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INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Computed tomography-guided cryoablation in treating adrenal metastases: a retrospective single-center study

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PURPOSE

To assess the effectiveness and safety of computed tomography (CT)-guided cryoablation for treating adrenal metastases (AMs).

METHODS

This study included 12 patients treated with 13 CT-guided cryoablation procedures for AMs between 2016 and 2020. Patients were selected based on specific criteria, including tumor size ≤5 cm and suitability for surgery. Procedures were performed by expert radiologists, with comprehensive monitoring for complications and regular post-treatment evaluations.

RESULTS

The primary technical success rate was 91.7%, with a secondary success rate of 100% following repeat procedures. Over an 8–24-month follow-up period, local tumor recurrence was observed in 16.7% of patients, and systemic progression occurred in five (41.6%) patients. The average overall survival duration was 26.4 ± 5.6 months.

CONCLUSION

CT-guided cryoablation is a feasible and effective treatment option for AMs, demonstrating high technical success rates and manageable complications.

CLINICAL SIGNIFICANCE

This study highlights CT-guided cryoablation as a promising treatment for AMs, offering a minimally invasive alternative to surgery with good local control and safety profile. Further research, including multi-center studies, is needed to confirm these findings.

KEYWORDS

Adrenal glands, cryotherapy, computed tomography, local treatment, oncology

The increasing occurrence of metastatic tumors in the adrenal glands, originating from various types of cancers, such as lung, breast, colorectal, hepatocellular carcinoma, and melanoma, presents substantial challenges in the field of oncology.[1-4]

Studies indicate that adrenal metastatic presence can be as high as 27% in patients with widespread cancer.[5,6]

While the efficacy of direct adrenal interventions is yet to be established through randomized studies, the role of surgical resection, particularly for isolated adrenal metastases (AMs), has gained recognition in observational studies.[7-11]

However, surgical procedures such as adrenalectomy are often hampered by individual health concerns and the intricacies of the operations, resulting in prolonged hospital admissions.[1-4]

In contrast, computed tomography (CT)-guided methods, such as radiofrequency and microwave ablation, have demonstrated encouraging 1-year survival rates without local re-

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currence, ranging from 70.5% to 82% in the treatment of AMs.[1-3]

As a CT-guided technique for treating AMs, cryoablation stands out among ablation methods due to its unique advantages. Unlike radiofrequency and microwave ablation, cryoablation allows for real-time visualization of the iceball, ensuring precise targeting and minimizing the risk of damaging surrounding tissues. This method also benefits from the cold-induced anesthesia effect, which reduces pain during the procedure and often eliminates the need for general anesthesia, leading to quicker recovery times.[12-16]

As a more recent development, CT-guided cryoablation of AMs offers several benefits, including clear visualization of the treated area, minimized discomfort, and expedited recovery, achieving promising results in recent studies, although its ultimate efficacy remains under evaluation.[17-24]

The purpose of this study is to evaluate the efficacy and safety of CT-guided cryoablation in the treatment of AMs in comparison with other established ablation techniques.

Methods

This study was conducted according to the guidelines of the Declaration of Helsinki. Ethical review and approval were waived for the study due to its retrospective nature. The study was approved by Armando Businco Oncology Hospital's Ethics Committee (decision no: 53/15, date: 14/12/2015).

The study involved 12 patients who received 13 CT-guided cryoablation procedures for AMs between January 2016 and December 2020.

Eligibility criteria included patients unsuitable for surgery, tumor size ≤5 cm, controlled or absent extra-adrenal tumors, and life expectancy ≥3 months. Exclusion criteria were adrenal vein invasion, significant coagulation disorders, active infections, or bleeding (Figure 1, Table 1).

Diagnosis involved patient history, abdominal CT/magnetic resonance imaging, and biopsy results, complemented by positron emission tomography-CT for detecting extra-adrenal tumors.

The procedures were performed by two expert interventional radiologists. Informed consent was secured from parents or guardians, and patients were briefed on possible complications. Prior to the procedure, the skin entry site was anesthetized using 1% lidocaine, and patients received conscious sedation with midazolam and tramadol. The interventions utilized a multidetector CT system (SOMATOM® go.Top 128, Siemens Healthineers, Erlangen, Germany). An initial non-contrast CT scan was performed to ascertain the morphological features of the lesion.

Following this, the cryoablation was conducted-with the patient in the prone position-utilizing a cryoablation system (Visual ICE™, Galil Medical-Boston Scientific, Arden Hills, MN, USA). This system was equipped with a single 17G insulated cryoprobe that could create ablation zones of varying diameters: IceSphere 1.5 (22 × 28 mm at –20 °C and 15 × 24 mm at –40°) and IceRod 1.5 (29 × 45 mm at –20 °C and 18 × 40 mm at –40°) (Figures 2, 3). Argon was used as the cryogen

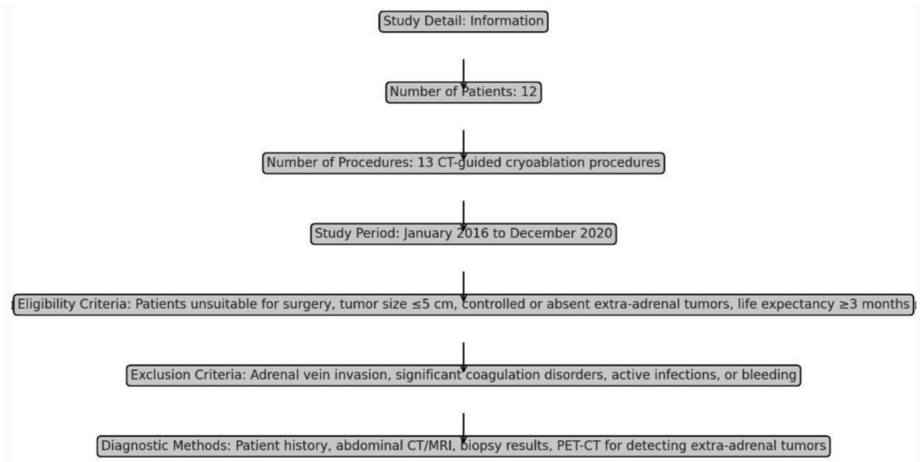

Figure 1. Flowchart of patient selection. CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.

Table 1. Patient characteristics and treatments

Patient	Age/sex	Primary tumor	Size of lesion in mm	Number of cryoprobes
1	74/M	NSCLC	24 × 18	2
2	78/F	NSCLC	18 × 28	1
3	65/F	RCC	17 × 11	1
4	68/M	NSCLC	32 × 22	2
5	64/F	RCC	2.5 × 2	2
6	67/M	SCLC	28 × 22	2
		SCLC	20 × 24*	2
7	45/F	Gastric cancer	30 × 24	3
8	57/M	NSCLC	20 × 26	2
9	58/M	NSCLC	30 × 22	2
10	63/F	NSCLC	28 × 21	1
11	54/M	SCLC	22 × 18	1
12	61/F	Synovial sarcoma	30 × 25	3

*Local recurrence treated with a second cryoablation. M, male; F, female; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer; RCC, renal cell carcinoma.

Main points

- Computed tomography-guided cryoablation achieved a high primary technical success rate of 91.7% and a secondary success rate of 100% in treating adrenal metastases (AMs).
- The procedure demonstrated good local control with a low recurrence rate, comparable to other ablation techniques.
- The safety profile was favorable, with no major complications reported, making cryoablation a viable option for patients unsuitable for surgery.
- The study suggests that cryoablation can effectively manage AMs while minimizing patient discomfort and recovery time.
- The findings support the need for further research to establish cryoablation as a standard treatment for AMs.

to create the iceball during the cryoablation process.

The cryoprobes were coaxially inserted into the adrenal lesions, as shown in Figure 2d. Scans were taken during the procedure to verify the placement and orientation of the instrument. The procedure involved a single 10-minute freezing cycle, followed by an 8-minute passive thawing phase. The freezing cycle was repeated twice. Post-freezing phase, non-contrast CT images were captured to evaluate the iceball's coverage and to identify any immediate complications.

To ensure patient safety, particularly in terms of managing the risk of hypertensive crises that can occur during interventional procedures on the adrenal gland, an anesthesiologist was present to continuously monitor vital parameters, including blood pressure. Additionally, an alpha-blocker was readily available in the operating room to promptly address any hypertensive emergencies.

Following the completion of the cryoablation procedures, abdominal CT images were acquired in all patients to detect early complications.

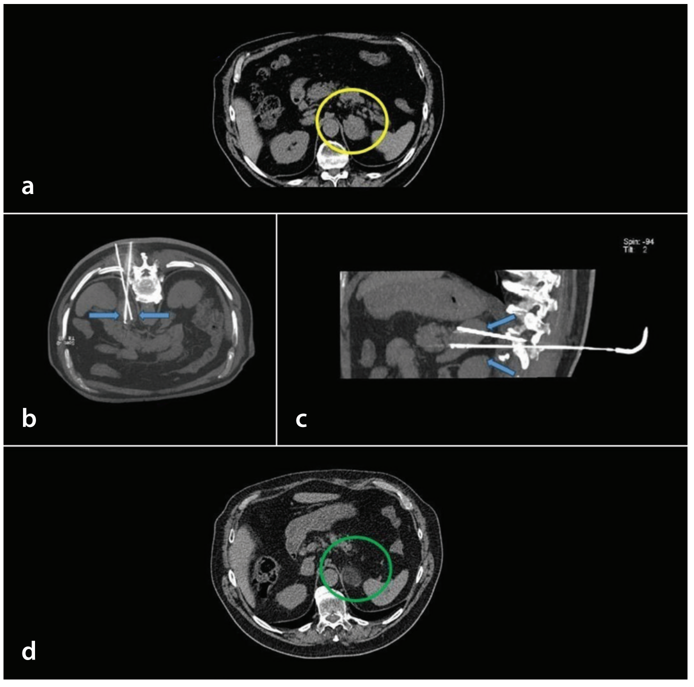

Figure 2. A 78-year-old woman with a history of non-small cell lung cancer with solid left adrenal metastasis [yellow circle in the preoperative computed tomography (CT) scan in **a**]. Treatment of the lesion with cryoablation using two Icesphere 1.5 cryoprobes (Visual ICE™, Galil Medical-Boston Scientific, Arden Hills, MN, USA), via posterior percutaneous access (blue arrows in the intraoperative axial scan image in **b** and in the sagittal plane reconstruction in **c**). Complete necrosis of the lesion in the CT follow-up (green arrow in **d**).

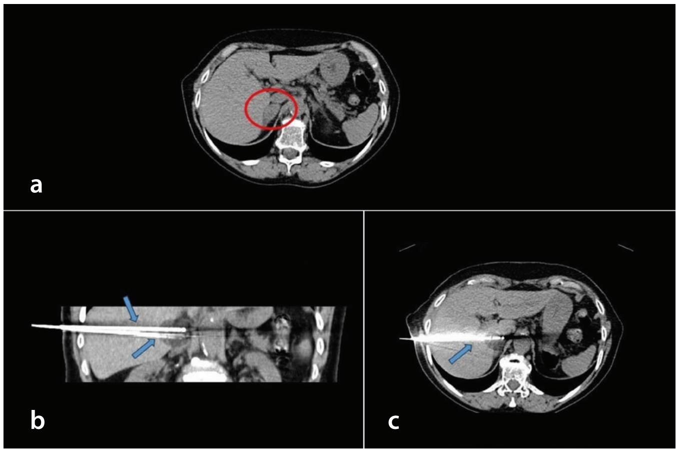

Figure 3. A 68-year-old man with a history of non-small cell lung cancer with solid right adrenal metastasis (red circle in the preoperative computed tomography scan in **a**). Treatment of the lesion with cryoablation using two Icesphere 1.5 cryoprobes (Visual IC™, Galil Medical-Boston Scientific, Arden Hills, MN, USA) via transhepatic access (blue arrows in the intraoperative reformatted coronal scan image in **b** and in the axial plane in **c**).

Patients were monitored during the first 24 hours and then discharged 1 day after the procedure if they were experiencing no discomfort.

Regular physical and laboratory evaluations, comprising blood cell count analysis, adrenal hormone measurements, and tumor marker monitoring based on the histological characteristics of the primary tumor, were conducted monthly.

Following adrenal cryoablation treatments and during the entire clinical and radiologic follow-up period, all the patients continued to receive their usual systemic therapies.

Regularly scheduled CT scans of the chest, abdomen, and pelvis, both with and without contrast, were conducted for patients at intervals of 1, 3, 6, and 12 months post-cryoablation, followed by biannual scans. The scanning protocols mirrored those used initially to evaluate the adrenal tumor lesions prior to the cryoablation.

Two months after the procedure, a complete disappearance of contrast enhancement in CT imaging was interpreted as a full response to the ablation treatment. By the 6^{th} month, any alterations in contrast enhancement or size increases of the treated areas seen in CT scans were indicative of potential recurrence or progression of the disease. The schedule for these radiological evaluations was largely influenced by the understanding that early post-procedure CT scans (within the first 30 days) can show intense enhancement of the treated areas due to the inflammatory response triggered by the cryoablation process.[20]

Hormonal analysis, including adrenal hormone levels, was conducted to assess the treatment's impact on adrenal function.

Statistical analysis

Statistical analysis was conducted to evaluate the outcomes of the cryoablation procedures. Descriptive statistics were used to summarize patient demographics, treatment characteristics, and follow-up data, including means, standard deviations, and percentages. For survival analysis, the Kaplan–Meier method was employed to estimate overall survival (OS) and progression-free survival (PFS) rates. The OS was defined as the time from the date of the first cryoablation procedure to the date of death from any cause, whereas the PFS was defined as the time from the first cryoablation procedure to the first documented evidence of disease progression or recurrence. The Kaplan–Meier curves were used to illustrate survival probabilities over time, and the corresponding 95% confidence intervals (CIs) were calculated.

Results

All cryoablation sessions were successfully completed, and no procedure-related complications were observed. The CT scans performed post-procedure confirmed the expansion of the iceball, extending 1 cm beyond the tumor borders, thus establishing an adequate safety margin.

Patient demographics and treatment overview:

- A total of 12 patients with AMs under went cryoablation treatment.
- Each patient presented with a single adrenal tumor.
- None of the patients had undergone adrenal resection prior to cryoablation.

Technical success:

- Complete tumor ablation, defined by the disappearance of any intratumoral arterial enhancement according to mRECIST criteria[17] was achieved in 11 out of 12 patients.
- This resulted in a primary success rate of 91.7%.
- One patient exhibited residual tumor activity at follow-up and required a sub sequent cryoablation session, which led to complete local tumor control, bringing the overall technical success rate to 100%.

Follow-up and recurrence:

- The follow-up period ranged from 8 to 24 months, with a mean duration of 16.3 ± 5.1 months.
- Six patients (50%) underwent additional systemic therapy post-cryoablation.
- Among this subgroup, three patients developed extra-adrenal tumors.
- Local tumor recurrence was observed in two patients (16.7%), occurring within a span of 6–20 months (median: 13 months).
- One of these patients underwent a sec ond cryoablation session due to local recurrence, after which no further local recurrences were detected in subse quent CT scans.

Systemic progression and mortality:

- Systemic progression was documented in five patients (41.7%):
  - Two cases of renal cancer recurrence
  - Two cases of non-small cell lung cancer recurrence
  - One case of multiple bone metastases
- During the study period, five patients died:
  - Four deaths were due to tumor progression
  - One death was due to heart failure
- The average OS duration was calculated to be 26.4 ± 5.6 months (95% CI: 20.2–32.6).

Discussion

In recent advancements in oncological treatment, cryoablation has emerged as a standout technique for addressing AMs.[15-19] This minimally invasive procedure has gained prominence due to its unique mechanism of action and significant clinical benefits, particularly when compared with other thermal ablation methods, such as radiofrequency and microwave ablation.

Cryoablation works by inducing cellular destruction through the rapid freezing of tumor tissue, leading to ice crystal formation within cells and subsequent cell death.[12] One of the key advantages of cryoablation is that it allows for visualization of the iceball in real-time using CT imaging. This real-time visualization enables precise monitoring of the ablation process, ensuring that the iceball extends beyond the tumor margins, which is critical for achieving a complete ablation and minimizing the risk of recurrence.[13,14] Additionally, the cold-induced anesthesia effect often results in a generally painless procedure, reducing or eliminating the need for general anesthesia, which is a significant benefit for patients who may be at higher risk for anesthesia-related complications.[15,16]

This single-center study contributes valuable insights into the efficacy and safety of CT-guided cryoablation for AMs. With 12 patients undergoing 13 procedures, we recorded a primary success rate of 91.7% and a secondary success rate of 100%, noteworthy when compared with existing literature where success rates for cryoablation, radiofrequency, and microwave ablation for AMs typically range from 70.5% to 82%.[1,2,19-25]

The high technical success rates observed in this study underscore the efficacy of cryoablation, particularly in achieving high primary complete ablation rates. Furthermore, the ability to perform follow-up cryoablations in cases of residual tumor activity enhances the overall efficacy of this treatment modality.[11-18]

In a study by Zhang et al.[22], CT-guided cryoablation for AMs demonstrated a primary technical success rate of 90.3% and a secondary success rate of 100% among 31 patients. The study reported a 19.4% local progression rate and favorable survival outcomes, with 1-, 3-, and 5-year local PFS rates at 80.6%, 37.8%, and 18.4%, respectively. These results further validate the high efficacy of cryoablation, particularly in cases where initial treatment might not fully eradicate the tumor.[22]

In 2021, Aoun et al.[23] assessed the technical feasibility and safety of percutaneous cryoablation for AMs in 34 patients. The local recurrence rate was 10% over 1.8 years. Recurrence was higher in tumors >3 cm. Major complications occurred in 5% of cases, with one directly linked to the procedure. Blood pressure increases were more significant in patients with residual adrenal tissue, but were manageable, especially with pre-treatment using alpha blockade.

Comparative studies further support the efficacy and safety of cryoablation. For example, in a meta-analysis by Pan et al.[25], the efficacy and safety of image-guided percutaneous thermal ablation for AMs were evaluated. The study revealed a 1-year local control rate of 80% and a 1-year OS rate of 77%, with severe adverse events occurring in 16.1% of cases and intraprocedural hypertensive crises in 21.9%. These findings align closely with the outcomes of the present study, where we observed that cryoablation effectively controlled local tumor progression with minimal complications.[25]

An added benefit of cryoablation is the reduced risk of major complications, such as hypertensive crises, which are often associated with other thermal ablation methods.[26,27]

In the present study, minor complications, primarily mild increases in blood pressure, were effectively managed without any reports of severe hypertensive crises. This aspect positions cryoablation as a potentially more favorable option for specific patient groups, particularly those who may be at higher risk for complications associated with other forms of thermal ablation.

However, it is important to acknowledge the limitations of this study. The retrospective design may have introduced selection bias, and the single-center nature, coupled with a small patient cohort, limits the generalizability of the findings. Consequently, while our results are promising, they highlight the need for multi-center randomized controlled trials to further validate the efficacy and safety of cryoablation in treating AMs and to explore its broader application across diverse patient populations.

In summary, this study reinforces the clinical efficacy of cryoablation for the treatment of AMs, particularly in achieving high primary complete ablation rates with a favorable safety profile. As the field of oncological treatment continues to evolve, cryoablation stands out as a compelling option, offering both precision and safety in the management of AMs.

In conclusion, CT-guided cryoablation is safe and effective in treating AMs, equating to other ablation techniques in terms of technical success, local tumor control, and the handling of complications.

These findings support the method's consideration as a practical alternative in oncological treatments, given its versatility in addressing various cancer types and its efficacy in both localized and systemic disease management.

Footnotes

Conflict of interest disclosure

The authors declared no conflicts of interest.

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