

## Radiofrequency ablation for hepatic hemangiomas: A consensus from a Chinese panel of experts

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## Abstract

Recent studies have shown that radiofrequency (RF) ablation therapy is a safe, feasible, and effective procedure for hepatic hemangiomas, even huge hepatic hemangiomas. RF ablation has the following advantages in the treatment of hepatic hemangiomas: minimal invasiveness, definite efficacy, high safety, fast recovery, relatively simple operation, and wide applicability. It is necessary to formulate a widely accepted consensus among the experts in China who have extensive expertise and experience in the treatment of hepatic hemangiomas using RF ablation, which is important to standardize the application of RF ablation for the management of hepatic hemangiomas, regarding the selection of patients with suitable indications to receive RF ablation treatment, the technical details of the techniques, therapeutic effect evaluations, management of complications, *etc.* A final consensus by a Chinese panel of experts who have the expertise of using RF ablation to treat hepatic hemangiomas was reached by means of literature review, comprehensive discussion, and draft approval.

**Key words:** Hepatic hemangiomas; Radiofrequency ablation; Consensus

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**Core tip:** Recent studies have shown that radiofrequency (RF) ablation therapy is a safe, feasible, and effective procedure for hepatic hemangiomas. It is necessary to formulate a widely accepted consensus among the experts in China who have extensive expertise and experience in the treatment of hepatic hemangiomas using RF ablation, which is important to standardize the application of RF ablation for the management of hepatic hemangiomas.

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## INTRODUCTION

Hepatic hemangioma is the most common benign tumor of the human liver, with an incidence of 0.4% to 20% in the general population and a prevalence of 0.4% to 7.3% incidentally found in autopsy<sup>[1-5]</sup>. Most incidentally identified and asymptomatic hepatic hemangiomas do not need medical interventions. However, therapies are warranted for giant hepatic hemangiomas ( $\geq 5$  cm) that cause significant symptoms or the peripherally located hemangiomas posing the risk of life-threatening spontaneous rupture and hemorrhage<sup>[6-10]</sup>.

Hepatic hemangiomas have been treated with a wide spectrum of therapies. Traditionally, surgical resection and surgical enucleation are the mostly used treatments of choice<sup>[6-10]</sup>. Minimally invasive therapies for hepatic hemangioma include transcatheter arterial embolization (TAE)<sup>[11-14]</sup>, radiation therapy<sup>[15,16]</sup>, and radiofrequency (RF) ablation<sup>[17-37]</sup>. Orthotopic liver transplantation has been performed as the treatment choice in rare circumstances<sup>[38]</sup>. In recent years, RF ablation has been increasingly used for managing hepatic hemangiomas due to its unique advantages compared with other therapies, such as minimal invasiveness, low cost, low incidence of complications, short duration of hospital stay, and increased patient compliance<sup>[17-37]</sup>. So far, 501 patients with hemangiomas treated by RF ablation have been reported in the literature<sup>[17-37]</sup>. A widely accepted consensus or guideline, embracing the selection of patients with suitable indications to receive RF ablation treatment, the application of the techniques, therapeutic effect evaluations, and management of complications, is needed to standardize the management of hepatic hemangiomas using RF ablation.

## CONSENSUS DEVELOPMENT

The literature search was performed with an inclusion of published articles during the period from 2003 to 2017. The searched database is Medline. Medical subject headings and free-text words were used for searches, including radiofrequency ablation and hepatic hemangioma. Twenty-one original research papers pertinent to RF ablation treatment for hepatic hemangiomas were included. Of the 21 included papers (501 patients), 13 (465 patients) came from China, including ten in English and three in Chinese<sup>[17-37]</sup>; two came from South Korea, in which 25 patients with hepatic hemangiomas underwent ultrasound-guided percutaneous RF ablation<sup>[21,25]</sup>; and Western experience contributed six case reports including 11 patients on the RF ablation for hepatic hemangiomas<sup>[18,23,24,26,30,36]</sup>. Studies were reviewed and selected for further screening analyses and for subsequent consensus studies.

Base on a comprehensive appraisal of the published original research articles related to RF ablation for hepatic hemangiomas, a Chinese panel of experts was contacted and convened by electronic mails and/or phone. The recruitment of the experts was determined based on the following comprehensive criteria: the number of reported cases using RF ablation for hepatic hemangiomas and the impact of the published articles. All the experts work in well-known, high-volume centers, and their clinical experiences are well documented in scientific papers. They reviewed both the literature and their institutional experience. The draft was completed by the corresponding author and his team and then was circulated to all participants for comments. The revised version was redistributed to the experts for approval or further comments. After more than nine months of electronic mail or, on occasion, face-to-face discussions, the final version of consensus was formulated.

## OVERVIEW OF HEPATIC HEMANGIOMAS

### *Pathology and clinical features*

Hepatic hemangioma is usually a solitary tumor mass, although multiple lesions may be present in both hepatic lobes in up to 40% of the patients. Hepatic hemangiomas include cavernous hemangioma, sclerosing hemangioma, hemangioendothelioma, and capillary hemangioma. It consists of blood-filled cavities fed by the hepatic arterial circulation, with walls lined by a single layer of endothelial cells, and manifests as a veritable chaotic entanglement of distorted blood vessels confined to a region as small as a few milliliters and as large as 10 cm, 20 cm, and even 40 cm<sup>[1-3]</sup>.

According to the diameter of hepatic hemangioma, it could be divided into three categories: small (<5 cm), giant (5-9.9 cm), and huge ( $\geq 10$  cm). Giant hemangiomas are also defined by a diameter larger

than 4 cm in the literature<sup>[1-5]</sup>.

### *Diagnosis*

In most situations, hepatic hemangiomas (especially when smaller than 4 cm) do not show any signs and/or symptoms, most likely being discovered incidentally during imaging investigations for other unrelated conditions. However, a few patients may present a wide variety of non-specific clinical symptoms such as pain in the right upper abdomen, decreased appetite, premature satiation sensation, nausea, vomiting, and abdominal discomfort such as sense of fullness and postprandial bloating (early or late). Spontaneous or traumatic rupture is the most severe complication. This has a catastrophic outcome if not promptly managed, and is the reason why correct diagnosis and management are extremely important<sup>[1-3]</sup>.

Hepatic hemangiomas can be specifically diagnosed by ultrasonography (US) or contrast-enhanced US, contrast-enhanced computed tomography (CT), and magnetic resonance imaging (MRI) because of their typical imaging characteristics<sup>[4]</sup>. On US images, hepatic hemangiomas present as a homogeneous, round or oval lesion with well-defined hyperechogenicity, and likelihood of posterior acoustic enhancement. Other imaging techniques, such as contrast-enhanced CT or MRI, are recommended for confirmation in case of inconclusive ultrasonographic results, or if a giant hemangioma requires treatment<sup>[4,5]</sup>. The typical hemangioma appears on CT or MRI scans as a hypointense, well-defined lesion, which after contrast injection shows peripheral nodular enhancement with progressive homogeneous centripetal filling.

## TRADITIONAL TREATMENT OF HEPATIC HEMANGIOMAS

Surgical procedure used to be the first choice of treatment for hepatic hemangiomas, including hemangioma enucleation, lobectomy (segmentectomy) or partial hepatectomy, and tumor suture or ligation<sup>[6-10]</sup>. Liver transplantation is used for rare cases which need medical intervention but the tumor is too large to undergo surgical resection, ruptures, or has hemorrhage combined with Kasabach-Merritt syndrome<sup>[38]</sup>. Surgical resection is rather invasive and associated with relatively high risks of perioperative morbidity (27%), mortality (3%) and long hospitalization<sup>[6-10]</sup>.

Radiation therapy can destroy the endothelial cells and smooth muscle cells of hepatic hemangiomas, consequently leading to thrombosis, necrosis, and fibrosis inside the tumors, which provides partial reduction in hemangioma size and relief of symptoms. Currently, radiation therapy is used rarely in hepatic hemangioma because it is not considered as a

curative therapy. Moreover, it may have the risks of radiation hepatitis, veno-occlusive disease, and hepatic neoplasia<sup>[15,16]</sup>.

TAE has been undertaken as an effective alternative treatment for managing hepatic hemangioma. Before TAE, hepatic arterial angiography is carried out to assess the blood supply to the tumor, tumor size, tumor number, tumor position, and intrahepatic vascular variants. The superselective catheterization of the hepatic arteries leading to the tumor body is followed by embolizing the tumor vessels using an embolization agent mixed with pingyangmycin or bleomycin. With the destruction of endothelial cells lining the blood sinus, thrombosis is formed to block the blood supply to the body of hemangioma. However, TAE is not considered as curative because recurrence is common due to vascular recanalization<sup>[34]</sup>. Moreover, the treatment may have disastrous complications, such as systemic embolization, biliary damage, and hepatic rupture as the size of tumors increases<sup>[11,12]</sup>. Several reports have advocated TAE as a temporizing and auxiliary preoperative procedure for huge hepatic hemangioma or spontaneously ruptured hemangiomas to decrease the risk of surgery<sup>[11-14,34]</sup>.

## HISTORY OF RF ABLATION FOR HEPATIC HEMANGIOMAS

RF ablation is performed by using RF-induced thermal energy to damage the endothelial lining vascular structures as a result of promoting thrombosis<sup>[18]</sup>, to induce necrotic coagulation<sup>[19]</sup>, as well as to destruct erythrocytes and cause vascular smooth muscle cell disappearance and fibrosis in the ablated zone<sup>[19]</sup>.

In 2003, Cui *et al.*<sup>[17]</sup> reported the first cohort of 12 patients who received the percutaneous RF ablation treatment for 15 hepatic hemangiomas (2.5-9.5 cm) under US guidance. In 2004, Zagoria *et al.*<sup>[18]</sup> reported the successful treatment of a symptomatic hepatic hemangioma (5.0 cm) using percutaneous RF ablation under CT guidance. A few more studies show that percutaneous RF ablation therapy is a safe, minimally invasive, and effective locoregional treatment for selected patients with hepatic hemangiomas<sup>[21,23]</sup>. In 2006, Fan *et al.*<sup>[20]</sup> reported the use of laparoscopic RF ablation therapy for treating 21 patients with 50 hepatic hemangiomas (5.5 cm  $\pm$  2.0 cm) located on the surface of the liver or adjacent to the gallbladder. The results showed that laparoscopic RF ablation therapy is a safe, feasible, and effective treatment option for patients with extrorse hemangiomas. In 2016, a prospective study demonstrated the benefits and disadvantages of laparoscopic RF ablation as compared with surgical resection for managing hepatic hemangioma<sup>[35]</sup>. Sixty-six patients with symptomatic-

enlarging hepatic hemangiomas (4 cm  $\leq$  diameter < 10 cm) either underwent laparoscopic RF ablation ( $n = 32$ ) or open resection ( $n = 34$ ). Laparoscopic RF ablation was associated with significantly shorter operative time (138 min vs 201 min,  $P < 0.001$ ) and less blood loss than open resection. Patients after laparoscopic RF ablation experienced significantly less pain and required less analgesia use, significantly shorter length of hospital stay, and lower hospital cost. The study showed that laparoscopic RF ablation, as a minimal invasive treatment option, is as safe and effective a procedure as open resection for patients with symptomatic-enlarging hepatic hemangiomas smaller than 10 cm.

During the initial period of RF ablation for hepatic hemangiomas, authors always selected and treated hepatic hemangiomas < 10 cm using RF ablation because of the lack of experience. Sporadic cases with huge hepatic hemangiomas were treated by RF ablation. Whether RF ablation should be accepted for treating huge hemangiomas is still in debate because of the requirement of long ablation time. Lengthy ablation time is prone to cause hemolysis, which can lead to the complications of hemoglobinuria, hemolytic jaundice, anemia, or even acute kidney injury (AKI)<sup>[25-36]</sup>. The incidence of complications post RF ablation is proportionally associated with the size of hemangiomas and the ablation time<sup>[28-36]</sup>. Park *et al.*<sup>[25]</sup> described the 100% ablation of 10 hepatic hemangiomas larger than 5 cm but less than 10 cm and an ablation in 60% (3/5) of hepatic hemangiomas  $\geq$  10 cm. Hence, they drew a conclusion that the best indication for RF ablation was giant hepatic hemangiomas, but huge hepatic hemangiomas were the comparative contraindication. Gao *et al.*<sup>[28]</sup> reported the same technical difficulties when they treated 17 huge hemangiomas  $\geq$  10 cm in 16 patients with RF ablation using cluster electrodes. In their study a high rate of complete ablation (82.4%, 14/17) was achieved, but ablation-related complications were seen in all the 16 patients with hemangiomas  $\geq$  10 cm, including significant systemic inflammatory responses and acute respiratory distress syndrome (ARDS, grade IV)<sup>[39]</sup>. Gao *et al.*<sup>[31]</sup> adopted two approaches to treat 21 large hemangiomas in 21 patients with the expectation of lessening the incidence of complications and achieving a higher success rate: (1) using cool-tip cluster electrodes; and (2) closely monitoring the patient's temperature and hemoglobinuria to warrant a termination of the procedure if the temperature exceeds 39 °C or signs of hemoglobinuria appeared. Complete ablation was achieved in 90.5% (19/21) of cases and ablation-related complications reduced to 47.6% (10/21). According to the Dindo-Clavien classification for complications<sup>[39]</sup>, all the complications were grade I (including hemoglobinuria in ten cases,

**Table 1** Indications and contraindications of radiofrequency ablation for hepatic hemangiomas

Indications
The maximum diameter of hemangiomas > 5 cm
Tumor gaining an enlargement of more than 1 cm within 2 yr
Persistent hemangioma-related abdominal pain or discomfort
Consent to receive the RF ablation
Contraindications
Severe bleeding tendency, platelets < 50 × 10 <sup>9</sup> /L, international normalized ratio > 1.5, severe platelet function disorders (prothrombin time > 18 s and prothrombin activity < 40%)
Malignant tumors
Kasabach-Merritt syndrome
Infection, especially biliary system inflammation
Low immune function
Severe primary organ failure such as the liver, kidney, heart, lung and/or brain

fever in four cases, hemolytic jaundice in three cases, anemia in one case, and elevated serum transaminase in four cases). Eighteen patients required one session and three patients with hemangiomas  $\geq 14.0$  cm required two sessions of RF ablation. This study by Gao *et al.*<sup>[31]</sup> showed that RF ablation for huge hepatic hemangiomas is minimally invasive, safe, and effective. Other studies reported the similar results<sup>[27,30]</sup>.

## INDICATIONS AND CONTRAINDICATIONS FOR RF ABLATION FOR HEPATIC HEMANGIOMAS

### Indications

Indications include: the maximum diameter of hemangiomas > 5 cm; on regular imaging follow-up, tumor gaining an enlargement of more than 1 cm within 2 years; persistent hemangioma-related abdominal pain or discomfort with the definite exclusion of other gastrointestinal diseases which cause the epigastric pain *via* gastroscopy examinations; patients' decline to receive surgical treatment but with the consent to receive the RF ablation (Table 1)<sup>[25-34]</sup>.

### Contraindications

Contraindications include: patients with severe bleeding tendency, platelets < 50 × 10<sup>9</sup>/L, severe platelet function disorders (prothrombin time > 18 s and prothrombin activity < 40%), international normalized ratio > 1.5, malignant tumors, Kasabach-Merritt syndrome, infection, especially biliary system inflammation, low immune function, and severe primary organ failure such as the liver, kidney, heart, lung and/or brain<sup>[28-34]</sup>. Anticoagulation and/or antiplatelet drugs should be discontinued at least 5-7 d prior to ablation (Table 1).

## ANESTHESIA PROTOCOLS

For percutaneous procedures, general anesthesia is recommended to prevent pain and discomfort during RF procedure. Controlled ventilation would reduce ablation attempts and increase the success rate while RF ablation is performed for patients under general anesthesia<sup>[31-35]</sup>.

## PROCEDURES OF RF ABLATION

RF ablation for hepatic hemangiomas can be performed *via* a percutaneous, laparotomy or laparoscopic approach. The diversity of approaches helps extend the scope of treatment indications<sup>[25-34]</sup>.

Hepatic hemangiomas deeply located in liver parenchyma are suited to be treated by percutaneous CT-guided RF ablation. After induction of general anesthesia, patients are placed in a supine position. Grounding is achieved by attaching two pads to the patient's thighs. The skin entry point of the RF electrodes is determined by the guidance of CT imaging. Under the monitoring and guidance of CT, the RF electrodes are percutaneously inserted through the liver to target the tumor. After CT images confirm the acting tip of the RF electrode is located in the tumor center, RF procedure is performed<sup>[28]</sup>.

Subcapsular hepatic hemangioma is suitable to be treated *via* a laparoscopic approach using US guidance<sup>[20,33,35]</sup>. Under general anesthesia, patients were placed in a supine position. After a pneumoperitoneum (CO<sub>2</sub> at 12 mmHg) is established, a thorough intraperitoneal exploration with a 30° laparoscope through a 10-mm umbilical port is performed. Another 10 mm subxiphoid port is created at the midline of abdomen and an additional 10 mm right or left lateral subcostal port is placed if needed, depending on the location of the hepatic hemangiomas. Under US guidance, the RF electrodes are introduced into the peritoneal cavity through the subcostal abdominal wall under the direct laparoscopic view and deployed into the tumor. The RF procedure is monitored by intraoperative US, which can increase the ability to guide the RF electrode placement and evaluate the efficacy of ablation. After ablation, the ablated lesion became hyperechoic because of outgassing from heated tissues. Laparoscopic biopsy of liver lesions before the ablation is not needed with the consideration of avoiding unnecessary bleeding. For the patients with gallbladder stones or simple hepatic cysts, laparoscopic cholecystectomy (LC) or deroofing of the hepatic cysts may be performed during ablation. LC had to be performed beforehand if the lesions are encroaching on the gallbladder fossa.

Laparotomy is more invasive than percutaneous and laparoscopic approaches. With the increasing

experiences in RF ablation and the improvement of laparoscopic techniques, laparotomy is only used for an alternative approach. In case of unexpected incidence of uncontrollable bleeding during the procedure *via* percutaneous and laparoscopic approaches, laparotomy needs to be performed for controlling the bleeding efficiently and preventing the occurrence of severe complications.

## TECHNICAL DETAILS TO BE NOTED

### **Common strategies of ablation for hepatic hemangiomas**

A transhepatic route for RF electrode placement to target the tumor is recommended to prevent bleeding from the electrode-poking site of hemangiomas. RF ablation is initiated at the treatment point close to the margin of the tumor to minimize the risk of bleeding and the heat sink effect. The heat sink effect refers to cooling by adjacent visible (>1 mm diameter) blood vessels when ablated tissues are heated. Overlapped ablation zones are warranted by repositioning the RF electrodes in the tumor mass repeatedly under the guidance and monitoring of CT or US imaging, ensuring a complete ablation of the tumors. An intratumoral ablation is necessary to minimize injuries to normal liver parenchyma and the needle tract ablation can prevent the incidence of needle puncture-induced bleeding<sup>[31]</sup>.

In the laparoscopic approach, the Pringle maneuver can be used to decrease the heat sink effect<sup>[28]</sup>. Furthermore, the laparoscopic approach also offers a direct vision of the entire RF procedure, which is helpful to identify and manage bleeding from the puncture site or tumor rupture<sup>[31-33]</sup>.

Based on our experience on treating 76 huge hepatic hemangiomas<sup>[31-33]</sup>, we prefer to use internally cooled cluster electrodes to treat the tumors by taking their advantage of achieving an efficient and much concentrated thermal energy in the tumor tissue, which is expected to reduce the incidence of ablation-related complications. Internally cooled cluster electrodes, for example Cool-tip ones, are straight electrodes without an array of prongs, and the tip is internally cooled by continuous infusion of cold saline. Thus, the temperature of the electrode itself is not extremely high, which is helpful to avoid the instant charring at the tissue around the probe and reduce tissue impedance. The efficient heat deposition creates a larger ablated zone within a shorter period of time. Another advantage of internally cooled electrodes is that they induce a sustaining high temperature in the tumor with limited "heat sink effect" caused by blood flow in the adjacent vessels, which can enhance the ablation effectiveness for the tumor tissue abutting the vessel. Moreover, a specially-designed Cool-tip

electrode is more visible under the guidance of CT or US imaging, which allows the accurate placement of the electrodes in the tumor without injuring the adjacent organs<sup>[31]</sup>.

### **Special strategies of ablation for huge hepatic hemangiomas**

Larger tumor size is a risk factor for ablation-induced complications. For huge hemangiomas, a few precautions should be taken to lessen the risk of severe complications and enable a successful treatment.

It is unnecessary to achieve a complete ablation of a large tumor using one ablation session if the patient shows the sign of elevating body temperature and hemolysis, considering the severe risk of hemolysis-induced AKI<sup>[36]</sup>. A repeat RF ablation session can be rescheduled to obtain the expected treatment effect<sup>[30]</sup>.

RF ablation combined with TAE could be an option to achieve a synergistic treatment effect for huge hepatic hemangiomas because the blockade of tumor blood supply by TAE can decrease the lesion size to some extent, facilitating the subsequent RF ablation and minimizing the risk of ablation-related complications. Additionally, the hyper-attenuation of iodized oil deposited in the tumor on CT images can facilitate the targeting placement of the RF electrodes in the tumor and thus increase the success rate of complete ablation<sup>[34]</sup>.

Laparoscopic resection of hemangioma boosted by intratumoral coagulation by RF ablation is a safe, effective option for treating huge hepatic subcapsular hemangiomas with low loss of blood and minimal complications. This technique lies in the advantage that a completely coagulated zone created by sequential RF ablation along the dissection margin warrants the successful removal of the tumor tissue without occluding the hepatic vessels before the tumor dissection. Compared with treating the tumor using RF ablation alone, this technique involves the ablation of the tumor tissue at the resection margin rather than the total hepatic hemangioma, thus shortens the ablation time and avoids the incidence of severe ablation-related complications<sup>[37]</sup>.

## COMPLICATIONS

### **Hemorrhage of hepatic hemangioma**

**Bleeding at the electrode entry site:** Due to the hypervascular nature of hepatic hemangioma and intratumoral high blood pressure, there is high risk of bleeding from the puncture site of the tumor. To prevent bleeding, the electrode needs to be advanced *via* a transhepatic approach to target the tumor and a needle tract ablation needs to be performed while withdrawing the electrode. When the RF electrode

placement is performed *via* laparotomy or laparoscopic approach, RF ablation should be launched from the exterior margin of the tumor from the beginning of a lower RF power<sup>[31-34]</sup>.

**Rupture of hepatic hemangioma:** Abrupt rupture of hepatic hemangioma could result in massive hemorrhage. For hemangiomas located in the surface of the liver, an improper advancement of the RF electrode directly through the tumor will lose the protection of liver parenchyma. In this context, the RF electrode puncture could induce massive bleeding from the electrode puncture site. On the other hand, when an extra-high RF output power is applied at the beginning of RF ablation, a rapid increase of intratumoral temperature and pressure will induce the burst force in the tumor, which will cause an abrupt rupture of the tumor and life-threatening bleeding. Under the direct view of laparoscopy, hemostasis procedure can be applied to the bleeding site such as applying ablation to stop bleeding. In case the bleeding is not controlled by these measures, a conversion to open surgery is advocated to achieve hemostasis.

#### **Puncture injury to adjacent organs**

The accidental injuries to the adjacent organs including the gallbladder, gastrointestinal organs, kidney, diaphragm, lungs, and heart need to avoid. While using multipolar expandable electrodes, the deployment of each prong of the electrodes need to be verified carefully<sup>[28,40]</sup>. The high visibility of Cool-tip electrodes on CT or US images facilitates the insertion of the electrodes in the tumor without causing accidental injury to adjacent organs<sup>[31]</sup>.

#### **Thermal injury to the pleura and diaphragm**

For hepatic hemangiomas situated in the subdiaphragm hepatic dome area, thermal injuries to the diaphragm frequently occur during RF ablation *via* the percutaneous approach<sup>[32]</sup>. The thermal injury to the diaphragm may manifest as the shoulder pain because the diaphragm and the shoulder skin are innervated by the same phrenic nerves arising from nerve roots C3, C4, and C5<sup>[32,41]</sup>. Diaphragmatic perforation and herniation were reported as major complications of RF ablation for hepatic tumors abutting the diaphragm in nine cases<sup>[41]</sup>. RF ablation injuries more frequently occur in cases with hepatic hemangiomas than hepatic cancers due to the high thermal energy and duration needed for large-sized hemangiomas. RF ablation *via* a laparoscopic approach can minimize the risk of diaphragm injury because the pneumoperitoneum can elevate the diaphragm to increase the operation space. Therefore, laparoscopic RF ablation therapy should be used as the first-line treatment for hepatic

hemangiomas abutting the diaphragm<sup>[32]</sup>.

#### **Thermal injury to the lung**

A patient with two huge hemangiomas in the right lobe (16.0 cm and 11.0 cm), treated with percutaneous RF ablation, developed ARDS immediately after an ablative time of total 250 min<sup>[28]</sup>. The major complication was resolved by conservative treatment<sup>[28]</sup>. The pathogenesis of ARDS needs to be investigated, and it is speculated that RF ablation of large quantity of tumor tissues induces significant systemic inflammatory responses<sup>[42-45]</sup>. Pre-ablation TAE as an adjuvant therapy or multiple ablation sessions is recommended to prevent the risk of ARDS<sup>[31,34]</sup>.

#### **Hemolysis**

**Hemolysis and anemia:** RF ablation poses a risk of predisposing huge hypervascular hepatic hemangiomas to the severe complication of hemolysis. Hemolysis can lead to various degrees of hemoglobinuria, hemolytic jaundice, anemia, or even AKI<sup>[28-31,36]</sup>.

**AKI:** AKI caused by ablation-induced hemolysis in patients with huge hepatic hemangiomas has been reported<sup>[36]</sup>. Hemoglobin is released upon erythrocyte destruction and is filtered by the glomerulus into the urinary space. In the urinary space, hemoglobin is degraded and releases heme pigments which can cause tubular injury. Furthermore, volume depletion enhances both vasoconstriction and the formation of obstructing casts, and also is of critical importance for the development of heme-induced AKI<sup>[36]</sup>.

Patients with huge hepatic hemangiomas should be sufficiently hydrated before RF ablation and during the procedure. When any signs or symptoms indicating hemolysis emerge in the course of RF ablation, such as rising body temperature and hemoglobinuria, the RF procedure should be terminated and a repeat RF ablation treatment may need to be rescheduled based on a comprehensive evaluation of the tumor<sup>[31]</sup>.

#### **Other complications**

Except for relatively severe RF ablation-related complications, some minor complications may take place, such as liver damage, fever, and skin burn injury at the site where the grounding pad is attached. The ablation-induced self-limiting liver injury can resolve within a short period of time without the need of any medication. The necrotic tissue of tumors can cause unspecific inflammatory reaction and mild hyperthermia. In case that the body temperature is higher than 39 °C, physical cooling can be used to alleviate the discomfort of hyperthermia. To prevent the burn injury to the skin in patients receiving long time RF ablation, multiple grounding pads can be

**Table 2** Ablation-related complications and preventive measures

Complication	Preventive measures
Bleeding at the electrode entry site	The electrode needs to be advanced <i>via</i> a transhepatic approach to target the tumor and a needle tract ablation needs to be performed while withdrawing the electrode. Radiofrequency (RF) ablation should be launched from the exterior margin of the tumor from the beginning of a lower RF power.
Rupture of hepatic hemangioma	Under the direct view of laparoscopy, hemostasis procedure can be applied to the bleeding site such as applying ablation to stop the bleeding. If it fails, a conversion to open surgery is advocated to achieve the hemostasis.
Puncture injury to adjacent organs	The high visibility of Cool-tip electrodes on computed tomography or ultrasonography images facilitates the insertion of the electrodes in the tumor without causing accidental injury to adjacent organs.
Thermal injury to the pleura and diaphragm	Laparoscopic RF ablation should be used as the first-line treatment for hepatic hemangiomas abutting the diaphragm.
Thermal injury to the lung	Pre-ablation transcatheter arterial embolization as an adjuvant therapy or multiple ablation sessions is recommended to prevent the risk of acute respiratory distress syndrome.
Hemolysis	The patients should be sufficiently hydrated before RF ablation and during the procedure. When any signs or symptoms indicating the hemolysis emerge in the course of ablation, the RF procedure should be terminated and a repeat RF ablation treatment may need to be rescheduled based on a comprehensive evaluation of the tumor.
Liver damage	The ablation-induced liver injury can resolve spontaneously without the need of any medication.
Fever	Physical cooling can be used to alleviate the discomfort of hyperthermia.
Skin burn injury	Multiple grounding pads can be applied or ice pad can be used to cool the skin with the contact of grounding pad.

applied or ice pad can be used to cool the skin with the contact of grounding pad<sup>[31-33]</sup>. The ablation-related complications and preventive measures are listed in Table 2.

## POST-TREATMENT EVALUATION

Contrast-enhanced CT or MRI can be used to evaluate the therapeutic effect of RF ablation for tumors one month after the treatment. On contrast-enhanced CT or MRI, complete ablation is defined as no nodular or irregular enhancement adjacent to the ablation zone and incomplete ablation is defined as irregular peripheral-enhanced foci in the ablation zone. In cases of complete ablation, subsequent CT or MRI examinations are repeated at a 6-mo interval<sup>[31-33]</sup>. Repeated RF ablation procedures are not needed unless the residual tumor is growing significantly or posing a risk of spontaneous rupture.

## CONCLUSION

RF ablation therapy is a safe, feasible, and effective procedure for hepatic hemangiomas, even for huge hepatic hemangiomas. RF ablation has the following advantages in the treatment of hepatic hemangiomas: minimal invasiveness, definite efficacy, high safety, fast recovery, relatively simple operation, and wide applicability.

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