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REVIEW

Influence of approach on outcome in radiofrequency ablation of liver tumors

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Abstract
In this article some recent data concerning the approach on radiofrequency ablation (RFA) of liver tumors are reviewed. Specifically, several critical statements between surgical and percutaneous approach are raised and discussed: (1) Open approach may lead to a higher complication rate; (2) Temporary occlusion of hepatic inflow during surgical approach may lead to a higher rate of ablation of the liver tumors; (3) Surgical approach may permit better targeting of the tumor to be ablated. (4) Surgical approach may discover additional liver tumors. Finally, several conclusions and recommendations are also addressed.

Contents

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The first radiofrequency ablation (RFA) of a liver tumor in the United States was performed in 1996 [1]. In only one decade the RFA technology has evolved quickly and easily found its way into the armamentarium of surgeons and radiologists. Several factors boosted the fast-growing interest in this technique: (1) the relative simplicity and low-cost and (2) the low morbidity rates associated with this procedure [2]. Nevertheless, in spite of the initial enthusiasm and improved developments several concerns have been raised: (1) high-degree variability of coagulation necrosis achieved by RFA in normally perfused liver which has been linked with high true local recurrence rates [3,4] and (2) promotion of intrahepatic growth of residual neoplastic cells because of possible, but not yet proven, immunologic and biological effects of heat trauma [5–10]. Therefore, the National Institute of Clinical Excellence (NICE) from the United Kingdom stated that: ''*Current evidence on the safety of radiofrequency ablation of colorectal metastases in the liver appears adequate. However, the evidence of its effect on survival is not yet adequate to support the use of this procedure without special arrangements for consent and for audit or research*'' [11]. In a more recent review the *Cochrane Library* concludes that local ablative therapy is probably useful in the treatment of colorectal liver metastases, but they need to be further evaluated in a randomized controlled trial [12]. This gives added importance to unreported but expected results of phase II randomized trials like the recently closed CLOCC 40004 trial from EORTC (chemotherapy + RFA *vs* chemotherapy alone) in spite of the lack of accrual in this study.

During this last decade of using RFA for liver tumors, the choice of the approach for this technique (percutaneous, laparoscopic or open laparotomy) has usually been dictated by the training and specialty of the physician performing the ablation [1,13]. Only lesions near the dome of the liver or at the edge of liver were usually deemed inappropriate for percutaneous RFA because of the risk of injury to the diaphragm or the stomach and the bowel, respectively [1,14–16]. Therefore, open approach has been considered essentially as an adjunct to operative resection [17,18] and the rate of its performance without hepatic resection may be extremely infrequent [19]. However, recent evidence suggests that the treatment approach chosen in RFA may influence outcome:

(1) On the one hand, Mulier et al. in a meta-analysis [20] including 5224 primary and secondary liver tumors demonstrated that surgical (laparoscopic or open laparotomy) approach resulted in superior local control of liver tumors. In the univariate analysis, factors with significantly less local recurrences included the following: small size, surgical (open or laparoscopic) approach, location away from large vessels, a 1-cm intentional margin, and a greater physician experience. In the multivariate analysis, significantly fewer local recurrences were observed for small size and for a surgical approach (Table 1). Thus, the global local recurrence rate after RFA of colorectal liver metastases was 3.5% after a surgical approach *vs* 26.4% after a percutaneous approach [21].
(2) On the other hand, similar conclusions were drawn in a retrospective study of a single specialized center including 228 hepatocelullar carcinomas treated by either a percutaneous or a surgical approach [22]. In this study, the 1-year and 3-year survival rate were significantly higher in patients with tumors of more than 3 cm in diameter when a surgical approach of the RF ablation procedure was performed.

Even though evaluation of current evidence from non-randomized studies may be hampered by the heterogeneity of patient selection, variety of techniques and devices in use or by experience and skill of those performing ablation some critical differences between surgical and percutaneous approach may be actually supported.

Open approach may lead to a higher complication rate

Livraghi et al. [14] in a multicenter study included 2320 patients with 3554 liver tumors treated with RFA clearly shown that the rate of combined death and major complications was 16.7 per 1000 patients for the radiologic centers and 60.2 per 1000 patients for the surgical centers. Likewise, independently Curley [23], and Poon [24] in their respective centers, demonstrated that open approach was associated with a higher complication rate in comparison to percutaneous approach. These results were obtained in spite of assuming that the life-threatening risk of thermal damage to neighboring organs is found almost exclusively in the percutaneous approach [25,26]. Nevertheless, this higher risk of complication rate was not encountered in laparoscopic approach [14,27–29]. Potential factors that may account for the higher risk of complication rate in the open approach are the following: (1) higher mobilization and manipulation of the liver as well as long abdominal incisions which have

Table 1 Local recurrence rate after radiofrequency ablation of hepatic tumors according to size and approach

Size (cm)	Percutaneous (%)	Laparoscopy/ laparotomy (%)
<3	16	3.6
3–5	25.9	21.7
>5	60	50

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been linked with a higher trauma [27,30]; (2) less experience and skill of surgical teams in performing ultrasound-guided RFA [14,19] and possible influence of learning curve in RFA of liver tumors [24,31,32]; and (3) possible selection bias in open approach group including the so-called high-risk location tumors more frequently or influence of concomitant liver resection when performing RFA [23,31].

Temporary occlusion of hepatic inflow during surgical approach may lead to a higher rate of ablation of the liver tumors

Flowing blood within the vessels acts as a heat sink and substantially limits the necrotizing effect of RFA treatment in the adjacent tissue leading to a reduced coagulation size and frequent irregular coagulation shape on the experimental setting [33–37]. In fact, it has been established that in theoretical calculations of temperatures and thermal damage, blood flow is the most important variable in determining the extend of tissue damage [38]. In clinical practice, the clamping of the hepatic artery and the portal vein (the Pringle maneuver) during intraoperative RFA procedure has been associated with a higher temperature in the targeted lesion [39], increase and less distorted coagulation [4,18,40–42]. These mechanisms have been linked to a better likelihood of complete tumor control globally [20] but mainly when treating large tumors (>3 cm in diameter) [39,40,43]. Given the relevance of the issue, occlusion of the blood flow has been tried and successfully performed laparoscopically [44,45] or even percutaneously where reduction of blood flow has been accomplished before RFA either through balloon catheter [46–48] or pharmacologically [49]. Nevertheless, several concerns with interruption of blood flow during RFA have been raised: (1) possible higher risk of portal vein thromboses mainly in cirrhotics [25,50–53] and (2) higher risk of histologic lesions to close bile ducts [53,54]. In any case and in spite of the increasing evidence of the efficacy of the manipulation of blood flow during RFA, several authors have described successful treatment of even perivascular lesions without using the Pringle maneuver [51,55,56].

Surgical approach may permit better targeting of the tumor to be ablated

It seems evident that the success of RFA is in large part dependent on the correct positioning of the ablation probe [57,58]. In this regard, surgical approach and especially the open approach may afford: (1) improved visibility and image resolution (no attenuation by the skin and subcutaneous tissue and wider window with no interposition of the ribs and bowel) with intraoperative ultrasound [39,59,60]; (2) greatest degree of control of probe delivery allowing free insertion of the electrodes at different angles with mobilization of the liver (if necessary). That may be especially relevant in so-called high-risk locations or when overlapping of the tumor is necessary [17,51,60]; and (3) finally, palpation of the liver may help accurate position of the electrode which may be especially advantageous while treating superficial tumors [17]. These advantages of the surgical approach may be especially relevant while treating large tumors (>3 cm in diameter) [39,60]. However, in spite of these theoretical advantages, many practitioners have found an intraoperative approach to be often limiting and awkward for tumors placed high and posterior in the right liver. Therefore, a posterior tumor in the right liver may be targeted easier through a percutaneous approach in a right-oblique lateral position [61].

Surgical approach may discover additional liver tumors

Elias et al. [59] collected 506 patients who underwent a partial hepatectomy and concomitant intraoperative RFA for colorectal liver metastases; these patients underwent preoperative ultrasonography and computed tomographic scan of the liver. They concluded that in at least one third of cases, surgical approach permits discovery and treatment with a curative intent of unsuspected intrahepatic or extrahepatic metastases that would not be treated by percutaneous RFA. Similarly, Scaife et al. [62] identified with intraoperative ultrasonography additional hepatic tumors in 27% who underwent hepatic resection after state-of-the-art preoperative computed tomography. Again, improved hepatic lesion detection by intraoperative ultrasound linked to manual palpation and visual inspection of intraperitoneal contents [17,42,60,63] likely account for these data.

Conclusion and recommendations

RFA of malignant liver tumors is a relatively recent treatment and limited definitive data regarding survival benefit are available but when some even recent series have demonstrated a recurrence rate that may reach 55% [64] some criticism about the technique is justified. In the present article we review several recent data concerning the approach in RFA of liver tumors. However, we must bear in mind that these evidences for the superiority of surgical approach in RFA of liver tumors come from retrospective comparative studies. Table 2 proposes

Table 2 Proposal of recommendations about approach in RFA

Favors surgical approach:
- Tumors located at liver periphery (consider better targeting of the tumor and better protection of neighboring organs with this approach)
- Tumors near hepatic or portal vein especially when >3 cm in diameter (consider temporary occlusion with this approach)

Favors percutaneous approach:
- Unfitness for major surgery
- Posterior, small and single tumor in the right liver (consider possible easier targeting with this approach in right-oblique lateral position)

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several specific recommendations about the approach in RFA of liver malignancies taking into account the data discussed above. In general terms we must state that, the less invasiveness and fewer risks of complications of the percutaneous approach during RFA may not outweigh the higher risk of tumor recurrence. In fact, the percutaneous approach may remain as a good option for patients at high-risk to tolerate a surgical approach [65]. For the rest of the patients, maybe a tailored approach of the patients should be warranted in the future and a surgical approach in RFA of a liver tumor should not be ruled out even if a liver resection is not planned in advance.

Conflict of Interest Statement

The author has no conflict of interest to declare.

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