Hepatic artery infusion chemotherapy (HAIC) is used primarily in patients with inoperable primary or metastatic hepatic tumors. During HAIC system implantation, the guide wire used to support the insertion of the catheter can damage the gastroepiploic artery resulting in intraperitoneal bleeding when percutaneous catheter placement and tip fixation method was used. Five cases complicated by gastroepiploic arterial hemorrhage are reported. Three were found to have active contrast extravasation during implantation. One had massive intraperitoneal hemorrhage several hours after implantation, and another had late-onset hemorrhage two months later. All hemorrhages were successfully controlled by transarterial embolization (TAE) from gastroepiploic artery.

Massive intraperitoneal hemorrhage resulting from the gastroepiploic artery is rare but can be lethal if not properly managed. Most literature regarding bleeding from gastroepiploic artery is mainly concerned with bleeding induced by gastroepiploic artery aneurysm rupture [1, 2, 3], penetrating stab wound [4], iatrogenic injury [5], or spontaneous rupture [6]. We report five cases of hemoperitoneum due to rupture of the gastroepiploic artery associated with HAIC catheter-port system implantation. They were successfully rescued by the intervention using TAE.

MATERIALS AND METHODS

In this paper, all patient data were collected under approval of the Institutional Review Board (IRB) in our hospital (registration number: CLH-0048). From July 2006 to December 2007, 155 patients with unresectable hepatic tumors received a total of 165 HAIC catheter-port system implantations. Of the 165 implantations, 141 were performed with tip fixation method. Of these 141 implantations, five patients had subsequent intraperitoneal hemorrhage as shown in Table 1.

In our tip fixation method, to prevent localized hematoma at puncture site after implantation of HAIC catheter-port system, we do not use sheath but use a 4-F RC1 catheter (Cordis. Super Torque; Europe, Roden, The Netherlands) as the guiding catheter for a 2.7-F micro-catheter (Progreat, Terumo Co., Tokyo, Japan) inserted coaxially to embolize all replaced and accessory hepatic arteries and identifiable extrahepatic tumor feeding arteries such as right and left inferior phrenic arteries, right adrenal arteries, right renal capsular arteries and omental arteries from gastroepiploic arteries to redistribute hepatic arterial inflow to single feeding artery from
<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Timing of bleeding</th>
<th>Embolic agent used</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>74</td>
<td>F</td>
<td>Multifocal HCC</td>
<td>During procedure</td>
<td>NBCA</td>
<td>Successfully stopped bleeding and partial remission for 7 months. Still alive.</td>
</tr>
<tr>
<td>2</td>
<td>39</td>
<td>M</td>
<td>Metastatic liver adenocarcinoma from unknown origin</td>
<td>Several hours after procedure</td>
<td>Gelfoam pledgets</td>
<td>Successfully stopped bleeding and partial remission for 17 months. Still alive.</td>
</tr>
<tr>
<td>3</td>
<td>53</td>
<td>M</td>
<td>Multifocal HCC with right portal vein thrombosis</td>
<td>Two months after procedure with significantly prolonged prothrombin time</td>
<td>Gelfoam pledgets</td>
<td>Successfully stopped bleeding but expired after ten days due to liver failure</td>
</tr>
<tr>
<td>4</td>
<td>54</td>
<td>M</td>
<td>Cholangiocarcinoma s/p modified hepatectomy with multiple recurrence within both lobes of liver</td>
<td>During procedure</td>
<td>NBCA</td>
<td>Successfully stopped bleeding and stationary disease for 10 months. Still alive.</td>
</tr>
<tr>
<td>5</td>
<td>56</td>
<td>F</td>
<td>Ascending colon carcinoma with multiple liver metastasis and extrahepatic portal veins thrombosis</td>
<td>During procedure</td>
<td>NBCA</td>
<td>Successfully stopped bleeding and partial remission for 9 months. Still alive.</td>
</tr>
</tbody>
</table>

HCC: hepatocellular carcinoma; NBCA: N-Butyl Cyanoacrylate

Figure 1. A 74 year-old woman, with hepatocellular carcinoma in the right lobe and multiple tumors in both lobes, underwent implantation of the HAIC catheter-port system in August 2007. HAIC catheter tip was placed in right gastroepiploic artery after passing through gastroduodenal artery. Active intraperitoneal contrast extravasation from left gastroepiploic artery (black arrow) was identified with contrast agent injected via a microcatheter passing coaxially through the HAIC catheter tip. After N-butyl cyanoacrylate (NBCA)-lipiodol mixture (1:2) was infused into left gastroepiploic artery via microcatheter, contrast extravasation was no longer appreciated (black arrow).
proper hepatic artery with metallic micro-coils (MicroNester/Embolization Coil, Cook, Bjaeverskov, Denmark). We also embolize the right gastric artery and identifiable accessory left gastric artery from left hepatic artery to prevent gastric and duodenal mucosa injury after initiation of HAIC. Before the Anthron P-U catheter (5-F heparin-coated polyurethane catheter; PU5070SDST; Anthron P-U catheter; Toray Medical Industries, Tokyo, Japan) is indwelt, we insert a 0.035-inch (Stiff type, Terumo, Tokyo, Japan) rather than a 0.018-inch guide wire from the 4-F RC1 catheter through anterior division of gastroduodenal artery and right gastroepiploic artery to left gastroepiploic artery to support the placement of the Anthron P-U catheter. By using this technique we reach almost one hundred percent success rate for implantation of HAIC catheter-port system in patients without previous embolization of gastroduodenal artery and without previous gastrectomy.

**Patient 1:**
A 74 year-old woman had a 10 cm-diameter hepatocellular carcinoma in right lobe of the liver and multiple smaller tumors in both lobes. She had received transarterial chemoembolization (TACE) twice but the results were suboptimal. She subsequently underwent HAIC catheter-port system implantation. After implantation, contrast extravasation was noted from the left gastroepiploic artery during the procedure. A micro-catheter was then inserted through the Anthron P-U catheter to reach the location of the bleeding and N-butyl cyanoacrylate (NBCA) (Histoacryl, B.Braun, Aesculap AG, Tuttingen/Germany)-lipiodol (Lipiodol Ultra Fluide, Guerbet, Roissy, France) mixture (1:2) was infused into left gastroepiploic artery to stop the bleeding.

**Patient 2:**
A 39 year-old man, with multiple hepatic metastases and unknown primary tumor origin, received systemic chemotherapy previously with poor response. Therefore, he underwent HAIC
catheter-port system implantation. However several hours after implantation, the patient complained of abdominal pain along with hypotension and tachycardia. Emergent CT showed massive intraperitoneal bleeding along the left upper quadrant of the abdomen near the spleen. The patient underwent angiography for suspected hemorrhage of the gastroepiploic artery and although the images did not show any significant contrast extravasation, based on the abdominal CT, the patient was treated with Gelfoam pledgets (Spongostan Film, Johnson & Johnson Medical, Gargrave, Skipton, U.K.) in the left gastroepiploic artery to stop the bleeding. The patient left the hospital several days later and follow-up CT showed his tumors had regressed (Fig. 2).

**Patient 3:**
A 53 year-old man, with hepatic tumors and right portal vein thrombosis, underwent implantation of the HAIC catheter-port system. The patient underwent also coumadinization for suspected right popliteal vein partial thrombosis. Unfortunately, two months after implantation he returned to our hospital with complaints of constant abdominal pain and tarry stools. The patient had an abnormal prothrombin time of 150.4 seconds, and an INR of 9.9. Considerable hemoperitoneum and contrast extravasation at the top of left abdomen were found on abdominal CT. Contrast extravasation from the branch of left gastroepiploic artery was also seen on angiography (Fig. 3), and Gelfoam pledgets were emergently injected into left gastroepiploic artery to stop the bleeding. Unfortunately, this patient died of liver failure 10 days later although the bleeding was controlled.

**Patients 4 and 5:**
A 54 year-old man with cholangiocarcinoma and multiple recurrences after resection of liver tumors and a 56 year-old woman with colon carcinoma complicated by multiple liver metastases and portal veins thrombosis, were both found to have active contrast extravasation from left gastroepiploic artery during implantation (same as Patient 1). After NBCA treatment, the bleeding was effectively stopped.

**DISCUSSION**
HAIC therapy is usually used for unresectable primary or metastatic hepatic tumors. It can also serve as adjuvant therapy for surgery [7,8], radiofrequency ablation [9,10], and transarterial chemembolization. Whether combined with systemic chemotherapy, the local tumor response rate can reach higher than 57.1% for unresectable liver metastases from colorectal cancer [11,12]. Recent reports
show that metastatic colorectal cancer treated with HAIC improved liver function and served as a bridge for surgery [13].

Percutaneous placement is a common method for the implantation of the catheter-port system [14,15]. Most researchers currently use a side-hole catheter and fix the catheter tip in the gastroduodenal artery rather than direct placement of the catheter in the hepatic artery. This reduces the occurrence of catheter dislodgement and improves the long-term patency rate.

During the catheter placement with our tip fixation method, the 0.035-inch guide wire is placed in the gastroepiploic artery as a support for catheter placement. In our experience, without the use of sheath the Anthron P-U catheter is difficult to be indwelt percutaneously with a 0.018-inch guide wire and a 0.035-inch guide wire will make the procedure more smoothly due to its higher rigidity and trackability. But during advancement of the Anthron P-U catheter through the arteries punctured, the guide wire in the gastroepiploic artery could suddenly advance and the gastroepiploic artery or its branches could be damaged or even be perforated if we did not hold the guide wire firmly and keep an eye on the tip of the guide wire. Otherwise, active and probably lethal bleeding could happen if neglected.

In our patient 1, 4 and 5, the active contrast extravasations from gastroepiploic artery were noted during the procedures immediately after the Anthron P-U catheter implantation because sudden advance of the tips of guide wires were appreciated. Gastroepiploic arteriographies were checked and the bleeders were successfully embolized with diluted NBCA via a micro-catheter inserted through the Anthron P-U catheter. In our patient 2, we probably neglected the injury of gastroepiploic artery during the implantation of HAIC catheter-port system and massive hemoperitoneum happened. Due to rapid clinical downhill occurring in the ward, the patient was then successfully treated with TAE. In our patient 3, the massive hemoperitoneum with active bleeding from left gastroepiploic artery was noted two months later closely related to inappropriate anticoagulation. We suggested the gastroepiploic artery could have been damaged during HAIC catheter implantation and then damaged artery bled due to bleeding tendency as a result of poor monitoring of anticoagulation.

Most hemoperitoneum from gastroepiploic artery reported in the literature are secondary to gastroepiploic artery aneurysm rupture, penetrating stab wound, or spontaneous rupture. A few cases are due to iatrogenic injury. The management options include expectant management, vessel ligation, vascular resection and TAE. According to the current literature, which is primarily in the form of case reports, most interventions involve surgical vascular ligations or resections [1, 6]. Until now, there is no report of HAIC catheter-port system implantation induced gastroepiploic arterial bleeding.

We report five patients receiving HAIC catheter-port system implantation complicated by hemorrhage that was successfully treated by TAE in left gastroepiploic artery. Gastroepiploic arterial bleeding should be monitored during the implantation. If hemoperitoneum is suspected, arteriography of gastroepiploic artery should be checked during the procedure from Anthron P-U catheter and the splenic artery should be checked for possible contrast extravasation from left gastroepiploic artery if gastroduodenal arteries were emoblized. Under suitable conditions, we suggest using NBCA for superselective embolization as it can efficiently stop bleeding. Even if contrast extravasation from the gastroepiploic artery is not detected at angiography, we suggest empirical use of gelfoam pledgets to stop bleeding.

CONCLUSIONS

HAIC therapy is commonly used for unresectable primary or metastatic hepatic carcinoma. If a stiff guide wire is placed in gastroepiploic artery via the gastroduodenal artery to support the pathway of catheter placement, gastroepiploic artery might be damaged by sudden inadvertent advance of guide wire with resultant intraperitoneal bleeding. The bleeding may occur during implantation, or several hours later, or may even be induced by inappropriate anticoagulation several months later. If we are aware of the possibility of gastroepiploic arterial bleeding, this complication can be identified earlier and treated appropriately to avoid a catastrophic outcome. According to our experience with TAE, embolization by using NBCA or gelfoam pledgets can efficiently stop the bleeding and prevent further complications. •
REFERENCES

肝動脈化療導管暨注射基座系統植入術導致胃大網膜動脈出血：五病例報告

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肝動脈化療經常是用在無法開刀的原發性或轉移性惡性肝腫瘤的治療方法，而在肝動脈化療導管暨注射基座系統植入時經常將導線置於胃大網膜動脈來做為支撐導管置入的路徑，所以在肝動脈化療導管暨注射基座系統植入過程中胃大網膜動脈可能會受到損害而有可能導致腹內之出血。若能早期發現出血，並適當止血就能避免更大的併發症產生。在此報告五例因肝動脈化療導管暨注射基座系統植入術造成胃大網膜動脈出血個案，包含三例於術中當場發現胃大網膜動脈顯影劑外漏現象，一例於術後數小時發現腹內大量出血，以及一例於術後兩個月後可能因右腳靜脈血栓使用抗凝血藥物（Coumadin）而導致的遲發性出血。在經過血管攝影檢查於胃大網膜動脈適當血管栓塞止血後均能達成有效止血。