Complications after percutaneous ablation of liver tumors: a systematic review

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Background: Although ablation therapy has been accepted as a promising and safe technique for treatment of unrespectable hepatic tumors, investigation of its complications has been limited. A physician who performs ablation treatment of hepatic malignancies should be aware of the broad spectrum of complications. Proper management is possible only if the physician Performing ablation understands the broad spectrum of complications encountered after ablation.

Objectives: To systematically review the complications after different ablation modalities: Radiofrequency ablation (RFA), microwave ablation (MWA) and Nano knife for the treatment of liver tumors and analyze possible risk factors that precipitate these complications.

Search methods: We performed electronic searches in the following databases: MEDLINE, EMBASE and COCHRANE. Current trials were identified through the Internet (from January 1, 2000 to January 1, 2014). We included only studies who specific mentioned complications after liver ablation therapy (RFA/MWA/Nano knife).

Main results: A total of 2,588 publications were identified, after detailed examination only 32 publications were included in the review. The included studies involved 15,744 participants. According to the type of technique, 13,044 and 2,700 patients were included for RFA and MWA. Analysis showed a pooled mortality of 0.15% for RFA, and 0.23% for MWA.

Conclusions: This systematic review gathers information from controlled clinical trials and observational studies which are vulnerable to different types of bias, never the less RFA and MWA can be considered safe techniques for the treatment of liver tumors.

Keywords: Liver tumors; liver metastases; percutaneous ablation; systematic review

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Introduction

Hepatocellular carcinoma (HCC) and colorectal liver metastases (CLM) are the two most common malignant liver tumors. Hepatic resection (HR) is the only curative option, but only 15-20% of patients with liver metastases from CRC (CRLMs) are suitable for surgical standard treatment (1). For the HCC group, less than 30% of patients with HCC are eligible for surgery, mainly because of the multiplicity of the lesions that often occurs in a background of chronic liver disease, bad liver function, and deteriorating general condition (2,3).

Several alternative treatments to control and potentially cure have been developed for use in patients with malignant liver tumors, whether primary or metastatic. Interventional therapies, such as percutaneous ethanol injection (PEI), radiofrequency ablation (RFA), microwave ablation (MWA) and Nano knife has been developed for treating malignant
RFA has gained wide acceptance by showing superior anticancer effects with low complications and mortality rate. Recently other emerging techniques such as MWA have attracted interest in clinical practice (4). However, these procedures will always entail some risks. Information regarding mortality and complications is absolutely essential for every intervention to permit an accurate assessment of the risks and benefits (5).

One of the greatest persistent problems in hepatic ablation has been the inability to establish quality standards in ablation complications, success, local recurrence after ablation, and nonablation hepatic recurrence. Reports from the literature are heterogeneous because of the study design, sample size, different technical approaches, and number of centers reporting complications and non-uniform terms as well as different parameters to calculate the rate of complications (6-9).

Major complications were defined as any symptom that developed after ablation and persisted for more than 1 week, or those that delayed hospital discharge, threatened the patient’s life, or led to substantial morbidity and disability (10). Major complication: included death, hemorrhage, RFA needle-track seeding, intra hepatic arterial pseudo aneurysm, RFA lesion abscess, perforation of gastrointestinal viscus, liver failure, biloma, biliary stricture, portal vein thrombosis, and hemothorax or pneumothorax requiring drainage, and minor complications including pain, fever, and asymptomatic pleural effusion.

Our goal was to bring the most updated literature regarding current used techniques (“what we really do”). The use of PEI has become less favorable in the face of new modalities such MWA and Nano knife, hence we decided to remove this technique from this review.

Ablation can be done either percutaneous or by surgery, in order to minimize bias related to surgery we decided to include only papers with percutaneous technique.

Materials and methods

Inclusion criteria

Randomized controlled trials (RCTs) and nonrandomized comparative studies assessing HCC or CRLM treated with RFA, MWA or Nano knife treatment were considered for review. Only patients aged over 18 were included. In order to exclude small studies, we only considered studies analyzing more than 50 patients for at least one technique.

Search strategy

A literature search was conducted on PubMed and EMBASE to identify clinical series of RFA, MWA and Nano knife procedures for liver tumours published between January 2000 and January 2014. Letters to the editors, supplements, review articles and case reports were excluded. The titles and abstracts of all potentially relevant trials were screened by one reviewer (LE). The full text articles of potentially relevant studies were obtained. Based on the full text article, another reviewer (HA) independently determined whether the study meets the inclusion/exclusion criteria.

Data collection

Information extracted from each study included: the number of patients, age and Child-Pugh score. The type of study were categorized as prospective, retrospective, observational or randomized trial and the type of intervention included RFA/MWA, the tumor according to type (HCC or metastasis). We extracted the data type for outcome measure using number of deaths, major complications and the description of the type of percutaneous ablative technique used.

Assessment of complications

In this study complications were reported in accordance with the guidelines recommended by the Working Group on Image-Guided Tumor Ablation (10).

The definition of major complication is an event that leads to substantial morbidity and disability, increasing the level of care, or results in hospital admission or substantially lengthened hospital stay (SIR classifications C-E) (Table 1). This includes any case in which a blood transfusion or interventional drainage procedure is required. All other complications are considered minor. It is important to stress that several complications, such as pneumothorax or tumor seeding, can be either a major or minor complications.

Results

The search on Medline and EMBASE databases provided a total of 2,588 citations (Figure 1). After screening title and abstract, 2,461 were discarded. The full text of the remaining 127 citations was examined in more detail, where 95 studies did not meet the inclusion criteria as described.
Finally 32 publications were included in the review.

**Characteristics**

**Study design, participants and interventions**

Of the 32 studies selected for the review, one was randomized trials and 31 were observational studies (Table 2). All the reports were published after 2000 (n=32). There were 29 studies using RFA only and 2 using MWA only. One observational study evaluated RFA versus MWA.

The included studies involved 15,744 participants. According to the type of technique, 13,044 and 2,700 patients were included for RFA and MWA respectively. The average age of patients ranged from 24 to 89 years. Mean tumor size treated ranged from 1.8 to 5.0 cm. In 16 studies, mortality and complications were primary outcomes.

**Specific outcomes**

Death and adverse events were assessed as secondary outcomes in 16 studies. Mean follow-up after treatment ranged from 10 to 137 months. For all percutaneous ablative techniques analyzed, mortality ranged from 0% to 0.88% and the pooled proportion was 0.16% (95% CI, 0.10-0.24%) by the random effects model. Individual analysis showed a pooled mortality of 0.15% for RFA, and 0.23% for MWA.

Major complication rates were 4.1% and 4.6% for RFA and MWA respectively. The most frequent major complication was hemorrhage intraperitoneal, subcapsular, pleural, biliary and retroperitoneal hemorrhage requiring blood transfusion (Table 3). Meanwhile the minor complication rates were 5.9% and 5.7% for RFA and MWA. There was no statistically significant difference in the mortality rates, major complications, and minor complications between the RFA and MWA groups (P>0.05).

**Discussion**

Ablation techniques have gained wide acceptance as a safe alternative to surgery in the management of early HCC and metastatic liver tumors (43,44). The effectiveness of RFA in the treatment of malignant liver tumors has been proven by a number of clinical studies and medical practice reports (45-48). Recently, developments in MWA technology have demonstrated its...
**Table 2** Baseline characteristics of studies included

<table>
<thead>
<tr>
<th>First author</th>
<th>Country</th>
<th>Year</th>
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<th>Age (years)</th>
<th>Child-Pugh class</th>
<th>Tumor number</th>
<th>Mean tumor size (cm)</th>
<th>Intervention</th>
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<tr>
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<td>1,136</td>
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Age recorded as mean ± SD or median [range]. NA, not available; RFA, radio frequency ablation; MWA, microwave ablation; HCC, hepatocellular carcinoma.
unique advantage (49,50). Although we intended to include Nano knife in our review there are no publications up to now that met our inclusion criteria and a solid conclusion could not be excreted.

Post ablation complications such as liver failure, intraperitoneal bleeding, abscess, bile duct injury, tumor seeding are very serious, and can be life threatening (51,52), other complication can prolonged hospitalization and increase morbidity. Being well aware of the complications and the choice of treatment method will lead to a more practical application and enable this procedure to be safer and more effective.

The results without heterogeneity show a mortality of 0.15% and 0.23% for RFA and MWA, respectively. The prevalence of major complications in the reported studies ranged from 1.52% to 4.7%, calculated by using a random effects model in the presence of significant heterogeneity, were 4.1% for RFA and 4.6% for MWA.

MWA-associated mortality was reported to occur in 0.002% according to a systematic review of this technique (53). Major complication rates have been reported to be higher with MWA than with RFA in a randomized trial. Our results indicated that MWA is a safe technique in terms of mortality and major complication rate. However, the results should be interpreted with caution and more reports including large number of patients are needed to make a solid conclusion.

The difference between the reported complication rates can be explained by several factors: single/multicenter studies, prospective/retrospective studies.

Prospective studies may report more accurately the number of participants lost to follow-up, the timing of collecting complications and the adequate predefined definitions for harms.

It is well understood that the risk of complications can be reduced by proficiency in technique and refinement in pretreatment assessments.

There are several strategies for decreasing complications after ablation of hepatic tumors (51). The first key strategy is prevention by not to perform ablation in patients at high risk, meticulous pre evaluation of candidates should be performed, especially in regard to coagulopathy, underlying hepatic reserve, and tumor proximity to major structures such as the bile duct or intestine. In a patient with correctable coagulopathy, ablation should be postponed until all parameters are corrected.

Early detection cannot reduce the frequency of complications such as infection or bleeding, but it can potentially minimize their clinical magnitude. Thus, the operator and other medical personnel should be knowledgeable about the spectrum of various complications after ablation because complications can be detected even during the procedure in some cases. Close immediate follow-up with clinical and laboratory data is also essential for early detection of complications.

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References


