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RAPID COMMUNICATION

A combination therapy of ethanol injection and radiofrequency ablation under general anesthesia for the treatment of hepatocellular carcinoma

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Abstract

AIM: To summarize the effects of laparoscopic ethanol injection and radiofrequency ablation (L-EI-RFA), thoracoscopic (T-EI-RFA) and open-surgery assisted EI-RFA (O-EI-RFA) under general anesthesia for the treatment of hepatocellular carcinoma (HCC).

METHODS: Time-lag performance of RFA after ethanol injection (Time-lag PEI-RFA) was performed in all cases. The volume of coagulated necrosis and the applied energy for total and per unit volume coagulated necrosis were examined in the groups treated under general (group G) or local anesthesia (group L).

RESULTS: The results showed that the total applied energy and the applied energy per unit volume of whole and marginal, coagulated necrosis were significantly larger in group G than those in the group L, resulting in a larger volume of coagulated necrosis in the group G. The rate of local tumor recurrence within one year was extremely low in group G.

CONCLUSION: These results suggest that EI-RFA, under general anesthesia, may be effective for the treatment of HCC because a larger quantity of ethanol and energy could be applied during treatment under pain-free condition for the patients.

Key words: Combination therapy; Ethanol injection; Radiofrequency ablation; General anesthesia, Local anesthesia

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INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most serious malignancies worldwide[1], especially in Asian countries due to the high exposure to hepatitis virus. Despite intensive efforts to develop novel treatment modalities for HCC, the prognosis of HCC remains relatively poor[2-4]. Although percutaneous ethanol injection (PEI) and percutaneous acetate injection (PAI) are frequently used for the treatment of HCC, these treatment modalities are considered to be effective for patients with relatively small, encapsulated HCC. By contrast, tumor ablation technologies such as microwave, laser, and radiofrequency ablation (RFA), have been shown to be reliable and effective for inducing thermally mediated coagulation necrosis of primary HCC[5-10] and metastatic liver cancer[11,12]. Among these treatment modalities, it is now possible to obtain larger areas of coagulated necrosis through innovative RFA technologies, while RFA now plays a central role in local treatment due to wider coagulated necrosis in fewer sessions without major complications compared with PEI and PAI. However, in contrast to its efficacy, several disadvantages have been pointed out, such as the limited coagulated necrosis induced by RFA and frequent local tumor recurrences[13,14]. To overcome these weaknesses, we have developed a novel combination therapy of percutaneous ethanol injection and radiofrequency ablation (PEI-RFA) and showed that combined use of ethanol prior to RFA was able to enhance the therapeutic effects with a smaller energy requirement compared with RFA alone[15-20]. Although PEI-RFA was shown to enlarge the area of coagulated necrosis, there are HCC cases that are difficult to treat with percutaneous RFA due to the location of the HCC. For example, HCC protruding from the surface of the liver are difficult to treat with RFA percutaneously due to the risk of tumor bleeding. Furthermore, HCC located closely to the diaphragm are difficult to treat with RFA percutaneously due to the poor visualization of the tumor by ultrasonography (US). For these HCC thus other appropriate RFA approaches are desirable. Furthermore, there are some HCC that can not be treated even with both laparoscopic and thoracoscopic approaches due to the location of the tumor, and open surgery-assisted RFA remains the only appropriate treatment. For these kinds of HCC, we applied the combination therapy of ethanol injection and RFA (EI-RFA) to laparoscopic, thoracoscopic, and open-surgery assisted treatments. We summarized and evaluated the effectiveness of laparoscopic-EI-RFA (L-EI-RFA), thoracoscopic-EI-RFA (T-EI-RFA), and open surgery-assisted-EI-RFA (O-EI-RFA) under general anesthesia.

MATERIALS AND METHODS

Patients

L-EI-RFA was performed in eight patients (5 male and 3 female; mean age 67 years) with HCC protruding from the surface of the left lobe of the liver (ranging from 1.0-3.0 cm in diameter). T-EI-RFA was performed in nine patients (6 male and 3 female; mean age 69 years) with HCC located closely to the diaphragm (ranging from 1.0-3.5 cm in diameter). O-EI-RFA was performed in five patients (4 male and 1 female ; mean age 63 years) with HCC located closely to the diaphragm (ranging from 1.0-2.5 cm in diameter). P-EI-RFA was performed in 40 patients (27 male and 13 female; mean age 65 years). All these studies were conducted with informed consent at the time of enrollment. The characteristics of the enrolled patients are shown in Table 1.

Treatment of time-lag EI-RFA

We previously reported that time-lag performance RFA after ethanol injection (time-lag P-EI-RFA) was effective for the treatment of HCC[20]. Time-lag PEI-RFA was performed under the real-time US guidance with a 3.5-MHz sector probe (TOSHIBA, Xario Prime Ultrasound, SSA-660A). RFA was performed by a Cool-tip RF System (RADIONICS, Burlington, USA)[21], a RTC system (RF3000 Generator, Boston Scientific, USA), and RITA system (Model 90, USA) according to the method described in our manuscripts[15,16]. Briefly, a 17-gauge RFA needle with an electrode of 3 cm in length was inserted into the center of tumor, followed by a 21-gauge PEI needle inserted into the liver tumor through the same attachment hole beside the echo probe. Pure ethanol (99.8%) was then slowly injected into the tumor. The volume of injected ethanol was always kept below double the estimated tumor volume. Five minutes after injection of ethanol into the tumor, the ablation was started with 30 W of power output followed by a stepwise increase of 20 W every 2-3 min. After the end of the ablation (50 W of power output), the circulating cooling water was stopped and the temperature of the RFA electrode was checked. The ablation was performed under impedance control. The ablation was terminated when the temperature of the RFA needle was > 65℃.

Table 1 Characteristics of patients enrolled in the present study

	Group G	Group L
Number of patients	22	40
Male/Female	15/7	27/13
Age (yr)		
Mean	64	65
Range	48-75	49-72
Tumor size (cm)		
Mean	2.8	2.9
Range	1.0-3.5	1.5- 3.3
Injected ethanol (mL)		
Mean	5.2	2.1
Range	2.0-15	1.5-2.5
Child-Pugh grade		
A	14	25
B	7	14
C	1	1

Laparoscopic time-lag EI-RFA (L-EI-RFA)

L-EI-RFA was performed for the HCC protruding from the surface of the liver. First, the laparoscope was inserted into the abdominal cavity beginning in the left-upper portion of the navel. RFA electrode and PEI needle were inserted at a second abdominal site according to the location of the tumor. A sonde was inserted into the abdominal cavity to lift up the liver when the HCC was protruding from the reverse surface of the liver. Under laparoscopic observation, a RFA electrode was directly inserted into the tumor, and then a 21-gauge PEI needle was inserted and ethanol was injected[18].

Thoracoscopic time-lag EI-RFA (T-EI-RFA)

T-EI-RFA was performed for HCC close to the right diaphragm. Patients were put under general anesthesia with one-lung (left lung) ventilation in a left-decubitus position. Three ports for the thoracoscope, End-fire laparoscopic probe (ALOKA UST-52109), and water-pouring tool were inserted into the pleural cavity through the intercostal space. After putting the collapsed right lung aside by a laparoscope, the End-fire laparoscopic probe was guided to the surface of the exposed diaphragm, and the tumor close to the diaphragm was identified by US (ALOKA ProSound SSD-3500). After visualizing the tumor by US, an RFA electrode was inserted into the tumor through the channel along the End-fire laparoscopic probe. A 21-gauge

Table 2 Comparison of the volume of coagulated necrosis and energy requirement between the groups treated with expandable and straight electrode

	T-S (cm)	ETOH (mL)	L (cm)	S (cm)	H (cm)	V (cm^3)	M (cm^3)	T-ENE (J)	T-ENE/V (J/cm^3)	T-ENE/M (J/cm^3)
Group L (*n* = 40)	2.0 ± 0.8	3.0 ± 1.9	3.5 ± 0.6	2.8 ± 0.4	3.0 ± 0.5	15.9 ± 5.2	10.1 ± 8.2	21565 ± 9631	1636 ± 791	2406 ± 1819
Group G (*n* = 15)	2.1 ± 0.8	6.1 ± 3.4	3.6 ± 1.1	3.2 ± 0.6	3.2 ± 0.8	22.5 ± 14.9	15.9 ± 12.1	37207 ± 20583	2409 ± 2045	3594 ± 2727
P value	0.56	0.0007	0.64	0.10	0.31	0.045	0.06	0.0095	0.10	0.11

Twenty-four HCC were treated with time-lag PEI-RFA with straight type electrode, while 15 HCC were treated with time-lag PEI-RFA with expandable type electrode. After treatment, the longest and the shortest diameters, and the height of the coagulated necrosis were estimated by helical dynamic CT and the approximation volume of total and marginal coagulated necrosis were calculated. Each datum expresses mean ± SD. Each abbreviation in the table is expressing as follows: T-S: Tumor size; EtOH: Amount of ethanol; L: Longest diameter; S: Shortest diameter; H: Height; V: Volume of coagulated necrosis; M: Volume of marginal coagulation; D: Duration of ablation; T-ENE: Total energy requirement; T-ENE/V: Energy requirement per unit volume for whole coagulation; T-ENE/M: Energy requirement per unit volume for inducing marginal coagulation.

PEI needle was inserted and pure ethanol or lipiodol containing ethanol was injected[19].

Open surgery-assisted time-lag EI-RFA (O-EI-RFA)

O-EI-RFA was performed for HCC which were difficult to treat with other EI-RFA approaches or when splenectomy was simultaneously performed to improve cirrhotic liver dysfunction accompanying severe esophageal varices or a decrease of platelet count. After exposing the liver and confirming the surface location of liver tumors by US, the RFA electrode was directly inserted into the liver tumors and time-lag EI-RFA was performed.

Evaluation of therapeutic efficacy

Five to seven days after treatment, plain or contrast enhanced CT was performed to evaluate the response to L-EI-RFA, T-EI-RFA, and O-EI-RFA. Tumor necrosis was considered to be complete when no foci of early enhancement were seen around the original regions.

Statistical analysis

Statistical analysis was performed using Statview Ⅱ (Version 5.0), statistical significance between the group L and group G was analyzed by a Chi-square test for independence and significant difference was accepted at $P < 0.05$.

RESULTS

Comparison of the volume of coagulated area and the applied energy requirement for total and unit volume coagulation in patients treated with EI-RFA under local anesthesia (group L) and general anesthesia (group G)

Group L (40 cases) received time-lag EI-RFA under local anesthesia, while group G (22 cases) received time-lag EI-RFA under general anesthesia. The patients underwent RFA therapy by means of the Cool-tip RF system, RTC system, and RITA system. No major adverse effects were observed in either group. Among treated cases, 40 cases in group L and 15 cases in group G (L-EI-RFA; 6 cases, T-EI-RFA; 8 cases, O-EI-RFA; 1 case) were treated with EI-RFA by means of the Cool-tip RF system. Between these patients treated by the Cool-tip RF system, the effect of EI-RFA was compared using several parameters drawn from the treatments. Comparison of the amount of injected ethanol, the volume of the induced coagulated necrosis, total applied energy for total and per unit volume coagulated necrosis in both groups are summarized in Table 2. The tumor size was approximately 3 cm in diameter in both groups, and no significant difference was detected between groups. Although the longest and the shortest diameter and the height of the coagulated necrosis did not show a significant difference between the groups, the mean values of all of these parameters in group G were higher than those in group L. Thus, the volume of total coagulated necrosis in group G was significantly larger than that in group L. Furthermore, the volume of marginal coagulated necrosis in group G was also larger than that in group L. According to the analysis of parameters which affect the volume of induced coagulated necrosis in EI-RFA, both the quantity of ethanol and applied energy for ablation in group G were significantly larger than those in group L. Because both, the volume of coagulated necrosis and total applied, energy, were increased in group G compared with group L, the applied energy per unit volume for whole and marginal coagulated necrosis were comparable. These results suggest that a higher volume of coagulated necrosis was induced in group G compared with group L because higher amounts of ethanol and energy for ablation could be applied.

Rate of local recurrence within a year in group G and L

Among the 22 patients treated with EI-RFA under general anesthesia (group G), local recurrence was observed in only one case (4.5%) within a year after the treatment. By contrast, local recurrence was detected within a year in four cases (10%) among the 40 cases treated with EI-RFA under local anesthesia (group L). Although the difference of the rate of local recurrence between group G and group L did not reach statistical significance, the rate was extremely low in group G. In one case (patient No. 21) with local recurrence, the volume of marginal coagulated necrosis around the original tumor was lower than in cases without recurrence.

Comparison of the effects of L-EI-RFA, T-EI-RFA, and O-EI-RFA

The results for treatment with L-EI-RFA, T-EI-RFA, and O-EI-RFA are summarized in the Table 3. L-EI-RFA was performed on the HCC located in the left lobe of the liver (segment 2-4) and T-EI-RFA was performed on the HCC of segment 8 of the liver close to the diaphragm (except for one HCC located in the segment 6). O-EI-RFA was performed on the liver HCC of segment 3, 7, and 8. The

Table 3 Results of L-EI-RFA, T-EI-RFA and O-EI-RFA

Location		T-S (cm)	Ins	EtOH (mL)	A-A (L x S x H) (cm)	V (cm^3)	M (cm^3)
L-EI-RFA							
No. 1	S3	1.5	Cool-tip	15	3.2 × 2.7 × 2.6	11.8	10.0
No. 2	S2	3.0	Cool-tip	8	4.2 × 4.2 × 4.2	38.7	24.0
No. 3	S4	1.5	Cool-tip	2	2.2 × 2.2 × 2.2	5.60	3.81
No. 4	S2	3.0	Cool-tip	7	6.7 × 5.0 × 3.7	64.8	50.7
No. 5	S3	2.5	Cool-tip	8	3.7 × 3.7 × 3.4	24.4	16.2
No. 6	S4	1.0	Cool-tip	7	2.2 × 2.2 × 2.3	5.83	5.30
No. 7	S2	1.5	RITA	2	4.0 × 4.0 × 4.0	33.0	31.0
No. 8	S2	1.5	RITA	2	3.5 × 2.5 × 3.0	19.0	17.0
T-EI-RFA							
No. 9	S6	2.5	Cool-tip	7	3.7 × .2 × 3.2	19.8	11.7
No. 10	S8	1.0	RTC	3	4.1 × 2.5 × 3.2	17.2	16.6
No. 11	S8	2.0	Cool-tip	12	4.2 × 4.2 × 3.7	34.1	30.0
No. 12	S8	2.5	Cool-tip	5	3.2 × 3.2 × 3.2	17.1	8.97
No. 13	S8	2.0	Cool-tip	4	3.0 × 3.0 × 2.5	11.8	7.59
No. 14	S8	2.0	Cool-tip	5	3.5 × 3.5 × 3.5	22.4	18.3
No. 15	S8	2.0	Cool-tip	5	4.5 × 3.0 × 3.5	24.7	20.5
No. 16	S8	3.5	Cool-tip	3	2.0 × 2.0 × 2.0	4.20	3.70
No. 17	S8	2.0	Cool-tip	4	2.5 × 2.5 × 4.0	13.1	8.90
O-EI-RFA							
No. 18	S3	1.5	RITA	2	3.3 × 2.5 × 3.0	13.0	8.90
No. 19	S8	2.5	Cool-tip	7	4.2 × 3.2 × 3.7	26.0	17.9
No. 20	S7	1.0	RTC	2	3.0 × 2.5 × 2.5	9.81	9.29
No. 21	S3	1.5	RTC	2	2.0 × 2.0 × 1.5	3.14	1.37
No. 22	S3	1.5	RTC	2	4.0 × 4.0 × 4.0	25.1	23.4

Eight HCC were treated with L-EI-RFA, Nine HCC were treated with T-EI-RFA and five HCC were treated with O-EI-RFA. Location of the tumor, tumor size (T-S), instruments for ablation (Ins), amounts of injected ethanol (EtOH), ablated area (A-A), [longest diameter (L) × shortest diameter (S) × height (H)], volume of coagulated necrosis (V) and volume of marginal coagulated necrosis (M) are shown.

approximate estimated volume of the original tumor, volume of whole and the marginal coagulated necrosis were calculated from the CT image after the treatments. In most treated cases, a larger volume of coagulated necrosis and marginal coagulated necrosis was induced compared with the volume of original tumor. In most patients treated with a large amount of ethanol (over 7 mL), larger volume of whole and marginal coagulated necrosis were induced in patients such as No. 2, 4, 5, 9, 11, and 19. The volume of whole and marginal coagulated necrosis was comparable in the patients treated with L-EI-RFA, T-EI-RFA, and O-EI-RFA.

Relationship between the amount of ethanol, applied energy, and the volume of coagulated necrosis

In group G, the induced coagulated necrosis increased with the amount of ethanol and applied energy. We previously showed that the amount of ethanol was positively correlated with the volume of coagulated necrosis in patients treated with P-EI-RFA using an RFA instrument equipped with a straight electrode (Cool-tip RF system)[19]. In the present study, the relationship between the amount of ethanol or applied energy and the volume of induced coagulated necrosis were evaluated in patients treated with EI-RFA under general anesthesia. Furthermore, the relationship between the product of the amount of ethanol and the applied energy *vs* the volume of coagulated necrosis was also analyzed. The results showed that both the amounts of injected ethanol and applied energy were significantly and positively correlated with the volume of coagulated necrosis (Figure 1A and B). The product of the amount of ethanol and the applied energy was also positively correlated with the volume of coagulated necrosis (Figure 1D). These results clearly indicated that both the amount of ethanol and applied energy were critical factors that regulate the volume of coagulated necrosis in the EI-RFA under general anesthesia.

Representative case treated with L-EI-RFA

By analyzing the effects of time-lag EI-RFA under general anesthesia, one point became evident: Total applied energy and the applied energy per unit volume of whole and marginal coagulated necrosis were significantly larger in patients treated under general anesthesia than in those treated under local anesthesia. This lead to the induction of a larger volume of coagulated necrosis. A representative case treated with T-EI-RFA was shown in our previous manuscript[22]. A case treated with L-EI-RFA is presented. One case with HCC successfully treated with L-EI-RFA is shown in Figure 2. An HCC (2 cm in diameter) was located in the S2 region of the liver protruding from the reverse surface and with an enhanced early vascular phase (Figure 2A) *via* dynamic CT. The laparoscope was inserted from the left-upper portion of the abdomen into the abdominal cavity and the liver was lifted by a sonde. An RFA electrode and PEI needle were percutaneously inserted into the center of the tumor, monitoring the depth of the inserted electrode by the linear type US. The electrode and needle were firstly inserted into the tumor from the upper surface of the liver (Figure 2B), and then inserted into the

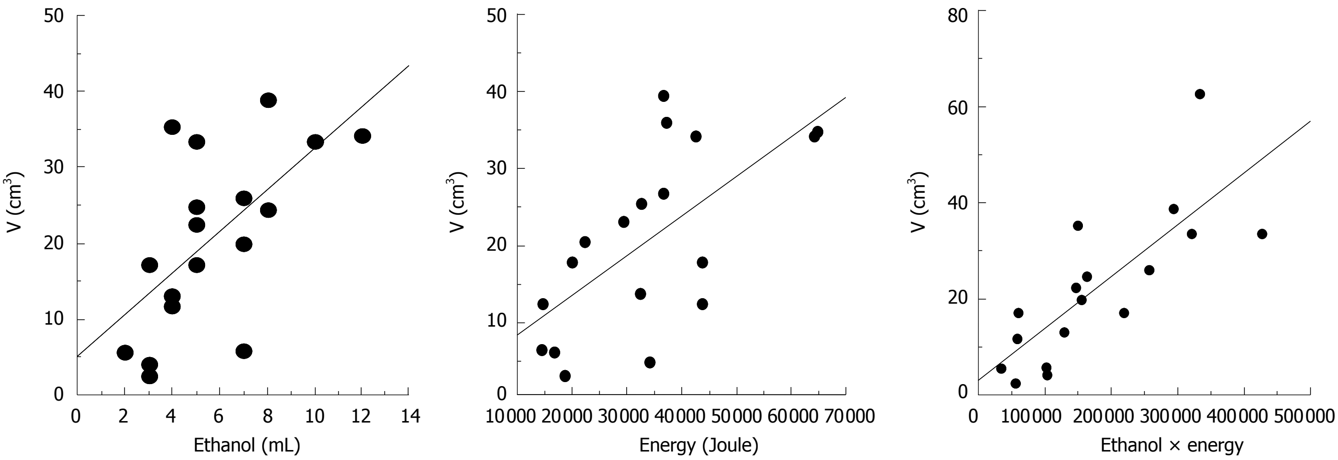

Figure 1 Relationship between the volume of coagulated necrosis induced and the amounts of ethanol injected or total applied energy or the product of the amounts of ethanol and the total applied energy. All the amounts of ethanol, total applied energy, or the products of the amount of ethanol and total applied energy showed a significant positive correlation with the volume of coagulated necrosis. (Ethanol *vs* volume, $r = 0.54$, $P = 0.018$; energy *vs* volume, $r = 0.61$, $P = 0.0057$; ethanol × energy *vs* volume, $r = 0.61$, $P = 0.0078$).

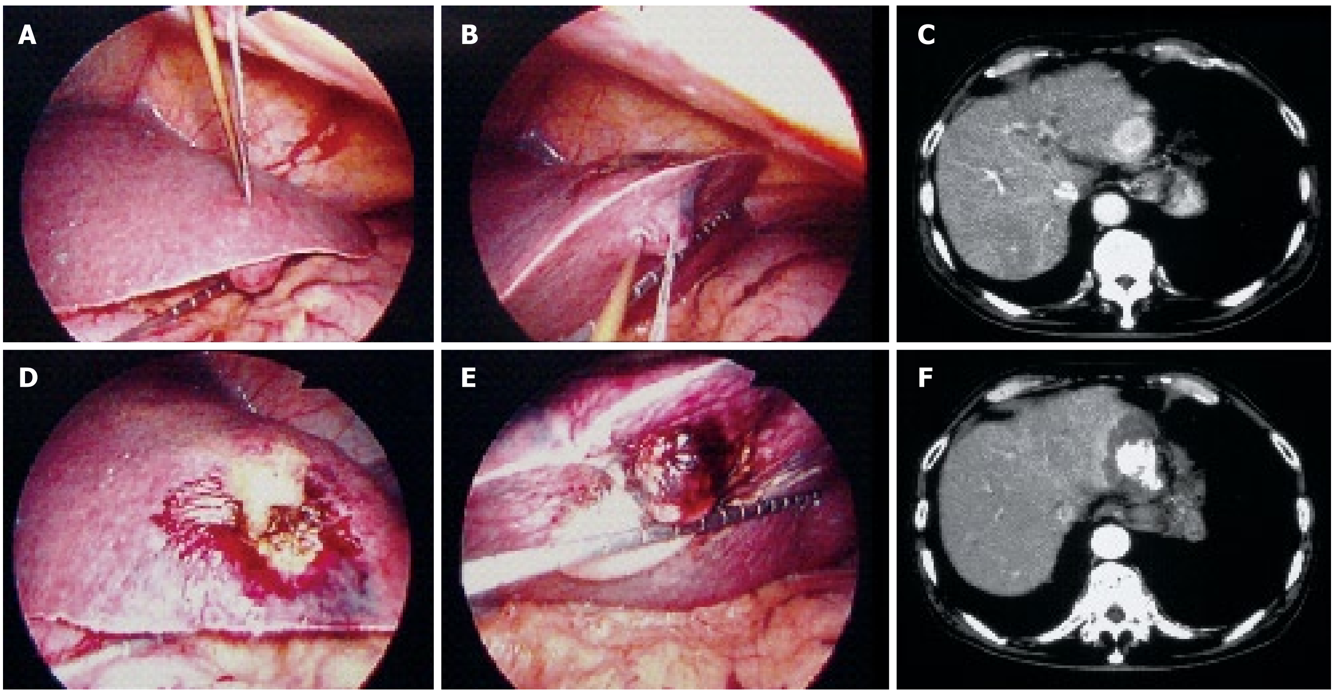

Figure 2 A case of HCC located on the reverse surface of the liver (S2 of the liver) treated with L-EI-RFA. A HCC (2 cm in diameter) showed an enhancement in early vascular phase of helical dynamic CT (**A**); RFA electrode and PEI needle were firstly inserted from the surface of the liver (**B**) and secondly inserted from the reverse surface of the liver (**C**); After injecting the ethanol containing 15% lipiodol, RFA was performed. Dynamic CT after the treatment showed lipiodol deposit associated with the original tumor and low density area was observed around the tumor (**D**); Laparoscopic observation of the tumor from the surface (**E**) and from the reverse surface (**F**) of the liver after the treatment.

tumor from the reverse surface of the liver (Figure 2C). We previously reported the usefulness of injecting the mixture of ethanol and lipiodol to visualize the original tumor by dynamic CT[23]. Therefore, a mixture of ethanol and lipiodol (15% lipiodol in ethanol) was injected into the tumor. Five minutes after injection of ethanol containing lipiodol, RFA was started at 30 W, and the power output was stepwise increased to 80 W by a Cool-tip RF system. During ablation, the tumor was constantly lifted by a sonde to prevent the transmission of heat to the mesentery. Abdominal dynamic CT taken after the operation clearly showed a lipiodol deposit associated with the tumor and the ablated region reached beyond the tumor (Figure 2D). A safety margin was shown to be sufficiently obtained by L-EI-RFA. The laparoscopic findings for the tumor after ablation are shown in Figure 2E and F.

DISCUSSION

HCC is one of the most serious and common malignancies worldwide[1,4]. As a treatment for HCC, RFA now plays a central role for local control of HCC, because RFA can induce wider coagulated necrosis in a few sessions compared with PEI which is frequently used for relatively small-encapsulated HCC. However, the region of coagulated necrosis induced by RFA is still limited and only considered applicable to tumors within a 3 cm diameter. Furthermore, it is also pointed out that relatively frequent local recurrences of tumor occur after RFA treatment. Therefore, the RFA technique could be further developed to improve the therapeutic effects of this treatment. To enhance the therapeutic effect of RFA, several treatment modalities have been applied in addition to local treatment[24-29]. As one of the optional combination therapies, we have developed a novel combination therapy of P-EI-RFA and showed that this combination therapy accurately enlarged the area of induced coagulated necrosis. Total applied energy and the applied energy per unit volume of whole and marginal coagulated necrosis was significantly lower in the P-EI-RFA than RFA alone. Furthermore, we found that the time-lag performance of RFA after ethanol injection (time-lag P-EI-RFA) resulted in a lower energy requirement per total and unit volume of coagulated necrosis than without time-lag performance of RFA after ethanol injection. In this regard, we suggest that time-lag P-EI-RFA can induce wider coagulated necrosis with a smaller energy requirement. Although P-EI-RFA was shown to enlarge the area of coagulated necrosis, there are HCC cases that are difficult to treat with the percutaneous RFA due to the location of the HCC. For these situations, we applied the combined therapy of ethanol injection and RFA (EI-RFA) with laparoscopic, thoracoscopic and open-surgery assisted. Among 22 patients treated with EI-RFA under general, the number of local recurrences was very small [1 case (4.5%)] and its frequency was kept in extremely low level. Analysis of the amount of injected ethanol, applied energy and the volume of coagulated necrosis showed that these parameters in the group treated with EI-RFA under general anesthesia were significantly larger than those in the group treated under local anesthesia. One of the most relevant differences between the EI-RFA under general anesthesia and local anesthesia is presence or absence of pain felt by the treated patients. We have reported in a series of analyses that P-EI-RFA under local anesthesia enabled a comparable coagulated necrosis with smaller energy requirement relative to RFA alone. P-EI-RFA was likely to be less invasive than RFA alone[16]. However, in the present study, the rate of local recurrence was reduced in the patients treated under general anesthesia compared with the patients treated under local anesthesia. Taken collectively, these results suggest that higher amounts of ethanol and energy administrated under pain-free conditions may result in a decreased rate of local tumor recurrences after RFA treatment. Indeed, although we still believe that PEI-RFA is less invasive for the treatment of HCC, we are sometimes obliged to cease the RFA treatment due to the pain felt by the patient during the percutaneous RFA treatment. Therefore, the results in the present study suggest that it is important to apply enough ethanol and energy for RFA treatment to decrease the local recurrence after percutaneous treatment as well as treatment under general anesthesia. For this purpose, it is beneficial to use anesthesia intravenously to decrease the pain felt by the patients during the percutaneous treatment as well. Patients under pain-free conditions during treatment may have a decreased rate of local tumor recurrence. Recently, it was reported that there were no differences in tumor control and complications under general anesthesia and analog-sedation in RFA treatment of pulmonary tumors[30]. This result is not in accordance with our results obtained during treatment of HCC. In the treatment of HCC located near the surface of the liver, patients often complain about pain originating from the membrane of the liver. In our patients, we usually use pentazocine and non-steroid anti-inflammatory drugs (NSAIDs) (if necessary diazepam is also used on a case by case basis) for the percutaneous RFA treatment. Therefore, it may be better to consider stronger pain relief during the treatment of percutaneous RFA treatment.

In conclusion, we compared the clinical effects, amounts of ethanol, and applied energy in P-EI-RFA between patients under general anesthesia and local anesthesia. The volume of induced coagulated necrosis, amounts of ethanol, and applied energy were significantly larger in the group treated under general anesthesia than that under local anesthesia. The rate of local tumor recurrence in the former group was kept at an extremely low level.

COMMENTS

Background

Radiofrequency ablation (RFA) plays a central role for the treatment of hepatocellular carcinoma (HCC) because this newly developed technology appears very effective to induce wider coagulated necrosis. However, several disadvantages have been pointed out for RFA and improvement of RFA technique will be desirable.

Research frontiers

RFA treatments are performed percutaneously under local anesthesia in many cases. Local tumor recurrence varies according to the location of tumor in the liver, size of tumors, and level of RFA technique. A few reports compared the effects of RFA treatment under local and general anesthesia.

Innovations and breakthroughs

This report showed that the total applied energy and the applied energy per unit volume of whole and marginal coagulated necrosis were significantly larger in the group treated under general anesthesia (group G) resulting in a larger volume of coagulated necrosis.

Applications

Patients under pain-free condition during treatment may have a decreased rate of local tumor recurrence. It thus may be better to consider stronger pain relief during the treatment of percutaneous RFA treatment.

Peer review

Dr. Kurokohchi and colleagues reported the advantage and features of the combination therapy of ethanol injection and radiofrequency ablation (EI-RFA) under general anesthesia for HCC. This manuscript arouses interest for readers and provides an important clue to effectively treat patients with HCC.

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