Contemporary Imaging of the Surgically Placed Hepatic Arterial Infusion Chemotherapy Pump

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Hepatic arterial infusion (HAI) of chemotherapy is a locoregional treatment strategy for hepatic malignancy involving placement of a surgically implanted pump or percutaneous port-catheter device into a branch of the hepatic artery. HAI has been used for metastatic colorectal cancer for decades but has recently attracted new attention because of its potential impact on survival, when combined with systemic therapy, in patients presenting with unresectable hepatic disease. Although various HAI device–related complications have been described, little attention has been given to their appearance on imaging. Radiologists are uniquely positioned to identify these complications given that patients receiving HAI therapy typically undergo frequent imaging and may have complications that are delayed or clinically unsuspected. Therefore, this article reviews the multimodality imaging considerations of surgically implanted HAI devices. The role of imaging in routine perioperative assessment, including the normal postoperative appearance of the device, is described. The imaging findings of potential complications, including pump pocket complications, catheter or arterial complications, and toxic or ischemic complications, are presented, with a focus on CT. Familiarity with the device and its complications will aid radiologists in playing an important role in the treatment of patients undergoing HAI therapy.

Hepatic arterial infusion (HAI) of chemotherapy is a locoregional treatment strategy for unresectable metastatic colorectal cancer confined to the liver. It is accomplished either by surgically implanting a pump-catheter system directly into a branch of the hepatic artery (HA) or by percutaneous placement of an arterial port catheter that ultimately terminates within the HA or one of its branches. Both strategies allow continuous arterial infusion of chemotherapy over a period of months to years while providing easy percutaneous access to the device. HAI can be used for downstaging before surgical resection, as an adjuvant therapy after curative resection, or for treatment of unresectable disease. It is also being explored for treatment of unresectable primary liver cancer, most notably cholangiocarcinoma. Though it has a relatively long history, HAI is still a specialized therapy that may not be familiar to all radiologists. Increasing interest in its use, however, may lead to more radiologists encountering the device in their practices in the coming years. Furthermore, the majority of HAI device–related complications may have ambiguous clinical presentations and may present in delayed fashion. Thus, these complications may be encountered by radiologists at practices other than the specialized centers where these devices are typically placed. Therefore, the goal of this article is to familiarize radiologists with the surgically placed HAI device and its imaging assessment, including its routine perioperative and normal postoperative appearance and a variety of its device-related complications.

The surgically placed HAI catheter and pump were first introduced in the 1960s for treatment of cancer metastatic to the liver, although the first pumps available at that time were of variable design and required an external power source. This therapy was made safer and more tolerable by an implantable pump introduced in the 1980s that could be used continuously without external power. From that time until the early 2000s, multiple randomized trials showed HAI to have a superior impact on tumor response in the

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liver compared with systemic chemotherapy. Although promising, these trials, summarized in a 2002 overview [1], failed to show a convincing beneficial impact on overall survival except when HAI was combined with systemic chemotherapy. Subsequently, a 2007 meta-analysis confirmed the lack of a survival advantage when HAI was used as a monotherapy [2].

On the other hand, mounting evidence over the last decade shows that neoadjuvant HAI, in combination with modern systemic chemotherapy, can have a dramatic impact on overall survival in patients with initially inoperable hepatic colorectal metastases confined to the liver because of its potential to downstage hepatic disease and enable curative resection. Combined systemic chemotherapy prevents disease progression outside of the liver from precluding resection, which offers the only potential for long-term survival in these patients. Authors from Memorial Sloan Kettering Cancer Center, for example, found a rate of 52% conversion to resectability in patients with initially inoperable colorectal liver metastases when HAI was combined with systemic therapy [3]; for comparison, these authors cited previous conversion rates of 13–27% in patients treated with systemic chemotherapy alone [4–7]. Conversion to resection in these patients predictably translated to improved overall survival: 3-year survival was 80% in patients who went on to resection compared with 26% in those who remained inoperable [3, 8, 9]. A 2017 case-control series from the University of Pittsburgh Medical Center similarly showed that overall survival was double (32 vs 15 months, respectively) in patients with unresectable colorectal liver metastases treated with both HAI and systemic therapy compared with systemic chemotherapy alone [10]. Results such as these have driven the expanding interest in HAI therapy for colorectal cancer. Meanwhile, at least 30 ongoing clinical trials are investigating HAI in the treatment of primary hepatic tumors such as cholangiocarcinoma and hepatocellular carcinoma [11].

The aim of HAI is to maximize the concentration of chemotherapy within hepatic tumors while minimizing the concentration in systemic circulation, thus maximizing therapeutic benefit while minimizing systemic adverse effects. This is achieved by two key mechanisms. First, tumors within the liver are selectively perfused by the hepatic arteries, whereas normal hepatocytes are primarily perfused by the portal veins. Therefore, arterial administration achieves much higher drug exposure in the tumor compared with the surrounding liver [12]. Second, hepatic extraction of select chemotherapy agents is high, such that the concentration in systemic circulation is low. For example, 5-fluoro-2′-deoxyuridine has a pharmacokinetic advantage (i.e., intrahepatic concentration relative to systemic concentration) of 100- to 400-fold when delivered arterially [13].

Once in place, the device is refilled by percutaneous injection every several weeks and requires regular refilling to maintain patency of the catheter. The several available pump devices all have similar mechanisms but are radiographically distinguishable. Until recently, the most commonly used device was the Codman 3000 infusion pump (Johnson & Johnson), which was discontinued in 2018. Other similar pump devices, such as the SynchroMed II (Medtronic) and IP 2000 V (Tricumed) infusion pumps, have been reconfigured and used with the original Codman cathe-

HIGHLIGHTS

- *HAI is a targeted therapy for cancer in the liver most often encountered at specialized treatment centers. Interest in its use, however, is growing.*
- *Surgical HAI devices are associated with unique complications, many of which may be detected at imaging. Even serious complications may not be clinically suspected.*
- *Radiologists play an important role in planning for HAI therapy and detecting its complications.*

Fig. 1—Comparison of hepatic arterial infusion (HAI) pump devices.
A, 57-year-old woman with unresectable cholangiocarcinoma receiving HAI therapy with Codman pump device (Johnson & Johnson). Axial CT image shows access hub (*asterisk*) at apex of device. Low-attenuation fluorocarbon (*arrows*) surrounds chemotherapy reservoir.
B and **C,** 68-year-old woman with metastatic colorectal cancer receiving HAI therapy with SynchroMed (Medtronic) pump device. Axial CT (**B**) and radiograph (**C**) show details of device. Compared with Codman device, SynchroMed device is more rectangular on axial CT (**B**) and, unlike Codman device, is not perfectly round when viewed *en face* on radiographs (**C**) or at fluoroscopy during access. Its superficial face is discontinuous at reservoir access hub (*asterisk*), whereas its deep face is flat and uninterrupted. Reservoir access hub is used to recharge pump with chemotherapy, and peripheral hub (*arrowhead*, **C**) can be accessed for direct injection of catheter, such as for perfusion imaging or direct angiography via device. Fluorocarbon (*arrow*, **B**) is confined to chamber deep to reservoir. Fluorocarbon expands as gas at body temperature to exert constant pressure on chemotherapy-filled bellows chamber, allowing continuous release.

ter for HAI. These pump devices are widely used for applications such as continuous intrathecal drug administration and are likely familiar to many radiologists. Although identifying the specific device model is usually unnecessary, radiologists should be familiar with the normal appearance and orientation of the device, with access hubs directed superficially toward the skin surface (Fig. 1). Visualization of the orientation of the device may not be possible on MRI because of the susceptibility artifact associated with the device but should be readily apparent on any CT image that includes the device or on a lateral radiograph of the abdomen. Given that many patients treated with HAI are surveilled with MRI, the device model is relevant for MRI safety. The Codman and SynchroMed pumps are considered MRI conditional and can be safely operated at both 1.5 and 3 T within parameters specified by the manufacturers. The SynchroMed pump can also stall while in the magnet bore and needs to be checked after the scan to confirm it has successfully restarted.

Routine Perioperative Imaging and Normal Postoperative Appearance of the Device

Most patients at our institution (Washington University School of Medicine) who are considered for HAI therapy undergo staging and surveillance with MRI. Our protocol includes multiphase contrast-enhanced imaging of the abdomen using gadoxetate disodium (Eovist, Bayer HealthCare) to define the extent of disease in the liver and to detect extrahepatic abdominal disease. Contrast-enhanced chest CT is performed to exclude thoracic disease. Depending on the MRI scanner, the patient, and the experience of the technologist performing the examination, MRI is not always adequate for defining the celiac and HA anatomy. A detailed assessment of this anatomy, either with catheter or CT angiography, is helpful for planning placement of the catheter. Branches of the HA distal to the catheter insertion and proximal to the liver that would result in extrahepatic delivery of chemotherapy, such as the right gastric artery, are routinely ligated at

TABLE 1: Summary of Hepatic Arterial Infusion Complications and Their Key Image Findings

Complication Type	Best Modality	Image Findings
Pump pocket	CT	
Flipped pump device		Ports facing deep
Hematoma		High-attenuation collection surrounding device
Infection		Rim-enhancing collection surrounding device
Catheter or arterial insertion	Multiphase CT	
Tip malposition		Retracted from or protruding into HA Change in position
Extravascular infusion		Growing lesion at insertion Fluid or fat stranding at insertion Peritoneal accumulation of ^{99m}Tc
Hepatic artery dissection		HA narrowing Presence or absence of dissection flap Blind-ending false lumen at angiography Absent intraoperative hepatic perfusion
Hepatic artery thrombosis		High-attenuation clot (acute) Obliteration (chronic) New intrahepatic disease progression
Pseudoaneurysm		Growing lesion at insertion Follows arterial enhancement Can mimic pseudocyst or lymph node if thrombosed or slow filling
Hemorrhage		Active extravasation or hematoma at insertion
Arterioduodenal fistula		Variable, often no direct findings
Refractory melena/anemia		
Arteriobiliary fistula		Hemobilia/biliary obstruction Pseudoaneurysm or hemorrhage near insertion
Toxic or ischemic	MRI/MRCP	
Hepatic infarction		Regional or peripheral hypoenhancement PV and HA thrombosis
Hepatic abscess		Overlap in appearance with metastases Recent hepatic infarct Preexisting biliary necrosis
Sclerosing cholangiopathy		Peripheral and extrahepatic strictures Bile lakes/necrosis

Note—HA = hepatic artery, PV = portal vein.

surgery. Similarly, the gallbladder is also removed at the time of surgery to prevent chemotherapy-induced cholecystitis resulting from infusion of the cystic artery.

If replaced or accessory arterial anatomy is identified, it is important to detail this anatomy unambiguously for surgical planning with reference to the known variations in celiac and HA supply [14]. In particular, identifying which HA supplies the gastroduodenal artery (GDA) is important given that the GDA will almost always be the target of catheter insertion. The GDA is preferred to other vessels because it is associated with fewer complications and is less likely to result in off-target perfusion. Once the anatomy is defined, the general approach is to ligate or embolize the vessels such that the only artery supplying the liver (usually the HA supplying the GDA) is infused with chemotherapy (Fig. 2). This is possible because, in most cases, cross perfusion develops via intrahepatic collateral pathways and allows the distribution of arterial perfusion in the liver to normalize over the course of several weeks [15–17]. Although older devices have included dual-catheter configurations that allowed cannulation of two separate vessels in the setting of variant anatomy, this approach has been abandoned in favor of devascularization. In patients with variant anatomy that is challenging to access or with a GDA that is deemed inadequate for cannulation, the catheter may be implanted directly into the HA, into the splenic artery, or into the HA by means of a saphenous vein graft conduit [18], but none of these approaches is common.

When implanted at the GDA, the catheter is positioned such that its tip is flush with the HA lumen and then fixed by tightening sutures around the vessel stump with the catheter inside. The catheter has beaded points near its tip that serve as anchors around which the suture can be tied to prevent slippage of the catheter once in place [19, 20]. Ideally, the catheter tip does not protrude into the lumen of the HA or terminate prematurely within the GDA vessel stump given that either position increases the risk for device failure and complications (discussed in more detail in the next section). Thus, the catheter tip position relative to the HA should be scrutinized on any contrast-enhanced CT examination and, to the extent possible, on any MRI examination performed after device placement. Coronal and sagittal planes are usually helpful in this assessment (Fig. 3).

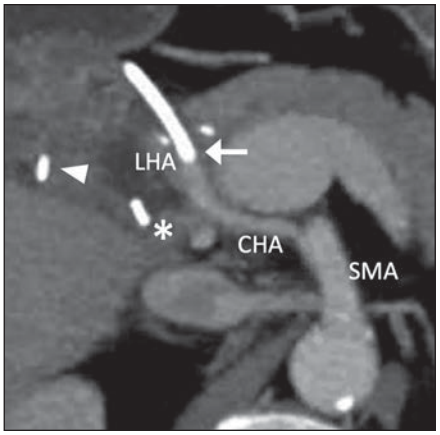

Fig. 2—61-year-old woman receiving hepatic arterial infusion (HAI) for metastatic colorectal cancer. Patient was found to have aberrant arterial anatomy on preoperative CT (not shown). Postoperative CT shows replaced common hepatic artery (CHA), which arises from superior mesenteric artery (SMA). CHA leads to small right hepatic artery (*asterisk*), which was ligated with clip at surgery, before continuing as left hepatic artery (LHA). In this case, LHA leads to gastroduodenal artery (GDA), and catheter tip (*arrow*) is implanted in ligated GDA stump. Gallbladder was also removed at surgery, as indicated by cholecystectomy clip (*arrowhead*).

After catheter placement, additional assessments are performed to ensure perfusion of the liver through the catheter is adequate and to exclude significant extrahepatic perfusion. The surgeon may inject the pump with methylene blue or phosphorescent dye while the patient is still on the operating table for direct visual confirmation. Following surgical placement, the de-

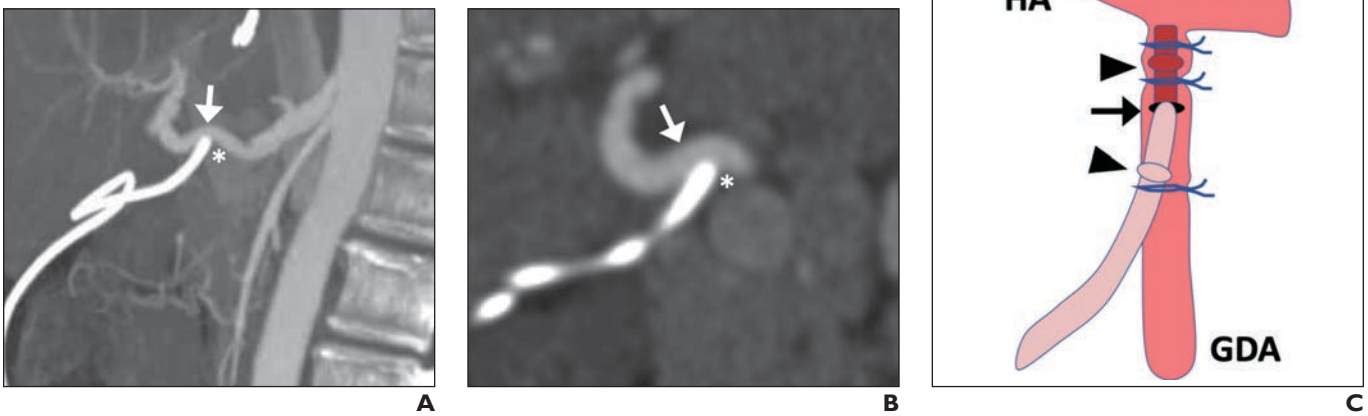

Fig. 3—57-year-old woman receiving hepatic arterial infusion for unresectable intrahepatic cholangiocarcinoma.
A and **B,** Contrast-enhanced oblique sagittal maximal-intensity-projection (**A**) and coronal (**B**) CT images show normal catheter tip position within ligated gastroduodenal artery (GDA) stump. Catheter tip (*asterisk*) touches but does not significantly protrude into opacified lumen of proper hepatic artery (*arrow*). GDA stump does not opacify with contrast around catheter, and exact site of GDA arteriotomy is not visible.
C, Diagram shows catheter at GDA arteriotomy (*arrow*). Of two beads (*arrowheads*), more distal bead at end of catheter is secured within GDA by sutures on either side. HA = hepatic artery, CHA = common hepatic artery.

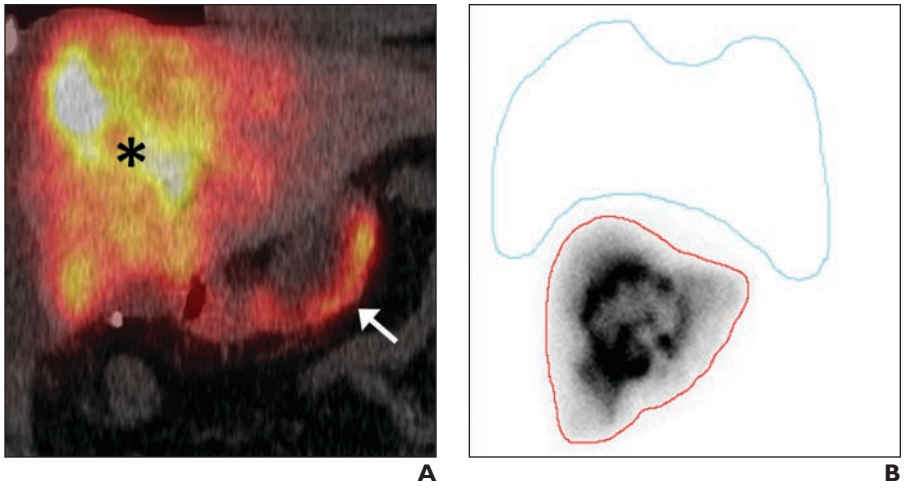

Fig. 4—Perfusion assessment in patients with hepatic arterial infusion pumps.
A, 69-year-old woman with unresectable intrahepatic cholangiocarcinoma who presented for routine postoperative pump perfusion study with SPECT/CT performed after injection of ^{99m}Tc macroaggregated albumin into pump. Coronal reconstruction of fused SPECT/CT images shows expected perfusion of liver, with asymmetrically increased uptake in right hemiliver (*asterisk*) due to underlying tumor and surgical devascularization. Extrahepatic activity in greater curvature of stomach (*arrow*) is also seen, which provoked repeat angiography to identify and embolize culprit vessel.
B, Diagram shows anterior planar imaging of the lungs (*blue outline*) and liver (*red outline*), acquired as part of postoperative perfusion study in 65-year-old woman with unresectable intrahepatic cholangiocarcinoma, to calculate pulmonary shunt fraction, which was normal in this case; 97.5% (*red outline*) and 2.5% (*blue outline*) of tracer activity localized to liver and lungs, respectively.

vice is routinely injected percutaneously with ^{99m}Tc macroaggregated albumin. More widely known for its role in ventilation-perfusion examinations, this tracer consists of radiolabeled particles that, because of their size, become trapped in capillary beds such as the hepatic sinusoids. At our institution, a nurse practitioner in medical oncology percutaneously accesses the direct injection port on the device and injects per manufacturer guidelines. A nuclear medicine technologist supplies the ^{99m}Tc macroaggregated albumin for injection. The standard dose for adults is 2 mCi (74 MBq) in 3 mL of 0.9% saline solution, given by hand injection over approximately 1 minute, followed by a heparinized saline flush. A 10-mL syringe is used to keep the injection pressure low. After administration is complete, the patient is transported from medical oncology to nuclear medicine. Anterior and posterior planar images of the lungs and upper abdomen are immediately obtained to allow calculation of the pulmonary shunt fraction. Then, a single-station SPECT/CT image centered on the upper abdomen is acquired to assess the distribution of radiotracer activity within the liver and to screen for sites of extrahepatic activity in the abdomen.

Ideally, the perfusion images will reveal activity throughout the liver. Asymmetric perfusion is expected and will likely normalize over the next several weeks if devascularization was performed for variant anatomy. Activity that localizes to the lungs or to the extrahepatic abdominal structures should not occur and would indicate collateral flow outside of the liver via the HA. The pulmonary shunt fraction is also routinely calculated at this time. A higher lung shunt fraction (≥ 20%) suggests that significant hepatic arteriovenous shunting is present, allowing the chemotherapy to escape first-pass metabolism within the liver and increasing the likelihood of systemic toxicity, especially in the gastrointestinal tract [21]. If extrahepatic perfusion is identified, repeat angiography can be performed to find the responsible arteries, which can then be embolized before initiation of chemotherapy (Fig. 4).

Complications of Hepatic Arterial Infusion

Complications of the surgically placed HAI device can be broadly categorized as related to the device at the pump pocket, involving the distal catheter or arterial insertion, or related to the toxic or ischemic effects of the arterial chemotherapy (Table 1). Complications of devices placed percutaneously by interventional radiology are distinct and are not covered in this review; these devices are not in use at our institution and are discussed elsewhere [22–26]. Similarly, interventional radiology techniques for salvaging complications in surgically placed HAI devices are beyond the scope of this article and are described elsewhere [27].

Most HAI device–related complications are best depicted by CT, which shows in detail the pump device, the catheter, and the adjacent structures within the porta hepatis. Because of the ligation clips and other surgical changes often encountered near the porta hepatis in patients with an HAI device, unenhanced CT of the abdomen can help distinguish these findings from arterial complications near the catheter tip. An arterial angiographic phase is useful for identifying any arterial complications. Finally, a portal venous phase is useful for assessing the liver and portal

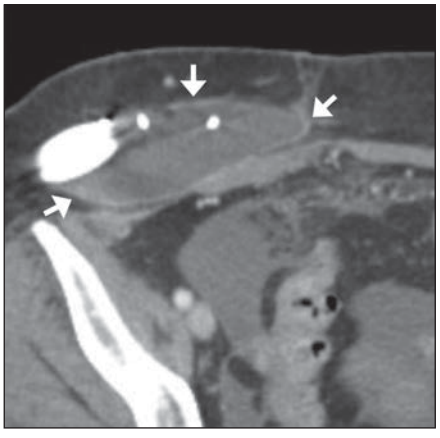

Fig. 5—54-year-old woman receiving hepatic arterial infusion for unresectable intrahepatic cholangiocarcinoma. Patient presented with new fever, tenderness, and erythema in region of pump device pocket. CT of device pocket shows rim-enhancing fluid collection (*arrows*) surrounding pump device. Aspiration confirmed abscess. Pump was removed during incision and drainage, and distal catheter was cut and internalized within abdominal cavity. Typical pump pocket hematoma may have more homogeneous, high-attenuating appearance, whereas seroma may show simple fluid attenuation without rim enhancement. In either case, aspiration or drainage may still be required if infection is clinically suspected or if fluid collection inhibits access to pump.

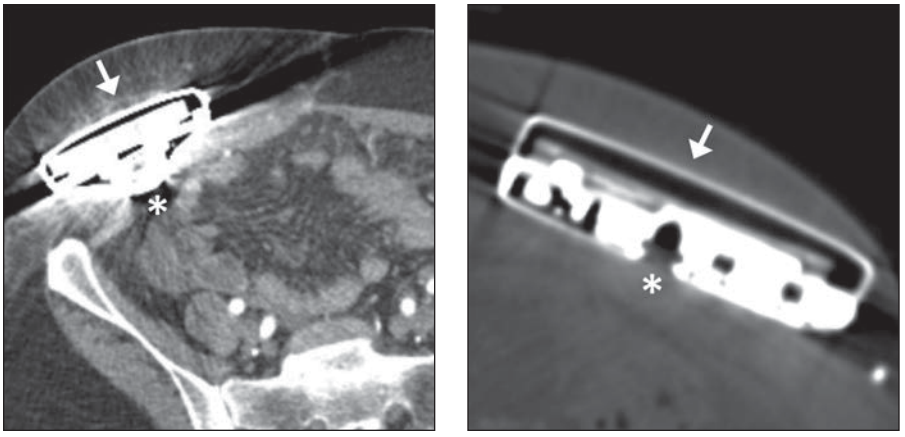

Fig. 6—Examples of flipped hepatic arterial infusion (HAI) devices.
A, 57-year-old woman receiving HAI for unresectable intrahepatic cholangiocarcinoma. Patient presented after pump could not be accessed in clinic. Axial CT image shows flipped Codman pump device (Johnson & Johnson) (*arrow*) with access port (*asterisk*) directed deep into device pocket. Surgical correction was required to enable timely access of pump.
B, 68-year-old woman with metastatic colorectal cancer. CT image shows flipped SynchroMed device (Medtronic) (*arrow*) with reservoir port (*asterisk*) directed deep into device pocket. This was not clinically suspected at imaging but also required timely surgical correction.

veins and for distinguishing suspected active extravasation from pseudoaneurysm in the setting of hemorrhage. At our institution, all of the aforementioned phases are combined in our CT protocol for suspected gastrointestinal bleeding, which we have adopted for assessment of suspected device-related HAI complications. This protocol uses an ROI threshold trigger of 100 HU on the descending aorta at the level of the diaphragm for the arterial phase followed by a scan at 60 seconds for the portal venous phase, in addition to the initial unenhanced phase. Other modalities including MRI, ultrasound, and SPECT/CT can serve as adjuncts in select cases, as illustrated in subsequent sections.

Complications of surgically placed HAI devices are not rare but reported rates have generally decreased over time. A large literature review, conducted in 2001, of HAI complication rates and toxicities in 4580 patients with both surgically implanted and percutaneous port-catheter devices found that the overall catheter-related complication rate approached 29% after 1990 compared with 42% before 1980 [28]. The most common reported

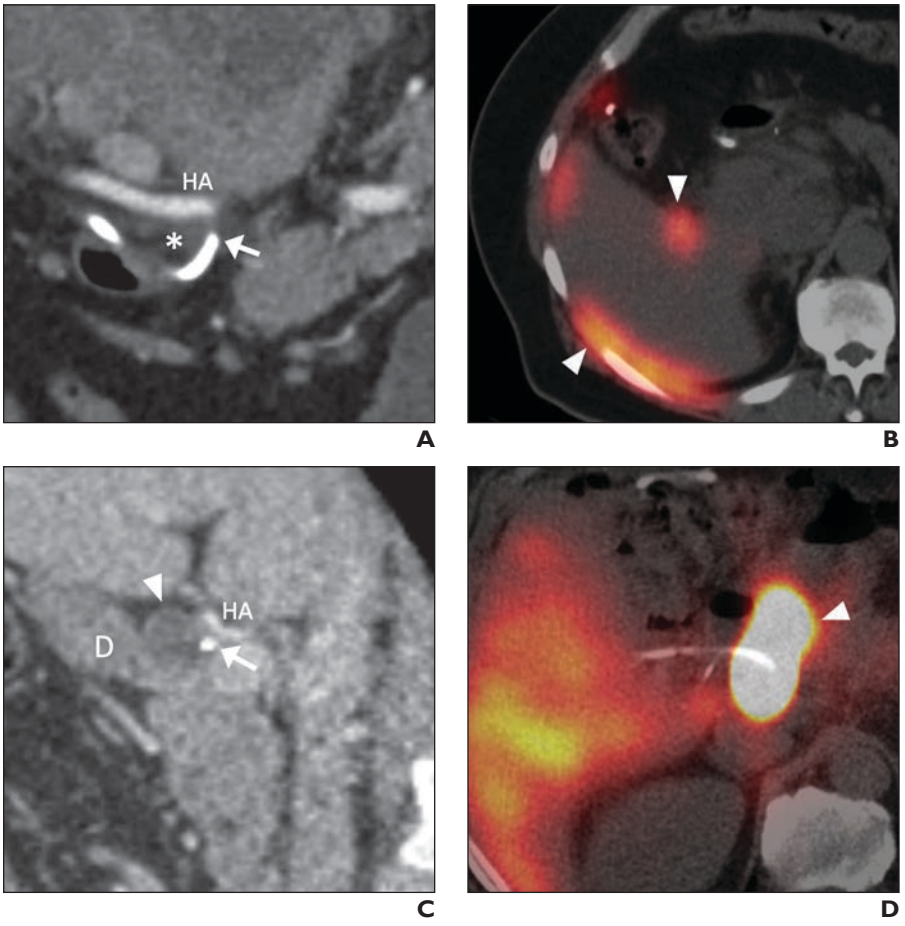

Fig. 7—Examples of catheter tip malposition in two patients who were receiving hepatic arterial infusion (HAI) for unresectable cholangiocarcinoma.
A, 71-year-old man who underwent CT after disease progression was noted in liver. Coronal CT image shows malposition of HAI catheter tip (*arrow*), which does not contact opacified hepatic artery (HA) lumen. Subtle fluid attenuation (*asterisk*) surrounds catheter tip near arteriotomy.
B, Same patient as in **A**. SPECT/CT image obtained after injection of pump with ^{99m}Tc macroaggregated albumin shows free tracer accumulation (*arrowheads*) outside of liver within peritoneal cavity.
C, 47-year-old man with enlarging lesion next to catheter tip at surveillance CT. Coronal CT image shows circumscribed, low-attenuating lesion (*arrowhead*) between catheter tip (*arrow*) and duodenum (D). Catheter tip is retracted from HA.
D, Same patient as in **C**. SPECT/CT perfusion study shows tracer accumulation within lesion (*arrowhead*), confirming pseudocyst of extravascular chemotherapy.

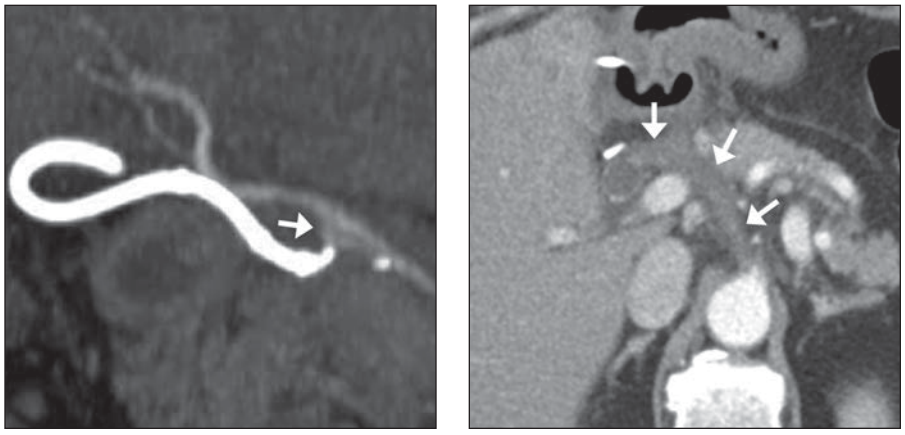

Fig. 8—Examples of hepatic artery (HA) dissection and thrombosis complications in two patients who were receiving hepatic arterial infusion.
A, 46-year-old woman with metastatic colorectal cancer. Intraoperative injection of methylene blue dye through catheter showed no perfusion of liver or adjacent organs (not shown). Coronal reconstruction of subsequent CTA shows dissection flap (*arrow*) dividing false lumen, where catheter tip terminates, from true lumen of HA. Dissection should also be suspected in setting of new HA narrowing, even when discrete flap is not visible.
B, 57-year-old woman with intrahepatic cholangiocarcinoma. Surveillance imaging showed new progression of disease in liver (not shown). Axial CT image at level of HA (*arrows*) shows indistinct, high-attenuation material filling vessel, consistent with complete HA thrombosis.

complications in that review were HA occlusion, catheter thrombosis, and catheter displacement [28]. Complication rates are lower at centers specializing in this therapy, especially when performed by more experienced surgeons [29].

Though many of these complications have long been recognized, they have received little attention with respect to imaging assessment. A 1993 review of the CT findings of arterial complications of HAI made several important observations that are reaffirmed by our experience [30]. However, CT technology has advanced significantly since that time, allowing more detailed assessment of the pump, catheter, and surrounding structures. Some attention has been given to imaging the toxic or ischemic effects of arterially infused chemotherapy [31–33], with sporadic mention of rarer device-related complications, such as arteriobiliary fistula [34, 35].

Although the clinical presentation of many device-related complications may be delayed and unsuspected, these complications can be life-threatening. Additionally, nonemergent complications may result in premature cessation of effective locoregional therapy. For these reasons, and because patients receiving HAI therapy are likely to undergo frequent imaging, radiologists are uniquely positioned to aid in prompt diagnosis of complications when they arise.

Pump Pocket Complications

Complications occurring at the pump device in the body wall include pump pocket seroma, hematoma, or infection. Postoperative seromas are common, especially in patients with more body wall fat. They are often found incidentally at postoperative imaging and do not typically require treatment. Hematoma and infection, on the other hand, are usually suspected clinically. In either case, CT or ultrasound may be helpful in defining the size of the collection and determining whether a sample may be aspirated for testing. Even a small hematoma can be problematic if it prevents access to the pump. Infection of the device pocket may necessitate removal of the device (Fig. 5).

Another pump device complication is flipping of the device within the pocket, which may or may not be clinically suspected depending on when the pump was last accessed. Therefore, distinguishing the superficial and deep faces of the device whenever possible is important to ensure proper orientation (Fig. 6). A flipped pump device requires timely surgical correction to restore access to the pump and to maintain patency of the pump catheter. Any complication at the device pocket that could interfere with percutaneous access is of some urgency because delayed management could result in device occlusion and failure. Such findings should prompt direct notification of the surgical team for potential correction.

Catheter and Arterial Complications

Radiologic diagnosis of catheter-related or arterial complications can be challenging even when these complications are

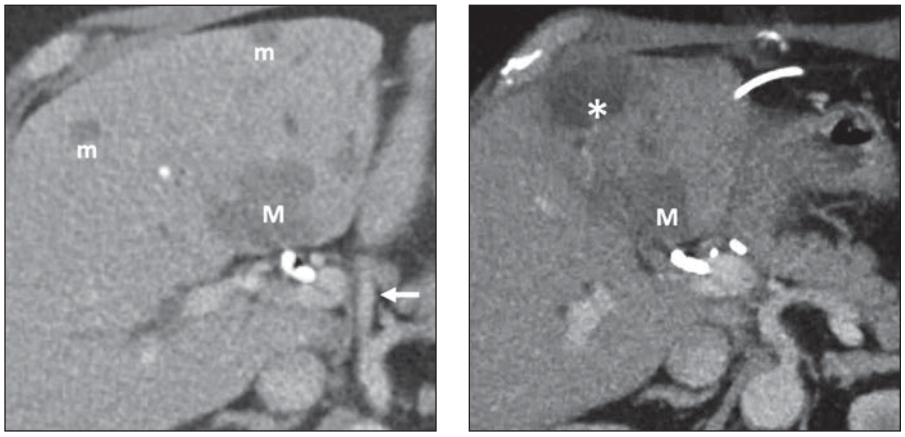

Fig. 9—70-year-old man who was receiving hepatic arterial infusion for intrahepatic cholangiocarcinoma.
A, Preoperative CT shows primary mass (M) and multiple small metastases (m) in adjacent liver. Hepatic artery (HA) (*arrow*) is patent. Left portal vein had previously thrombosed and is not visualized.
B, Subsequent CT performed for fever and right upper quadrant pain shows new peripheral, wedge-shaped region of hypoenhancement (*asterisk*) in left hemiliver, consistent with liver infarction. Primary mass (M) is also seen. HA is thrombosed and no longer visible.

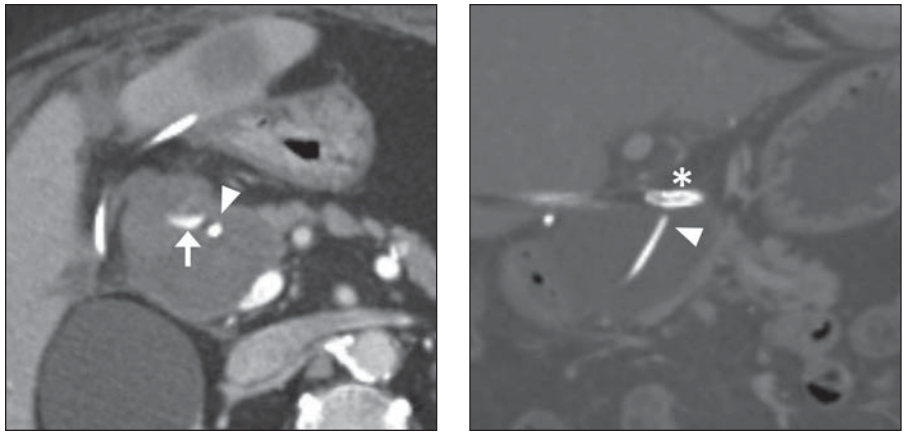

Fig. 10—83-year-old woman receiving hepatic arterial infusion therapy for unresectable intrahepatic cholangiocarcinoma. Patient presented to emergency department with acute abdominal pain 2 months after device placement.
A, Axial CT image shows hyperattenuating collection (*arrowhead*) surrounding distal portion of catheter, consistent with hematoma. Blush of contrast material (*arrow*) is seen within hematoma and adjacent to presumed arteriotomy site, suggesting active extravasation. Catheter angiography confirmed active extravasation near catheter tip, presumably from gastroduodenal artery (GDA) arteriotomy. Stent was placed across GDA origin with resolution of bleeding.
B, Coronal image from follow-up CT performed days later shows catheter tip (*arrowhead*) and adjacent stent within HA (*asterisk*) across GDA origin.

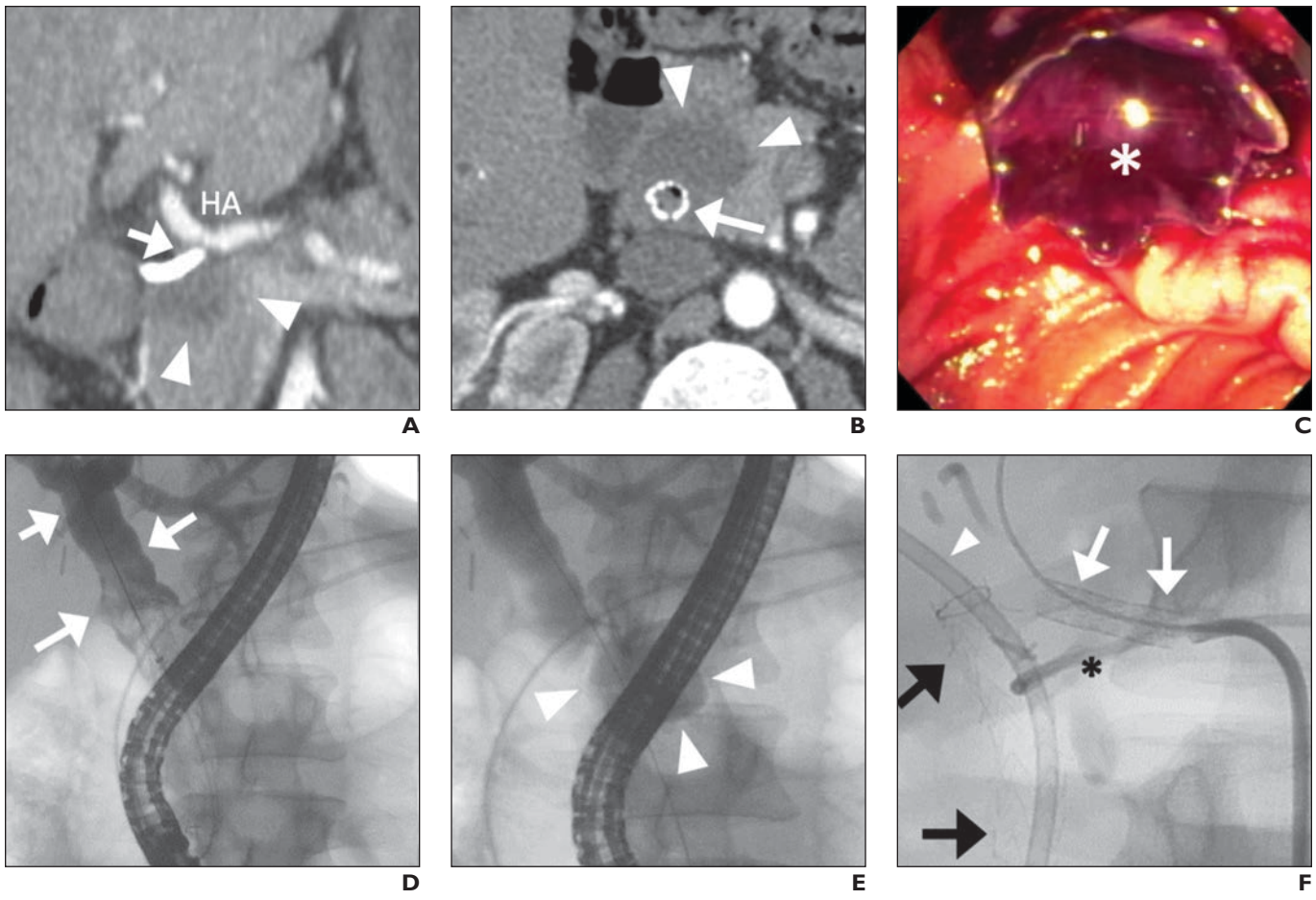

Fig. 11—36-year-old man receiving hepatic arterial infusion (HAI) for metastatic colon cancer with acute abdominal pain and anemia.
A, Coronal CT image at initial presentation shows new retraction of HAI catheter tip (*arrow*) from hepatic artery (HA) lumen and new low-attenuating globular lesion (*arrowheads*). Angiography (not shown) was negative for pseudoaneurysm or active bleeding. Patient's symptoms resolved, and no intervention was performed. Patient presented again with new clinical and laboratory evidence of biliary obstruction, for which metallic bile duct stent was placed.
B, Axial CT image shows bile duct stent (*arrow*) and enlarged low-attenuating globular lesion (*arrowheads*) seen in **A**. Despite stenting, biliary obstruction continued to worsen.
C and **D,** ERCP image (**C**) and radiograph (**D**) show complete obstruction of stent by clotted blood (*asterisk*, **C**) with upstream biliary dilation (*arrows*, **D**).
E, During stent exchange, brisk hemorrhage was encountered from bile duct. Cholangiography shows new opacification of globular lesion (*arrowheads*) communicating with biliary tree, consistent with pseudoaneurysm that had fistulized with biliary tree.
F, After bile duct stents were reinserted, catheter angiography (not shown) confirmed bleeding pseudoaneurysm arising from gastroduodenal artery (GDA) stump. Subsequent angiography shows stent (*white arrows*) placed within HA across GDA origin to treat bleeding pseudoaneurysm. Close proximity of distal HAI catheter (*asterisk*) to bile duct, now containing plastic (*arrowhead*) and metallic (*black arrows*) biliary stents, is also seen.

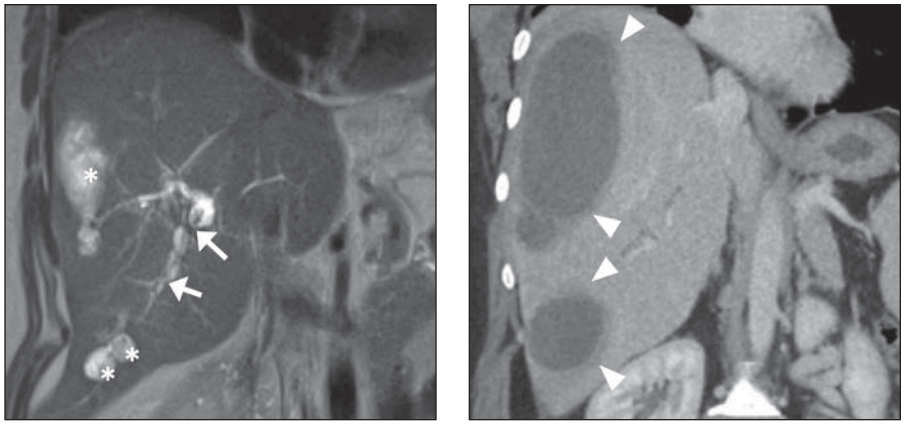

Fig. 12—48-year-old woman receiving hepatic arterial infusion (HAI) for metastatic colon cancer and presenting with hyperbilirubinemia, right upper quadrant pain, and fever.
A, MRI/MRCP performed before presentation shows intrahepatic biliary strictures causing beaded appearance of ducts (*arrows*). Well-circumscribed T2-hyperintense lesions (*asterisks*) in communication with bile ducts are consistent with necrotic biliary lakes secondary to chemotherapy-induced sclerosing cholangiopathy.
B, CT performed at presentation shows enlargement of biliary collections, which are surrounded by halos of edema (*arrowheads*), consistent in this clinical setting with cholangitis and biliary abscess formation. Ultrasound-guided aspiration of largest collection yielded pus and numerous mixed gram-positive cocci.

clinically suspected. The relevant vessels of the celiac axis are small and can be difficult to examine, especially if an arterial phase is not included in the study. Vascular anatomy may also be distorted by the devascularization performed before placement of the catheter. Surgical clips or embolization coils near the catheter tip can create streak artifact and obscure or distract from subtle findings. The GDA, where the catheter tip almost always resides, is also in proximity to multiple important structures in the porta hepatis, all of which may be affected by various complications.

When evaluating an HAI device on CT, we advise starting at the catheter tip and its juncture with the HA using coronal and sagittal reconstructions. As noted previously, the HAI catheter tip is optimally positioned at the GDA origin without protruding significantly into the HA lumen or terminating prematurely within the GDA stump. Protrusion into the HA may partially impede arterial flow, promoting turbulence and increasing the risk of HA thrombosis. On the other hand, if the catheter terminates prematurely within the GDA stump or becomes retracted, the lumen of the stump becomes a nidus of more stagnant flow, potentially resulting in the development of a thrombus that can occlude the catheter and/or propagate into the HA. Additionally, the added exposure of the GDA wall to the chemotherapy, which otherwise would be rapidly carried away by brisk flow in the HA, may result in weakening or injury to the vessel, leading to either extravascular infusion of chemotherapy or hemorrhagic complications. These possibilities are further illustrated in the following case examples.

Catheter Tip Malposition and Extravascular Infusion

Deviation of the catheter tip from the ideal position at the GDA origin, or any change in its position from a prior study, should prompt careful inspection for related complications. If the catheter tip retracts or becomes loose within the GDA stump, extravascular infusion of chemotherapy, with or without associated bleeding, is possible. This can occur early and come to light during workup of a suspected device malfunction or may be diagnosed months to years after device placement. Extravascular infusion may manifest on CT as subtle stranding or fluid attenuation surrounding either the catheter or the HA near the catheter tip. The extravascular chemotherapy can also form a loculated fluid collection, or pseudocyst, adjacent to the catheter, appearing as a circumscribed oval or round lesion of variable attenuation. This can easily be mistaken for an enlarging periportal lymph node. Such findings can be further examined with a ^{99m}Tc macroaggregated albumin perfusion study with the tracer injected through the device to establish whether extravascular infusion is present (Fig. 7). If this is not confirmed, the other diagnosis to consider is a thrombosed or slow-filling pseudoaneurysm.

Hepatic Artery Dissection and Thrombosis

In our experience, HA dissection results from arterial injury at the time of catheter placement and is clinically suspected in the perioperative setting. In this context, digital subtraction angiography can be performed through the direct injection port of the pump device. Complementary CT angiography can also be performed with IV contrast material. Dissection of the celiac axis arteries, including the HA, may manifest with a visible dissection flap on CT or direct angiography, but this is not always seen. A more consistent finding is vessel narrowing along the length of dissection due to nonopacification or thrombosis of the false lumen. If the catheter tip terminates in the false lumen of the dissection, the HA may not opacify during direct catheter injection (Fig. 8A).

Similar to dissection, HA thrombosis can occur in the perioperative or immediate postoperative period, in which case prompt diagnosis is essential to salvage the pump. Alternatively, it can occur in a delayed fashion and go clinically unrecognized, manifesting only as progression of the patient's disease. With this in mind, detection of new disease progression in a patient receiving HAI therapy should prompt careful evaluation of the device and the HA. In the usual scenario in which the patient is restaged with MRI, newly suspected disease progression should prompt the radiologist to consider whether CT is necessary for confident exclusion of HA thrombosis and for more definitive assessment of the catheter tip and adjacent structures (Fig. 8B).

Hepatic Infarction

Portal vein thrombosis or occlusion is encountered commonly in the setting of either metastatic colorectal cancer or primary hepatic malignancy and, when detected preoperatively, is a contraindication to HAI pump placement. This is because thrombosis of the HA in these patients is much more likely to precipitate a hepatic infarct. Patients with hepatic infarction may present

for evaluation of nonspecific or right upper quadrant abdominal pain or other clinical or laboratory evidence of hepatic dysfunction or failure (Fig. 9). As with new disease progression in these patients, a new hepatic infarct should prompt careful investigation of the HA. If the infarct was detected on restaging MRI, the radiologist should again consider whether CT is necessary to adequately assess the arteries and the device.

Hemorrhagic Complications

Hemorrhage at the GDA arteriotomy or stump can manifest in different ways, including hematoma, pseudoaneurysm, or active extravasation. Hemorrhage suspected to derive from a complication at the GDA arteriotomy or stump may ultimately require placement of a stent across the GDA origin, or even embolization of the entire HA, if bleeding is life-threatening or does not resolve (Fig. 10). Because of the proximity of the arteriotomy and GDA stump to the duodenum and the common bile duct, either subacute hemorrhage or a pseudoaneurysm that is initially undetected can eventually progress to an arterioduodenal or arteriobiliary fistula. Recognizing the acute imaging manifestations of bleeding and pseudoaneurysm, which are best depicted on multiphase CT or catheter angiography, can be straightforward when clinically suspected. However, in our experience, arteriobiliary fistulas (Fig. 11) and arterioduodenal fistulas often present in a delayed and insidious fashion, and a variety of imaging and other tests are often required to reach the correct diagnosis. Arterioduodenal fistulas at the catheter insertion may appear similar to arterioenteric fistulas at other locations, manifesting with recurring unexplained episodes of pain, melanotic stool, and anemia. CT, tagged RBC scintigraphy, endoscopy, or catheter angiography studies may not achieve a definitive diagnosis. One such case at our institution (not shown) ultimately required empiric HA embolization to control the patient's bleeding. A more unusual presentation, with frank erosion of the HAI catheter through the duodenal wall visualized at endoscopy, has also been reported [31]. Recognition of these complications requires a high index of suspicion in patients with suggestive clinical features (e.g., worsening biliary obstruction, anemia, or melena).

Toxic and Ischemic Complications

Finally, the caustic effects of HAI chemotherapy are not limited to the GDA but may also affect the downstream vessels of the arterial tree. Damage to the small vessels of the arterial peribiliary plexus can result in ischemic cholangiopathy, which mimics idiopathic primary sclerosing cholangitis, with resulting strictures, biliary necrosis, and cholangitis or abscess formation [36]. One distinction between ischemic cholangiopathy secondary to HAI and primary sclerosing cholangitis is the propensity of HAI to cause strictures at the confluence of hepatic ducts or in the common bile duct in addition to peripheral strictures within the liver [32]. Unlike hemorrhagic and device-related complications centered at the catheter insertion or device pocket, ischemic cholangiopathy is often best depicted on MRCP (Fig. 12).

Conclusion

The role of HAI in the treatment of selected patients with metastatic colorectal cancer is evolving and may expand in the coming years, including for treatment of other cancers such as intrahepatic cholangiocarcinoma. Radiologists at centers currently or soon to be offering this therapy play an important role in the planning and perioperative assessment of the surgically placed HAI device. Radiologists in wider practices or in the emergency setting may encounter patients with this device when they present with delayed or clinically unsuspected complications. In either setting, the imaging evaluation of the HAI device can be challenging but is facilitated by an understanding of the HAI device and a familiarity with the spectrum of its unique complications and their imaging appearances.

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