Percutaneous Radiofrequency Ablation Treatment of Hepatocellular Carcinoma in Caudate Lobe Using Expandable Electrodes

Somrach Thamtorawat, M.D.*, Torpong Claimon, M.D., Satit Rojwatcharapibarn, M.D.*, Pradesh Ghimire, M.D.*, Trongtum Tongdee, M.D.*, Jirawadee Yodying, M.D. * Walailak Chaiyasoot, M.D.***

**Department of Radiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand, **Department of Radiology, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok 10300, Thailand.*

ABSTRACT

Objective: To evaluate the outcome of radiofrequency (RF) ablation using expandable electrodes in the treatment of hepatocellular carcinoma (HCC) located in the caudate lobe.

Materials and Methods: Between January 2011 and April 2017, 29 consecutive patients with HCC at the caudate lobe were treated with RF ablation using expandable electrodes. The electrodes were placed on the targeted tumor under combined ultrasound and computed tomography (CT) guidance for each tumor in all the patients. Out of the 29 cases, 19 (65.5%) were accessed via the left hepatic lobe. The technical success, primary efficacy, local tumor progression, secondary efficacy, overall survival, and complications were evaluated. Univariate analysis was performed of the various prognostic factors for technical success, primary efficacy, and local tumor progression.

Results: The technical success rate was 86.2%, primary efficacy was 89.7%, and secondary efficacy was 82.8%. The local tumor progression (LTP) rate was 12.3% at one year and 31.5% at two years. The median time of LTP was 6.9 months. The overall survival rate was 85.8% at one year and 57.1% at two years. Ten patients died during the follow-up period (mean 22.5 months; with a range of 3.6–53.2 months). A minor complication of asymptomatic biloma was found in one patient (3.5%). Small-sized tumors (≤2 cm) and Spiegel's lobe location had significantly better treatment outcomes (p = 0.007 and 0.045, respectively).

Conclusion: Radiofrequency ablation using expandable electrodes is feasible and safe in treating HCCs located in the caudate lobe, especially for small-sized tumors (≤2 cm).

Keywords: Caudate lobe; Expandable electrodes; Hepatocellular carcinoma; Radiofrequency ablation (Siriraj Med J 2021; 73: 541-548)

INTRODUCTION

Treatment of hepatocellular carcinoma (HCC) in the caudate lobe, to date, is challenging due to the deep location; proximity to the IVC and main portal vein; the unique anatomy of the caudate lobe, including the arterial feeder, the portal venous supply, and the draining vein (directly to the IVC), and the complex biliary drainage, either by surgical resection, or through percutaneous ablation, or via transarterial treatment.[1-4]

With regard to the surgical resection of HCC in the caudate lobe, Tanaka et al.'s study in 20 patients showed a relatively poor prognosis compared to procedures

Corresponding author: Satit Rojwatcharapibarn
E-mail: satit.roj@mahidol.ac.th
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ORCID ID: https://orcid.org/0000-0003-4079-9104
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performed at other locations, owing to the intraoperative blood loss, longer duration of operation, higher chances of post-operative complications, and more frequent intrahepatic recurrent rate, and a significantly poor survival rate.[3]

There are a limited number of studies on percutaneous RF ablation of HCC in the caudate lobe. Seror et al. studied 10 cases that underwent percutaneous RF ablation in the caudate lobe, with 8 cases being HCC. All the procedures were performed using single straight needle electrode. The results showed that percutaneous RF ablation had a high technical success rate (about 90%), without major complications. However, the local recurrence rate was relatively high, compared to other locations, possibly due to the heat sink effect from the adjacent large vessels, which made it hard to achieve an adequate ablation margin.[5]

In Yamakado et al.'s study, percutaneous RF ablation was performed in 6 cases of HCC in the caudate lobe, also, using a single straight needle electrode.[6] The difference was in the use of CT scan as imaging guidance in all the cases. The results showed not only a higher technical success rate of 100%, but also had the ability to achieve local tumor control in all the cases, with a mean follow-up period of 10 months.

Nishigaki et al.'s study in 2012 performed percutaneous RF ablation in 20 patients with HCC in the caudate lobe, which also showed similar results, with a 100% technical success rate without major complications. In these cases, however, the local recurrence rate was relatively high (22.3%) compared to at the other locations (4.5%).[7]

With regard to an alternative treatment of HCC in the caudate lobe with transarterial chemoembolization (TACE), Kim et al. showed that the key to achieving treatment efficacy was a successful super-selection of the caudate artery. However, local tumor progression (LTP) was still relatively high (about 64%).[8]

In terms of combined treatment using TACE and RF ablation for treating HCC in the caudate lobe, Fujimori et al. (2012) and Hyun et al. (2016) also used a single straight electrode needle in both studies.[9,10] Similar results were noted, without significant difference in the results between RF ablation used alone and in combined treatment regarding the local tumor control. However, with regard to the survival rate, the combined treatment was seen to be better.[11,12] For some small HCCs, combined treatment is effective that are not visible in unenhanced CT and ultrasound.[13]

Since relatively fewer studies have been reported regarding the use of percutaneous RF ablation for the treatment of HCC in the caudate lobe, and all the prior studies used a non-expandable RF ablation electrode, the purpose of this study was to evaluate the outcome of RF ablation using an expandable electrode in the treatment of HCC located in the caudate lobe in experienced hands.

MATERIALS AND METHODS

This is a retrospective study performed over the period January 2011 to April 2017. After approval from the institutional review board, with protocol number (Si 109/2017 (EC2)), the electronic records in the radiological information system (RIS) were searched for patients with HCC in the caudate lobe who had underwent RF ablation.

Out of a total of 1,292 ablation procedures in the liver, including 1,251 RF ablations, 19 IRE (irreversible electroporation), and 22 microwave ablations, the records of 29 patients with HCC at the caudate lobe treated with RF ablation by an expandable electrode were obtained. The patients included 21 males and 8 females with mean age of 65.4 ± 10.8 years old. All the patients had liver cirrhosis, mostly with an etiology of hepatitis B (n = 13) (Table 1). Child-Pugh classifications A and B were obtained in 24 patients and 5 patients, respectively. Serum alpha-fetoprotein (AFP) levels with the mean and median values of 109.0 and 5.69 ng/ml, respectively, (range, 1.0-2,444.0 ng/ml) were noted.

Tumor characteristics

The diagnosis of HCC at the caudate lobe was based on either the imaging criteria or the pathological results. The mean size of the tumor was 1.78 ± 0.80 cm (range 0.7 - 4.0 cm). Tumor size was classified into two categories (size ≤2 cm; n = 18, and >2 cm; n = 11). Location of the tumor was classified according to three sub-segments of the caudate lobe: Spiegel's lobe (48.3%), paracaval portion (41.4%), and caudate process (10.3%) (Table 1). There were 7 lesions (24.1%) that underwent TACE before the ablation treatment.

RF ablation procedure

Percutaneous RF ablation procedures were performed by one of the five interventional radiologists in our institution, who had at least three years' experience. The procedures were performed under intravenous sedation, using expandable RF electrodes (Leveen needle electrode; Boston Scientific, Marlborough, Massachusetts, USA). All the procedures were performed under combined ultrasound (iU22; Philips Healthcare, Amsterdam, the Netherlands) and CT (Optima CT660; GE Healthcare, Chicago, Illinois, USA) guidance, as the standard protocol in the institution. Depending on the tumor size and

TABLE 1. Patient demographics and tumor characteristics.

Patients' characteristics	
Age (years)	65.4 ± 10.8 (range, 34–84)
Sex (male: female)	21:8
Etiology of liver cirrhosis	
Chronic hepatitis B	13 (44.8%)
Chronic hepatitis C	7 (24.1%)
Cryptogenic cirrhosis	6 (20.7%)
NASH	2 (6.9%)
Alcoholic cirrhosis	1 (3.5%)
Child-Pugh classification	
A	24 (82.8%)
B	5 (17.2%)
AFP Median	5.69 ng/ml
	(range, 1.0–2,444.0)
Tumor characteristics	
Mean tumor size (cm)	1.78 ± 0.80 (range, 0.7–4.0)
Size classified	
≤ 2 cm	18 (62.1%)
> 2 cm	11 (37.9%)
Tumor location	
Spiegel's lobe	14 (48.3%)
Paracaval portion	12 (41.4%)
Caudate process	3 (10.3%)
Prior TACE treatment of the lesion	7 (24.1%)
Subcapsular location	18 (64.3%)
Perivascular location	16 (57.1%)

Abbreviations: NASH, Non-alcoholic steatohepatitis; AFP, Alpha-fetoprotein; TACE, Transarterial chemoembolization

the depth from the skin, the diameter and the length of the RF electrode were determined by the performing physicians. Three types of access route were used: supine approach through the left lobe, right anterior approach, and right posterior approach (Fig 1). The aim of the ablation treatment was to cover the visualized tumor area and to generate a sufficient ablation zone of at least 5 mm margin, which was could be as an echogenic cloud on the real-time ultrasonography.

The imaging assessment protocol at this institution includes multiphase CT of the liver or MRI of the liver with a hepatocyte specific agent; performed at 1, 3, 6, 9, and 12 months after the ablation, and thereafter every 3-6 months. The treatment response definitions were based on the Society of Interventional Radiology Standardization of Terminology and Reporting.[14]

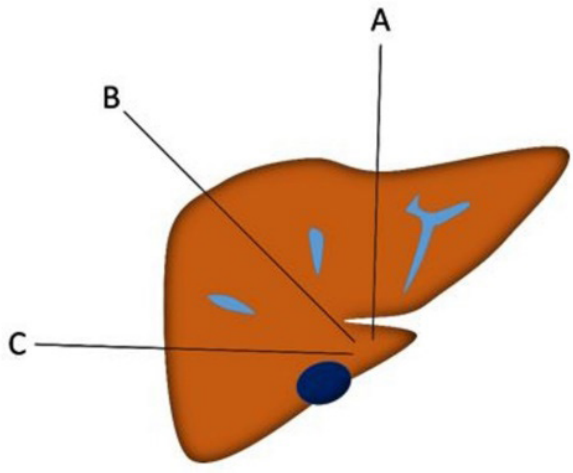


Fig 1. Schematic diagram showing three access sites for the caudate lobe approach;
A. – left lobe approach
B. – right anterior approach
C. – right posterior approach

Treatment response assessment

Technical success was determined as complete ablation of a targeted tumor at one month imaging follow-up. Primary efficacy was achieved if there was disappearance of the tumor at the ablation site without evidence of a residual viable tumor at three months imaging follow-up. Local tumor progression (LTP) was determined as any imaging follow-up after three months showing evidence of a recurrent tumor. Secondary efficacy was defined as successful local tumor control by re-ablation of the LTP using RF ablation.

Follow-up concluded at the time of death, liver transplantation, or the last clinical follow-up evaluation. The primary endpoints of the study were LTP and control of the tumor growth. The secondary endpoint of the study was the overall survival rate.

Complications were analyzed by imaging findings, clinical symptoms, and laboratory examinations after treatment and were ranked according to the SIR standard classification.[15]

Risk factors analyzed

Risk factors related to LTP include the tumor size, location of the tumor, proximity to the large vessels, and proximity from the liver capsule and the adjoining critical organs that might be injured during ablation. Perivascular location was established as the tumor abutting vessels >3 mm in diameter. Subcapsular location was defined as a tumor located less than 10 mm from the liver capsule. Adjoining critical organs at risk were contemplated if located <10 mm from the tumor.

Statistical analysis

Analysis of the data was done by using the chi-square test to determine whether technical success, primary efficacy, secondary efficacy, and local tumor progression were related to the size of the tumor (classified as ≤2 cm and >2 cm), access route, and location of the tumor, prior to TACE treatment, and the Child–Pugh classification. Kaplan–Meier analysis was used to assess the survival rate and local tumor progression rate.

All the statistical analyses were performed using IBM SPSS Statistics for Windows version 23.0 (IBM Corporation, Armonk, New York). A difference with $p < 0.05$ was considered to be statistically significant.

RESULTS

Primary efficacy and technical success rate

Among the 29 patients treated by RF ablation using expandable electrodes, four lesions demonstrated residual disease upon imaging at one month after ablation. The technical success rate of the first session was 86.2%. One lesion had another RF ablation session and achieved complete tumor ablation within three months (Fig 2). Two lesions had re-ablation but the follow-up imaging still showed residual disease. In one lesion, re-ablation treatment was not performed because of multiple intrahepatic distant recurrence; hence TACE was performed instead. The primary efficacy rate was 89.7%, as 26 of the 29 tumors had complete tumor control at three months follow-up imaging.

Univariate analysis (Table 2) showed better technical success ($p = 0.014$) and primary efficacy ($p = 0.045$) in the smaller tumor group (≤2 cm), as compared to the larger tumor group (>2 cm). With regard to the location (Table 3), the technical success was statistically significant in the tumor located at Spiegel's lobe and in the caudate process (100% technical success; $p = 0.042$). In terms of the access site (Table 3), the primary efficacy was significantly better in the left lobe approach (100% primary efficacy; $p = 0.033$) compared to the right anterior or right posterior approach. The rest of the various tumor-related prognostic factors, such as the patient's age and sex, Child-Pugh score, prior TACE treatment of the lesions, perivascular or subcapsular location, vessel in ligamentum venosum, and the depth from the skin, showed no statistically significant results in both technical success and primary efficacy.

Local tumor progression rate and secondary efficacy rate

Local tumor progression (LTP) occurred in five of the 29 tumors. Two tumors were successfully treated by additional RF ablation with a secondary efficacy

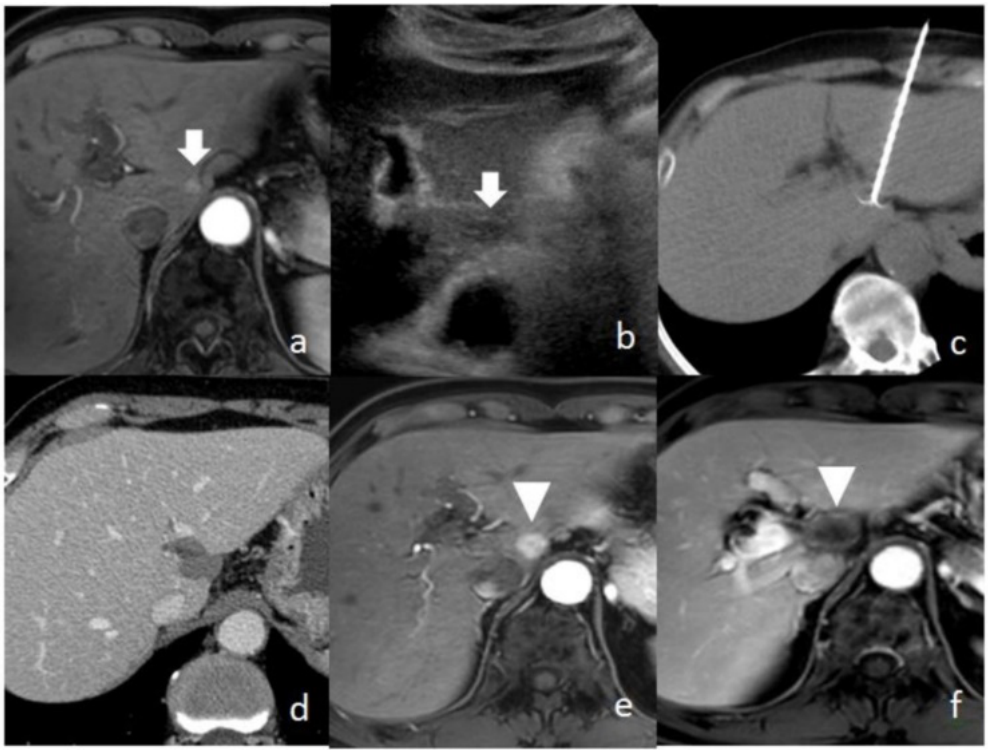


Fig 2. A 71 year-old man with a 1 cm HCC in Spiegel portion of caudate lobe (arrow in a, b) RF ablation was performed via anterior left lobe approach (c). CT after ablation showed complete ablation (d). At two years follow up, MRI showed local tumor progression (arrowhead in e). Second RF ablation was performed by using the same technique and complete ablation was achieved (arrowhead in f).

TABLE 2. Univariate analysis of the tumor characteristics and results between tumor size.

Variables	Tumor size ≤2 cm	Tumor size >2 cm	*P*-value
No. tumors	18	11	
Age (years)	68.6 ± 9.2	60.1 ± 11.6	.291
Sex			
Male	13 (72.2%)	8 (72.7%)	.976
Female	5 (27.8%)	3 (27.3%)	
Child–Pugh score			
A	13 (72.2%)	11 (100%)	.126
B	5 (27.8%)	0 (0%)	
Prior TACE treatment	2 (28.6%)	5 (71.4%)	.071
Location of tumor			
Spiegel lobe	11 (61.1%)	3 (27.3%)	
Paracaval portion	4 (22.2%)	8 (72.7%)	.024
Caudate process	3 (16.7%)	0 (0%)	
Perivascular	7 (41.2%)	9 (81.8%)	.054
Subcapsular	10 (58.8%)	8 (72.7%)	.689
Vessel in ligamentum venosum	2 (11.1%)	3 (27.3%)	.339
Access site			
Left lobe	14 (77.8%)	5 (45.5%)	
Right anterior	2 (11.1%)	3 (27.3%)	.267
Right posterior	2 (11.1%)	3 (27.3%)	
Results			
Technical success	18 (100%)	7 (63.6%)	.014
Primary efficacy	18 (100%)	8 (72.7%)	.045
LTP	3 (16.7%)	3 (37.5%)	.330
Secondary efficacy	17 (94.4%)	7 (63.6%)	.054

Abbreviations: TACE, Transarterial chemoembolization; LTP, Local tumor progression

TABLE 3. Univariate analysis of the prognostic factors for technical success, primary efficacy, and local tumor progression.

Variable	Technical success		Primary efficacy		Local tumor progression (LTP)	
	(%)	(*P*-value)	(%)	(*P*-value)	No LTP (%)	(*P*-value)
Prior TACE treatment						
Present	71.4%	0.238	85.7%	1.000	2 (33.3%)	0.596
Absent	90.9%		90.9%		4 (20.0%)	
Location of tumor						
Spiegel's lobe	100%		100%		4 (28.6%)	
Paracaval portion	66.7%	0.042	75%	0.136	2 (22.2%)	0.829
Caudate process	100%		100%		0 (0%)	
Vessel in ligamentum venosum						
Present	80%	0.553	80%	0.446	2 (50%)	0.218
Absent	87.5%		91.7%		4 (18.2%)	
Perivascular						
Present	75%	0.113	81.3%	0.238	5 (29.4%)	0.624
Absent	100%		100%		1 (12.5%)	
Subcapsular						
Present	88.9%	0.601	94.4%	0.284	3 (23.1%)	1.000
Absent	80%		80%		3 (25%)	
Access site						
Left lobe	94.7%		100%		5 (26.3%)	
Right anterior	60%	0.105	60%	0.033	0 (0%)	1.000
Right posterior	80%		80%		1 (25%)	

Abbreviation: TACE, Transarterial chemoembolization

rate of 82.8%. Three patients with LTP had no further ablation treatment due to disease progression. One developed pulmonary metastasis, another had concomitant cholangiocarcinoma proven by tissue biopsy and both were subjected to systemic chemotherapy. Another patient had deterioration of liver function and was treated with palliative care. Kaplan–Meier analysis showed LTP rates of 12.3% at one year and 31.5% at two years. The median time of LTP was 6.9 months (Fig 3A).

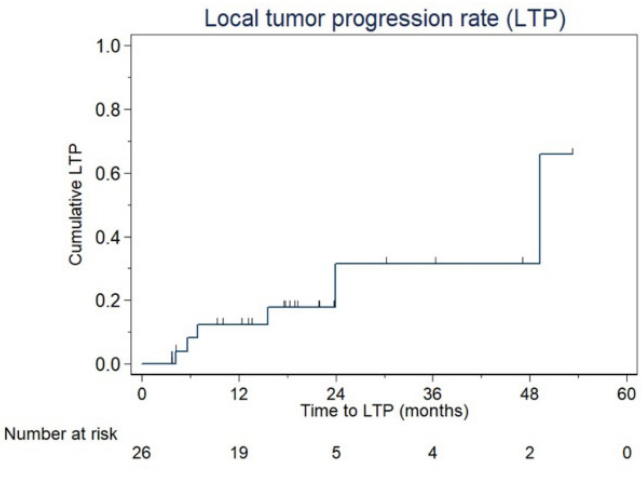
Univariate analysis also showed a high LTP rate and low secondary efficacy in the larger tumor group (>2 cm), but not significant statistically (p = 0.054). (Table 2).

Follow-up period and overall survival rate

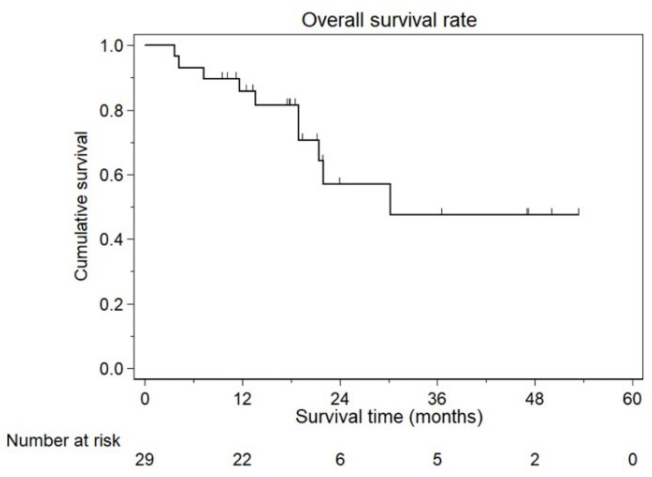
The mean follow-up period was 22.5 ± 14.3 months (range, 3.6–53.2 months). Ten patients died during the follow-up period. One patient underwent liver transplantation. The overall survival rate was computed by using Kaplan–Meier analysis, which showed survival rates of 85.8% at one year and 57.1% at two years (Fig 3B).

Complications

There were no major complications encountered. No procedure-related death occurred. Only one case developed a minor complication of asymptomatic biloma (3.5%), which resolved spontaneously.



3A



3B

Fig 3. Kaplan-Meier analysis; (A) Local tumor progression rate (B) Overall survival rate

DISCUSSION

For the curative treatment of HCC, RF ablation is an alternative to surgical resection. Nevertheless, the treatment of HCC located in the caudate lobe is still challenging to date due to the complex anatomy and deep location.[1-4]

This study showed an 86.2% technical success rate and 89.6% primary efficacy rate, which are comparable with the prior study by Seror et al. (2005), where treatment was done by RF ablation alone using non-expandable electrodes.[5] This study also used a combination of ultrasound and CT guidance for the needle electrode placement in all cases, which may have been a major key in achieving the technical success of the RF ablation in the tumors deeply situated in the caudate lobe. The advantage of the expandable electrode seems to be allowing a more precise estimation of the ablation zone, which can be visualized in the image guidance from the reconstructed non-contrast CT scan. However, a disadvantage is the difficulty to deploy the expandable electrode in the limited space of the caudate lobe.

This study demonstrated the advantage of the RF ablation of tumors in the caudate lobe using expandable electrodes in the smaller tumor group (≤2 cm), which showed better results with statistical significance for technical success (p = 0.014) and the primary efficacy (p = 0.045) compared to the larger tumor group (>2 cm). Similar results were reported by Hyun et al. using combined transarterial treatment with RF ablation.[10]

The LTP rate of the present study (12.3% at one year and 31.5% at two years) showed a higher rate compared to RF ablation done in other locations.[5-7] These could be due to multifactorial causes, like inadequate ablation margins, difficulty of needle repositioning in the limited space of the caudate lobe, and the heat sink effect due to the proximity to the large vessels, including the IVC and the main portal vein.

Regarding the access route of the RF electrode, this study mainly involved the use of the left lobe approach (65.5%), which was probably due to the majority of the tumors being located in the Spiegel's lobe (48.3%), which could be accessed by using this approach. The technical success rate of the left lobe approach also was the highest (94.7%) as long as the primary efficacy was 100%, also showing statistical significance (p = 0.033). This might be due to the tumors in the Spiegel's lobe seemingly able to be well-visualized in the ultrasonography, probably as the depth from the skin was mostly shorter compared to the other locations. Also there is likely less heat sink effect for tumors in the Spiegel's lobe because of the greater distance to the large vessels.

The left lobe approach may increase the risk of bleeding, due to the needle piercing the liver capsule twice and also penetrating the ligamentum venosum, in which an accessory/replaced left hepatic artery or accessory left gastric artery may be present.[5] A variant artery in ligamentum venosum causing a limitation for the left lobe approach was observed in five patients; comprising accessory left hepatic artery in four patients and accessory left gastric artery in one patient. Four of these were accessed by using the left lobe approach. There was no evidence of bleeding, but we need to be catious in this matter.

Limitations of this study include its retrospective design, non-randomized control, and small number of patients, which may have caused some selection bias

and a difference in the results. Multivariate analysis also itself has inherent limitations that need to be taken into account. A longer follow-up period should be achieved for a better evaluation of the overall survival and LTP.

In conclusion, radiofrequency ablation using expandable electrodes is feasible and safe in treating HCCs located in the caudate lobe, especially for small-sized tumors (≤2 cm).

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