm [1], spontaneous bleeding and rupture have been reported in more than 30% of adenomas larger than 5cm and may have significant clinical consequences [2-7]. An undefined subset of patients present with symptoms of bleeding, ranging from minor upper abdominal pain to hypovolemic shock, requiring emergency care. Other patients have vague complaints of abdominal discomfort, fatigue, or elevated liver function tests in a routine blood test. Cross-sectional imaging of the liver is the first step in diagnosis of HCA with or without bleeding. Computer Tomography (CT) and Magnetic Resonance (MR) imaging with a liver specific hepatobiliary contrast agent play an important role [8].

Characteristics of contrast enhancement of the adenoma during arterial phase of dynamic imaging, no uptake of contrast on hepatobiliary phase of MR imaging [8], intratumoral fat and glycogen (9), and signs of bleeding (10). Active arterial bleeding in HCA might be evident on contrast enhanced, cross-sectional imaging studies. When control of bleeding is required, selective transarterial embolization (TAE) of the feeding artery is the treatment of choice in medical centers with an interventional radiology department [11]. Oral contraceptive (OC) use has been associated with growth of HCA and possible increased risk of bleeding [12]. Therefore, treatment of HCA first of all consists of discontinuation of OC. This might result in shrinking or stabilization of growth of adenomas [13]. When the HCA does not reduce in size below 5cm, resection is advocated, because of the continued increased risks of bleeding and malignant transformation in this patient group [1]. To improve treatment strategies for patients suffering from bleeding HCA, bleeding needs to be better defined.

With this study we aimed to devise a grading system for bleeding in HCA according to the extent of bleeding relative to the adenoma and surrounding liver parenchyma. Secondly, we aimed to assess outcomes of observation and interventions in patients with bleeding in HCA.
Assessment of bleeding characteristics on MR and CT imaging

Methods

This study is part of a prospective study including all patients referred with suspicion on HCA or focal nodular hyperplasia (FNH) from January 2008 until May 2012 [8]. All patients with an established diagnosis of HCA were selected (n = 45). All patient data were collected in a designated prospective database. Standard of reference was diagnosis based on either histopathology or imaging (MRI Primovist® [6] or CT imaging). The institutional Medical Ethics Committee approved the study and a written informed consent was obtained from all patients. Case characteristics were noted and symptoms at time of presentation were assessed with a questionnaire. Baseline and post-treatment visual analogue scale (VAS) were used to assess pain and discomfort [14].

Diagnosis of Hepatocellular adenoma

Diagnosis of HCA was preferably made by MR imaging of the liver using hepatobiliary Gadolinium EOB-DTPA contrast (Primovist®, Bayer, Germany (Eovist® in the United States). Diagnosis of HCA was based on intra-tumoral hemorrhage, fat and/or glycogen, and arterial enhancement of the adenoma with subsequent loss of intensity compared to surrounding liver tissue in the hepatobiliary phase [8]. Multiphase CT imaging of the liver was only rendered diagnostic in the presence of an arterial enhancing adenoma with clear signs of hemorrhage and without suspicion on malignant disease [15]. Histopathological samples were obtained either by resection and/or liver biopsy from tumoral tissue. Systematic biopsy was performed until 2011, as of which time MR imaging with Primovist® was proven sensitive for diagnosis of HCA [8]. Morphological characteristics of HCA include: hepatocellular proliferation without cytonuclear atypia in which solitary arterioles are seen and portal tracts are lacking, with a well-developed reticulin framework without pseudoglandular or thickened trabecular growth patterns.

Characteristics on MR and CT imaging

Liver adenomas were evaluated by one abdominal radiologist (SSKSP) with over 10 year experience with liver imaging, according to the following characteristics: number of adenomas (a max of 10 – largest adenomas were assessed per patient), segmental location of adenomas, depth of adenomas in relation to the liver capsule: intrahepatic (adenomas more than 1cm distance to the liver capsule); subcapsular (any part of the adenoma within 1cm distance of the liver capsule); exophytic (any part of the adenoma bulging beyond the contours of the liver).

Assessment of bleeding

Signs of bleeding on CT imaging included intra- or peri-adenomal, irregular hypodense areas, without contrast enhancement. Or irregular, non-enhancing hyperdense areas, consistent with a recent bleeding or clot. These signs, in combination with free abdominal fluid were considered compatible with rupture of the bleed into the abdominal cavity. On MR inhomogeneous, non-enhancing areas of hypo- or hyperintensity on T1 w and T2 were regarded as consistent with bleeding. High intensity areas on T1 w sequence were regarded as acute bleeding. Signal loss on gradient sequences was regarded as sign of old bleeding (hemoglobin). If both CT and MR images were available, MR images were considered superior and used for evaluation (exception: when motion artefacts or technical difficulties intervened with the quality of the images). Bleeding was scored as Grade I (intratumoral), Grade II (intrahepatic) or Grade III (extrahepatic: rupture into the peritoneal cavity). If no remnant of tumor tissue was found on imaging bleeding was graded as confined within the liver (intrahepatic; Grade II) or extrahepatic (Grade III). Hemorrhage in histopathologic specimens was not evaluated as histopathology in this prospective patient cohort was designed to be used as HCA diagnostics and samples were taken from vital, non-bleding, and non-necrotic areas for evaluation. Size of the adenoma and area(s) of bleeding were noted on baseline imaging and if follow-up took place, these factors were re-assessed over time.

In all patients diagnosed with HCA, oral contraceptives were discontinued as initial treatment. Patients with adenomas smaller than 5 cm underwent follow-up. Adenomas larger than 5 cm were considered for resection. If patients presented with signs of acute bleeding, a contrast enhanced CT scan was performed in an emergency setting. In the absence of signs of intra-abdominal rupture (free fluid) and hemodynamic stability, patients were admitted and observed. In case of hemodynamic instability, extensive intrahepatic bleed, rupture of the adenoma into the abdominal cavity, or extravasation on CT imaging, superselective catheterization of the hepatic arterial branches and embolization (TAE) were performed.

Statistical analysis

Statistical analysis is per patient using SPSS 20 (IBM Corporation, Chicago, IL). Descriptive statistics were used to assess study population. Mann Whitney test was used to assess continuous data. Pearson’s Chi square, Fisher’s exact, and Spearman correlation tests were used for categorical data analyses. Statistical tests were evaluated at the 5% level of significance.

Results

In all 45 patients (median age 39 years, 1 male) a total of 105 adenomas were evaluated. Final diagnosis of HCA was confirmed by histopathological examination in 42/45 patients (30 resection specimens; 12 histological biopsies) and in 73 adenomas (57 resection specimens; 16 biopsies). In the remaining 3 patients, MR and/or CT imaging were regarded diagnostic for HCA (with a total of 14 adenomas). If multiple adenomas occurred, all adenomas with similar radiological characteristics as the diagnostic adenoma were considered the same diagnosis. Patient characteristics are summarized in Table 1.
Grading of bleeding

**Patient characteristics**

| Age | median years (range) | 39 (22 - 60) |
| Male / Female | 1 : 44 |

**Oral contraceptive use (OC)**

- Discontinuation before diagnosis | median months |
  - 13 (69) |
- Discontinuation at time of diagnosis | 31 (29) |

**Body Mass Index (BMI)**

- Normal | (< 25) |
  - 11 (24) |
- Overweight | (25 - 30) |
  - 13 (29) |
- Obesity | (30 - 40) |
  - 16 (36) |
- Morbidly obese | (40 <) |
  - 5 (11) |

**Hepatic steatosis**

- Mild | 17 (38) |
- Intermediate | 3 |
- Severe | 7 |

**Number of adenomas**

- Solitary (%) | 14 |
- 2-5 (%) | 16 |
- 6-9 (%) | 6 |
- 10+ (%) | 9 |

**Diagnosis**

| Patients | n = 45 | Adenomas | n = 195 |
| Histopathology | 42 | 73 |
| Biopsy | 16 |
| Resection | 57 |
| Imaging | 3 | 122 |

**Size**

| medium cm (range) | 68* (0 - 250) | 24 (10 - 250) |

**Location**

- Left liver (%) | 58 (30) |
- Right liver (%) | 137 (70) |
- Intrahepatic (%) | 82 |
- Subcapsular (%) | 89 |
- Exophytic (%) | 24 |

Results are summarized in Table 2. All 45 patients underwent MR and/or multiphase CT imaging. Bleeding was seen in 42/195 adenomas (22%), in 29/45 patients (64%) and in 23 out of 31 (74%) patients with multiple lesions, more than 1 bleeding occurred (Table 3). Most bleeding sites were confined to the adenoma and graded accordingly as Grade I (29/42: 69%). In 9 adenomas the bleeding spread intrahepatically (Grade II, 21%), and in 4 adenomas the bleeding had ruptured into the peritoneal cavity (Grade III, 10%). Sixteen of 45 patients (36%) were asymptomatic at presentation and were analyzed for incidental adenomas after finding of elevated liver function tests, or imaging for unrelated causes. Four patients presented with minor symptoms of abdominal discomfort showing signs of intratumoral bleeding in 5 cases (median VAS 1: 0-2); 12 patients had chronic abdominal complaints with 3 cases of intratumoral bleeding, 1 intrahepatic, and 1 extrahepatic bleeding (median VAS 7: 4-7); 14 patients had severe pain of acute onset showing signs of bleeding in 13/14 patients with additional intrahepatic expansion in 2 cases, and extrahepatic breach in 3 cases (median VAS 8: 7-10). Symptoms, bleeding and treatment are summarized in Table 2. Location of HCA in relation to the liver capsula was ‘intrahepatic’ in 82/195, ‘subcapsular’ in 89/195, and ‘exophytic’ in 24/195 adenomas. Exophytic adenomas showed more bleeding (16/24; 67%) compared to intrahepatic (9/82; 11%) and subcapsular (17/89; 19%) adenomas (P < 0.001). None of the intrahepatic adenomas showed extrahepatic grade III bleeding (n = 82).

![ROC curve representing the size of the bleeding site and the correlation with the need for TAE in patients. The larger the bleeding site, the more likely the patient required intervention. The cut-off, most specific and sensitive size was 68 mm (dotted line; specificity 96%; sensitivity 73%), and most sensitive and specific was 88 mm (striped line; sensitivity 84%; specificity 98%).](image-url)
Chapter 5

Grading of bleeding

Treatment and follow-up is summarized in Table 2. Emergency care with TAE was indicated in 7 patients: Grade I bleeding in 2 patients with bleeding-area 40 and 62 mm, Grade II in 2 patients with bleeding-area of 60 and 153, and Grade III bleeding in 3 patients with a median intrahepatic bleeding-area of 75 mm (50-160 mm). The size of the bleeding-area was significant for the need of TAE regardless of grading score (P = 0.017). Size of the bleeding-area of 60 mm or more was most specific (96%) and sensitive (73%) (Figure 1). Figure 2 shows an example of resected adenomas with additional findings of granulomatous lesions (16). Preventive TAE was performed in two patients: a Jehovah witness after an episode of intratumoral bleeding and another patient pre-operatively to reduce risk of bleeding during resection of a giant HCA of 25 cm. Emergency care with laparotomy was indicated for bleeding in two patients; one patient was unstable while no interventional radiologist was available at the hospital of presentation and the other patient required laparotomy for abdominal compartment syndrome after massive bleeding. Elective resection was performed in 29/45 (64%) patients, with 57 adenomas (median size 64 mm; 10-250 mm). Radiological signs of bleeding were seen in 18/29 (62%) patients and 21/57 (37%) adenomas: Grade I, Grade II, and Grade III. One subclinical, new Grade I bleeding was seen in an adenoma during follow-up (after 22 months the adenoma had decreased 42% in size to 21 mm and showed a small area of bleeding of 2 by 7 mm). 36 adenomas with signs of bleeding enrolled in follow-up had a mean decrease in area of bleeding of 38% (median follow-up 15 months). Patients who had discontinued OC use at time of presentation had no more signs of bleeding compared to the group who discontinued OC well before presentation (P = 0.665). Fifty percent of all included women had been pregnant at least once before diagnosis of HCA was made. One of these patients presented with bleeding of HCA during the 17th week of her first pregnancy, classified as extrahepatic (Grade III) on MRI (Figure 2). This patient was successfully treated with TAE. 22 months after first presentation she suffered a Grade I re-bleed for which elective resection was performed.

Table 2 — Treatment

<table>
<thead>
<tr>
<th>Table 2 — Treatment</th>
<th>Patients (n = 45)</th>
<th>Lesions (n = 195)</th>
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<tr>
<td><strong>Transarterial embolization</strong></td>
<td><strong>VAS Baseline</strong></td>
<td><strong>Lesion size</strong></td>
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<tr>
<td>Emergency care</td>
<td>Grade I bleeding</td>
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<tr>
<td></td>
<td>Grade II bleeding</td>
<td>2 (7-10)</td>
</tr>
<tr>
<td></td>
<td>Grade III bleeding</td>
<td>3 (6-5-7)</td>
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<tr>
<td></td>
<td>Preventive care</td>
<td>2 (0-10)</td>
</tr>
<tr>
<td><strong>Resection</strong></td>
<td>VAS Baseline</td>
<td>29 (0-10)</td>
</tr>
<tr>
<td></td>
<td>VAS Post</td>
<td>18 (0-10)</td>
</tr>
<tr>
<td></td>
<td>No bleeding</td>
<td>11 (0-8)</td>
</tr>
<tr>
<td><strong>No resection</strong></td>
<td>VAS Baseline</td>
<td>16 (0-10)</td>
</tr>
<tr>
<td></td>
<td>VAS Post</td>
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<tr>
<td></td>
<td>Follow-up (median 19 months)</td>
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<td>3 (9-5-10)</td>
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<td></td>
<td>Follow-up (median 22 months)</td>
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<td>Follow-up (median 16 months)</td>
<td>5 (0-5)</td>
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<tr>
<td></td>
<td>Follow-up (median 20 months)</td>
<td>110 (0-104)</td>
</tr>
</tbody>
</table>

**TREATMENT & FOLLOW-UP**

Treatement and follow-up is summarized in Table 2. Emergency care with TAE was indicated in 7 patients: Grade I bleeding in 2 patients with bleeding-area 40 and 62 mm, Grade II in 2 patients with bleeding-area of 60 and 153, and Grade III bleeding in 3 patients with a median intrahepatic bleeding-area of 75 mm (50-160 mm). The size of the bleeding-area was significant for the need of TAE regardless of grading score (P = 0.017). Size of the bleeding-area of 60 mm or more was most specific (96%) and sensitive (73%) (Figure 1). Figure 2 shows an example of resected adenomas with additional findings of granulomatous lesions (16). Preventive TAE was performed in two patients: a Jehovah witness after an episode of intratumoral bleeding and another patient pre-operatively to reduce risk of bleeding during resection of a giant HCA of 25 cm. Emergency care with laparotomy was indicated for bleeding in two patients; one patient was unstable while no interventional radiologist was available at the hospital of presentation and the other patient required laparotomy for abdominal compartment syndrome after massive bleeding. Elective resection was performed in 29/45 (64%) patients, with 57 adenomas (median size 64 mm; 10-250 mm). Radiological signs of bleeding were seen in 18/29 (62%) patients and 21/57 (37%) adenomas: Grade I, Grade II, and Grade III. One subclinical, new Grade I bleeding was seen in an adenoma during follow-up (after 22 months the adenoma had decreased 42% in size to 21 mm and showed a small area of bleeding of 2 by 7 mm). 36 adenomas with signs of bleeding enrolled in follow-up had a mean decrease in area of bleeding of 38% (median follow-up 15 months). Patients who had discontinued OC use at time of presentation had no more signs of bleeding compared to the group who discontinued OC well before presentation (P = 0.665). Fifty percent of all included women had been pregnant at least once before diagnosis of HCA was made. One of these patients presented with bleeding of HCA during the 17th week of her first pregnancy, classified as extrahepatic (Grade III) on MRI (Figure 2). This patient was successfully treated with TAE. 22 months after first presentation she suffered a Grade I re-bleed for which elective resection was performed.

Table 3 — Number of lesions and bleeding

<table>
<thead>
<tr>
<th>Table 3 — Number of lesions and bleeding</th>
<th>Total patients</th>
<th>Radiology of lesions</th>
</tr>
</thead>
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<td>Bleeding</td>
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<td>7</td>
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<tr>
<td><strong>Multiple lesions</strong></td>
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<td></td>
</tr>
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<td></td>
<td>No bleeding</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>One bleeding adenoma</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Multiple bleedings adenomas</td>
<td>10</td>
</tr>
</tbody>
</table>

Grade of bleeding
In this prospective study of patients with HCA, 64% of the patients showed radiological signs of bleeding. We propose a clinical grading system to classify the severity of bleeding according to imaging features that can be used to direct therapy. Grade I bleeding is confined to the tumor and can usually be observed, requiring no active treatment. Grade II bleeding extends into the liver parenchyma whereas Grade III bleeding represents rupture of the parenchyma and bleeding beyond the confines of the liver capsule into the abdominal cavity. We advise to treat all active bleeding sites, bleeding sites of over 6 cm, and Grade III bleeding, with selective TAE of the feeding branch of the hepatic artery.

Clinical presentation of patients with bleeding may differ according to the severity of bleeding. Acute rupture of bleeding HCA requires emergency admission and resuscitation of the patient. Whereas a decade ago, the acute phase of intraparenchymal and intrahepatic bleeding (Grade II and III) with hemodynamic instability usually required laparotomy and control of the bleeding by packing of the liver, management has now shifted towards selective TAE. This technology is available in most large medical centers with state-of-the-art interventional radiology. In case of semi-acute bleeding, for example large intratumoral (Grade I) or intrahepatic (Grade II) bleeding without hemodynamic instability, TAE can be performed to prevent further bleeding. In our experience, an additional effect of TAE might be relief of pain, as presumably, the local pressure in the liver is reduced by proximal occlusion of the bleeding vessel(s). For these reasons, we treat patients presenting with (semi-)acute bleeding sites of >6 cm and all Grade III bleeding with TAE. Most patients with small Grade I bleeding do not experience substantial discomfort and might not even seek medical attention.

Another risk for bleeding was the relation of HCA to the liver capsule. Exophytic adenomas bled more often than intraparenchymal or subcapsular adenomas, and intrahepatic adenomas did not cause Grade III bleeding. The pressure of surrounding liver parenchyma most likely prevents bleeding to spread. These findings have direct inferences for management as patients presenting with HCA with exophytic growth, or patients with large adenomas and concomitant obesity must be informed of the higher risks of severe bleeding. Preventive treatment options like TAE could be considered in these high risk patients, however this is an area of debate and will need further study. In our view, preventive TAE is of potential value in patients with increased risk of bleeding, patients unfit for surgery, or in patients who have increased surgical risks such as a Jehovah’s witness refusing blood transfusion.

Another issue is ‘what to do after bleeding of HCA’. First of all, we advise a wait-and-see policy whether or not the adenoma required TAE of an active bleeding site. After the acute phase, it is difficult to ascertain which parts of the adenoma constitute the original HCA and which parts are due to the bleeding, i.e. represent hematoma or clot. With time, the hematoma is cleared resulting in decrease of size of the adenoma as noted in 38% of adenomas in this series, leaving intact part(s) of the HCA at the site for assessment. In this series, one of the patients with severe Grade III bleeding underwent TAE, after which no residual HCA tumor could be found on follow-up imaging and hence, no resection of the tumor needed to be performed. Because of the intratumoral bleeding and rupture, part of the original tumor is destructed. This phenomenon we reported previously in 16 patients who underwent planned, delayed resection of the bleeding site after a bleeding episode of HCA [17]. Histopathologic examination of the resection specimen revealed necrosis and fibrosis at the site of the bleeding in 7 patients (43%) with detectable remnants of HCA [17]. We are now more conservative in resection of HCA after bleeding.

As a result of the abovementioned policy, we undertook delayed resection in only two of the four patients that suffered Grade III bleeding in this study. Recurrent bleeding within the remnants of the same adenoma was encountered in one patient (Grade I), after which she underwent a segmental liver resection.

**Figure 2**

A: Transverse arterial MR image of a 34-year-old woman who during the 17th week of pregnancy experienced severe acute upper abdominal pain. A large arterial enhancing adenoma in segment 2/3 of the liver is seen (arrow) with a hypodense area consistent with bleeding (white arrowhead). With abdominal free fluid this bleed was categorized as an extraparenchymal grade III bleeding. Therefore the feeding hepatic arteries to the adenoma were selectively embolized. The fetus remained under extra care during the remaining pregnancy and the baby was healthy although prematurely delivered in the 34th week.

B: Transverse arterial CT image of the same woman 22 months after first presentation. After successful TAE the pain and discomfort subsided until similar less intense pain occurred again. Imaging was performed showing a smaller adenoma in the left liver (white arrow). However, a new grade I bleeding was seen in the tumor.

C: Intra-operative image showing the exophytic adenoma in the left liver (white arrow). Spread through the liver, small greyish adenomas were present (arrowheads). Frozen section revealed granulomatous inflammation [16].
Adenomas in the other two patients did not require subsequent resection as the adenoma was undetectable. Likewise, 5 out of 9 adenomas with Grade II bleeding were resected. During follow-up none of the other adenomas presented with bleeding and all adenomas decreased in size or remained stable. On the basis of these experiences we advise a wait-and-see policy after TAE, even after severe Grade II and Grade III bleeding. The adenoma should be reassessed after 3-6 months, and secondary resection is only considered when there is evidence of residual HCA >5cm, or severe persisting abdominal complaints. Following this strategy, many adenomas do not require subsequent resection and can safely be observed.

Importantly, the differential diagnosis of HCA is hepatocellular carcinoma (HCC), and especially after bleeding it is difficult to distinguish HCA from HCC. In young women without cirrhosis, hepatitis, or other underlying (parenchymal) liver disease with a normal alpha fetoprotein, diagnosis of HCC is unlikely [18]. However, in male patients who present with bleeding adenoma in the liver and have not been taking androgenic hormones, suspicion on HCC should be high [19]. These patients are not elaborated herein, as the primary diagnosis of HCC excluded them from the present study. The only one male patient included in this study, did present with typical signs of HCA, without underlying parenchymal disease or history of malignancy. Even though the adenoma was smaller than 5 cm (the current standard to advise resection), the adenoma was resected with generous margins. Final histopathological diagnosis in this patient was steatotic HCA without signs of malignancy.

This study has some limitations. First of all bleeding was only assessed on imaging and was not corroborated with histopathology. The study design of the prospective patient cohort included histopathology as reference for diagnosis of HCA and not as reference for bleeding. Therefore specimens were obtained from vital tumor tissue and bleeding was not prospectively noted and correlated to imaging. Using radiology as standard of reference for bleeding enabled us to assess every HCA in the liver and to accurately evaluate the proposed grading system in regard with clinical presentation. Finally, imaging was evaluated by one abdominal radiologist and no inter-observer analysis was performed.

**Conclusions**

We propose a grading system of bleeding for HCA in which intratumoral (Grade I) and intrahepatic (Grade II) bleeding larger than 6cm, and extrahepatic (Grade III) bleeding should be treated with TAE, while most small, grade I intratumoral bleeding do not need treatment. After the acute phase of bleeding with or without treatment with TAE, adenomas should be reassessed in time; in the absence of (remnants of) HCA >5cm after 3 months, further observation may be restricted to patients with large exophytic adenomas.

**References**