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# Percutaneous ablation in perivascular-HCC: impact of liver parenchyma and characteristics of vascular structures on the outcomes

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AIM: Percutaneous radiofrequency ablation (RFA) is a standard treatment for small-HCC (<3 cm). However, some features such as proximity to intrahepatic vascular structures (perivascular location) seem to be related to short- and long-term outcomes. The aims of the study were to investigate the features related to ablation success and local tumor progression (LTP) in patients submitted to percutaneous ablation for perivascular-HCC.

MATERIALS AND METHODS: From January 2010 to May 2021, 132 perivascular-HCC nodules ablated with US-guided single probe percutaneous RFA were retrospectively analyzed. Univariate analysis and multivariable Cox regression model were used to identify factors that were independently related to ablation success and LTP-free survival.

RESULTS: The overall ablation success rate was 71.9% (n=95). Morbidity and mortality rates were 4.0% and 0.0%. The features related to ablation success: nodule size (≤20 mm vs. >20 mm) (OR 2.442, p=0.031), major vascular structures diameter (3–5 mm vs ≥ 5 mm) (OR 2.167, p=0.037) and liver parenchyma (cirrhosis vs no-cirrhosis) (OR 2.373, p=0.033). The following features resulted independently related to better LTP-free survival: nodule size ≤20 mm (HR 2.802, p=0.003), proximity to glissonean pedicles (HR 1.677, p=0.028), and major vascular structure diameter <5 mm (HR 1.987, p=0.041).

CONCLUSIONS: Perivascular location confirmed to be a difficult and unfavorable indication for percutaneous ablation for HCC nodules. However, perivascular nodules not suitable for surgery with low-risk features (size <20 mm, proximity to glissonian pedicles and vascular diameter <5 mm) may be treated with RFA with satisfactory outcomes.

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## Introduction

Hepatocellular carcinoma (HCC) represents about 80% of primary liver cancers, with an increasing incidence with advancing age in all populations. Liver cirrhosis represents the main risk factor, mostly associated with an evident etiology, such as chronic viral hepatitis (B or C), and alcohol intake.[1] Recently, metabolic associated fatty liver disease (MAFLD) is becoming a relevant cause of HCC, particularly in developed countries.[2–5] Based on this knowledge, surveillance's protocols, developed during years, could favor an early diagnosis and therefore the optimal tailored treatment.[6] According to Barcelona Clinic Liver Cancer (BCLC) guidelines, liver transplantation, surgical resection, and local ablative techniques, remain the curative therapeutic options among which to choose based on tumor burden, liver function and the patient's clinical condition. Local ablative techniques (LAT), as radiofrequency ablation (RFA) and microwave ablation (MWA), represent a standard of treatment in selected cases of HCC not fit for surgery, as a single HCC nodule <20 mm in diameter (very-early HCC, BCLC 0) and up to 3 nodules ≤30 mm (early HCC BCLC A).[7]

The mechanism of cell death in RFA is based on the frictional heat generated using high-frequency alternating current. Heat produces coagulative necrosis of the tumor and allows extension of the necrosis to a "safety ring" in the peri-tumoral tissue, which might eliminate small-undetected satellites.[8]

As emerged from randomized studies, LAT is effective as resection, with similar results in overall survival (OS) and disease-free survival (DFS), with the advantage of shorter hospitalization and less morbidity.[9–11] In addition, LAT could be considered as "bridge" or "downstaging" treatment prior to liver transplantation for reducing the drop-out rates due to the tumor progression.[12]

However, some features, such as nodule size and perivascular location, have been demonstrated to be related to a higher rate of failure ablation and local tumor progression (LTP). The real impact of these features is still debated.[13–15]

The aims of the study were to investigate the features related to ablation success and local tumor progression (LTP) in patients submitted to percutaneous ablation for perivascular-HCC.

## Materials and Methods

From January 2010 to May 2021, 798 nodules were ablated with 624 procedures in 356 patients and were retrospectively analyzed. The inclusion criteria of the study were as follows: age >18 years, radiological or histological diagnosis of small-HCC (<3 cm) and ablation performed by ultrasound (US)-guided percutaneous single probe RFA. Therefore, 663 HCC nodules, ablated with 570 procedures in 314 patients, were included.

Finally, 611 nodules treated with 514 procedures in 291 patients were evaluated for the study according to the following exclusion criteria: presence of macrovascular invasion (n=3), patients with follow up imaging not performed in the local radiology department (n=49).

Perivascular nodules were defined as nodules with distance ≤5 mm to major vascular structures. A major vascular structure was defined as an artery, portal branch or hepatic vein with a diameter larger equal or higher than 3 mm. Among the 611 nodules ablated, 132 were perivascular and were included in the study.

Diagnosis of HCC was based according to imaging techniques (US, CT, or MRI) showing an arterial enhancement and wash out pattern on delayed phase or with a combined criteria of an imaging technique and serum alpha-fetoprotein (AFP) level greater than 400 ng/dl. A fine-needle biopsy was performed in patients with uncertain diagnosis**.** All patients were submitted to complete liver function tests (bilirubin, alkaline phosphatase, AST, ALT, GGT, albumin, prothrombin time), blood count, creatinine level, and chest x-rays.

Indication to LAT was proposed and discussed during the multidisciplinary team meeting, in presence of surgeons, oncologists, hepatologists and interventional radiologists.

On the preoperative imaging (CT or MRI), major vascular structures were defined glissonean pedicles or hepatic veins up to second degree division or with a diameter at least 3 mm. For each nodule, the shortest distance either in axial, coronal or in the sagittal plane between the edge of the nodule and the major vascular structure was measured, likewise, the shortest distance between the nodule and the liver capsule. In addition, the main diameter of the vascular structure nearest the nodule was measured.

Every patient underwent abdominal US-scan from 1 to 4 weeks before the planned procedure to establish the feasibility of the ablation.

Radiofrequency ablation was performed in an operating room setting by the liver surgeon while the expert interventional radiologist provided US guidance. Once the patient was under conscious sedation or general anesthesia, the best approach to target the lesion was selected.

An electrode-needle type probe, connected to a radiofrequency generator was utilized in all patients. During the study period, we used RITA electrode (Balmer Medical SA, Switzerland) from 01/2010 to 07/2017, V-Tip or Jet-Tip electrode (RF Medical Co, Korea) from 07/2017 to 04/2020 and Amica HS electrode (Mermaid Medical, Denmark) from 04/2020 to 05/2021.

The probe was inserted into the center of the nodule preferably along its main axis, and the parameters of the radiofrequency generator were set to achieve an ablation

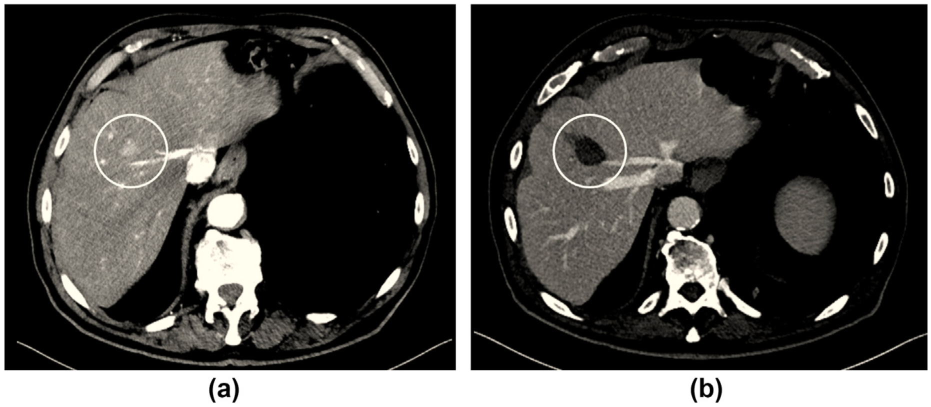


**Figure 1** Ablation success of perivascular HCC of 1.7cm in Sg8 who underwent percutaneous ablation. (a) Preoperative CT image with nodule of HCC (white circle) in Sg8 in proximity to glissonian pedicles of Sg8 and Hepatic Vein; (b) postoperative CT image with ablated area (white circle)

zone that included the nodule and at least a 5 mm margin all around.[16] The result of ablation was assessed with contrast-enhanced CT performed 30 days after the procedure. Ablation success was defined as the complete ablation of nodules in the absence of residual tumor after two consecutive procedures (Fig 1).

Post-operative outcomes were prospectively collected and reported according both to the Society of Interventional Radiology (SIR) Standards of Practice Committee guidelines and to Dindo-Clavien classification system.

Patients were monitored every 3 months for the first two years after LAT by contrast enhanced-US (CEUS) or CT/MRI, alternatively. The successively follow-up was performed by CEUS or CT/MRI, alternatively, every 6 months for three years. In each case, imaging study was associated with clinical examination, liver function test and AFP level.

Hepatic recurrences were divided in local tumor progression (LTP) when it occurred within 10 mm from the previously ablated area, and intrahepatic recurrence (IR) when a new nodule occurred more than 10 mm away from the ablated area[16] (Fig 2).

Written informed consent was obtained in all patients before the procedure. The local ethics committee approved the study protocol. Data collection and analysis were performed according to the institutional guidelines conforming to the ethical standards of the Helsinki Declaration.

### *Statistical analysis*

Statistical analysis was performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY). Continuous variables were reported as medians with interquartile ranges (IQRs) and compared among groups using the unpaired t test or Mann-Whitney U test as appropriate. Categorical variables were reported as totals and frequencies and compared using the chi-square test or Fisher's exact as appropriate. Only nodules who underwent complete ablation were considered for LTP risk and survival analyses. Univariate analysis was used to identify the preoperative clinical and radiological features related to ablation success and LTP. A p-value $\leq$0.05 was regarded as statistically significant, and the selection criteria for entering features into multivariate analysis. The Kaplan-Meier method was used to estimate the LTP-free survival probabilities, which were compared using the log-rank test. A multivariable Cox regression model was used to identify factors that were independently related to LTP-free survival to estimate

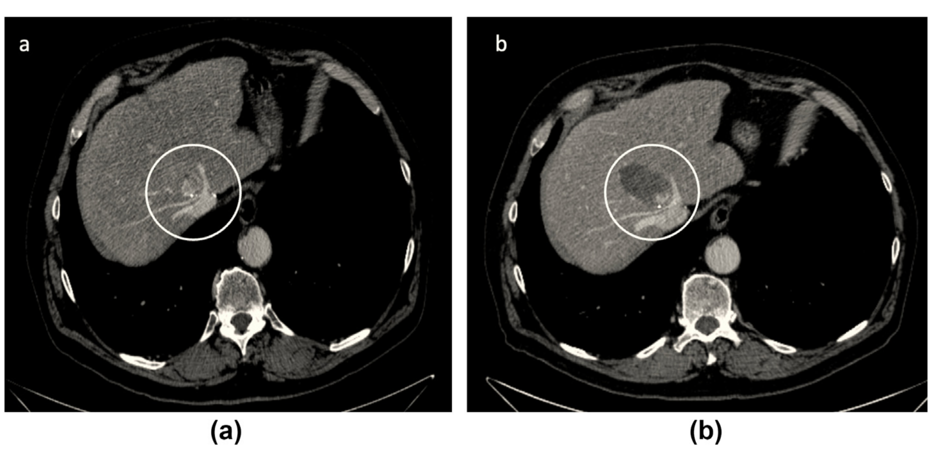


**Figure 2** Local tumor progression of ablated perivascular HCC at the hepatocaval confluence. (a) Preoperative CT image with nodule of HCC (white circle) at the hepatocaval confluence; (b) the 6 months follow-up post-ablation CT image with ablated area and local tumor progression (white circle) in proximity of hepatic veins

**Table 1**
Study population baseline patients' characteristics.

| Features | Study population n (%) |
|---|---|
| **Number of patients** | 101 |
| **Gender**, male | 76 (75.2) |
| **Age, median, years (IQR)** | 72 (66–79) |
| **HCC etiology** | |
| Viral | 51 (50.4) |
| Alcohol intake | 29 (28.8) |
| Metabolic | 13 (12.9) |
| Unknown | 8 (7.9) |
| **Cirrhosis** | 80 (79.2) |
| **Child-Pugh** | |
| A5 | 69 (68.4) |
| A6 | 20 (19.9) |
| B7 | 7 (6.9) |
| B8 | 4 (3.9) |
| B9 | 1 (0.9) |
| **Previous HCC treatment** | |
| None | 43 (42.5) |
| TACE | 28 (27.8) |
| Surgery | 9 (8.9) |
| Ablation | 8 (7.9) |
| Multi-treatment (TACE and/or Surgery and/or Ablation) | 13 (12.9) |

TACE: trans-arterial chemo-embolization.

hazard ratios with 95% confidence intervals (95% C.I.), adjusting for potential confounders. The follow up period ranged from 6 to 138 months with a median follow up period of 27 months (IQR 13–44).

## Results

### *Baseline characteristics*

Among 101 patients, the male sex was predominant (75.2%, n=76). Median age was 72 years (66–79). The detailed baseline characteristics of the study population are reported in Table 1.

Considering the RFA procedures, one nodule was ablated in 76.4% (n=94) of the cases, two nodules in 19.5% (n=24), and three nodules in 4.1% (n=5).

The overall postoperative complications rate was 4% (n=5). According to Dindo-Clavien classification resulted Grade I, 1.7% (n=2), Grade II, 1.7% (n=2), and Grade III, 0.7% (n=1), respectively. Postoperative mortality was null (Table 2).

Among the 132 nodules ablated, the median nodule size was 22 mm (15–30). The median distance from the surface was 17 mm (9–23). The vascular structure nearest the nodule was glissonean pedicle in 39.4% (n=52) and hepatic vein in 60.6% (n=80).

According to the ablation difficulty score (ADS),[13] nodules were divided into ADS 0 0.7% (n=1), ADS 1 31.1% (n=41), and ADS 2 68.2% (n=90). The ablation success rate was 71.9% (n=95) (Table 3).

### *Features related to ablation success*

The following features resulted related to ablation success: nodule size (≤20 mm vs. >20 mm) (OR 2.442, CI 95% 1.086–5.494, p=0.031), major vascular structures diameter (3–5 mm vs ≥ 5 mm) (OR 2.167, CI 95% 1.048–4.956, p=0.037) and liver parenchyma (cirrhosis vs no-cirrhosis) (OR 2.373, CI 95% 1.023–6.099, p=0.033). The distance from liver surface and proximity to glissonian pedicles or hepatic vein did not reach the statistical significance (p=0.548 and p=0.337, respectively) (Table 4).

**Table 2**
Study population procedures' characteristics.

| Features | Ablation procedure tot 123 n (%) |
|---|---|
| **Nodules per ablation** | |
| 1 | 94 (76.4) |
| 2 | 24 (19.5) |
| 3 | 5 (4.1) |
| **Intraoperative CEUS** | 26 (21.2) |
| **Post-procedural Complications** | 5 (4) |
| **Dindo-Clavien** | |
| I | 2 (1.7) |
| II | 2 (1.7) |
| III | 1 (0.7) |
| **SIR grading** | |
| A | 0 (0) |
| B | 3 (2.4) |
| C | 1 (0.7) |
| D | 3 (2.4) |
| **Post-operative Mortality** | 0 (0) |
| **Length hospital stay, days, median (IQR)** | 1 (1–1) |
| **Length hospital stay, days, mean (SD)** | 1.24 (±0.94) |

CEUS: contrast-enhanced US; SIR: Society of Interventional Radiology.

**Table 3**
Nodules' baseline characteristics.

| Features | Ablated nodules tot 132 n (%) |
|---|---|
| **Number of patients** | 101 |
| **Number of procedures** | 123 |
| **Nodules segment location** | |
| Sg1 | 2 (1.5) |
| Sg2 | 6 (4.5) |
| Sg3 | 3 (2.3) |
| Sg4 | 14 (10.6) |
| Sg5 | 20 (15.2) |
| Sg6 | 17 (12.9) |
| Sg7 | 22 (16.7) |
| Sg8 | 48 (36.3) |
| **Nodule size, median, mm (IQR)** | 22 (15–30) |
| ≤ 20 mm | 75 (56.8) |
| > 20 mm | 57 (43.2) |
| **Distance from surface, median, mm (IQR)** | 17 (9–23) |
| ≤ 5 mm | 17 (12.8) |
| > 5 mm | 115 (87.2) |
| **Proximal major vascular structure** | |
| Glissonean pedicle | 52 (39.4) |
| Hepatic vein | 80 (60.6) |
| **Ablation Difficulty Score (ADS)** | |
| 0 | 1 (0.7) |
| 1 | 41 (31.1) |
| 2 | 90 (68.2) |
| **Complete ablation after one procedure** | 89 (67.4) |
| **Ablation Success**[a] | 95 (71.9) |

[a] after two consecutive procedures.

**Table 4**
Features related to Ablation Success.

| Features | Ablation success % (n) | *p values* | OR | I.C. 95% | *p values* |
|---|---|---|---|---|---|
| **Nodule size** | | | | | |
| ≤ 20 mm | 78.7 (59/75) | 0.039 | 2.442 | 1.086–5.494 | 0.031 |
| > 20 mm | 63.2 (36/57) | | Ref | - | |
| **Distance from surface** | | | | | |
| > 5 mm | 72.2 (83/115) | 0.548 | | | |
| ≤ 5 mm | 70.6 (12/17) | | | | |
| **Major vascular structure** | | | | | |
| Glissonian pedicles | 75.0 (39/52) | 0.337 | | | |
| Hepatic veins | 70.0 (56/80) | | | | |
| **Major vascular structure diameter** | | | | | |
| 3–5 mm | 79.5 (58/73) | 0.027 | 2.167 | 1.048–4.956 | 0.037 |
| ≥ 5 mm | 62.7 (37/59) | | Ref | | |
| **Liver parenchyma** | | | | | |
| Cirrhotic | 76.4 (81/106) | 0.023 | 2.373 | 1.023–6.099 | 0.033 |
| Non cirrhotic | 53.8 (14/26) | | Ref | - | |

### *Features related to LTP-free survival and survival analysis*

Among the ablation success cohort (71.9%, n=95), the major vascular structure nearest the nodule was a Hepatic vein in 58.9% (n=56), and glissonian pedicle in 41.1% (n=39). The median diameter of the nearest vascular structure was 5 mm (4–6). A diameter 3–5 mm resulted in 38.9% (n=37), and ≥5 mm in 61.1% (n=58).

The LTP-FS at 1-, 3-, and 5-years according with nodule size resulted 86.1%, 61.4%, and 61.4% versus 48.3%, 17.6%, and 17.6% (p<0.001) (Fig 3A). The LTP-FS at 1-, 3-, and 5-years for nodules distant >5 mm from liver surface were 75.7%, 48.9%, 48.9% versus 45.5%, 27.3%, 27.3% for nodules distant <5 mm, respectively (p=0.020) (Fig 3B). The LTP-FS at 1-, 3-, and 5-years for nodules near to glissonian pedicles was 86.8%, 58.4%, 58.4% versus 62.1%, 38.5%, 38.5% for nodules near hepatic veins, respectively (p=0.028) (Fig 3C). The LTP-FS at 1-, 3-, and 5-years according with major vascular structure

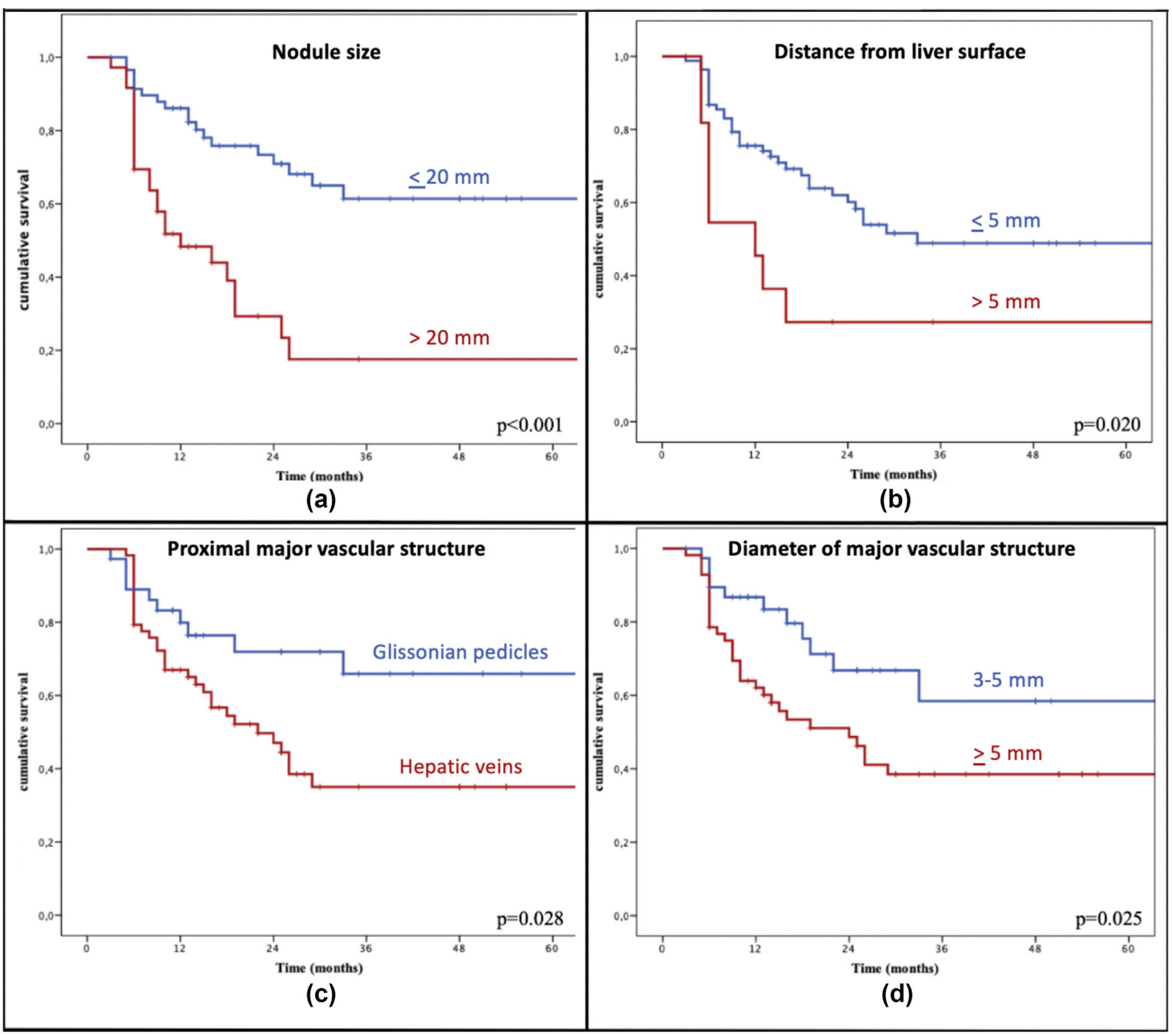


**Figure 3** Local tumor progression-free survival in perivascular nodules. (a) Nodule size (≤20 mm, blue > 20 mm, red), log rank test p<0.001; (b) distance from liver surface (>5 mm, blue; ≤5 mm, red), log rank test p = 0.020; (c) type of major vascular structure proximity (glissonian pedicles, blue; hepatic veins, red), log rank test p = 0.028; (d) diameter of major vascular structure (3–5 mm, blue; ≥ 5 mm, red). Log rank test p = 0.025

**Table 5**
Features related to LTP-free survival among perivascular nodules.

| Features | 1 year LTP-free survival % | *p values* | HR | I.C. 95% | *p values* |
|---|---|---|---|---|---|
| **Nodules Size** | | | | | |
| ≤ 20 mm | 86.1 | <0.001 | 2.802 | 1.416–5.542 | 0.003 |
| > 20 mm | 48.3 | | | | |
| **Distance from surface** | | | | | |
| > 5 mm | 75.5 | 0.020 | 1.543 | 0.661–3.602 | 0.316 |
| ≤ 5 mm | 45.5 | | | | |
| **Major vascular structure** | | | | | |
| Glissonian pedicles | 86.8 | 0.028 | 1.677 | 1.032–3.382 | 0.028 |
| Hepatic veins | 62.1 | | | | |
| **Major vascular structure diameter** | | | | | |
| 3–5 mm | 79.9 | 0.025 | 1.987 | 1.042–4.194 | 0.041 |
| ≥ 5 mm | 67.0 | | | | |
| **Liver parenchyma** | | | | | |
| Cirrhotic | 67.1 | 0.019 | 5.497 | 0.742–8.722 | 0.095 |
| Non cirrhotic | 83.3 | | | | |

diameter resulted 79.9%, 65.9%, and 65.9% versus 67.0%, 35.0%, and 35.0%, respectively (p=0.025) (Fig 3D). The LTP-FS at 1-, 3-, and 5-years according with liver parenchyma (cirrhosis vs. no cirrhosis) resulted 67.1%, 51.5%, and 41.9% versus 83.3%, 83.3%, and n/a, respectively (p=0.019). On multivariable analysis, the following features resulted independently related to LTP-free survival (LTP-FS): nodule size ≤ 20 mm (HR 2.802, IC 95% 1.416–5.542, p=0.003), proximity to glissonean pedicles (HR 1.677, IC 95% 1.032–3.382, p=0.028), and major vascular structure diameter < 5mm (HR 1.987, IC 95% 1.042–4.194, p=0.041) (Table 5).

## Discussion

Despite the proven efficacy of RFA in the treatment of HCC,[14,17–19] previous researchers have shown significant variability in ablation success depending on nodule and patient characteristics. In a recent manuscript, size <20 mm, hyper- or hypo-echogenity, non-perivascular and deeper locations of the nodules, and cirrhotic liver are the features related to ablation success, ranging from 93.5% to 71.3%.[13] In the present study, features related to ablation success were nodule size <20mm (OR 2.442, CI 95% 1.086–5.494, p=0.031), proximity to vascular structure 3–5 mm (OR 2.167, CI 95% 1.048–4.956, p=0.037) and cirrhotic liver (OR 2.373, CI 95% 1.023–6.099, p=0.033). Regarding the characteristics of parenchyma, Livraghi *et al.* proposed a relationship between ablation success and liver cirrhosis, known as “oven effect”.[20] In a study concerned on thermal conductivity, they hypothesized that the fibrotic liver parenchyma functions as a thermal insulator which concentrates heating in the tumor tissue.

The local tumor progression (LTP) after complete ablative treatment represents another important outcome for defining the effectiveness of RFA. As an ablation success, some features have been highlighted as influencing this result.[14,17,19,21,22] In the present series, small nodules (<20mm) and non-perivascular location (>5 mm) resulted to be significantly related with higher LTP- FS.

The predictive value of nodule size on LTP has been extensively studied. The “from center-to- periphery” direction of the heat from the energy source explains the temperature decrease together with distance from the electrode to the nodule margin, particularly for monopolar electrode tip.[23] Lee *et al.* reported that size ≥ 20 mm resulted the main independent factor for LTP (HR 2.1, CI 95% 1.05–3.86, p<0.05) in a series of 467 single HCC ≤ 30 mm.[19] A similar result was shown by Huang *et al.* in a series of 109 single HCC ≤ 50 mm, the cut-off of 20mm in size resulted to be an independent factor for LTP (HR 2.374, CI 95% 1.229–4.588, p=0.01).[24]

Other studies reported a size of 30 mm as a predictor for LTP.[17,21,22]

In contrast to the size of the nodule, the relationship between nodule and major vascular structures is still debatable. When nodules are near the vessels, it could decrease accumulation of heat and result in “heat sink” effect, which is considered an important cause of LTP.[25] Previous studies investigated the use of percutaneous balloon occlusion of liver vessels, while performing RFA for HCC nodules, to mitigate the impact of “heat sink effect”.[26,27] De Baere *et al.* reported that RFA with hepatic vein or portal vein branches occlusion provides equal LTP rates for tumors < 35 mm abutting vessels ≥ 4 mm and the same-size tumors away from vessels.[27] Other researchers investigated the use of hydrodissection, while performing LAT for liver nodules, to obtain a larger ablation area and protect surrounding organs or structures.[28,29] Garnon *et al.* treated 3 patients with centrally located liver tumors, performing hydrodissection of portal vein before ablation and reporting an increase in the safety margins. However, the rationale and the real advantage of using hydrodissection in the setting of RFA for perivascular nodules is still controversial.

Yang *et al.* reported the perivascular location (considered within 10mm to intrahepatic vessels) as an independent risk factor for LTP (HR 2.580, CI 95% 1.564–4.257, p<0.001).[22] Other studies reported similar results, considering perivascular HCC as nodules abutting large veins or directly in contact with them.[14,19] By contrast, a meta-analysis by Lai *et al.* showed a controversial influence of perivascular location on LTP (OR 2.12, CI 95% 0.99–4.56, p=0.05), advocating potential limitations as a correct classification of major vascular structures.[25]

The present series confirms the impact of perivascular localization on LTP, also provides some additional detailed data such as the classification and size of the vascular structures involved. In particular, the main vascular diameter nearest the nodule resulted related to higher LTP-FS if < 5 mm. Previously, Loriaud *et al.* in a series of perivascular HCC nodules, founded larger veins as an independent risk factor for LTP (HR 3.886, CI 95% 1.401–10.8, p=0.009), caused by a more significant reduction of coagulative necrosis near peri-venous areas.[30]

Furthermore, the proximity to glissonean pedicles, compared to Hepatic veins, resulted related to better LTP-FS, suggesting different impact of in-flow and out-flow vessels on “heat-sink” effect. Previous authors reported a higher LTP with glissonean pedicles, advocating a more frequent risk of intrahepatic neoplastic progression in presence of vascular thermal injury.[18,19,31] By contrast, Chen *et al.* reported a worse LTP for peri-hepatic veins versus non peri-hepatic veins nodules (44.4% vs. 26.2%, HR 1.98, CI 95% 1.15–3.4, p=0.013), but not a difference in the glissonean group (p=0.46).[14] These results may be explained by the presence of a reduced portal flow (but not hepatic flow) in cirrhotic patients, with a less significant reduction in heat capacity (and therefore “heat-sink” effect) for nodules proximal to glissonean pedicles.[32]

In the present study, the overall LTP-FS at 1- and 5-years resulted 84.5% and 67.1%, coherently with previous studies, which varies from 86.9% to 64% and from 79.9% to 24%, respectively.[14,17,19,21,22] However, significant differences may be observed among subgroups. A significant difference in LTP-FS was observed for perivascular nodules (p<0.001), similar to the results reported by Kim *et al.* (LTP-FS of 72.9% vs. 84.5% at 1-year, p=0.022),[21] and by Chen *et al.* (LTP-FS at 1- and 5-years of 53.7% and 68.7% vs. 71.9% and 85.1%, respectively, p=0.012).[14]

However, in the perivascular group, the presence of low risk features (<20 mm, proximal to glissonian pedicles and vascular diameter <5mm) was related to significantly better results in LTP-FS at 1- and 5- years (Fig 3A and B-C).

The present study had several limitations. The retrospective and monocentric design of the study could reflect in a selection bias. Moreover, only the nodules treated with US-guided single probe RFA were included. Other researchers reported that perivascular location could have a lesser impact on ablation success and LTP when employing other technologies such as microwave ablation (MWA), cryoablation or irreversible electroporation (IRE).[33–37] In a series of 144 patients with perivascular nodules treated with RFA or MWA, An *et al.* reported that the treatment modality was an independent prognostic factor for LTP (RFA vs. MWA: HR 7.861, 95% CI 1.642–37.635, p=0.010).[34] Wada *et al.* conducted a comparison of the clinical outcomes of different ablative modalities such as RFA, MWA, and IRE. In both unmatched (p=0.028) and propensity score-matched cohorts (p=0.005), IRE showed significantly better local tumor control than RFA. In this study, 33.3% of tumors treated with IRE were located adjacent to major portal branches, which was statistically more frequent than others, and no LTP was observed in patients treated with IRE.[37] However, US-guided single probe RFA continues to be the most spread and worldwide used technology to treat liver nodules. The findings of this study could be beneficial in improving and tailoring the selection of patients who are willing to receive local treatment.

In conclusion, percutaneous radiofrequency ablation is confirmed to be effective for treating HCC nodules not suitable for surgery. However, perivascular location confirmed to be a difficult and unfavorable indication for percutaneous ablation for HCC nodules. Nevertheless, perivascular nodules not suitable for surgery with low-risk features (size <20 mm, proximity to glissonian pedicles and diameter of vascular structures <5 mm) may be treated with percutaneous RFA with satisfactory outcomes. Further studies and external validation are needed to confirm our results.

## Ethics

The local ethics committee approved the study protocol. Data collection and analysis were performed according to the institutional guidelines conforming to the ethical standards of the Helsinki Declaration.

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## Author contribution

**Guarantor of integrity of the entire study:** Simone Conci.
**Study concepts and design:** Simone Conci; Andrea Ruzzenente.
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**Clinical studies:** N/A.
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## Conflict of Interest

The authors declare no conflict of interest.

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