CLINICAL STUDY

Consolidation of Hepatic Arterial Inflow by Embolization of Variant Hepatic Arteries in Preparation for Yttrium-90 Radioembolization

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ABSTRACT

Purpose: Before yttrium-90 (^{90}Y) radioembolization administration, the authors consolidated arterial inflow by embolizing variant hepatic arteries (HAs) to make microsphere delivery simpler and safer. The present study reviews the technical and clinical success of these consolidation procedures.

Materials and Methods: Preparatory and treatment angiograms were retrospectively analyzed for 201 patients. Variant HAs were coil-embolized during preparatory angiography to simplify arterial anatomy. Collateral arterial perfusion of territories previously supplied by variant HAs was evaluated by digital subtraction angiography (DSA), C-arm computed tomography (CT), and technetium-99m (^{99m}Tc)–macroaggregated albumin (MAA) scintigraphy, and by follow-up evaluation of regional tumor response.

Results: A total of 47 variant HAs were embolized in 43 patients. After embolization of variant HAs, cross-perfusion into the embolized territory was depicted by DSA and by C-arm CT in 100% of patients and by ^{99m}Tc-MAA scintigraphy in 92.7%. Uniform progressive disease prevented evaluation in 33% of patients, but regional tumor response in patients who responded supported successful delivery of microspheres to the embolized territories in 95.5% of evaluable patients.

Conclusions: Embolization of variant HAs for consolidation of hepatic supply in preparation for ^{90}Y radioembolization promotes treatment of affected territories via intrahepatic collateral channels.

ABBREVIATIONS

^{99m}Tc = technetium-99m, CHA = common hepatic artery, CR = complete response, DSA = digital subtraction angiography, EORTC = European Organization for Research and Treatment of Cancer, GDA = gastroduodenal artery, HA = hepatic artery, LHA = left hepatic artery, MAA = macroaggregated albumin, PD = progressive disease, PET = positron emission tomography, PHA = proper hepatic artery, PR = partial response, RECIST = Response Evaluation Criteria In Solid Tumors, RHA = right hepatic artery, SD = stable disease, SMA = superior mesenteric artery, SPECT = single photon emission CT

Radioembolization is becoming a preferred option for intraarterial treatment of hepatic malignancy (1). However, hepatic artery (HA) anatomy is highly variable, and as many as 45% of patients may exhibit nonstandard anatomy with portions of the liver supplied by variant HAs (2). In the presence of multifocal hepatic neoplasia, intended tumor targets may be supplied by standard and variant HAs, making it impossible to radioembolize all targets by administration from one arterial site. Each site of catheterization and administration requires a complete delivery setup and catheter, introduces risk of nontarget radioembolization or contamination, and produces radioactive waste (3).

Preexisting intrahepatic collateral pathways can result in intrahepatic recruitment of blood flow from one segment or lobe to another (4–10). Surgical or endovascular elimination of variant arterial anatomy rarely causes ischemia or hypoperfusion of the liver (4,6–8). Intentional elimination of variant

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None of the authors have identified a conflict of interest.

From the SIR 2010 Annual Meeting.

This article includes an appendix available online at www.jvir.org.

J Vasc Interv Radiol 2011; 22:1364–1371

DOI: 10.1016/j.jvir.2011.06.014

arteries could potentially amalgamate the HA inflow into one major artery, simplifying the administration and improving the completeness of intraarterial therapy (7). Consolidation of inflow could also improve safety of administration of radioembolic microspheres in patients with variant HAs by preventing reflux into the left gastric, gastroduodenal, and superior mesenteric vascular beds. We hypothesized that intrahepatic collateral pathways are robust enough to allow passage of 30-μm microspheres so that tumors originally perfused by variant HAs could be treated via these pathways after elimination of the variant HAs. We retrospectively reviewed the results of our attempts to consolidate arterial inflow by analyzing postembolization imaging (digital subtraction angiography [DSA], C-arm cone-beam computed tomography [CT], and technetium-99m [^{99m}Tc] macroaggregated albumin [MAA]–scintigraphy) and evaluating differential territorial tumor response.

MATERIALS AND METHODS

Patient Cohort

We retrospectively reviewed all preparatory and treatment angiograms in 201 patients treated for unresectable hepatic malignancy from June 2004 to November 2010. Patients ranged in age from 20 to 92 years (mean, 60.1 y; median, 61 y), and underwent radioembolization treatment with SIR-Spheres (Sirtex, Lane Cove, Australia) or TheraSphere (MDS Nordion, Ottawa, Ontario, Canada). Iterative data on seven patients who underwent repeat radioembolization were also included. All data were handled in compliance with the Health Insurance Portability and Accountability Act. The institutional review board of the authors' institution approved this retrospective study.

Angiography and Classification of Arterial Anatomy

Mesenteric arterial anatomy was previewed on all preprocedural cross-sectional imaging (CT or magnetic resonance [MR] imaging). All patients underwent abdominal aortography with injection of contrast medium at the level of T8 to portray intra- and extrahepatic vessels supplying the liver. DSA and contrast-enhanced C-arm CT were performed while injecting contrast medium into the dominant HA (ie, proper HA [PHA] or common HA [CHA]), and hepatic territories devoid of enhancement were identified. Selective catheterization of the mesenteric vessels confirmed the anatomy of the superior mesenteric artery (SMA), CHA, PHA, gastroduodenal artery (GDA), left HA (LHA), and right HA (RHA). Anatomy was identified as standard, accessory (ie, segmental or subsegmental variant supply), or replaced (ie, lobar or whole-liver variant supply). Patients were categorized according to the Michels classification (2) (**Appendix**, available online at *www.jvir.org*); a few rare variants not included in Michels classification were also identified and catalogued.

Consolidation of Inflow by Embolization

All patients underwent standard HA endovascular skeletonization to eliminate visible hepaticoenteric routes of possible nontarget radioembolization. In addition, variant HAs were identified and evaluated for suitability for embolization to consolidate HA inflow into simpler or safer anatomy. Before embolization, contrast-enhanced DSA and C-arm CT were performed to delineate the hepatic territory supplied by the variant HA and to identify tumors within. The variant HAs were embolized with use of 0.018-inch coils (VortX [Target Therapeutics/Boston Scientific, Natick, Massachusetts], Tornado and MicroNester [Cook, Bloomington, Indiana], and/or Azur [Terumo, Somerset, New Jersey), 0.035-inch coils (Tornado and/or Nester; Cook), or vascular plugs (AMPLATZER or AMPLATZER II; AGA Medical, Plymouth, Minnesota), depending on the size of the embolized artery and the tortuosity of the access. In cases in which the dominant tumor burden was supplied by a large variant HA, the standard HA was the one embolized, resulting in consolidated supply from the variant HA. Consolidation by embolization was performed only if doing so could result in fewer sites of administration, improved selectivity of treatment, and/or reduced risk of nontarget radioembolization.

Imaging Evaluation of Consolidation and Vascular Redistribution

After embolization of targeted variant HAs, contrast-enhanced DSA and C-arm CT were repeated from the main HA (ie, PHA or CHA) to reevaluate completeness of hepatic perfusion. Special attention was paid to confirm restoration of intrahepatic perfusion of territories previously supplied by variant HAs. From the planned site of yttrium-90 (^{90}Y) administration, 1 mCi of ^{99m}Tc-MAA was injected for scintigraphy. Patients underwent planar and single photon emission CT (SPECT) imaging to calculate lung shunt fraction and to characterize the intrahepatic distribution of injected tracer. On the day of the treatment procedure, contrast-enhanced DSA and C-arm CT were repeated just before administration of microspheres. Any evidence of unsuccessful consolidation was addressed in the same way as during the preparatory angiography procedure.

Follow-up cross-sectional imaging by CT, positron emission tomography (PET), or MR imaging was obtained on all surviving patients 2–3 months after treatment and approximately every 3 months thereafter. Individual tumor responses were measured by Response Evaluation Criteria In Solid Tumors (RECIST; version 1.1) for CT and MR imaging or by European Organization for Research and Treatment of Cancer (EORTC) criteria for PET (11,12). Specifically, radiographic response of individual tumors previously supplied by a variant HA and now dependent on intrahepatic collateral vessels after consolidation were compared with the control response measured in tumors not dependent on the development of intrahepatic collateral vessels (**Fig. 1**). Uniform response (complete response [CR], partial response [PR], or stable disease [SD]) of tumors distributed in territories supplied and not supplied by embolized vessels was interpreted as evidence of suc-

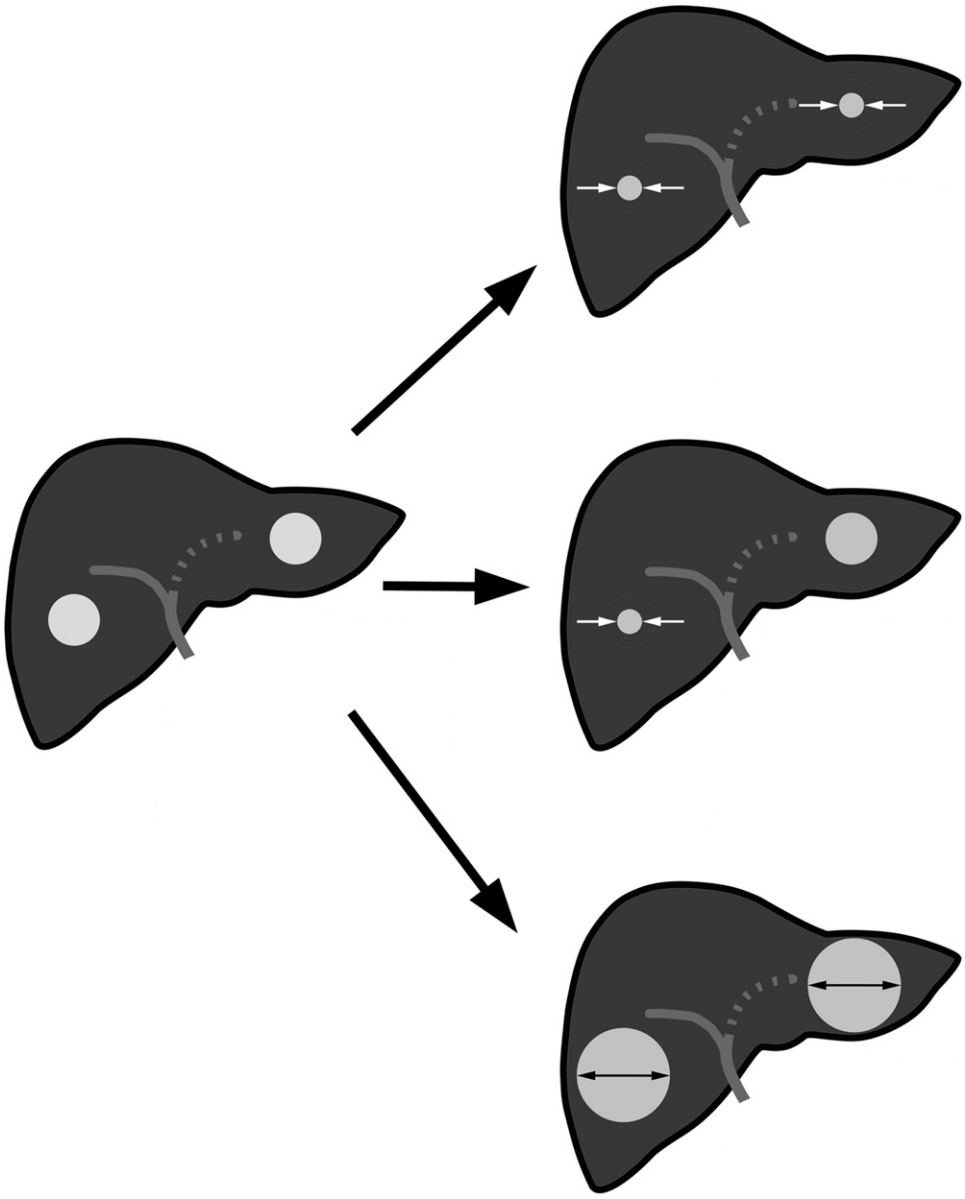

Figure 1. Assessment of microsphere distribution based on radiographic tumor response is modeled in this liver in which the left-lobe tumor is perfused via intrahepatic collateral circulation after embolization of a variant LHA. If all tumors responded positively (top), we interpreted this as evidence of good distribution of microspheres through the collateral circulation. If asymmetric response was noted, with inferior response in the tumor perfused by collateral circulation (middle), we interpreted this as evidence of inadequate distribution of microspheres. If all tumors uniformly progressed (bottom), distribution of microspheres was not evaluable because even direct administration in the right lobe did not result in therapeutic response, suggesting poor tumor biology and resistance to radioembolization.

cessful distribution of radioembolic microspheres via intrahepatic collateral vessels into territories originally supplied by variant HAs. Inferior response of tumors distributed in territories previously supplied by variant HAs compared with responding tumors in the territories not supplied by embolized vessels was interpreted as unsuccessful delivery of radioembolic microspheres to these territories.

Uniform progressive disease (PD) of all intrahepatic tumors (including those previously supplied by variant HAs and those never supplied by variant HAs) could not be interpreted in evaluating the success of consolidation and microsphere delivery because such progression indicated radioembolization-resistant tumor biology, and even tumors that directly received microspheres showed PD.

RESULTS

Arterial Anatomy in Patient Cohort

A total of 73 patients (36.3%) had variant HAs; the other 128 patients (63.7%) had standard HA anatomy or underwent previous resection that eliminated variant HAs. The

Table 1. Patient Demographics and Treatment Details in Patients with Variant Hepatic Artery

Parameter	Value
Age	
Mean	59.7
Range	22–81
Sex (M/F)	42/31
Tumors	73 (100)
Primary (HCC, cholangiohepatoma)	19 (26.7)
Metastatic*	54 (73.3)
Type of microsphere used	
SIR-Spheres	58 (78.7)
TheraSphere	15 (21.3)
Territory of liver treatment	
Whole liver (all with SIR-Spheres)	49 (67.1)
PHA or CHA single administration	29 (39.7)
Two lobar administrations, single procedure	15 (20.5)
Two lobar administrations, different sessions	5 (6.8)
Right lobe only	13 (17.8)
Right lobe and segment IV	6 (8.2)
Left lobe only	3 (4.1)
Segment IV only	1 (1.4)
Left lobe and segment VIII	1 (1.4)

Note.—Values in parentheses are percentages. CHA = common hepatic artery, HCC = hepatocellular carcinoma, PHA = proper hepatic artery.
* Metastases from colorectal carcinoma, neuroendocrine carcinoma, ocular melanoma, pancreatic adenocarcinoma, renal cell carcinoma, urothelial transitional cell carcinoma, sarcoma, breast carcinoma, lymphoma, or nonsmall cell lung carcinoma.

Table 2. Arteries Embolized for Consolidation in Patients (N = 43) with Variant HA (N = 47)

Arteries Embolized	No. of Pts.
Variant arteries	35 (81.3)
aLHA from LGA	14 (32.6)
rLHA from LGA	10 (23.2)
aRHA from SMA	4 (9.3)
MHA from GDA	2 (4.7)
rRHA from SMA	1 (2.3)
aRHA from CHA	1 (2.3)
aRHA from GDA	2 (4.7)
rLHA from LGA and aRHA from SMA	1 (2.3)
Nonvariant arteries	6 (14.0)
MHA	3 (7.0)
PHA	1 (2.3)
LHA	1 (2.3)
MHA and PHA	1 (2.3)
Variant and nonvariant arteries	2 (4.7)
rLHA and MHA	2 (4.7)

Note.—Values in parentheses are percentages. aLHA = accessory left hepatic artery, aRHA = accessory right hepatic artery, CHA = common hepatic artery, GDA = gastroduodenal artery, HA = hepatic artery, LGA = left gastric artery, LHA = left hepatic artery, MHA = middle hepatic artery, PHA = proper hepatic artery, rLHA = replaced left hepatic artery, rRHA = replaced right hepatic artery, SMA = superior mesenteric artery.

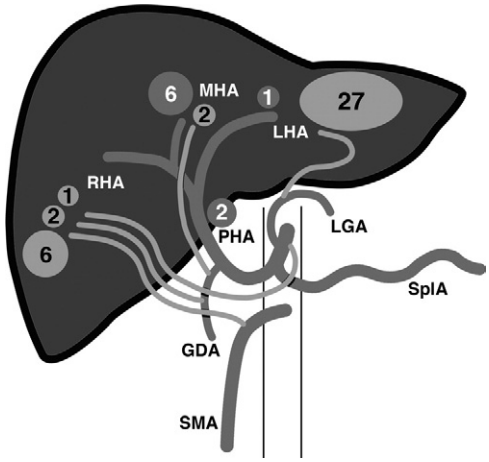

Figure 2. Distribution of variant HAs that were embolized for consolidation is depicted in light gray. Accessory and replaced arteries arising from the left gastric artery (*LGA*) and SMA are shown as totals. Normal HAs that were embolized for consolidation are shown in dark gray, and include middle HA, LHA, and PHA. Normal arteries were embolized when the tumor burden was predominantly perfused through a dominant variant HA, which was then chosen as the vessel for radioembolic administration. SplA = splenic artery; MHA = middle hepatic artery.

73 patients had a total of 85 variant HAs amenable to consolidation (42 men, 31 women; age range, 22–81 y). Details about demographics, type of radioembolization microsphere used, and territory of liver treated are listed in **Table 1**. The majority of patients had diffuse bilobar metastatic disease and required whole-liver treatment. Single-session whole-liver treatment was frequently performed to limit the potential for tumor progression in an untreated lobe, and also to minimize reimbursement issues. Of the 73 patients who had variant HAs, the majority 61 (83.6%) exhibited only a single variant artery, and 12 (16.4%) had two variant HAs. The distribution of variant HAs according to the Michels classification is listed in an Appendix available online at *www.jvir.org*.

A total of 38 variant HAs in 37 patients underwent coil embolization to consolidate the HA vasculature, and patients and individual variant HAs embolized are listed in **Table 2** and diagrammed in **Figure 2**. Not all patients who underwent consolidation had variant HAs embolized, as some had dominant tumor supply from the variant HA and therefore underwent consolidative embolization of the nonvariant artery instead. Eight patients (18.6%) underwent embolization of a nonvariant artery, including six middle HAs, two PHAs, and one LHA (**Table 2**). Two patients underwent embolization of a variant and a nonvariant artery, one underwent embolization of two variant HAs, and one underwent embolization of two nonvariant arteries.

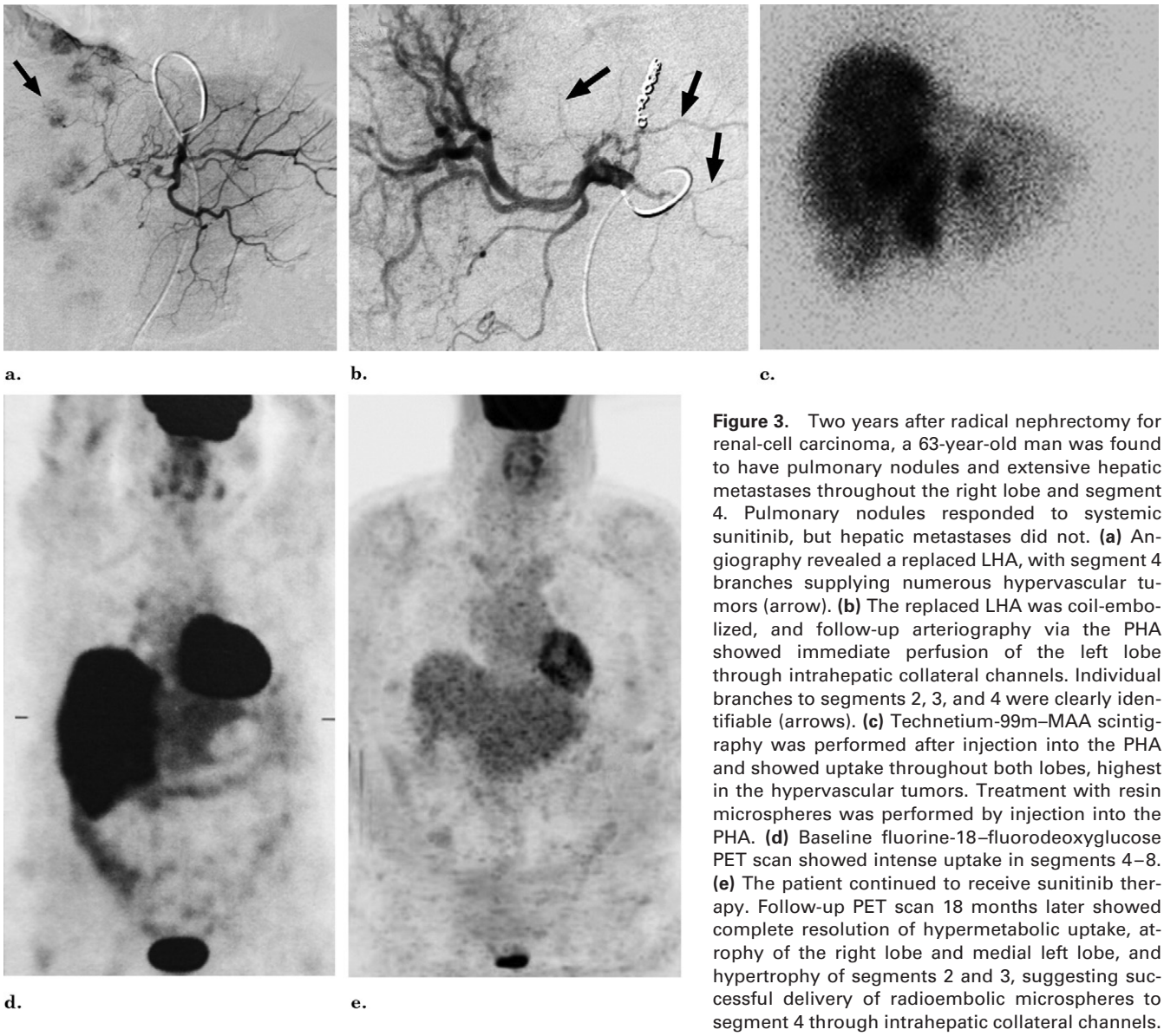

Figure 3. Two years after radical nephrectomy for renal-cell carcinoma, a 63-year-old man was found to have pulmonary nodules and extensive hepatic metastases throughout the right lobe and segment 4. Pulmonary nodules responded to systemic sunitinib, but hepatic metastases did not. **(a)** Angiography revealed a replaced LHA, with segment 4 branches supplying numerous hypervascular tumors (arrow). **(b)** The replaced LHA was coil-embolized, and follow-up arteriography via the PHA showed immediate perfusion of the left lobe through intrahepatic collateral channels. Individual branches to segments 2, 3, and 4 were clearly identifiable (arrows). **(c)** Technetium-99m–MAA scintigraphy was performed after injection into the PHA and showed uptake throughout both lobes, highest in the hypervascular tumors. Treatment with resin microspheres was performed by injection into the PHA. **(d)** Baseline fluorine-18–fluorodeoxyglucose PET scan showed intense uptake in segments 4–8. **(e)** The patient continued to receive sunitinib therapy. Follow-up PET scan 18 months later showed complete resolution of hypermetabolic uptake, atrophy of the right lobe and medial left lobe, and hypertrophy of segments 2 and 3, suggesting successful delivery of radioembolic microspheres to segment 4 through intrahepatic collateral channels.

The other 34 variant HAs (40%) in 30 patients (41.1%) were not embolized for consolidation: 15 patients with 16 variant HAs underwent whole-liver treatments involving division of the dose between a normal and a variant HA or between two variant HAs. Two of these were procedures staged to lessen side effects in patients in frail condition with poor performance status. Thirteen were treated by sequential lobar infusions on the same day to allow administration distal to hepaticoenteric anastomoses too small to embolize with coils. Eighteen variant HAs in 15 patients were not embolized because the patients underwent subselective lobar or segmental treatments and consolidation was not necessary. Two patients with Michels type IX anatomy did not require consolidation because they had only single HA inflow. No patient experienced any adverse events as a result of arterial consolidation. Overall, 38 of 58 patients (65.5%) with variant HAs treated with resin microspheres and five of 15 patients (33.3%) treated with glass microspheres underwent consolidative embolization.

Evaluation of Intrahepatic Collateral Perfusion

Two patients were not evaluable by scintigraphy because variant HAs were only discovered at the time of microsphere administration, after scintigraphy had already been completed. Upon reviewing the available imaging on the 43 patients with variant HAs who underwent consolidative embolization, perfusion of the hepatic territory previously supplied by the embolized vessel was confirmed by DSA in 43 of 43 patients (100%), by contrast-enhanced C-arm CT in 39 of 39 patients (100%; the earliest patients in the series were treated before the availability of C-arm CT), and by scintigraphy in 38 of 41 patients (92.7%) (**Figure 3**). In five patients, the immediate postembolization DSA and C-arm

Table 3. Perfusion and Tumor Response in Territories Previously Supplied by Variant HAs

Imaging Modality	Perfusion of Previously Variant-supplied Territory vs Internal Control	
	Homogeneous	Hypoperfused
DSA	43 (100)	0
C-arm CT	39 (100)	0
^{99m}Tc-MAA scintigraphy	38 (92.7)	3 (7.3)
Response per RECIST (PR/SD)	21 (95.5)	1 (4.5)
Total with response	22 (66.7)	
Uniform PD*	11 (33.3)	

Note.—DSA = digital subtraction angiography, MAA = macroaggregated albumin, PD = progressive disease, PR = partial response, RECIST = Response Evaluation Criteria In Solid Tumors, SD = stable disease.
* Not evaluable for microsphere distribution.

CT studies were equivocal or discordant with one another, likely because of incomplete immediate development of intrahepatic collateral flow. The presence of intrahepatic collateral flow after maturation of collateral channels became unequivocal in all five patients by the time of the treatment procedure a mean of 17.7 days later. No repeat scintigraphy was performed on any patients.

Follow-up Assessment of Therapeutic Effects

Among the patients with variant HA for whom follow-up imaging was available, 25 were followed by CT, three by PET only, three by MR imaging, and two by CT and PET. Uniform PD was found in 11 patients (33.3%) with variant HAs who had adequate imaging follow-up, and distribution of microspheres was not evaluable in these patients.

Excluding patients with uniform PD and patients with insufficient follow-up imaging, uniform PR and SD responses were found in 21 of 22 patients (95.5%) with embolized variant HAs (**Table 3**). Inferior response was found in only one patient (4.5%), in whom all lesions regressed more than 30% in diameter (ie, PR by RECIST) except for the single lesion previously supplied by a variant HA, which remained stable in size. This lesion was previously supplied by an accessory right HA originating from the GDA, and would have posed very high risk to treat via this route. Embolization of the GDA resulted in recruitment of collateral flow from the SMA rather than from intrahepatic collateral routes, requiring adjunctive coil embolization of the SMA branch on the day of treatment. One year after radioembolization treatment, all other lesions in this patient had disappeared on CT and were photopenic on PET scan (ie, CR), but the poorly responding lesion remained stable in size with a specific uptake value of 4.7 (ie, SD). The patient underwent wedge resection of the lesion, and surprisingly, histopathologic analysis revealed radioembolic microspheres in and around the tumor. Presumably, the inferior response was caused by a sublethal density of microsphere deposition, but no other lesions were resected for comparison. Although not completely successful, consolidation resulted in stabilization of this lesion and allowed the patient to become a candidate for resection. The other patient who underwent consolidative embolization on the day of treatment showed uniform PD, so microsphere distribution was not evaluable.

Of the five patients who had equivocal collateral perfusion by DSA and C-arm CT after embolization but showed improved perfusion by the day of treatment, three showed uniform good response, one showed uniform PD, and one did not undergo follow-up imaging. Of the three patients who showed scintigraphic evidence of hypoperfusion of the target territory, uniform PD in two precluded evaluation, but uniform good response in the other patient suggested adequate delivery of microspheres. This suggested that ^{99m}Tc-MAA scintigraphy is an imperfect simulation of microsphere distribution, either because intrahepatic collateral channels may exhibit hypertrophy in the interim between scintigraphy and the time of treatment, or the size and biochemical reactivity of MAA particles results in distribution that does not replicate that of microspheres.

DISCUSSION

Hepatic radioembolization with ^{90}Y-impregnated microspheres is a promising emerging treatment for patients with primary or metastatic hepatic malignancy, but the presence of variant HA anatomy poses certain risks and inconveniences. The potential complications resulting from nontarget radioembolization can be far more severe than those resulting from nontarget chemoembolization or bland embolization (13). Administration of radioembolic microspheres into variant HAs originating from the SMA, left gastric artery, or GDA is likely to entail high risk for gastrointestinal complications because these arteries may have numerous enteric branches in close proximity to the hepatic branches, and even a small amount and distance of reflux could result in complications. This heightened risk is lesser with glass microspheres than with resin, but could be further avoided by consolidation and administration from another safer route, such as from a nonvariant HA. In addition, segmental consolidation and flow redistribution may allow more targeted treatments that spare more normal liver (4).

The closed-source formulation of the microspheres and the high flux rate of each individual microsphere also introduce special handling risks (3). Microspheres are especially likely to lodge or accumulate in crevices such as at a Luer connection (3). Therefore, the entire delivery apparatus, including vial, catheter, and tubing, must be removed and disposed of intact to prevent spillage and contamination (3). Unlike chemoembolization, the option of iterative repositioning of the catheters for serial administrations in

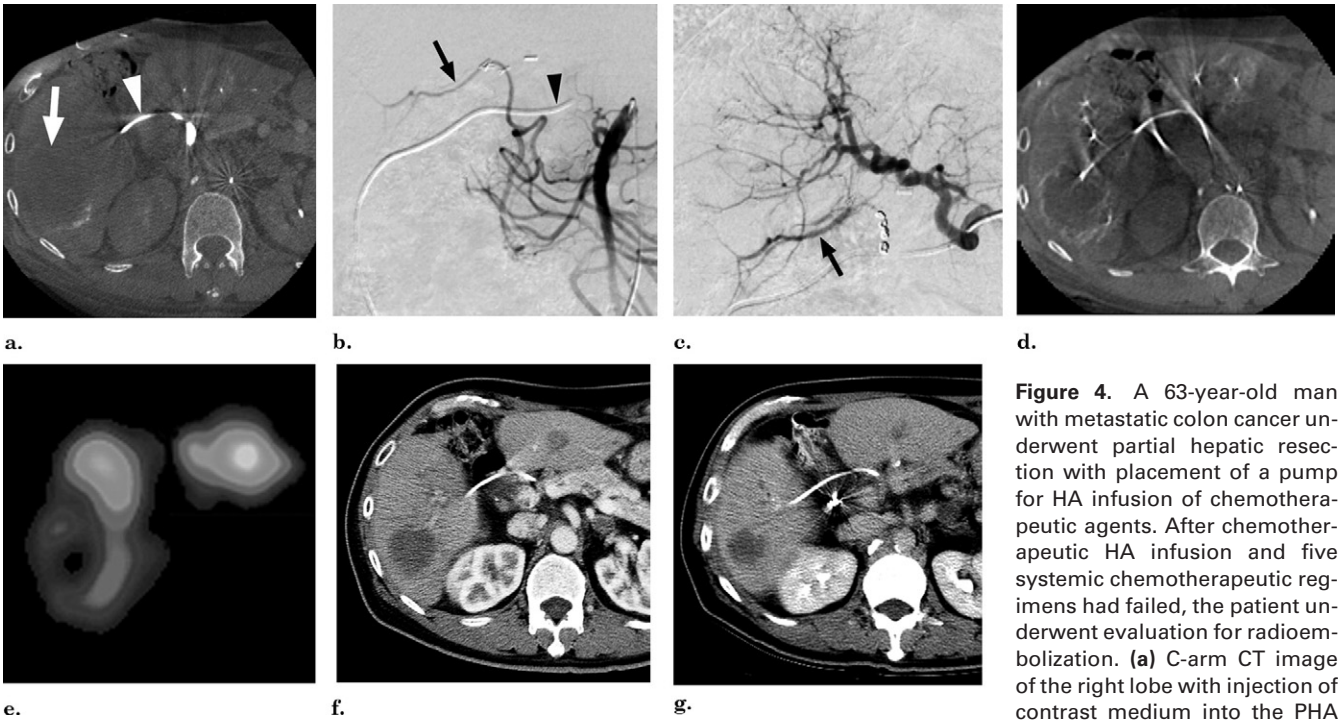

Figure 4. A 63-year-old man with metastatic colon cancer underwent partial hepatic resection with placement of a pump for HA infusion of chemotherapeutic agents. After chemotherapeutic HA infusion and five systemic chemotherapeutic regimens had failed, the patient underwent evaluation for radioembolization. **(a)** C-arm CT image of the right lobe with injection of contrast medium into the PHA showed rim enhancement of the dominant lesion only in segment 6, without enhancement of the anterior rim in segment 5 (arrow). Note the hepatic infusion catheter sutured into the GDA (arrowhead). **(b)** Arteriography of the SMA revealed an accessory RHA leading to segment 5 (arrow). Radioembolization via this accessory RHA would have been feasible but highly risky for reflux and nontarget radioembolization. Note again the hepatic infusion catheter with its tip at the origin of the GDA (arrowhead). **(c)** PHA arteriogram after coil embolization of the accessory RHA demonstrated intrahepatic collateral circulation perfusing the segment 5 artery (arrow). **(d)** Repeated contrast-enhanced C-arm CT image showed complete circumferential enhancement of the dominant lesion. **(e)** Axial SPECT image after injection of ^{99m}Tc into the PHA also confirmed perfusion of the entire liver, including segment 5. Note the photopenic area centered on the tumor, likely representing central necrosis. **(f)** Baseline diagnostic CT scan and **(g)** follow-up scan 3 months later at the same level of the SPECT image confirmed uniform response of the anterior and posterior aspects of the tumor as well as lesions found in other segments, suggesting successful distribution of radioembolic microspheres into segment 5 via intrahepatic collateral vessels.

different anatomic locations is very limited, and multiple sites of administration require multiple catheterizations with new catheters. Administration is most expeditious when the arterial anatomy requires the fewest catheterizations. Similarly, consolidation can also simplify the administration of ^{99m}Tc-MAA. However, consolidation extends the duration and cost of preparatory angiography, a disadvantage that must be weighed for each patient.

Not all patients undergoing radioembolization stand to benefit from inflow consolidation, and we found reason to consolidate inflow in only 59% of eligible patients in our cohort. If a segment was supplied by a variant HA but was free of tumor, avoiding consolidation avoided unneeded treatment of this segment. Likewise, solitary tumors fed by variant HAs were treated selectively when considered safe, without unneeded radiation to the remainder of the liver. Consolidation should be considered only in patients in whom a therapeutic advantage would result. These advantages would be most likely to occur in patients with diffuse, multifocal disease requiring whole-liver treatment, a situation more commonly encountered with resin microspheres; in fact, we consolidated HA supply in patients treated with resin microspheres twice as frequently as in those who received glass microspheres. However, advantages may also be seen in lobar or smaller target territories and for selective glass microsphere treatment, when nontarget radioembolization is a high risk. For instance, an accessory LHA could be embolized to allow treatment of the entire left lobe via a middle HA. Overall, we found more advantageous situations involving variant left HAs as a result of their smaller size and greater abundance of hepaticoenteric communications.

An alternative to consolidation would be to use multiple microcatheters and to use glass microspheres to limit reflux. However, this would also entail multiple vials and setups, additional radioactive waste, and additional opportunities for spillage. In addition, selective treatment of the smallest territories can be hampered by difficulty in accurate preparation of an appropriately small dose, especially with resin microspheres.

The existence of intrahepatic collateral networks has long been known (4–10). Early angiographic studies (5) demonstrated small arterial communications present in the hilum of most patients linking the left and right lobes. These interlobar collateral vessels became more evident after balloon occlusion (10) or ligation (6) of one or the other lobar arteries, but were sparse and poorly visualized

on angiography of normal individuals with intact arteries (9) (**Fig S1**). Similarly, perfusion of a hepatic segment via preexisting intrahepatic collateral pathways was demonstrated angiographically after interruption of a variant HA (7). Perfusion through these collateral pathways was demonstrated by injection of starch microspheres or MAA, although uniform distribution was not always seen acutely after arterial interruption, raising the issue of baseline luminal diameter and capacity of these collateral pathways (8). This potential limitation of the consolidation technique became evident in the single case of clinical failure in our cohort, in which consolidation was only partially achieved by coil embolization. Repeat embolization on the day of treatment achieved consolidation as shown by contrast medium enhancement, but asymmetric tumor response suggested poor microsphere distribution, perhaps caused by insufficient time to allow intrahepatic collateral channels to mature enough to permit passage of 30-μm particles.

The main uncertainty of the present study was the questionable correlation between imaging and the distribution of therapeutic microspheres. Resin microspheres range in size from 29 μm to 35 μm, whereas glass microspheres range from 15 μm to 35 μm (1). Water-soluble contrast medium molecules measure only approximately 1.5 nm in diameter (14) and easily pass through even the smallest capillary beds. Technetium-99m–MAA particles vary widely in size, ranging from 10 μm to 90 μm, with as many as 10% of the particles measuring less than 10 μm (15). Technetium-99m–MAA particles are therefore most similar in size to microspheres, but still do not exactly replicate the behavior and distribution of radioembolic material.

The truest test of arterial redistribution would require pathologic comparison of tissue from directly perfused regions with tissue from regions previously supplied by variant HAs to eliminate the possibility that all good responses were caused by adjuvant systemic therapy. None of our patients have undergone transplantation or multiple lesion resections; in the absence of histopathologic proof, angiographic evidence of cross-perfusion—in which C-arm CT has become an indispensable tool (16) (**Figure 4**)—and radiographic evidence of tumor response must serve as endpoints in evaluating the success of this technique. However, the inability to determine microsphere distribution in patients with uniform PD became a limitation of the present study: in the worst case scenario of all these patients actually having poor distribution, the overall clinical success of consolidation would have been achieved in only 21 of 33 patients (63.6%).

In conclusion, in patients who undergo embolization of variant HAs, reperfusion of nearly all territories previously supplied by these arteries is possible via intrahepatic collateral channels, and tumors in these territories can be successfully treated by radioembolization microspheres that apparently traverse these channels. Consolidation of HA inflow allowed simplification of radioembolization by reducing the number of sites of administration necessary to treat all targeted tumors, and facilitated treatment of targeted tumors in territories supplied by variant HAs.

ACKNOWLEDGMENTS

The authors thank Dr. A.K. Hosni for expert statistical advice.

REFERENCES

1. Lewandowski RJ, Sato KT, Atassi B, et al. Radioembolization with 90Y microspheres: angiographic and technical considerations. Cardiovasc Intervent Radiol 2007; 30:571–592.
2. Michels NA. Newer anatomy of the liver and its variant blood supply and collateral circulation. Am J Surg 1966; 112:337–347.
3. American College of Radiology/American Society for Radiation Oncology/Society of Interventional Radiology. ACR-ASTRO-SIR Practice guideline for radioembolization with microsphere brachytherapy device (RMBD) for treatment of liver malignancies. Available at http://www.acr.org/SecondaryMainMenuCategories/quality_safety/guidelines/ro/RMBD.aspx. Accessed March 6, 2011.
4. Bilbao JI, Garrastachu P, Herraiz MJ, et al. Safety and efficacy assessment of flow redistribution by occlusion of intrahepatic vessels prior to radioembolization in the treatment of liver tumors. Cardiovasc Intervent Radiol 2010; 33:523–531.
5. Redman HC, Reuter SR. Arterial collaterals in the liver hilus. Radiology 1970; 94:575–579.
6. Koehler RE, Korobkin M, Lewis F. Arteriographic demonstration of collateral arterial supply to the liver after hepatic artery ligation. Radiology 1975; 117:49–54.
7. Chuang VP, Wallace S. Hepatic arterial redistribution for intraarterial infusion of hepatic neoplasms. Radiology 1980; 135:295–299.
8. Civalleri D, Scopinaro G, Simoni G, et al. Starch microsphere-induced arterial flow redistribution after occlusion of replaced hepatic arteries in patients with liver metastases. Cancer 1986; 58:2151–2155.
9. Chen WJ, Ying DJ, Liu ZJ, He ZP. Analysis of the arterial supply of the extrahepatic bile ducts and its clinical significance. Clin Anat 1999; 12:245–249.
10. Tohma T, Cho A, Okazumi S, et al. Communicating arcade between the right and left hepatic arteries: evaluation with CT and angiography during temporary balloon occlusion of the right or left hepatic artery. Radiology 2005; 237:361–365.
11. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 2009; 45:228–247.
12. Young H, Baum R, Cremerius U, et al. Measurement of clinical and subclinical tumour response using [18F]-fluorodeoxyglucose and positron emission tomography: review and 1999 EORTC recommendations. European Organization for Research and Treatment of Cancer (EORTC) PET Study Group. Eur J Cancer 1999; 35:1773–1782.
13. Riaz A, Lewandowski RJ, Kulik LM, et al. Complications following radioembolization with yttrium-90 microspheres: a comprehensive literature review. J Vasc Interv Radiol 2009; 20:1121–1130.
14. Andersen R, Stordahl A, Aase S, Laerum F. Intestinal permeability of x-ray contrast media iodixanol and iohexol during bacterial overgrowth of small intestines in rats. Dig Dis Sci 2001; 46:208–213.
15. Hung JC, Redfern MG, Mahoney DW, Thorson LM, Wiseman GA. Evaluation of macroaggregated albumin particle sizes for use in pulmonary shunt patient studies. J Am Pharm Assoc 2000; 40:46–51.
16. Louie JD, Kothary N, Kuo WT, et al. Incorporating cone-beam CT into the treatment planning for yttrium-90 radioembolization. J Vasc Interv Radiol 2009; 20:606–613.

APPENDIX

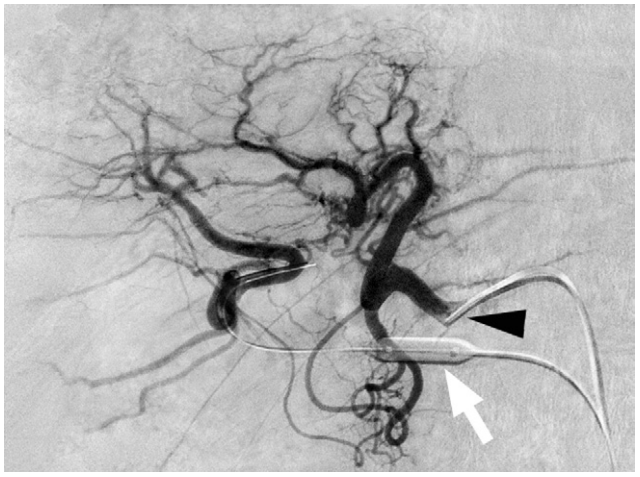

Figure S1. A 59-year-old man with bilobar metastases from colon carcinoma underwent preparatory angiography for radioembolization. A large replaced RHA originating from the SMA supplied a minority of tumors, whereas the majority were supplied by the PHA. To evaluate presence and adequacy of intrahepatic collateral channels, a 6-mm balloon was introduced from contralateral femoral access and inflated in the replaced RHA (white arrow), and an angiogram was obtained with injection of contrast medium into the CHA (black arrowhead). The entire territory originally supplied by the replaced RHA was immediately perfused through robust intrahepatic collateral channels. The replaced RHA was then embolized with two AMPLATZER I plugs. The replaced RHA was embolized rather than the smaller PHA because the majority of tumors were supplied by the PHA. This patient underwent whole-liver treatment by single-site administration in the PHA. Only two patients with unusually large variant HAs underwent balloon test occlusion to simulate embolization before actual embolization.

Table S1. Anatomy and Incidence of Variant HAs

Type	Anatomic Description	Incidence in Present Study
Michels classification		
I	RHA, MHA, and LHA originate from celiac axis (normal anatomy)	—
II	RHA and MHA originate from celiac axis, rLHA originates from LGA	15 (20.5)
III	MHA and LHA originate from celiac axis, rRHA originates from SMA	20 (27.4)
IV	MHA originates from celiac axis, rRHA originates from SMA, and rLHA originates from LGA	6 (8.2)
V	RHA, MHA, and LHA originate from celiac axis, aLHA originates from LGA	14 (19.2)
VI	RHA, MHA, and LHA originate from celiac axis, aRHA originates from SMA	5 (6.8)
VII	RHA, MHA, and LHA originate from celiac axis, aRHA originates from SMA, aLHA originates from LGA	0
VIII	Combined patterns: (i) rRHA and aLHA or (ii) aRHA and rLHA	4 (5.5)
Type IX	Entire hepatic trunk originates from SMA	2 (2.7)
Type X	Entire hepatic trunk originates from LGA	0
Other variants		
—	aRHA from GDA	3 (4.1)
—	MHA from GDA	2 (2.7)
—	rRHA from CHA and aLHA from LGA	1 (1.4)
—	aRHA from CHA and rLHA from LGA	1 (1.4)

Note.—Values in parentheses are percentages. aLHA = accessory left hepatic artery, aRHA = accessory right hepatic artery, CHA = common hepatic artery, GDA = gastroduodenal artery, HA = hepatic artery, LGA = left gastric artery, LHA = left hepatic artery, MHA = middle hepatic artery, RHA = right hepatic artery, rLHA = replaced left hepatic artery, rRHA = replaced right hepatic artery, SMA = superior mesenteric artery.