Laparoscopic-Assisted Ablation of Hepatic Tumors: A Review

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Abstract

Keywords

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Thermal ablation of hepatic tumors has been an evolving field over the last two decades. It is used in the treatment of both primary and metastatic neoplasms, and with evolutions in the technology, there has been an increasing interest in treating lesions where hepatic resection is not an option. Laparoscopic or minimally invasive surgical procedures have also advanced during this same time period, and the interface of these tools has been associated with the genesis of a new approach for treating hepatic lesions which are located in difficult to reach locations or found immediately adjacent to other intra-abdominal organs. This review summarizes the published literature focusing on the treatment of primary and metastatic neoplasms located in the liver, including a review of outcomes.

Objectives: Upon completion of this article, the reader will be able to identify the role of laparoscopic assistance during microwave or radiofrequency ablation of liver tumors.

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Georg Kelling performed the first laparoscopic procedure in his laboratory in 1901.¹ In the late 20th century due to advancements in lens design and optical projection, laparoscopy achieved global acceptance. The field has progressed from a purely diagnostic instrument to one capable of advanced intervention. Laparoscopy is extensively used in patients with benign disease, as well as those with advanced

malignancy. Over the past 15 years, there has been a growing interest in utilizing laparoscopy to facilitate the delivery of thermoablative therapies for primary (►Fig. 1) and secondary tumors of the liver. This article will provide a summary and insight into the current state of laparoscopic thermal ablation in hepatic malignancies.

The local ablative modalities most frequently used to treat liver tumors are radiofrequency (RF) and microwave (MW). For this reason, other local ablative therapies, such as cryotherapy, ethanol injection, and laser-induced thermotherapy will not be discussed. RF is delivered via an insulated probe with an exposed tip. The RF generator provides an alternating current causing the oscillation of ions, resulting in a tissue temperature of up to 100°C. The heat dissipates throughout the tissue surrounding the probe, and the increase in local temperature results in protein denaturation ultimately leading to cellular destruction and tissue necrosis.² Although it provides a similar result MW energy ablation functions through a different mechanism, the MW generator produces electromagnetic radiation (EMR) within the MW spectrum, which is absorbed by water molecules. This EMR causes molecular rotation, resulting in the creation of thermal energy within the tissue leading to coagulative necrosis.³ In

Figure 1 A microwave ablation antenna (black arrow) is demonstrated within the hepatic parenchyma during ablation. A four-way ultrasound probe (white arrow) is located immediately adjacent to the microwave antenna.

either technique, ablation zones are predetermined by limiting the amount of energy supplied, or by the time the tissue is exposed to the energy source.

RF ablation (RFA) and MW ablation (MWA) have been described as a treatment for primary and secondary malignancies in the liver. The most common applications are in patients with hepatocellular carcinoma (HCC), and in those with hepatic metastases from colorectal carcinoma (colorectal cancer liver metastases [CRLM]).^{4–20} The indications for laparoscopic RFA or MWA can be divided into patient-specific and tumor-specific categories. In discussing indications for laparoscopic thermal ablation, it should be noted that surgical resection with tumor-free margins remains the accepted gold standard of therapy for both HCC and CRLM.^{21–26}

The most frequent presentation of HCC is in the setting of cirrhosis. Additional risk factors for the development of HCC include concomitant infection with hepatitis C and/or hepatitis B.²⁷ Typically, these patients are not eligible for partial hepatectomy due to insufficient hepatic reserve and are subsequently evaluated for alternative options, including but not limited to thermal ablation or liver transplantation.²⁸ With regard to CRLM, patients often undergo thermal ablation due to the presumption that they would be unable to tolerate the magnitude of partial hepatectomy due to comorbidities. Tumor-specific characteristics can also limit patients' options in treating either HCC or CRLM. Patients with technically unresectable disease, multicentric disease, and bilobar disease are also candidates for laparoscopic thermal ablation.

Safety/Morbidity/Mortality

The safety of laparoscopic RFA and MWA is well described in the literature. Complication rates vary from 2 to 62%.^{4,5,10–12,14,16,19,20} Morbidity from RFA ranges from 2 to 45%,^{4,11,12,14} whereas the rates for MWA range from 16 to 62%.^{4,5,20} The majority of complications are minor; however, deaths have been reported after both procedures.^{4,9}

Efficacy

Hepatocellular Carcinoma

RFA and MWA treatment in HCC are local modalities typically used in patients who are not candidates for surgical resection. Since anatomic resections are not possible, the necessity for complete ablation is vital. Incomplete laparoscopic ablation rates from 5.6 to 13% have been published^{5,6}; local recurrence rates range from 2.9 to 22% with a varying range of follow-up.^{5,6,9} In addition to local recurrence, intrahepatic recurrence and the development of de novo malignancies poses a significant clinical challenge. In a retrospective review of 92 patients undergoing laparoscopic RFA for HCC, Karabulut et al noted a new liver recurrence in 57% of patients with a median follow-up of 19 months. This was in comparison to a 46% recurrence rate in 92 patients undergoing liver resection for HCC ($p = 0.167$).⁹ Similarly, Santambrogio et al published a regional recurrence rate of 30% after laparoscopic RFA for HCC in 102 patients during an unspecified time of follow-up.⁶

The effects of laparoscopic thermal ablation on survival have also been described. Swan et al published a 1-year survival rate of 72.3% in 54 patients with HCC and cirrhosis following laparoscopic MWA.⁵ Berber et al found a similar 1-year overall survival rate of 78% after laparoscopic RFA in 66 cirrhotic patients with HCC.⁸ Ballem et al describe a 3-year survival rate of 21% in 104 patients undergoing 122 ablations for HCC using RF.⁷ In the 66 patients presented by Berber et al, a 3-year survival rate of 38% was achieved.⁸ When reported, 5-year survival rates ranged from 8.3 to 21%.^{7,9}

Several authors have shown an increased survival advantage based on child class.^{5,7,8} Swan et al show a 1- and 2-year overall survival rate of 71 and 63% for Child A cirrhotics, whereas this falls to 65 and 52% in Child B and C, respectively.⁵ Ballem et al and Berber et al found similar median survival in their respective subgroup analyses based on the degree of hepatic dysfunction. In both studies, median survival for Child A was 28 to 29 months, but only 5 to 5.9 months for Child C patients^{7,8} (Berber et al⁸ reached statistical significance with a p value < 0.001).

Colorectal Liver Metastases

Similar to HCC, $< 20\%$ of patients presenting with liver metastases from colorectal carcinoma are eligible for curative resection.²⁹ In addition, local recurrence rates have been problematic for these patients. The local recurrence rates range from 9.2 to 34%.^{13,15,16} Over a 10-year experience with 130 patients, Kennedy et al showed a local recurrence rate of 9.2%. However, a subgroup analysis restricted to patients with tumors > 3 cm in size demonstrates local recurrence rates blossoming to 19.6%.¹⁶ Aksoy et al described a de novo recurrence rate of 43% in 252 patients with CRLM undergoing laparoscopic RFA. Multivariate analysis of this group showed patients with a tumor size > 5 cm were twice as likely to recur locally when compared with patients with tumor size < 3 cm. They also showed patients with an ablation margin of < 1 cm retained a similar risk when compared with those with a margin > 2 cm.¹³ Berber et al also

demonstrated that local tumor control improved with larger ablation margins.¹⁵

Five-year survival rates for hepatic resection in CRLM are as high as 59%.^{30–33} Laparoscopic RFA has been unable to match this efficacy in survival. Aksoy et al reported a 5-year survival rate of 47% in 252 patients; however, the inclusion criteria were limited to those with tumors ≤ 3 cm.¹³ Hammill et al described a retrospective review of 101 patients undergoing laparoscopic RFA for CRLM. Upon review of preoperative imaging, a blinded hepatobiliary surgeon determined 64 of those patients were technically resectable. The 5-year survival for those who were technically resectable was 48.7 versus 18.4% for those deemed unresectable.¹² Two different studies demonstrate similar 5-year survival rates of approximately 30%.^{14,16}

Other Secondary Malignancies

Laparoscopic RFA has been described in multiple secondary hepatic malignancies other than metastatic colorectal cancer. Outcomes from laparoscopic RFA treatment of liver metastases from breast cancer, neuroendocrine tumors, melanoma, sarcoma, and others have been published.^{34–36} These are primarily case reports and small clinical series. Given the paucity of data, laparoscopic thermal ablation should not be considered in the algorithm for standard treatment of these tumors.

Laparoscopic Ultrasound

One of the major advantages of laparoscopic thermal ablation is the inherent surgical staging that precedes an intervention. Some clinicians have advocated for diagnostic laparoscopy before open partial hepatectomy for cancer to ensure a patient's candidacy for curative resection.²⁹ The rationale for this approach is to avoid the morbidity associated with laparotomy for those patients who would not benefit from the planned resection. This concept can be applied to laparoscopic thermal ablation as well. Santambrogio et al reported on 153 HCC nodules identified preoperatively by transcutaneous ultrasound, triple-phase computed tomography (CT), or magnetic resonance imaging (MRI). Only one patient had an MRI. At the time of operation, laparoscopic ultrasound located 26 new malignant lesions that were missed by preoperative imaging. These tumors ranged in size from 4 to 23 mm.⁶ In a series of 72 cirrhotic patients with a variety of malignant hepatic tumors, Salama et al identified 19 new malignant lesions with ultrasound at the time of laparoscopy. Preoperative imaging included triple-phase CT and MRI. The median diameter of these tumors was not specified.¹⁸

Conclusion

Current results with laparoscopic thermal ablation have not demonstrated efficacy that would allow either laparoscopic RFA or MWA to supplant surgical resection as primary therapy for either HCC or CRLM. However, the role of laparoscopic RFA and MWA continues to evolve. The reported complication rates associated with laparoscopic MWA are

surprisingly frequent considering it is a minimally invasive approach. However, the vast majority of the literature on laparoscopic MWA involves patients with HCC and cirrhosis. It is well established that cirrhotic patients are high-risk surgical candidates, and as such more likely to incur postoperative morbidity. The complication rates with MWA are more likely related to the patients underlying liver disease rather than the modality itself.

Laparoscopic RFA and MWA have also been criticized for unacceptable local recurrence rates. Although the rates are higher than surgical resection, the data are impacted by selection bias. The majority of studies reporting on the topic of ablation involve patients allocated to thermal ablation by some means other than randomization. The heterogeneity of the population treated with laparoscopic thermal ablation makes it extremely difficult to draw any meaningful conclusions regarding the efficacy of laparoscopic RFA or MWA. In addition to the questions arising from the selection criteria of the patient population, the impact of heterogeneity of the modalities used must also be studied. Padma et al described the evolution of generators used in RFA, as well as those available for MWA; advances in generators and probes over the last 10+ years likely contribute to some of the differences in outcomes. In addition, RFA and MWA are not equal modalities. MWA provides higher intratumoral temperatures, a more predictable ablation zone, and it is not susceptible to the "heat sink" phenomenon that afflicts RFA.³

Hepatic thermal ablation can be delivered via an open, laparoscopic, or percutaneous approach.¹⁷ The percutaneous approach relies solely on radiographic staging and can be limited by the anatomic location of the tumor(s) within the liver. Some of these anatomic limitations can be overcome with laparoscopic assistance that provides a different trajectory for placement of the ablation probes. In addition, laparoscopy may provide some benefit in detecting subtle extrahepatic disease, which may alter the planned course of treatment.

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