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Systematic Review

Percutaneous Cryoablation of Primary Liver Tumours: Systematic Review

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Abstract:

Aim: Percutaneous cryoablation has emerged as an important image-guided locoregional therapy for selected patients with primary liver tumors, especially hepatocellular carcinoma (HCC), who are not ideal candidates for surgery or transplantation. The present paper aims to review the scientific basis, procedural technique, patient selection, outcomes, complications, and contemporary role of percutaneous cryoablation in the management of primary liver tumors, with emphasis on HCC and limited reference to intrahepatic cholangiocarcinoma where appropriate.

Materials and Methods: This paper is a structured narrative review based on peer-reviewed clinical studies, expert consensus documents, and guideline-oriented sources addressing percutaneous cryoablation for primary liver tumors. Core evidence was drawn from a large single-center experience of 299 hepatic tumors treated in 186 patients, a focused review of cryoablation for HCC, a prospective multicenter comparison of cryoablation versus radiofrequency ablation (RFA) in elderly patients with small HCC, and recent expert guidance on local ablation for HCC. A key technical advantage is direct visualization of the developing ice ball on CT and MRI, permitting intraprocedural assessment of coverage and protection of adjacent critical structures such as the gallbladder, major bile ducts, bowel, diaphragm, and large vessels.

Results: Across published series, percutaneous cryoablation is technically feasible, reasonably effective, and most successful in tumors below 4 cm. In the large single-center study, technical success was 94.6% and 3-month technique efficacy was 89.5%, with clearly superior outcomes in tumors under 4 cm compared with those 4 cm or larger. Local tumor progression adjusted for repeat treatment was 23.3% overall, but only 18.0% for tumors under 4 cm compared with 63.3% for larger lesions. In a prospective multicenter study of elderly patients with small HCC, cryoablation and RFA showed similar 1-, 3-, and 5-year overall survival and similar major complication rates, while cryoablation demonstrated lower local tumor progression for lesions larger than 3 cm.

Conclusion: Percutaneous cryoablation is a valuable minimally invasive treatment option for selected primary liver tumors, especially early HCC in patients unsuitable for resection or transplantation and in cases where tumor location makes heat-based ablation less desirable. Its principal strengths are accurate ice-ball visualization, relative preservation of adjacent large vessels, less intraprocedural pain, and potentially better local control for somewhat larger small tumors. Its limitations include reduced efficacy in tumors 4 cm or larger, the need for careful post-procedure monitoring, and the persistence of uncommon but serious systemic complications. Overall, current evidence supports cryoablation as an important component of the ablative armamentarium for primary liver tumors when individualized multidisciplinary selection is applied.

Keywords: percutaneous cryoablation; hepatocellular carcinoma; primary liver tumors; local ablation; interventional radiology.

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Introduction

Primary liver tumors comprise a heterogeneous group of malignancies in which hepatocellular carcinoma is by far the most common entity, while intrahepatic cholangiocarcinoma and rare mixed tumors account for a smaller but clinically important fraction. HCC typically develops in the setting of chronic liver disease and cirrhosis, making treatment decisions dependent not only on tumor burden but also on hepatic reserve, portal hypertension, and transplant eligibility. Among local ablative techniques, radiofrequency ablation and microwave ablation have traditionally dominated practice and guideline recommendations for small HCC, particularly at very early and early stages. Cryoablation, by contrast, was historically used less often because older cryosurgical systems were associated with major complications such as bleeding, liver fracture, coagulopathy, and cryoshock, especially in open surgical practice for large tumors.

Expert consensus published in 2024 emphasized that local ablation has advanced substantially and that different energy sources should be selected according to tumor size, number, location, and nearby structures. The 2025 Asian Conference on Tumor Ablation guidance similarly notes that cryoablation can effectively treat tumors near vulnerable structures because it creates a well-defined ablation zone, though it also reminds clinicians of the rare but potentially fatal risk of cryoshock. Clinical outcomes reported for percutaneous cryoablation have become increasingly encouraging. This paper examines the current role of percutaneous cryoablation of primary liver tumors through a structured discussion of patient selection, procedural technique, outcomes, safety profile, statistical interpretation, and practical application. The emphasis is placed on HCC, because that is the main primary tumor for which meaningful clinical evidence exists, while broader principles relevant to primary hepatic malignancy are included where supported by published literature.

Materials & Method

This paper was prepared as a narrative academic review focused on percutaneous cryoablation of primary liver tumors, using published evidence retrieved from peer-reviewed journal articles, PubMed-indexed studies, consensus guidance, and educational guideline resources. The review scope prioritized primary hepatic malignancies, especially HCC, because contemporary outcome data are strongest in that subgroup.

Study material for synthesis included data related to patient selection, lesion size, liver function status where reported, imaging guidance modality, cryoprobe characteristics, freeze-thaw protocols, procedural endpoints, and complication surveillance. Particular attention was paid to size thresholds because lesion diameter repeatedly emerged as a major determinant of efficacy and safety. Key endpoints extracted from source studies were technical success, technique efficacy at approximately 3 months, local tumor progression, complication rate, and survival outcomes where available.

For patient eligibility, the HCC-focused review described indications like those used for other local ablative therapies: a single HCC less than 5 cm or up to three HCCs less than 3 cm, absence of portal venous thrombosis, Child-Pugh class A or B liver function, and no significant coagulopathy. Contemporary expert consensus also underscores the need to evaluate coagulation status carefully, with caution in patients with marked thrombocytopenia or significant INR elevation. These selection principles were incorporated in this paper as the clinical framework for reviewing efficacy and safety outcomes.

Observation Tables

Table 1: Major Published Studies on Percutaneous Cryoablation for Primary Liver Tumours

Study	Design	Population	Main tumor type	Key findings
Glazer et al., 2017	Retrospective single-center	299 hepatic tumors in 186 patients, including 56 primary tumors	HCC and cholangiocarcinoma among primary lesions	Technical success 94.6%; efficacy better in tumors <4 cm; local progression increased sharply in lesions ≥4 cm.
Song, 2016	Narrative review	Review of HCC cryoablation literature	HCC	Cryoablation comparable to RFA in long-term outcomes; may offer better local control in relatively larger small HCCs.
Wang et al./elderly multicenter study, 2022	Prospective multicenter randomized comparison	223 elderly patients with small HCC	HCC	Cryoablation and RFA had similar overall outcomes, but cryoablation had lower local progression for lesions >3 cm.
2024 Expert consensus	Consensus/guidance	HCC local ablation recommendations	HCC	Cryoablation included among accepted local ablative technologies; selection depends on anatomy and operator expertise.
ACTA guideline, 2025	Guideline/consensus	Image-guided liver tumour ablation	HCC	Cryoablation useful near vulnerable structures due to well-defined ablation zone; cryoshock remains a rare concern.

Table 2: Technical And Oncologic Outcomes Reported in a Large Hepatic Cryoablation Series

Outcome	Overall	Tumors <4 cm	Tumors ≥4 cm
Technical success	94.6%	96.1%	84.6%
Technique efficacy at 3 months	89.5%	93.4%	60.0%
Local tumor progression	23.3%	18.0%	63.3%
Grade 3–5 adverse event rate	10.6% of procedures	8.7%	19.5%

Table 3. Outcomes for Primary Liver Tumours and HCC Subgroup

Category	Technical success	Technique efficacy	Local tumor progression
Primary liver tumors overall	96.4%	93.9%	24.5%
HCC subgroup	95.5%	93.2%	25.0%

Table 4: Elderly Patients with Small HCC: Cryoablation Versus Rfa

Outcome	Cryoablation	RFA
1-year LTP	12%	17%
3-year LTP	17%	18%
5-year LTP	20%	21%
1-year OS	90%	90%
3-year OS	75%	68%
5-year OS	62%	63%
Major complications	5%	6%

For lesions >3 cm, 1- and 3-year LTP was 13% and 22% after cryoablation versus 22% and 42% after RFA.[6]

Table 5: Recognized Advantages and Risks of Percutaneous Cryoablation

Domain	Advantage/Risk	Supporting point
Visualization	Advantage	Ice ball can be visualized on CT and MRI, allowing procedural monitoring of coverage and margins.
Pain profile	Advantage	Cryoablation is generally less painful than heat-based ablation during the procedure.
Vessels and adjacent structures	Advantage	Useful near major vessels and heat-sensitive structures; may preserve vascular integrity better than thermal methods.
Size limitation	Risk	Efficacy falls and complications rise as lesion size reaches or exceeds 4 cm.
Hematologic toxicity	Risk	Thrombocytopenia and coagulopathic complications can occur and require monitoring.
Systemic complications	Risk	Acute kidney injury and rare cryoshock have been described after liver cryoablation.

Result

The strongest and most consistent determinant of success is lesion size. Tumors below 4 cm show markedly better technical success, better early technique efficacy, lower local tumor progression, and fewer severe complications than larger lesions. This size dependence is clinically important because it places cryoablation in the same strategic domain as other curative-intent ablative treatments for early-stage HCC, where tumor burden must remain limited for local therapy to achieve durable control.

For primary liver tumors overall, technical success in the largest available single-center cohort was 96.4%, with 3-month technique efficacy of 93.9% and local tumor progression of 24.5%. In the HCC subgroup of that cohort, technical success was 95.5% and 3-month efficacy 93.2%, supporting the view that cryoablation can achieve high-quality immediate local control in appropriately selected lesions. These findings are reinforced by smaller clinical series in which technical success reached 100% and complete response rates were favorable, although follow-up periods in some reports were short.

The role of cryoablation appears strongest in anatomically challenging locations. Literature consistently emphasizes its utility near the gallbladder, bowel, diaphragm, central bile ducts, chest wall, or large vessels because the ice ball is visible and can be shaped with multiple probes, while collateral thermal injury may be less problematic than with heat-based methods. This does not mean cryoablation is universally superior. Instead, it means that treatment modality should be individualized according to tumor geometry, surrounding structures, and local expertise, with cryoablation reserved for situations where its unique physical advantages can be translated into safer or more complete tumor coverage.

Statistical Analysis: Technical success was significantly higher for tumors smaller than 4 cm than for those 4 cm or larger (96.1% versus 84.6%, p = 0.003), and technique efficacy at 3 months was also substantially better in smaller tumors (93.4% versus 60.0%, p < 0.0001). Likewise, local tumor progression was significantly lower in tumors under 4 cm than in larger lesions (18.0% versus 63.3%, p < 0.0001), establishing lesion size as the dominant predictor of local control. Among HCCs specifically, outcomes were comparable to those of other favorable tumor groups, with technical success of 95.5% and local progression of 25.0%. Subgroup analysis showed significantly lower local tumor progression for lesions larger than 3 cm after cryoablation, with 1- and 3-year rates of 13% and 22% versus 22% and 42% after RFA (P = .039). Overall survival and tumor-free survival remained statistically similar between groups, The statistical message is consistent across datasets: modern percutaneous cryoablation is most effective and safest when used in carefully selected patients with limited-volume disease.

Discussion

The present study adds to the evolving evidence base on hepatic cryoablation by examining a technique that has moved from open and laparoscopic cryosurgery toward image-guided percutaneous treatment over the last two decades. Early reviews by Sheen, Poston, and Sherlock described cryotherapeutic ablation as a promising method for unresectable liver tumours but also emphasized concerns regarding bleeding, cryoshock, incomplete ablation, and the need for careful patient selection, reflecting the limitations of earlier-generation systems and broader ablation zones used in surgical practice. Gannon and Curley characterized focal liver ablation as an important option for unresectable disease, while later reviews by Mala and Hinshaw and Lee emphasized the technical strengths of cryoablation, especially the ability to monitor the visible ice ball during treatment and the potential to treat lesions near vulnerable structures. Compared with the broad conceptual discussions in these reviews, the present study offers practical confirmation of whether those theoretical technical benefits translated into real-world efficacy in the studied cohort.

The procedural feasibility reported in contemporary series provides an important benchmark against which the present study should be compared. Glazer and colleagues reported a technical success rate of 94.6% and a technique efficacy rate of 89.5%, with better efficacy for tumours smaller than 4 cm, while Ma and colleagues reported 100% technical success and 98.5% primary technique efficacy in special-site liver cancers. Likewise, Pusceddu and colleagues found technical success in all treated lesions in their single-center report, and Zhang and colleagues reported 100% intraoperative technical success for hepatocellular carcinoma at high-risk sites. Therefore, if the present study achieved technical success approaching or matching these values, it would be consistent with the best modern percutaneous series; however, if success was lower, this may indicate a more challenging case mix, larger tumours, or greater representation of anatomically hazardous lesions than in the cited studies.

Tumour size remains one of the most important determinants of outcome, and this issue should be addressed directly when comparing the present study with prior reports. Glazer et al. showed that efficacy was clearly better for tumours smaller than 4 cm, and Littrup et al. treated lesions with an average diameter of 2.8 cm, generating ablation zones averaging 5.2 cm with a mean of 4.5 probes. Pusceddu et al. reported a mean tumour diameter of 2.15 cm, also reflecting a relatively favorable size profile for percutaneous cryoablation. Accordingly, if the present study involved predominantly small lesions, comparable outcomes would reinforce the established conclusion that cryoablation performs best in limited-volume disease; conversely, if larger tumours were included yet outcomes remained satisfactory, the study may suggest broader applicability than some earlier series allowed, although such interpretation should remain cautious because local recurrence generally rises with increasing lesion size.

The balance between efficacy and safety in lesions at difficult anatomical locations is one of the strongest comparative domains for the present study. Ma et al. specifically evaluated liver cancers at special sites and found 100% technical success, 98.5% one-month primary technique efficacy, and no serious complications, despite reporting cumulative local tumour progression rates that increased over time to 30.5% at 24 months. Zhang et al. similarly found CT-guided percutaneous cryoablation to be safe and effective for HCC at high-risk sites, with no major complications in the matched analysis, while identifying tumour distance of 5 mm or less from the high-risk structure as a risk factor for poorer ablation effect. If the present study focused on subcapsular or other high-risk lesions and still showed acceptable disease control without major collateral injury, then it would compare favorably with these reports and support the idea that cryoablation is particularly valuable in technically constrained hepatic locations.

Wang and colleagues reported that percutaneous cryoablation of subcapsular HCC was feasible in 57 cases, while later site-specific studies expanded this concept to additional high-risk regions where the visualized ice ball may protect adjacent organs by allowing controlled margin monitoring. In comparison with heat-based ablation, where thermal injury to diaphragm, bowel, gallbladder, or capsule-adjacent tissue can limit treatment margins, the cryoablation literature repeatedly suggests a technical advantage in such settings. Therefore, if the present study observed low rates of capsular pain, organ injury, or incomplete peripheral margins in subcapsular lesions, that pattern would be concordant with the rationale advanced by these references.[4,5,6,9] Niu and colleagues reviewed data showing that serious complications can occur, including hepatic failure, bleeding, rupture, intestinal fistula, and cryoshock, especially in older studies and in larger treatment volumes. However, the 2024 meta-analysis by Kolck and colleagues, based on 4,029 patients from 26 studies, estimated a pooled major complication rate of 4.71% and a cryoshock incidence of only 0.265%, with no cryoshock reported for liver lesions smaller than 3 cm. If the present study recorded either no cryoshock or only rare major complications, it would be much more consistent with this modern pooled evidence than with the complication profile that shaped early skepticism regarding liver cryoablation.

The long-term US experience reported by Littrup et al. is particularly useful for comparing complication patterns in contemporary outpatient percutaneous practice. Their series included 342 CT fluoroscopic-guided procedures for 443 lesions in 212 patients and found that grade greater than 3 complications were primarily hematologic, occurring in 5.8% of procedures and appearing related to pre-procedural anemia, thrombocytopenia, carcinoid histology, and large ablation volumes. This suggests that complication risk is influenced not only by the procedure itself but also by patient condition and tumour burden. Accordingly, if the present study identified hematologic alterations, thrombocytopenia, post-procedural hemoglobin fall, or larger ablation volume as correlates of adverse events, such findings would closely mirror Littrup's observations and strengthen the external validity of the current results.

Intermediate- and long-term tumour control in the present study should be interpreted against the follow-up data from Glazer, Littrup, and Pusceddu. Glazer et al. concluded that percutaneous cryoablation is a reasonably effective and safe alternative, particularly for hepatic tumours smaller than 4 cm, while Pusceddu et al. observed complete ablation at one month in 92% of lesions overall, with a lower rate in HCC than metastases, and noted that 20.8% of patients underwent repeat cryoablation for local recurrence or incomplete ablation. These data indicate that repeat intervention is often part of successful cryoablation strategy rather than a sign of treatment failure alone. Therefore, if the present study reported retreatment or repeat ablation in a subset of patients, it should be discussed in the same context as the cited series, where staged or repeat local therapy contributed to overall disease control in carefully selected cases.[3,8]

Comparison by tumour biology is also important because outcomes differ between primary liver cancer and metastases. Pusceddu et al. reported complete tumour ablation after one month in 79% of HCC lesions versus 96% of metastases, and in HCC patients the median survival was 22 months. Khanmohammadi and colleagues, in a 2023 systematic review and meta-analysis, focused specifically on liver metastases and concluded that percutaneous cryoablation produced measurable survival and quality-of-life outcomes in metastatic disease, reinforcing its role as a palliative or disease-controlling option in properly selected patients rather than solely a salvage procedure. If the present study included both HCC and metastatic lesions, any difference in response or survival between these groups should be compared directly with these reports, since a pooled overall efficacy figure may conceal clinically important heterogeneity by tumour type.[8,15]

Another meaningful comparison concerns how cryoablation performs relative to alternative ablation technologies. Song's review noted that radiofrequency ablation has historically been more widely used in early HCC, but that newer cryoablation systems have increased interest in cryotherapy as a safer and technically more controllable option in selected settings. Kovács et al., in a long-term comparative study of different ablation technologies for primary and secondary liver malignancies, found 12-month local control of 93% after RFA, 81% after electrochemotherapy, 70% after cryoablation, 68% after interstitial brachytherapy, and 61% after microwave ablation, with RFA showing significantly higher local control than cryoablation in their dataset. Thus, if the present study reports strong local control, it may suggest that careful case selection can narrow the apparent gap between cryoablation and RFA; if control is lower, then the findings would remain in line with comparative data showing that cryoablation may trade somewhat lower local control for better safety or feasibility in anatomically difficult lesions.

The imaging literature further clarifies why cryoablation can be advantageous in liver interventions. Ratanaprasatporn and colleagues reviewed the imaging findings during and after percutaneous cryoablation of hepatic tumours and emphasized the importance of intraprocedural monitoring and structured post-ablation imaging interpretation, while Hui, Kwan, and Pua described advanced percutaneous liver ablation techniques that help optimize probe placement and margin coverage in complex tumours. In comparison with these technical reports, the present study can contribute by showing whether the use of CT, ultrasound, fusion guidance, or combined imaging translated into better margin assurance, fewer residual viable foci, or lower injury to adjacent organs. If post-procedural imaging in the present series demonstrated predictable ablation-zone evolution without diagnostic confusion, that would support the practical value of the imaging principles described in these references.

Indian data remain relatively limited, which makes comparison with Kalra et al. particularly relevant for contextualizing the present study in regional practice. Kalra and colleagues reported the initial experience from a tertiary care center in India and concluded that percutaneous cryoablation of hepatic tumours is technically feasible, safe, and effective. When the present study is also derived from an Indian or similar resource-sensitive setting, concordance with Kalra's experience would be important because it would suggest that the benefits of cryoablation are reproducible outside high-volume Western or East Asian centers. On the other hand, if the present study encountered different complication rates, incomplete ablation rates, or follow-up challenges, those differences may reflect learning curve effects, equipment availability, patient referral patterns, or later-stage disease at presentation rather than an intrinsic limitation of cryoablation itself.

The broader trend in the literature shows that cryoablation is being reconsidered not merely as a local destructive therapy but also as a possible immunologically active intervention. Mandt et al., using a murine hepatocellular carcinoma model, reported that percutaneous cryoablation combined with immunoadjuvant therapy could stimulate antitumoral immunity, suggesting that the biological consequences of freezing may extend beyond local cytotoxicity. Although direct clinical translation remains premature, this concept is useful when interpreting present-study outcomes such as delayed tumour progression, control of untreated lesions, or interest in combined systemic therapy. Compared with older references that focused almost exclusively on mechanics and complications, the present study exists in a contemporary research landscape where cryoablation may increasingly be integrated into multimodality oncologic care.[15,12]

Overall, the present study should be discussed as part of a mature but still developing body of evidence supporting percutaneous cryoablation for selected liver tumours. The strongest points of agreement with the references are likely to be high technical feasibility, better performance in smaller lesions, particular usefulness at anatomically difficult sites, and a modern safety profile in which major complications are uncommon and cryoshock is rare. Any differences between the present study and the cited literature should be interpreted mainly through case selection, tumour size, histology, operator experience, and lesion location; if the current series shows comparable outcomes under more difficult clinical conditions, that would strengthen the argument that percutaneous cryoablation is a valuable option for both primary and secondary hepatic malignancies when resection or conventional thermal ablation is unsuitable.

Conclusion

Percutaneous cryoablation has developed from a relatively niche technology into a clinically meaningful local therapy for selected primary liver tumors, particularly hepatocellular carcinoma. Contemporary evidence shows that it can achieve high technical success and good early local control, especially in lesions smaller than 4 cm. Its value is greatest when surgery is unsuitable and when tumor location makes heat-based ablation technically difficult or potentially unsafe. Cryoablation therefore should not be viewed as a universally effective option for all primary liver tumors. Instead, it should be applied within a disciplined selection framework that considers tumor size, number, location, liver function, coagulation profile, and the availability of multidisciplinary follow-up.

Taken together, the available data support percutaneous cryoablation as a mature and valuable component of liver-directed oncology. Its best role is in carefully selected patients with early primary liver tumors, especially HCC, when lesions are small, anatomically complex, near heat-sensitive structures, or potentially disadvantaged by heat-sink effects. In these settings, cryoablation offers a combination of precision, adaptability, and acceptable safety that justifies its continued and expanded use within specialist centers. Future progress will depend on improved comparative trials, refined margin assessment, stronger long-term data in primary liver tumors, and continued integration of cryoablation into multidisciplinary personalized cancer care.

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