

# Thermal Ablation of Renal Tumors under Ultrasound Guidance and Conscious Sedation: A Retrospective Experience

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## ABSTRACT

**Purpose:** Computed tomography (CT) guidance and general anesthesia have recently been recommended as the approach of choice for percutaneous ablation of small renal cell carcinoma (RCC), whereas ultrasound (US) guidance and conscious sedation have been tagged as inadequate. Aim of the study was to assess the safety and effectiveness of percutaneous thermal ablation of small RCC under ultrasound (US)-guidance and conscious sedation. **Methods:** The records of 74 patients with small RCC ( $\leq 5$  cm), who underwent US-guided thermal ablation under conscious sedation were retrospectively reviewed. Conscious sedation was usually induced by means of intravenous bolus of midazolam 50–100  $\mu\text{g}/\text{kg}$  plus continuous infusion of a 25  $\mu\text{g}/\text{mL}$  solution of remifentanyl at a rate of 0.05  $\mu\text{g}/\text{kg}/\text{min}$ . Technical success, technical efficacy, local tumor progression (LTP), primary and secondary efficacy rates, complication rate, and 1-, 3-, and 5-year survival rates were analyzed. **Results:** No procedure needed to be converted to general anesthesia, and all tumors were treated according to the protocol, with a technical success of 100%. One patient died after surgical intervention for bowel perforation and other 2 patients experienced grade 3 complications. Mortality rate and major complication rate were 1.3% and 2.7%, respectively. One-month technical efficacy was 100%. LTP was observed in 4/74 patients, with a primary efficacy rate of 94.6%. Two of them underwent successful thermal ablation and secondary efficacy rate was, therefore, 97.3%. The median follow-up was 38 months (range 1–130 months). No patient died for tumor progression. 1-, 3-, and 5-year survival rates were 94%, 80.5%, and 60%, respectively. **Conclusion:** US guidance and conscious sedation remain valid alternatives to CT guidance and general anesthesia for the percutaneous ablation of small RCC.

**Key words:** Conscious sedation, renal cancer, thermal ablation, ultrasound

## INTRODUCTION

Renal cell carcinoma (RCC) is increasingly diagnosed in T1a stage ( $\leq 4$  cm), mainly due to incidental imaging findings.<sup>[1]</sup> Partial nephrectomy is the first option to treat T1a RCC, as it maintains oncologic outcomes comparable to total nephrectomy while better preserving renal function.<sup>[2]</sup> In the last years, percutaneous image-guided thermal ablation is gaining increasing interest as a valid option for patients with small renal cancer who are unsuitable for surgery, as they have a lower complication rate and

are more nephron sparing, while obtaining 90–100% of successful ablation.<sup>[3,4]</sup> The cardiovascular and interventional radiology society of Europe (CIRSE) guidelines recommend radiofrequency ablation (RFA) and cryoablation (CRA) as the ablation modalities of choice; moreover, they suggest that microwave ablation (MWA) may represent a promising technique, as it can produce larger ablation volumes than RFA and is only slightly influenced by the heat sink effect.<sup>[5,6]</sup> Furthermore, quite recently, laser ablation (LA) has been reported to be an effective and safe alternative to RFA, CRA, or MWA in patients with increased risk of bleeding.<sup>[7]</sup> Whatever

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ablation technique was used, historically the approach under ultrasound (US) guidance and conscious sedation, with the patient in supine, lateral, or prone position according to the best acoustic window to reach the target, was mostly used worldwide.<sup>[8-10]</sup> In the last years such an approach has been questioned,<sup>[5]</sup> and recently computed tomography (CT) guidance and general anesthesia, with the patient in prone position, have strongly been recommended in the Annual Meeting of CIRSE as the standard approach for percutaneous ablation of RCC.<sup>[11]</sup>

In this retrospective study, we evaluated the safety and effectiveness of percutaneous thermal ablation of small RCC under US-guidance and conscious sedation.

## METHODS

The data of 74 patients (43 males and 31 females, age range 51–87 years) with small RCC, who underwent US-guided thermal ablation under conscious sedation from April 2006 to December 2019, were retrospectively reviewed. Approval of the Ethics Committee of our hospital was obtained (protocol 2019/104) and patients' informed consent was waived. Inclusion criteria were: Refusal or contraindications to surgery because of comorbidity or advanced chronic renal failure; long-axis diameter of the tumor  $\leq 5$  cm; absence of distant metastases, lymph node involvement, or renal vein invasion; tumor location at least 5 mm from the major calyces or pelvis; and informed consent to undergo the procedure. Exclusion criteria were: Distance of the tumor  $< 5$  mm from the bowel and impossibility to displace bowel by at least 10 mm from the tumor; platelet count  $< 50,000/\mu\text{L}$ ; international normalized ratio  $> 1.5$ ; and final histopathologic diagnosis of a benign lesion. In 27 patients, the diagnosis was obtained by percutaneous biopsy, in 47 patients, the diagnosis was based on the imaging findings, and biopsy was performed before thermal ablation. Long-axis and short-axis diameters of the tumors ranged from 13 mm to 50 mm (median 25) and from 12 mm to 48 mm (median 22 mm), respectively. RFA was used to treat tumors with long-axis diameter up to 3 cm, MWA was used to treat lesions with long-axis diameter exceeding 3 cm. LA was used to treat tumors with long-axis diameter up to 3 cm that were judged at high risk of bleeding owing to their deep location, or antiplatelet therapy that could not be discontinued.<sup>[7]</sup>

### Ablation procedures

All thermal ablations were carried out under US-guidance. The patients underwent preliminary US examination in supine, prone, and right or left lateral position to assess the best acoustic window to reach the target. Afterward, the lesions were examined by contrast-enhanced US (CEUS) to assess tumor vascularity using a 2.4 mL intravenous bolus of an 8 mL solution of sulfur hexafluoride microbubbles stabilized by a phospholipid shell as US contrast agent

(SonoVue®, Bracco, Milan, Italy). The CEUS clips were stored to allow a comparison with post-ablation changes of vascularity. If the distance of the tumor was  $< 10$  mm from the bowel, hydrodissection was performed by instilling 5% dextrose solution to obtain an at least 10-mm safety margin between the bowel and the tumor; if hydrodissection was unsuccessful, ablation procedure was not carried out. Conscious sedation was induced by means of i.v. bolus of midazolam 50–100  $\mu\text{g}/\text{kg}$  plus continuous infusion of a 25  $\mu\text{g}/\text{mL}$  solution of remifentanyl at a rate of 0.05  $\mu\text{g}/\text{kg}/\text{min}$ . If necessary, an i.v. bolus of propofol 1% 0.5 mg/kg, followed by continuous infusion at a rate of 1–2 mg/kg/h, was also administered. Vital signs were continuously monitored throughout the ablation procedure.

RFA was performed using an internally-cooled system, a generator with a maximum power output of 200 W, and a 17-gauge needle electrode with a 2- or 3-cm exposed tip, according to the size of the tumor (Cool-tip RFA System, Valleylab, Boulder, CO, U.S.A). MWA was performed using an internally-cooled system with a miniaturized device on the tip of the MWA antenna as a remedy to back heating effects (AMICA MWA System, HS Hospital Service, Aprilia, Italy). MWA procedures were carried out using a generator with a frequency of 2450 MHz and maximum power output of 140 W, and 14- or 16-gauge antennas with energy delivery output between 70 and 100 W for 8–10 min, according to the size of the tumor. LA was performed using a semi-conductor diode system (EchoLaser, Elesta Srl, Florence, Italy) with a wavelength of 1064 nm and a multi-source device that enables to use up to four 300  $\mu\text{m}$  fibers at once, that were inserted into the nodules through 21-G Chiba needles.<sup>[12,13]</sup> Two and three laser fibers were used for tumors with long-axis diameter up to 14 mm and larger than 14 mm, respectively, and 1800 J per fiber was delivered in 6 min according to the technique described elsewhere.<sup>[7]</sup>

After the end of the procedures, the patients underwent CEUS to assess the completeness of ablation. If an avascular zone with no enhancement completely covering the tumor was observed, ablation was judged complete [Figures 1a and b]. When some residual foci with vascular enhancement were depicted in the ablation zone, the treatment was completed under CEUS guidance [Figures 2a-c].

### Follow-up

All patients were followed up until death or the time the data were censored (June 30, 2020). Contrast-enhanced CT or CEUS if the patients had reduced renal function were performed 30 days after thermal ablation. Afterward, contrast-enhanced CT or CEUS were carried out every 3 months for the first 2 years, then every 6 months.

Technical success, technical efficacy, primary and secondary efficacy rate, and local tumor progression (LTP) were

recorded and defined according to the recommendations of the International Working Group on the Image-guided Tumor Ablation.<sup>[14]</sup> Complications were recorded and

classified according to the CIRSE classification system for complications reporting.<sup>[15]</sup>

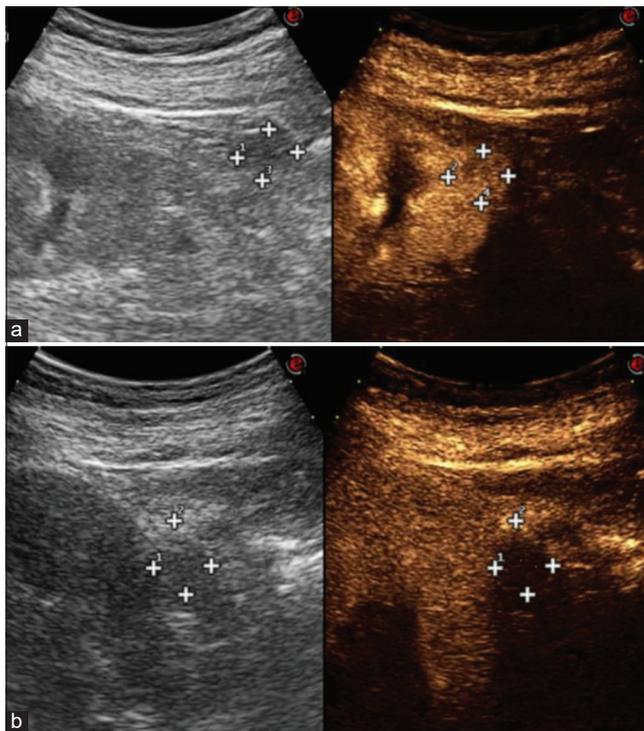
### Statistical analysis

Overall survival (OS) for the entire population and OS for the patients treated with RFA, MWA, and LA were estimated using the Kaplan–Meier method and were calculated from the date of the ablation procedure to patients death or June 30, 2020. All analyses were performed using a statistical software program (STATA 13.0 for Windows; StataCorp., College Station, TX, U.S.A.).

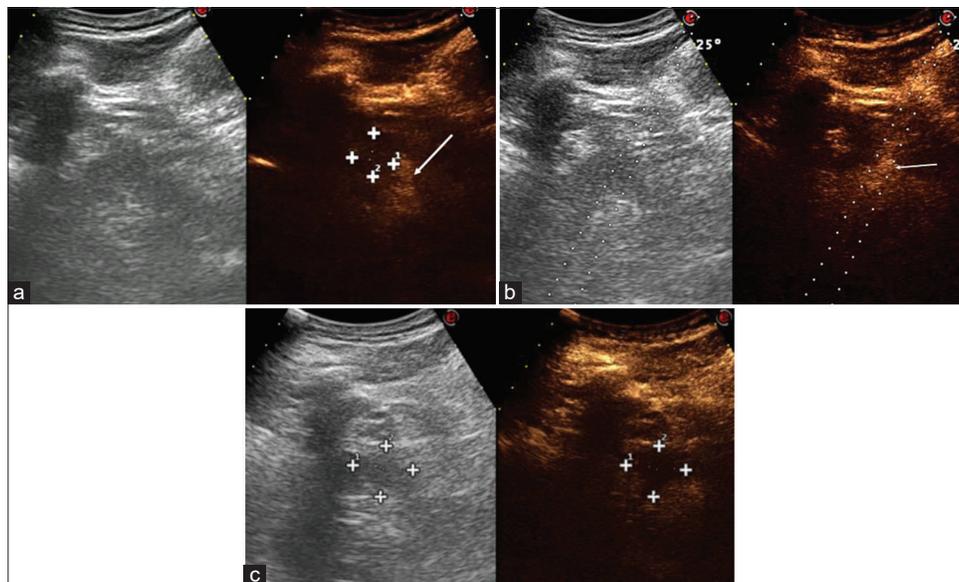
## RESULTS

Main characteristics of patients and tumors are reported in Table 1.

Forty-seven patients underwent RFA, 15 MWA, and 12 LA. In sixty-nine cases, the patients were treated in supine or lateral position, just in five cases (6.7%), they were placed in prone position. In nine patients, post-procedural CEUS depicted residual viable tumor tissue, and the treatment was completed by CEUS-guided RFA, MWA, or LA. No procedure needed to be converted to general anesthesia and all tumors were treated according to protocol and were completely covered by the ablation zone, with a technical success of 100%. One patient died after surgical intervention for bowel perforation following MWA of a  $38 \times 30$  mm RCC in the left kidney, despite an apparently successful hydrodissection. Two patients experienced Grade 3 complications: A genitofemoral nerve injury and a skin burn in the site of the needle insertion, respectively. Both complications resolved after adequate



**Figure 1:** Complete tumor ablation. (a) CEUS scan showing an exophytic inhomogeneous enhancing nodule in the upper pole of the left kidney (cross-shaped markers); (b) post-ablation CEUS scan showing a non-enhancing zone completely covering the nodule (cross-shaped markers)



**Figure 2:** Incomplete tumor ablation and retreatment under CEUS guidance. (a) Post-ablation CEUS scan showing residual enhancing tissue (arrow) in the lateral margin of the ablation zone (cross-shaped markers); (b) the residual enhancing tissue (arrow) is targeted for retreatment under CEUS guidance (dotted lines); (c) post-retreatment CEUS showing a non-enhancing zone completely covering the residual viable tissue (cross-shaped markers)

Table 1: Patients and tumors characteristics

Age/ sex	Kidney	Tumor size (long axis x short axis)	Ablation technique	Date of ablation	Major complications	LTP (treatment)	Date of death	Cause of death
78/F	Right	25x21 mm	RF	05/04/06	No	No	09/09/13	Heart failure
65/M	Left	22x18 mm	RF	11/13/06	No	No	10/28/14	Car accident
70/M	Right	23x20 mm	RF	07/09/07	No	No	02/14/18	Stroke
75/F	Right	29x25 mm	RF	11/09/07	No	No	04/18/12	Stroke
70/F	Right	24x20 mm	RF	12/03/07	No	No	07/23/14	Heart failure
74/M	Left	24x21 mm	RF	06/02/08	No	No	03/22/15	Pneumonia
72/M	Right	30x25 mm	RF	12/10/08	No	No	05/30/16	Lung cancer
70/F	Right	24x20 mm	RF	10/06/08	No	No	11/24/18	Cirrhosis
76/F	Right	26x22 mm	RF	03/15/09	No	No	04/12/15	Renal failure
79/M	Left	30x25 mm	RF	05/29/09	No	Yes (RF)	10/14/17	Colon cancer
68/F	Left	22x20 mm	RF	08/18/09	No	No	Alive	--
72/M	Left	30x26 mm	RF	06/06/10	No	No	06/23/14	Heart Attack
65/F	Right	25x20 mm	RF	12/03/10	No	No	Alive	--
72/F	Left	20x15 mm	RF	12/17/10	No	No	08/29/15	Stroke
62/M	Left	30x26 mm	RF	03/14/11	No	No	Alive	--
79/F	Right	19x17 mm	RF	09/21/11	No	No	12/18/18	Renal failure
73/M	Left	24x20 mm	RF	11/02/11	No	No	Alive	--
85/F	Left	30x26 mm	RF	05/08/13	No	No	11/23/17	Heart failure
77/M	Right	22x20 mm	Laser	07/08/13	No	No	09/12/17	Endocarditis
65/F	Right	26x21 mm	RF	08/21/13	No	No	Alive	--
58/M	Left	18x16 mm	Laser	08/21/13	No	No	Alive	--
68/M	Right	26x24 mm	RF	08/21/13	No	No	Alive	--
73/M	Left	16x14 mm	Laser	08/28/13	No	Yes (Laser)	07/16/17	Larynx cancer
51/M	Left	14x12 mm	Laser	09/12/13	No	No	Alive	--
69/F	Right	30x28 mm	RF	09/12/13	No	No	03/23/17	Pancreatitis
77/F	Right	15x12 mm	Laser	02/27/14	No	No	Alive	--
69/M	Right	28x24 mm	RF	02/27/14	No	Yes (RF)	Alive	--
80/F	Left	13x12 mm	Laser	05/15/14	No	No	Alive	--
82/F	Right	50x48 mm	MW	10/08/15	No	No	Alive	--
73/M	Left	27x22 mm	RF	10/08/15	No	No	Alive	--
83/F	Right	25x23 mm	RF	03/17/16	No	Yes (RF)	Alive	--
80/M	Left	20x17 mm	Laser	06/05/16	No	No	10/12/17	Broncopneumonia
87/F	Left	37x30 mm	MW	09/29/16	No	No	Alive	--
52/M	Left	18x15 mm	Laser	11/13/16	No	No	08/19/19	Colon cancer
85/M	Left	25x23 mm	RF	11/24/16	No	No	Alive	--
69/F	Right	23x20 mm	Laser	01/13/17	No	No	Alive	--
73/M	Right	22x18 mm	RF	02/23/17	No	No	08/20/18	Heart Attack
85/M	Left	50x46 mm	MW	03/19/17	No	No	01/24/19	Stroke
81/M	Right	24x22 mm	RF	04/06/17	No	No	Alive	--
81/F	Left	30x25 mm	RF	04/20/17	No	No	12/21/17	Stroke
81/F	Left	22x20 mm	RF	04/20/17	No	No	02/21/19	Stroke
84/M	Right	28x22 mm	RF	06/15/17	No	No	01/24/19	Broncopneumonia

(Contd...)

Table 1: (Continued)

Age/ sex	Kidney	Tumor size (long axis × short axis)	Ablation technique	Date of ablation	Major complications	LTP (treatment)	Date of death	Cause of death
81/F	Right	34×28 mm	MW	07/13/17	No	No	Alive	--
83/F	Right	29×24 mm	RF	08/24/17	No	No	Alive	--
74/M	Left	16×14 mm	Laser	09/21/19	No	No	Alive	--
81/F	Left	30×20 mm	RF	09/28/17	No	No	Alive	--
72/F	Left	18×15 mm	Laser	12/21/17	No	No	07/30/19	Sepsis
76/M	Right	24×20 mm	RF	12/21/17	No	No	Alive	--
66/M	Right	45×37 mm	MW	01/11/18	No	No	Alive	--
80/M	Left	35×32 mm	MW	03/01/18	No	No	Alive	--
82/M	Right	50×43 mm	MW	03/23/18	No	No	Alive	--
79/M	Left	40×30 mm	MW	06/28/18	No	No	Alive	--
81/F	Left	38×30 mm	MW	08/17/18	Colon perforation (Death)	No	09/29/18	Colon perforation
80/F	Right	16×12 mm	Laser	09/20/18	No	No	Alive	--
78/M	Left	24×20 mm	RF	09/20/18	No	No	Alive	--
70/M	Left	16×12 mm	RF	10/05/18	No	No	Alive	--
81/M	Right	28×22 mm	RF	12/21/18	No	No	Alive	--
82/M	Left	50×45 mm	MW	01/31/19	No	No	Alive	--
79/M	Right	40×32 mm	MW	02/14/19	Genitofemoral nerve injury	No	03/04/19	Heart attack
83/F	Right	39×32 mm	MW	02/27/19	No	No	Alive	--
83/M	Left	18×16 mm	RF	05/30/19	No	No	Alive	--
85/M	Right	18×15 mm	RF	06/04/19	No	No	Alive	--
71/M	Left	30×28 mm	RF	06/06/19	No	No	Alive	--
72/M	Left	16×12 mm	RF	06/20/19	No	No	Alive	--
80/F	Right	25×23 mm	RF	06/21/19	No	No	Alive	--
57/M	Right	16×13 mm	RF	06/21/19	No	No	Alive	--
81/M	Left	35×30 mm	MW	07/10/19	Skin burn	No	09/14/19	Endocarditis
80/M	Right	35×34 mm	MW	07/11/19	No	No	Alive	--
65/M	Left	45×35 mm	MW	07/19/19	No	No	Alive	--
69/F	Left	24×20 mm	RF	07/19/19	No	No	Alive	--
61/F	Right	19×14 mm	RF	08/01/19	No	No	Alive	--
67/M	Left	18×12 mm	RF	09/18/19	No	No	Alive	--
81/M	Left	14×12 mm	RF	11/21/19	No	No	Alive	--
76/F	Right	18×16 mm	RF	12/19/19	No	No	Alive	--

LTP: Local tumor progression

treatment with no post-procedure sequelae. No complication of conscious sedation was observed. On the whole, mortality rate and major complication rate were 1.3% and 2.7%, respectively.

CT or CEUS performed 1 month after the procedure showed successful ablation of 74/74 tumors and technical efficacy was 100%. LTP occurred 3–10 months after thermal ablation in 4/74 patients, and primary efficacy rate was 94.6%. Two of them

underwent successful CEUS-guided RFA and LA, whereas 1 of them experienced tumor recurrence after retreatment with RFA and underwent surgery, and 1 patient was not retreated owing to the inability to displace the colon from the tumor recurrence. Secondary efficacy rate was, therefore, 97.3%.

The median follow-up was 38 months (range 1–130 months, mean 45.1 ± 36). Twenty-eight patients died 1–127 months

after thermal ablation: One owing to complications following the ablation procedure and 27 for causes other than renal cancer. No patient died for disease progression. Forty-six patients were still alive 6–130 months after ablation, and 44 of them were disease free.

One-, 3-, and 5-year OS was 94%, 80.5%, and 60% for the entire population, respectively [Figure 3]. No difference in OS was observed among the subgroups of patients treated with RFA, MWA, and LA [Figure 4].

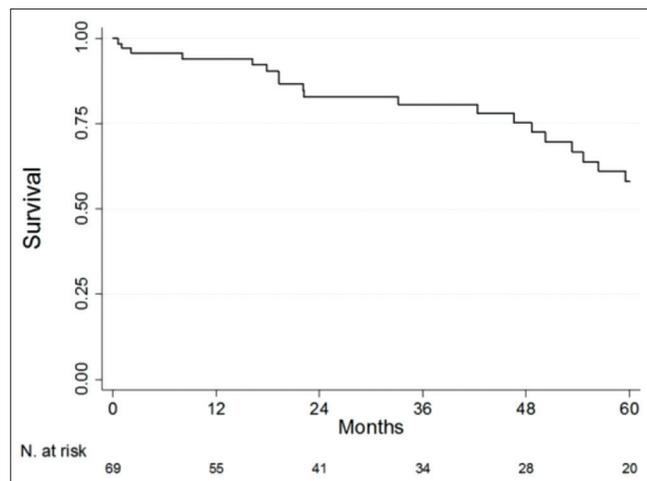
## DISCUSSION

Surgical intervention is worldwide considered the first choice for the treatment of RCC. However, in the last years, percutaneous thermal ablation has evolved into a valid alternative for the treatment of T1a RCC, with oncological outcomes comparable to surgery and lower complication

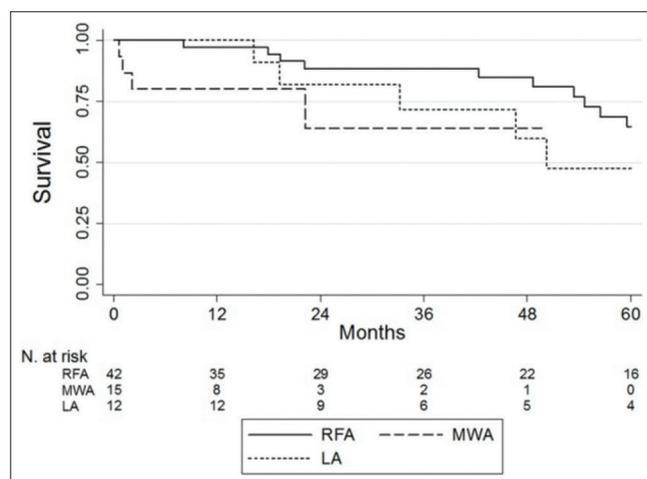
rate.<sup>[1,3,4,16]</sup> Moreover, the availability of an effective minimally invasive technique such as thermal ablation is turning the current opinion about the role of active surveillance that for a long time has been recommended for T1a tumors in patients unsuitable for surgery.<sup>[17,18]</sup> Quite recently, the CIRSE guidelines suggested that active surveillance should be reserved just for patients who are not suitable for ablation for age or comorbidities.<sup>[5]</sup>

The best imaging method to guide percutaneous ablation of RCC is widely being discussed. US remains the most used method of guidance, due to its availability, low cost, lack of radiation exposure, and the considerable advantage to enable the real-time monitoring of each step of the ablation procedure, as well as to place the patients in the most suitable position to reach the target.<sup>[1,9,10]</sup> Moreover, the use of US contrast medium after the end of the procedure allows to assess the completeness of the ablation and to guide the immediate retreatment if residual viable foci of tumor tissue are detected. Indeed, the post-procedural assessment of the completeness of ablation has been proven to increase primary technical efficacy,<sup>[19]</sup> and in our series, CEUS enabled to detect 9/74 (12.2%) residual viable tumor foci and to guide the retreatment, with a technical success and technical efficacy of 100%. In this regard, a prior study suggested that CEUS is as effective as CECT or MRI in the assessment of residual or recurrent tumors after RFA,<sup>[20]</sup> and quite recently this observation has been confirmed by other authors.<sup>[21]</sup> However, US can be limited by inherent patient characteristics, and sometimes the exact anatomical relationship with the surrounding organs (particularly the bowel loops) cannot be easily delineated.<sup>[5]</sup> Moreover, gas formation during the procedure can limit the adequate visualization of the ablation zone, making post-procedural assessment hard.<sup>[1]</sup> For these reasons, the recent CIRSE guidelines did not recommend US as the guidance modality of choice and suggested that CT or MRI guidance should be preferred.<sup>[5]</sup> However, there are no studies in the literature that compared both effectiveness and complication rates of US-guided, CT-guided, and MRI-guided thermal ablation, so the superiority of one imaging modality over the others has never been proved.<sup>[10,22]</sup>

Another debated issue is the ideal anesthesiologic regimen to perform the ablation procedure. General anesthesia undoubtedly ensures better pain control than conscious sedation and reduces patient anxiety or panic, but it is not free of risks such as myocardial infarction, stroke, and malignant hyperthermia.<sup>[23]</sup> On the other hand, conscious sedation is more painful but does not require intubation, and several relative contraindications to general anesthesia such as impairment of lung function do not preclude its use.<sup>[1]</sup> Although most percutaneous ablations of renal tumors are currently performed under conscious sedation, there is a widespread belief that general anesthesia can ensure a better outcome. However, data to support such a belief are weak. A



**Figure 3:** Survival curve for all patients from tumor ablation to death or June 30, 2020



**Figure 4:** Overall survival curves for patients treated with RFA, MWA, and LA

study reported that general anesthesia can decrease the number of sessions required to achieve complete tumor ablation in early-stage hepatocellular carcinoma, but no difference was observed in 2-year OS and recurrence-free survival rate in comparison with conscious sedation.<sup>[23]</sup> Other authors reported excellent initial success rates of CT-guided RFA under general anesthesia, but no comparison with conscious sedation was done.<sup>[24]</sup> Finally, general anesthesia was reported to provide better intermediate outcomes than conscious sedation in RFA ablation of small RCC, but the results of the study are fairly questionable.<sup>[25]</sup> Indeed, in the conscious sedation group (just ten patients vs. 41 patients in the general anesthesia group) LTP occurred in 40% of cases that are a surprisingly high rate when compared with all studies published in literature on US-, CT-, or MRI-guided ablation of renal tumors.<sup>[1,3,4,7,8-10,16,19]</sup> Furthermore, excellent results were reported in a study comparing two types of conscious sedation in US-guided RFA of liver tumors.<sup>[26]</sup> Despite the lack of clear evidence of superiority of a type of anesthesia over the other one, as well as of an imaging technique of guidance over the others, the need for standardization of percutaneous thermal ablation of renal tumors has recently been advocated, and a prone CT-guided approach under general anesthesia has been recommended.<sup>[11]</sup> Conversely, US guidance and conscious sedation have been tagged as inadequate.<sup>[11]</sup> We think such statements reflect more the personal opinion and experience of some skilled interventional radiologists than the proven finish line of all skilled interventional radiologists. There are a lot of papers in literature reporting excellent results of ablation of RCC under US guidance and conscious sedation that are comparable to those obtained with CT or MRI guidance and general anesthesia.<sup>[1,3,7-10,20,22,27]</sup> According to these prior reports, our experience confirms that US-guided ablation under conscious sedation of RCC is as safe and effective as the other ablation approaches. US guidance enabled to detect and confidently target the tumors, and conscious sedation allowed to complete all the interventions, with no need to convert any procedure to general anesthesia and with a technical success of 100%. LTP after one or two ablation sessions was 5.4% and 2.7%, respectively, and was comparable to that reported in literature for CT-guided ablation under general anesthesia.<sup>[23,28,29]</sup> One cancer-related death occurred 1 month after thermal ablation because of complications of the procedure, whereas 73/74 patients (98.7%) are still alive or died for causes other than RCC. Likewise, also our major complication rate (2.7%) resulted in the range of that reported in literature for the other ablation approaches (1.6–6%).<sup>[1,5,30]</sup>

## CONCLUSIONS

Although our study is retrospective, concerns just our experience with US-guided ablation of RCC under conscious sedation, and has no control group treated with other approaches, our results compare well with those reported in literature for CT-guidance and general anesthesia.

According to many prior reports,<sup>[1,3,7-10,20,22,27]</sup> our experience suggests that US guidance and conscious sedation remain valid alternatives to CT guidance and general anesthesia in the percutaneous ablation of small RCC.

Each modality of guidance and anesthesia has advantages and disadvantages<sup>[11]</sup> that make them more or less suitable in each particular setting. We do not think there is an ideal approach for all the patients and all the tumors, but we believe the time is ripe for an individually tailored approach based on tumor and patient characteristics to select the optimal modalities of guidance and sedation in each single case.

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