Journal of Interventional Medicine 5 (2022) 51–56

Contents lists available at ScienceDirect

Journal of Interventional Medicine

journal homepage: www.keaipublishing.com/cn/journals/journal-of-interventional-medicine/

Advances in the interventional therapy of hepatocellular carcinoma originating from the caudate lobe

Shanmiao Ke

The Second Affiliated Hospital of Nanchang University, Department of Gastroenterology, Nanchang, 330006, China

ARTICLE INFO

Keywords:
Liver neoplasms
Transcatheter arterial chemoembolization
Radiofrequency ablation
Microwave ablation
Percutaneous ethanol injection
Efficacy
Safety analysis

ABSTRACT

Hepatocellular carcinoma originating from the caudate lobe, also known as segment I hepatocellular carcinoma, is difficult to treat because of its special location, complex vascular supply, and the proximity of important vessels, bile ducts, and organs. This research is conducted to examine the efficacy and safety of interventional therapy for hepatocellular carcinoma in the caudate lobe.

Conclusion: Superselective chemoembolization and ablation techniques for the treatment of caudate lobe hepatocellular carcinoma still need to be improved. The combination of multiple interventional methods and the application of multiple imaging techniques can improve the effectiveness and safety of interventional therapy for hepatocellular carcinoma in the caudate lobe. Multidisciplinary treatment is also essential to improve the prognosis of patients with caudate lobe hepatocellular carcinoma.

1. Introduction

The independent portal venous supply and venous drainage of the caudate lobe allow hepatocellular carcinoma (HCC) in the caudate lobe to frequently invade vessels, such as the portal and inferior vena cava, and the frequent formation of cancer thrombi can result in early intra- or extra-hepatic metastases. For resectable hepatocellular carcinoma in the caudate lobe that meets Milan's criteria, surgical treatment has better recurrence-free survival and overall survival (OS) than radiofrequency ablation (RFA)[1]; however, in some cases, surgical resection carries the risk of heavy bleeding and high early recurrence rates. In contrast, minimally invasive interventions, including endovascular and extravascular interventions, have the advantages of being safe and effective with minimal impact on liver function and are increasingly becoming the choice of treatment for unresectable caudate lobe HCC. Among the interventions, the efficacy of percutaneous RFA for caudate lobe tumors meeting the Milan criteria is significantly better than that of superselective transcatheter arterial chemoembolization (TACE).[2]

2. Transcatheter arterial chemoembolization

The OS and progression-free survival (PFS) rates are significantly higher with superselective TACE for caudate lobe HCC than with non-superselective TACE.[3] Because of the variable and complex vascular supply of the caudate lobe and the fact that the caudate artery mostly originates proximal to the hepatic artery, non-superselective TACE is ineffective for the treatment of caudate lobe hepatocellular carcinoma.[4,5] Alterations in the proximal hepatic artery supply to the caudate lobe and the source of the supplying artery may make TACE difficult to treat HCC in the caudate lobe.[6,7] The technical success rate of superselective embolization is currently about 62–85% according to available studies.[2,8–10] Multiple caudate lobe supply arteries significantly affect the success rate of superselective embolization, local tumor recurrence and survival in TACE for HCC in the caudate lobe.[8–10] The highest 1,2,3-year survival rates for HCC in the caudate lobe treated with superselective TACE are currently 89.0–92%, 79–80.8%, and 62.0–65%, respectively.[2,8] In theory, multiple repeat embolizations may reduce tumor recurrence, but the arteries supplying the HCC in the caudate lobe that recurs after endovascular intervention are frequently altered during subsequent chemoembolization therapy,[11] making repeat chemoembolization difficult. The caudate arteries can initially originate from the extrahepatic arteries,[12] and the right inferior phrenic artery (RIPA) is the most common extrahepatic artery.[12–14] Other less common vessels supplying recurrent tumors include the right gastric artery, the left gastric artery, the pancreatic artery and the adrenal artery.[5,7,11] The possibility of extrahepatic arterial supply, such as the RIPA, should therefore not be overlooked during hepatic arteriography. In addition, poor or thin collateral arteries have been shown on imaging to thicken and supply recurrent tumors after TACE is completed or even become the main tumor-supplying artery. The caudate artery can overlap with other hepatic arteries and be difficult to identify on digital subtraction

E-mail address: ncdxefy201909@163.com.

https://doi.org/10.1016/j.jimed.2022.03.002
Received 10 December 2021; Received in revised form 1 March 2022; Accepted 5 March 2022

Abbreviation

HCC	hepatocellular carcinoma
RFA	radiofrequency ablation
TACE	transcatheter arterial chemoembolization
RIPA	right inferior phrenic artery
CE-US	contrast-enhanced ultrasound
CE-CT	contrast-enhanced CT
MWA	microwave ablation
LTP	local tumor progression
OS	overall survival
RFS	recurrence-free survival
DFS	disease-free survival
PFS	progress free survival
PTCLI	percutaneous transhepatic chemotherapy-lipiodol injection
TACE-RFA	transcatheter arterial chemoembolization combined with radiofrequency ablation
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
SIRT	selective internal radiation therapy
NS-RFA	normal saline-enhanced radiofrequency
HRFA	hydrochloric acid-enhanced radiofrequency ablation

angiography (DSA), so it has been suggested that full and adequate intra- and postoperative angiography of the right and left hepatic arteries and multiple angiograms should be performed to avoid missing tumors.[9] C-arm computed tomography (CT) can identify more than 90% of the tumor-supplying arteries of HCC in the caudate lobe and clearly show their origin and anatomy and the vascular extent of embolized branches, preventing non-target embolization and detection of residual tumor.[15] Stereo magnification angiography has also been used in some studies. Selective hepatic artery embolization of the caudate lobe artery carries the risk of stenosis of the main bile duct in the porta hepatis, especially with repeated TACE treatment.[16] When C-arm CT or CT suggests bile duct enhancement, complete obstruction of the caudate artery should be avoided, or a finer catheter may be advanced distal to the caudate artery, as the bile duct arteries tend to originate proximally.[16] Collateral flow from other caudate arteries can reverse the flow in the embolized artery, causing the emboli to retreat, and it is therefore recommended that the microcatheter should be advanced distal to the anastomotic branch to avoid accidental extensive embolization. For the diagnosis of residual tumor after TACE, the diagnostic performance of contrast-enhanced ultrasonography (CEUS) for residual tumor after TACE was considered superior to that of contrast-enhanced CT (CE-CT) in the study by Liu et al.[17] DB-TACE can be used in caudate arteries which are impossible to treat with superselective TACE, avoiding damage to normal liver parenchyma and improving the aggregation of chemoembolization material.[18]

3. Percutaneous ablation

3.1. Thermal ablation

3.1.1. Efficacy, complications and the influencing factors of thermal ablation

Microwave ablation (MWA) does not rely on heat conduction and is less affected by the dissipative effect than RFA,[19] so MWA may be more widely used than RFA. According to current studies,[20–23] the initial complete ablation rate of ultrasound-guided RFA or MWA for HCC in the caudate lobe was approximately 76.9–93.5%, with the tumor diameter significantly affecting the initial complete ablation rate. According to related reports,[20–25] the incidence of more serious complications such as obstructive jaundice, bleeding, infection, and bile leakage was approximately 13.3–15.4%, but no procedure-related deaths were observed. Studies by Chen et al.[23] and Kariyama et al.[25] showed better survival and prognosis in ultrasound-guided RFA for HCC in the caudate lobe within the Milan criteria. Studies by Cui et al.[22] and Li et al.[24] showed that the 1-, 3- and 5-year survival rates of HCC in the caudate lobe treated with ultrasound-guided thermal ablation could reach 84.6–91.6%, 76.9–83.3% and 46.1–66.7%, respectively, but some studies[20–22,25] suggested that recurrence was easy after thermal ablation, with recurrence rates as high as 38.5% within 1 year, and 41.7% at 3 years. According to the present researchers, the factors affecting the efficacy and prognosis of thermal ablation are summarized as follows: Thermal ablation, especially RFA, is affected by the heat deposition effect of large veins and the restricted access to the puncture electrode. (1) Adjacent large vessels: one study[26] found that partial ablation of the spigelian lobe, paraventricular, and caudate margins achieved adequate ablation in 25%, 40% and 100% of cases, respectively, and that the difference in ablation outcome was clearly related to sites such as adjacent large veins or the hepatic pericardium. Dou et al.[19] have also found that the ablation effect is compromised by the increased thermal settling effect of thermal ablation when the tumor is located in the paraventricular portion of the vena cava. A research[20] indicated that a distance of <0.5 cm between the tumor and the inferior vena cava is a high-risk factor for residual tumor. (2) Tumor diameter: the incidence of distant metastases and survival can be significantly affected when the diameter of HCC in the caudate lobe is greater than 2 cm.[27] (3) Ablation margins: according to an existing study,[19] thermal ablation combined with alcohol ablation still only achieved margins of more than 5 mm in 55% of patients, while 22.2% of patients who underwent conformal ablation or had margins less than 5 mm, had local tumor progression (LTP) during a certain follow-up period, and only 9.1% of patients with at least 5 mm margins had LTP. This is particularly important for patient survival but remains difficult for patients with caudate lobe HCC.

3.1.2. Location and shape of hepatocellular carcinoma in the caudate lobe

The location and shape of the tumor are closely related to the outcome of radiofrequency ablation treatment.[28,29] The following methods are available to address the specific location and shape of HCC in the caudate lobe: (1) Artificial Pleural effusion can improve imaging under ultrasound of the tumor at the top of the liver but cannot reduce the possibility of diaphragmatic injury.[30] On the other hand, artificial ascites not only improves ultrasound imaging, but also minimizes damage to intra-abdominal vessels, bile ducts, and organs from the puncture needle.[31] (2) The positioning adjustment of RFA electrodes is difficult and the puncture route is restricted, which may lead to insufficient ablation margins, so it is particularly important to choose a suitable puncture route. In addition, a multidirectional approach can compensate for the limited puncture route, but a transthoracic route should be avoided because it is more prone to serious complications such as hemothorax and pneumothorax.[32] (3) Applying conformal ablation can ensure the maximum ablation area and reduce the number of perforations.[31] Bypass ablation can avoid puncturing large vessels and bile ducts. Parallel orientation can expand the contact surface between the ablation needle and the vessel and reduce the heat dissipation effect, but it may not be applied at complex vessels.

3.1.3. Reduction of the thermal dissipation effect of vessels

The thermal dissipation effect of vessels can reduce thrombosis and vascular injury, which can also lead to residual tumors. For the heat sink effect, in addition to conformal, bypass, and parallel ablation methods, the following methods are available: (1) Masashi et al.'s study[33] showed that multi-electrode RFA significantly increased the rate of complete tumor necrosis, improved relapse-free survival (RFS) of patients and reduced the rate of LTP without increasing serious complications. In contrast, Serror et al.[34] reported that complete necrosis of tumors adjacent to large vessels could only be achieved using a multi-electrode technique. However, another research[31] has also concluded that the

increased number of multipolar perforations and repositioning of electrodes can increase the risk of tumor implantation and needle tract dissemination. It was also concluded that reinsertion of electrodes significantly increases the risk of penetrating blood vessels, bile ducts, etc. Whether multipolar ablation can improve prognosis still needs to be confirmed by numerous clinical studies. (2) Physiological saline-infused radiofrequency ablation (NSRFA) and hydrochloric acid-enhanced radiofrequency ablation (HRFA) increases the conductivity around the radiofrequency electrode. The electrode can be placed in the center of the lesion, allowing the formation of an ablation zone larger than 5 cm with a single electrode, thus increasing the volume of ablation without serious complications. Thus, they are expected to be used for the treatment of large caudate lobe HCC.[35]

3.1.4. Reduction of serious complications such as bile duct injury and tumor implantation

To prevent the occurrence of bile duct injury, the electrode needs to be kept more than 5 mm from the bile duct[36]; and endoscopic nasobiliary drainage tube cooling[37] is a preventive measure against bile duct injury. To prevent tumor implantation, the use of larger electrodes and multiple perforations should be avoided, and the normal liver parenchyma should be crossed as far as possible before entering the tumor. There are special ablation techniques for tumors in special locations to avoid tumor implantation in the abdominal cavity. For example, ablation of exophytic HCC in the caudate lobe should be performed by ablating the intrahepatic portion first, blocking the blood supply to the exophytic portion, and gradually increasing the radiofrequency ablation energy, thus improving the safety of ablation.

3.1.5. Guidance modalities for thermal ablation

(1) Influenced by the deeper location of the caudate lobe, real-time ultrasound often displays poorly, which may easily cause damage to important structures along the puncture path. After guiding to complete ablation, it is still recommended to enhance CT to clarify residual lesions. (2) The 1-, 3-, and 5-year survival rates, and 1-, 3-, and 5-year disease-free survival (DFS) rates of stereo ultrasound guiding multi-needle RFA,[38] were roughly comparable with ultrasound-guided RFA[1]; and the value and safety of its application needs to be further investigated. (3) Some scholars[39] found that the LTP rate of ultrasonography-guided ablation was significantly lower than that of ultrasound, and the application of ultrasonography also has great potential. (4) Other scholars used CT-guided thermal ablation of HCC in the caudate lobe to achieve a complete ablation rate of 100% without serious complications.[40] (5) At present, combined guidance of ultrasound and CT has been applied in some studies, and Bao et al.[41] treated 33 cases of HCC in the caudate lobe with CT combined with ultrasound-guided MWA. The complete ablation rate was 100%, and the recurrence rate was only 9.3% in 8–16 months, but the incidence of surgery-related grade IV complications was still 2/33, which shows that the combined guidance is more effective, but still cannot completely guarantee the safety of ablation. In contrast, fusion imaging guidance techniques combining the advantages of real-time imaging with ultrasound or ultrasonography and high resolution CT or magnetic resonance imaging (MRI) have also been applied,[42,43] suggesting better safety and good prospects for application. (6) Laparoscopic or open ablation can significantly shorten the distance of needle puncture and has the significant advantage of allowing direct visualization of the lesion. In Jiang et al.'s study, laparoscopy-guided RFA was used to treat 27 cases of HCC in the caudate lobe with a mean diameter of 2.8 cm. The survival rates at 1, 2, 3, 4, and 5 years reached 96.3%, 88.9%, 74.1%, 74.1%, and 62.9%, respectively, while the DFS rates at 1, 2, 3, 4, and 5 years reached 92.6%, 52.9%, 44.4%, 33.3%, and 33.3%, with only minor adverse effects.[44] A similar study by Jiang et al.[45] treated 10 cases of tumors with an average diameter of 2.6 cm, and displayed a complete ablation rate of 100%, survival rates of more than 2 years in all cases, confirming safety and effectiveness.

3.2. Cryoablation

In recent years, the application of cryoablation has gradually increased, and several studies have found that cryoablation is significantly safer for HCC near the base of the diaphragm, the heart, or other vital organs.[46–49] Both studies[50,51] found that cryoablation significantly reduced major vascular complications such as peritumoral vascular thrombosis and liver infarction, and it was found to be more effective in controlling local tumor progression, comparable to radiofrequency ablation. In another study,[52] cryoablation for HCC in high-risk sites also significantly reduced the rate of local tumor progression compared with microwave ablation but did not improve the overall survival, or recurrence-free survival. However, it was less effective for tumors larger than 4 cm in diameter than for smaller tumors in terms of technical effectiveness, local tumor progression, and occurrence of adverse effects.[53] Minimum ablation margins <5 mm are also an important prognostic factor for cryoablation of LTP.[54] The use of multi-slice spiral CT guidance to improve efficacy and reduce complications has been suggested in a study.[55] The use of MRI-CT fusion imaging to evaluate cryoablation margins in hepatocellular carcinoma has also been suggested.[56] Despite the lack of clinical studies on cryoablation of caudate lobe HCC, cryoablation has shown very good potential application for the treatment thereof.

3.3. Chemical ablation

Ethanol ablation is less capable of complete ablation than thermal ablation, has a low effective margin reach rate, a high recurrence rate, and is only used for tumors less than 3 cm in diameter or lesions in high-risk locations such as near vessels. In theory, alcohol can destroy the vessels around the tumor, as well as tumors that may metastasize through microvessels after thermal ablation; or make the tissues around the electrode less susceptible to carbonization, promote heat conduction, and reduce the heat sink effect, which can be used as a complementary treatment to reduce the residual tumor after thermal ablation. But whether e*thanol ablation* can improve the prognosis of patients undergoing thermal ablation for caudate lobe carcinoma, remains to be proven. In contrast, other stronger chemical ablation agents, such as acetic acid and hydrochloric acid, demonstrate good efficacy in the ablation of tumors at other sites and may be a better choice for caudate lobe hepatocellular carcinoma.

4. Combination of various interventions

4.1. Transcatheter arterial chemoembolization combined with thermal ablation

Transcatheter arterial chemoembolization can reduce the heat dissipation effect of other arteries or portal vein57, and reduce the probability of tumor metastasis or tumor size to improve the safety of thermal ablation. In addition, segmental TACE can improve the visibility of small HCCs that are not easily detected by conventional examination through enhanced contrast or iodinated oil injection, making CT-guided percutaneous radiofrequency ablation possible.[58,59] Tissue necrosis after TACE can enhance the thermal ablation effect of RFA; moreover, tissue necrosis after thermal ablation makes it easier for chemotherapeutic agents to spread, so the two interventions can be mutually reinforcing. Studies on the treatment of HCC in the caudate lobe[32,60,61] have shown that although combined interventions are still subject to the inherent limitations of each intervention, the combination of the two significantly increased the rate of complete tumor destruction, which could reach 90–100%, with survival rates of 100%, 80.8% and 80.8% at 1, 3 and 5 years for HCC in the caudate lobe with a diameter <2 cm.[60] For HCC in the caudate lobe within *Milan* Criteria, 1-, 3- and 5-year survival rates of 94.4%, 86.6%, and 67.5%, respectively, were achieved,[32] which are significantly higher than those of studies with superselective TACE

alone.[2,8] In addition, the reproducibility of the combination therapy may also significantly improve OS. This therapy has shown good efficacy in large HCC in the caudate lobe in one study,[62] which has achieved a mean survival of more than 2 years by treating 5.0–8.1 cm diameter tumors with TACE combined with hydrochloric acid-enhanced RFA. However, some scholars[63] concluded that there are no differences in LTP, OS, and RFS between TACE-RFA and RFA for patients with small (≤3 cm) HCC. Therefore, TACE-RFA was not recommended for the first-line treatment of small HCC. However, Kim et al.[63] have shown that TACE-RFA is better than TACE alone for small HCC and is therefore recommended for situations where RFA is not appropriate. In contrast, Fujimori et al.[32] recommended combination therapy for patients with intrahepatic tumors smaller than 5 cm in diameter and liver function Child-Pugh scores equal to or less than 7. In their study[64] treating HCC at other sites, Liu et al. found that combination therapy induces more thrombosis or segmental liver infarction than RFA monotherapy. In the study of Hyun et al.,[60] combination intervention for HCC in the caudate lobe also identified one case of portal vein thrombosis resulting in asymptomatic liver infarction. This is possibly because the reduced heat dissipation effect of TACE increased the likelihood of large vein thrombosis. Previous studies have reported complications after TACE-RFA, including liver infarction, liver failure, bile duct stricture with cholestasis, liver abscess, and arterial hemorrhage.[65] It has also been shown that the combination of TACE and RFA can increase the incidence of complications.[63] However, it is clear from the available studies[32,60,61] that all complications, with the exception of the increased likelihood of liver infarction due to portal vein thrombosis, may occur with a single intervention. Therefore, clinical decisions should be made by assessing the risk of venous thrombosis and reducing the possible complications of a single intervention by various measures to prevent a superposition of the respective complications.

4.2. Transcatheter arterial chemoembolization combined with chemical ablation

Percutaneous transhepatic chemotherapy-lipiodol injection (PTCLI) has good tracer properties and conformability, and reduces damage to the normal liver, so it has great value for application. Dai et al.[66] compared TACE combined with PTCLI or RFA for the treatment of HCC and found that PTCLI treatment had fewer complications and good results. Liu et al.[67] found that the complete inactivation rate of TACE combined with PTCLI for giant HCC was 58.3% (42/72), which was higher than the 31.8% (14/44) in the combined MWA treatment group. One study[68] used TACE and CT-guided PTCLI to treat exophytic HCC in the caudate lobe without serious complications such as liver failure, tumor necrosis, and hemorrhage from tumor rupture, showing that it is safe and reliable.

4.3. Cryoablation combined with other interventional methods

Cryoablation has also been used in combination with other interventional methods. Combining cryoablation with radiofrequency ablation to take advantage of their respective strengths can ensure the efficacy and safety of the treatment. It has also been found that the total clinical efficacy of TACE combined with cryoablation for unresectable large hepatocellular carcinoma can reach 93.5% with an overall adverse effect rate of only 12.9%, thus effectively improving the cellular immunity of patients.[69]

5. Ultrasound endoscopy

Ultrasound endoscopy-guided laser ablation for HCC in the caudate lobe has been reported.[70] The study showed that it significantly reduced complications, but further studies are required to establish the efficacy thereof. Ultrasound endoscopy-guided thermal ablation and chemical ablation have been used for the treatment of liver carcinoma in other areas and have great potential for the treatment of caudate lobe liver carcinoma.

6. Multidisciplinary treatment

6.1. Combination of interventional therapy with immunotherapy or molecular targeted therapy

Ablative therapy can induce peripheral immune responses. One study showed that combined immunotherapy can still be safe for the treatment of advanced HCC with complications such as hepatic insufficiency, rash, pruritus, autoimmune pneumonia, colitis, and thyroid dysfunction.[71] A prospective study found that sequential nonspecific immunotherapy after RFA was effective in extending the overall survival time of patients with early-stage HCC compared with RFA alone.[72] A retrospective study by Yang et al.[73] found 86.6%, 77.4%, and 66.0% disease control rates at 1, 3, and 6 months, respectively, in TACE combined with immunotherapy for intermediate-stage hepatocellular carcinoma. Although one case of fatal lung injury, abnormal thyroid function and reactive cutaneous capillary hyperplasia occurred in most patients, the efficacy was still greater. A randomized controlled trial[74] and a retrospective study[75] confirmed that TACE combined with sorafenib significantly improved the efficiency of treatment relative to TACE alone. Another retrospective study[76] found that TACE combined with sorafenib for inoperable patients was well tolerated and safe, although toxic side effects associated with sorafenib were observed.

6.2. Combination of interventional therapy with radiation therapy

Radiation therapy alone has been used in the treatment of caudate lobe HCC and has shown positive outcomes.[77–79] Other radiation therapy methods, such as stereotactic radiation therapy and selective internal radiation therapy (SIRT), have been used as additional options for local treatment. Brachytherapy can be used for the treatment of residual caudate lobe tumors that cannot be completely ablated. In an existing study,[80] transarterial chemoembolization and I^{125} seed implantation for caudate lobe HCC had an objective response rate of 60.0% and a median OS of 35 months, while biliary tract injury only occurred in about 5% of cases, suggesting that it could become a new treatment option.

6.3. Combination of interventional therapy with surgery etc.

Interventional therapy has been used in combination with surgery, radiotherapy, and targeted therapy. One study[81] has used hepatic artery embolization prior to surgery and concluded that it improves the prognosis of patients without significantly increasing the difficulty or reducing the safety of the procedure. On the other hand, it is now also recommended that small resectable tumors should be avoided for local treatment.[82]

7. Summary

In the interventional treatment of hepatocellular carcinoma in the caudate lobe, the efficacy of super-selective TACE is still influenced by the multiple origins of the caudate lobe arteries, pending the development of hepatic arteriography techniques. Combining multiple image-guided methods can improve the efficacy and safety of ablative interventions. The sequential combination of multiple intervention methods is the trend of interventional treatment for HCC in the caudate lobe. Multidisciplinary treatment is also essential to improve the prognosis of patients with HCC in the caudate lobe.

Declaration of competing interest

The authors declare no conflict of interest.

References

1. Xie W, Tan J, Li B, et al. Comparison of hepatic resection with percutaneous ablation for hepatocellular carcinoma in the caudate lobe within milan criteria. *J Gastrointest Surg*. 2022;26:323–332.
2. Lee BC, Liu KL, Wu CH, et al. Comparison of radiofrequency ablation and transarterial chemoembolization for hepatocellular carcinoma in the caudate lobe. *Cardiovasc Intervent Radiol*. 2018;41:1699–1707.
3. Yan L, Ren Y, Qian K, et al. Superselective transarterial chemoembolization for unresectable or "ablation unsuitable" hepatocellular carcinoma in the caudate lobe: a real world, single-center retrospective study. *Front Oncol*. 2021;11, 678847.
4. Braat MN, van den Hoven AF, van Doormaal PJ, et al. The caudate lobe: the blind spot in radioembolization or an overlooked opportunity? *Cardiovasc Intervent Radiol*. 2016;39:847–854.
5. Kim HC, Miyayama S, Chung JW. Selective chemoembolization of caudate lobe hepatocellular carcinoma: anatomy and procedural techniques. *Radiographics*. 2019; 39:289–302.
6. Yoon CJ, Chung JW, Cho BH, et al. Hepatocellular carcinoma in the caudate lobe of the liver: angiographic analysis of tumor-feeding arteries according to subsegmental location. *J Vasc Intervent Radiol*. 2008;19:1543–1550. quiz 1550.
7. Miyayama S, Yamashiro M, Yoshie Y, et al. Hepatocellular carcinoma in the caudate lobe of the liver: variations of its feeding branches on arteriography. *Jpn J Radiol*. 2010;28:555–562.
8. Kim HC, Chung JW, Jae HJ, et al. Caudate lobe hepatocellular carcinoma treated with selective chemoembolization. *Radiology*. 2010;257:278–287.
9. Yuan HJ, Liu FY, Li X, et al. Clinical effect of ultraselective transcatheter arterial chemoembolization in treatment of hepatocellular carcinoma originating from the caudate lobe: an analysis of 13 cases. *Zhonghua Gan Zang Bing Za Zhi*. 2017;25: 744–748 (Chinese).
10. Wang HM, Zhao Y, Zhang JH, et al. Transcatheter hepatic artery chemoembolization for caudate lobe liver cancer. *Chin J Clin*. 2012;6:1060–1061.
11. Miyayama S, Yamashiro M, Hattori Y, et al. Angiographic evaluation of feeding arteries of hepatocellular carcinoma in the caudate lobe of the liver. *Cardiovasc Intervent Radiol*. 2011;34:1244–1253.
12. Miyayama S, Yamashiro M, Sugimori N, et al. Blood supply to the caudate lobe of the liver from the right inferior phrenic artery: observation by cone-beam computed tomography during arteriography. *Abdom Radiol (NY)*. 2020;45:2851–2861.
13. Miyayama S, Yamashiro M, Shibata Y, et al. Arterial blood supply to the caudate lobe of the liver from the proximal branches of the right inferior phrenic artery in patients with recurrent hepatocellular carcinoma after chemoembolization. *Jpn J Radiol*. 2012;30:45–52.
14. Woo S, Kim HC, Chung JW, et al. Chemoembolization of extrahepatic collateral arteries for treatment of hepatocellular carcinoma in the caudate lobe of the liver. *Cardiovasc Intervent Radiol*. 2015;38:389–396.
15. Choi WS, Kim HC, Hur S, et al. Role of C-arm CT in identifying caudate arteries supplying hepatocellular carcinoma. *J Vasc Intervent Radiol*. 2014;25:1380–1388.
16. Miyayama S, Yamashiro M, Okuda M, et al. Main bile duct stricture occurring after transcatheter arterial chemoembolization for hepatocellular carcinoma. *Cardiovasc Intervent Radiol*. 2010;33:1168–1179.
17. Liu M, Lin MX, Lu MD, et al. Comparison of contrast-enhanced ultrasound and contrast-enhanced computed tomography in evaluating the treatment response to transcatheter arterial chemoembolization of hepatocellular carcinoma using modified RECIST. *Eur Radiol*. 2015;25:2502–2511.
18. Soga S, Kuwamura H, Edo H, et al. Double balloon-occluded transarterial chemoembolization (double B-TACE) for hepatocellular carcinomas located in the caudate lobe. *Cardiovasc Intervent Radiol*. 2020;43:162–164.
19. Dou JP, Yu J, Cheng ZG, et al. Ultrasound-guided percutaneous microwave ablation for hepatocellular carcinoma in the caudate lobe. *Ultrasound Med Biol*. 2016;42: 1825–1833.
20. Zhou YZ, Zhu RL, Wang ZZ, et al. Curative effect analysis of ultrasound-guided percutaneous radiofrequency ablation for caudate lobe hepatocellular carcinoma. *Zhonghua Gan Zang Bing Za Zhi*. 2021;29:690–695 (Chinese).
21. Peng Y, Cui D, Li W, et al. Ultrasound-guided percutaneous microwave ablation for hepatocellular carcinoma originating in the caudate lobe: a pilot clinical study. *J Cancer Res Therapeut*. 2021;17:764–770.
22. Cui D, Ding M, Li WJ, et al. Ultrasound-guided percutaneous microwave ablation in the treatment of large hepatocellular carcinoma in the cauda lobe(a report of 13 cases). *Liver*. 2020;25:355–358.
23. Chen X. *Clinical Study of Ultrasound-Guided Radiofrequency Ablation in the Treatment of Malignant Tumors of the Caudate Lobe of Liver with Diameter ≤5cm*. Zhengzhou University; 2019:1–47.
24. Li Q, Liu CC, Gao HD, et al. Comparison of ultrasound-guided percutaneous radiofrequency ablation and surgical resection in the treatment of hepatocellular carcinoma of caudate lobe. *Liver*. 2020;25:693–694, 698.
25. Kariyama K, Nouso K, Wakuta A, et al. Percutaneous radiofrequency ablation for treatment of hepatocellular carcinoma in the caudate lobe. *AJR Am J Roentgenol*. 2011;197:W571–W575.
26. Nishigaki Y, Tomita E, Hayashi H, et al. Efficacy and safety of radiofrequency ablation for hepatocellular carcinoma in the caudate lobe of the liver. *Hepatol Res*. 2013;43:467–474.
27. Liu B, Long J, Wang W, et al. Predictive factors of treatment outcomes after percutaneous ablation of hepatocellular carcinoma in the caudate lobe: a retrospective study. *BMC Cancer*. 2019;1:699.
28. Kwon HJ, Kim PN, Byun JH, et al. Various complications of percutaneous radiofrequency ablation for hepatic tumors: radiologic findings and technical tips. *Acta Radiol*. 2014;55:1082–1092.
29. Cha DI, Lee MW, Rhim H, et al. Therapeutic efficacy and safety of percutaneous ethanol injection with or without combined radiofrequency ablation for hepatocellular carcinomas in high risk locations. *Korean J Radiol*. 2013;14:240–247.
30. Kim YJ, Lee MW, Park HS. Small hepatocellular carcinomas: ultrasonography guided percutaneous radiofrequency ablation. *Abdom Imag*. 2013;38:98–111.
31. Kim JW, Shin SS, Heo SH, et al. Ultrasound-guided percutaneous radiofrequency ablation of liver tumors: how we do it safely and completely. *Korean J Radiol*. 2015; 16:1226–1239.
32. Fujimori M, Takaki H, Nakatsuka A, et al. Combination therapy of chemoembolization and radiofrequency ablation for the treatment of hepatocellular carcinoma in the caudate lobe. *J Vasc Intervent Radiol*. 2012;23:1622–1628.
33. Hirooka M, Ochi H, Hiraoka A, et al. Multipolar versus monopolar radiofrequency ablation for hepatocellular carcinoma in the caudate lobe: results of a propensity score analysis. *Hepatol Res*. 2017;47:658–667.
34. Seror O, N'Kontchou G, Van Nhieu JT, et al. Histopathologic comparison of monopolar versus no-touch multipolar radiofrequency ablation to treat hepatocellular carcinoma within Milan criteria. *J Vasc Intervent Radiol*. 2014;25: 599–607.
35. Deng HX, Huang JH, Lau WY, et al. Hydrochloric acid enhanced radiofrequency ablation for treatment of large hepatocellular carcinoma in the caudate lobe: report of three cases. *World J Clin Cases*. 2019;7:508–515.
36. Liu N, Gao J, Liu Y, et al. Determining a minimal safe distance to prevent thermal injury to intrahepatic bile ducts in radiofrequency ablation of the liver: a study in dogs. *Int J Hyperther*. 2012;28:210–217.
37. Ogawa T, Kawamoto H, Kobayashi Y, et al. Prevention of biliary complication in radiofrequency ablation for hepatocellular carcinoma-Cooling effect by endoscopic nasobiliary drainage tube. *Eur J Radiol*. 2010;73:385–390.
38. Schullian P, Laimer G, Putzer D, et al. Stereotactic radiofrequency ablation of primary liver tumors in the caudate lobe. *HPB*. 2020;22:470–478.
39. Liu F, Yu X, Liang P, et al. Contrast-enhanced ultrasound-guided microwave ablation for hepatocellular carcinoma inconspicuous on conventional ultrasound. *Int J Hyperther*. 2011;27:555–562.
40. Dong J, Li W, Zeng Q, et al. CT-guided percutaneous step-by-step radiofrequency ablation for the treatment of carcinoma in the caudate lobe. *Medicine (Baltim)*. 2015; 94, e1594.
41. Bao XZ. The clinical efficacy and safety of CT combined with ultrasound-guided microwave ablation in the treatment of patients with caudate lobe liver cancer. *Med Equip*. 2019;32:81–82.
42. Lee MW, Rhim H, Cha DI, et al. Percutaneous radiofrequency ablation of hepatocellular carcinoma: fusion imaging guidance for management of lesions with poor conspicuity at conventional sonography. *AJR Am J Roentgenol*. 2012;198: 1438–1444.
43. Kunishi Y, Numata K, Morimoto M, et al. Efficacy of fusion imaging combining sonography and hepatobiliary phase MRI with Gd-EOB-DTPA to detect small hepatocellular carcinoma. *AJR Am J Roentgenol*. 2012;198:106–114.
44. Jiang K, Zhang W, Su M, et al. Laparoscopic radiofrequency ablation of solitary small hepatocellular carcinoma in the caudate lobe. *Eur J Surg Oncol*. 2013;39:1236–1242.
45. Jiang K, Su M, Liu Y, et al. The feasibility and safety of laparoscopic one-off complete radiofrequency ablation for hepatocellular carcinoma in caudate lobe. *Med J Chin Peoples Lib Army*. 2013;38:355–358.
46. Wang L, Liu C, Liu J, et al. MRI-guided cryoablation of hepatic dome hepatocellular carcinomas using 1-T open high-field-strength scanner. *AJR Am J Roentgenol*. 2019; 212:1361–1369.
47. Kwon JH, Won JY, Han K, et al. Safety and efficacy of percutaneous cryoablation for small hepatocellular carcinomas adjacent to the heart. *J Vasc Intervent Radiol*. 2019; 30:1223–1228.
48. Ma J, Wang F, Zhang W, et al. Percutaneous cryoablation for the treatment of liver cancer at special sites: an assessment of efficacy and safety. *Quant Imag Med Surg*. 2019;9:1948–1957.
49. Zhang W, Gao X, Sun J, et al. Percutaneous argon-helium cryoablation for small hepatocellular carcinoma located adjacent to a major organ or viscus: a retrospective study of 92 patients at a single center. *Med Sci Mon Int Med J Exp Clin Res*. 2021;27, e931473.
50. Kim R, Kang TW, Cha DI, et al. Percutaneous cryoablation for perivascular hepatocellular carcinoma: therapeutic efficacy and vascular complications. *Eur Radiol*. 2019;29:654–662.
51. Cha SY, Kang TW, Min JH, et al. RF ablation versus cryoablation for small perivascular hepatocellular carcinoma: propensity score analyses of mid-term outcomes. *Cardiovasc Intervent Radiol*. 2020;43:434–444.
52. Zhou L, Chen CX, Pan ZB, et al. Ultrasound -guided percutaneous microwave ablation versus cryoablation for treatment of hepatocellular carcinoma on the high-risk location. *Chin J Interv Radiol (Electr Ed)*. 2019;7:190–196.
53. Glazer DI, Tatli S, Shyn PB, et al. Percutaneous image-guided cryoablation of hepatic tumors: single-center experience with intermediate to long-term outcomes. *AJR Am J Roentgenol*. 2017;209:1381–1389.
54. Kim DK, Han K, Won JY, et al. Percutaneous cryoablation in early stage hepatocellular carcinoma: analysis of local tumor progression factors. *Diagn Interv Radiol*. 2020;26:111–117.
55. Yan QH, Xu DG, Shen YF, et al. Observation of the effect of targeted therapy of 64-slice spiral CT combined with cryoablation for liver cancer. *World J Gastroenterol*. 2017;23:4080–4089.
56. Chen C, Xu LC, Wang Y, et al. Assessment of the cryoablation margin using MRI-CT fusion imaging in hepatic malignancies. *Clin Radiol*. 2019;74:652.e21–652.e28.
57. Hyun D, Cho SK, Shin SW, et al. Treatment of small hepatocellular carcinoma (≤2 cm) in the caudate lobe with sequential transcatheter arterial chemoembolization and radiofrequency ablation. *Cardiovasc Intervent Radiol*. 2016;39:1015–1022.

58. Yamakado K, Nakatsuka A, Takaki H, et al. Subphrenic versus nonsubphrenic hepatocellular carcinoma: combined therapy with chemoembolization and radiofrequency ablation. *AJR Am J Roentgenol*. 2010;194:530–535.
59. Takaki H, Yamakado K, Sakurai H, et al. Radiofrequency ablation combined with chemoembolization: treatment of recurrent hepatocellular carcinomas after hepatectomy. *AJR Am J Roentgenol*. 2011;197:488–494.
60. Hyun D, Cho SK, Shin SW, et al. Treatment of small hepatocellular carcinoma (≤2 cm) in the caudate lobe with sequential transcatheter arterial chemoembolization and radiofrequency ablation. *Cardiovasc Intervent Radiol*. 2016;39:1015–1022.
61. Sheng SP, Sun B, Zheng JS, et al. Transcatheter hepatic arterial chemoembolization combined with CT guided radiofrequency ablation for treatment of primary liver cancer in caudate lobe. *Chin J Interventional Imaging Ther*. 2017;14:391–395.
62. Deng HX, Huang JH, Lau WY, et al. Hydrochloric acid enhanced radiofrequency ablation for treatment of large hepatocellular carcinoma in the caudate lobe: report of three cases. *World J Clin Cases*. 2019;7:508–515.
63. Kim W, Cho SK, Shin SW, et al. Combination therapy of transarterial chemoembolization (TACE) and radiofrequency ablation (RFA) for small hepatocellular carcinoma: comparison with TACE or RFA monotherapy. *Abdom Radiol (NY)*. 2019;44:2283–2292.
64. Liu BX, Kuang M, Lei YY, et al. Ultrasound-guided percutaneous radiofrequency ablation to treat hepatocellular carcinoma in the caudate lobe. *Chin J Hepatobil Surg*. 2018;24:654–658.
65. Liu Z, Gao F, Yang G, et al. Combination of radiofrequency ablation with transarterial chemoembolization for hepatocellular carcinoma: an up-to-date meta-analysis. *Tumour Biol*. 2014;35:7407–7413.
66. Dai QM, Chen Y, He L, et al. Sequential combination therapy of three minimally invasive methods for the treatment of massive hepatocellular carcinoma. *J Clin Res*. 2010;27:1050–1053.
67. Liu WY. *Contrastive Study of the Treatment for Solitary Large HCCs Using TACE Plus Percutaneous Transhepatic Chemotherapy-Lipiodol Injection and MWA Respectively*. Southern Medical University; 2018:1–50.
68. Wu HJ, Cui N, Li GJ, et al. The imaging features and interventional treatment of exogenous caudate lobe liver cancer. *Chin J Gen Surg*. 2011;5:42–44.
69. Xu W, Wang X, Wu ZY, et al. Efficacy of transcatheter arterial chemoembolization combined with cryoablation for unresectable large hepatocellular carcinoma and the effect on cellular immunity. *Chin J Clinic Oncol Rehabil*. 2019;26:1039–1042.
70. Di Matteo F, Grasso R, Pacella CM, et al. EUS-guided Nd:YAG laser ablation of a hepatocellular carcinoma in the caudate lobe. *Gastrointest Endosc*. 2011;73:632–636.
71. Duffy AG, Ulahannan SV, Makorova-Rusher O, et al. Tremelimumab in combination with ablation in patients with advanced hepatocellular carcinoma. *J Hepatol*. 2017;66:545–551.
72. Yao SY, Zhou JP, Chen YY, et al. Radiofrequency ablation combined with non-specific sequential immunotherapy for early hepatocellular carcinoma: a prospective study. *Chin J Gen Surg*. 2018;17:377–382.
73. Yang Qiuyu, Ning Wei, Xu Hao, et al. Correlation analysis of short-term efficacy and efficacy of TACE combined with camrelizumab in the treatment of advanced liver cancer. *J Med Imag*. 2021;31:1212–1219.
74. Xu X, Meng Q. Drug effect analysis of sorafenib combined with transcatheter arterial chemoembolization in the treatment of advanced hepatocellular carcinoma. *Pak J Pharm Sci*. 2018;31(4):1751–1755. Special.
75. Yue Yanxiao, Ning Shangkun, Liu Jibing, et al. Comparative analysis of the efficacy of interventional therapy and interventional therapy combined with targeted drugs for advanced primary liver cancer. *Chin J Oncol Prevent Treat*. 2021;28:788–791.
76. Liu Guangyu, Liu Ying, Zhang Yuewei. TACE combined with sorafenib in the treatment of advanced HCC preliminary evaluation of the efficacy and safety. *Electr J Liver Tumor*. 2018;5:19–23.
77. Iizumi T, Okumura T, Sekino Y, et al. Long-term clinical outcomes of patients receiving proton beam therapy for caudate lobe hepatocellular carcinoma. *J Radiat Res*. 2021;62:682–687.
78. Lee SU, Yoon SM, Cheng JC, et al. Multi-institutional retrospective study of radiotherapy for hepatocellular carcinoma in the caudate lobe. *Front Oncol*. 2021;11, 646473.
79. Okazaki S, Shibuya K, Shiba S, et al. Carbon ion radiotherapy for patients with hepatocellular carcinoma in the caudate lobe carbon ion radiotherapy for hepatocellular carcinoma in caudate lobe. *Hepatol Res*. 2021;51:303–312.
80. Yan L, Chen L, Qian K, et al. Caudate lobe hepatocellular carcinoma treated with sequential transarterial chemoembolization and iodine 125 seeds implantation: a single-center retrospective study. *Cancer Manag Res*. 2021;13:3901–3912.
81. Wu XS, Li ML, Wu WG, et al. The role of preoperative TACE on hepatocellular carcinoma located in caudate lobe. *Zhonghua Wai Ke Za Zhi*. 2013;51:780–783 (Chinese).
82. Chung YK, Hwang S, Ko GY, et al. Long-term complete response after transcatheter arterial chemoembolization and stereotactic body radiation therapy in a patient with hepatocellular carcinoma at the caudate lobe. *Ann Hepatobiliary Pancreat Surg*. 2018;22:274–281.