

Thoracoscopic Microwave Coagulation Therapy for Hepatocellular Carcinoma

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ABSTRACT

Thoracoscopic microwave coagulation therapy (MCT) is a new therapeutic approach for hepatocellular carcinoma (HCC) in segments VII and VIII, which allows minimal access to the tumor and complete tumor ablation. In this study, four patients with HCC in segments VII and VIII underwent thoracoscopic MCT as a less invasive therapeutic option due to advanced liver cirrhosis and/or severe complications. Tumor sizes ranged from 15 to 30 mm in diameter and the tumors were well differentiated in 2 patients, moderately in one and poorly in one patient. Microwave irradiation was performed at an 80W output with a 60-sec duration via a thoracoscopic route and the total duration ranged from 4 to 24 min (mean:17 min). Patients recovered rapidly to preoperative conditions and no mortality was occurred. Complications were observed in one patient, including pleural effusion and fever elevation, but were cured conservatively. Postoperative computed tomography (CT) showed complete tumor ablation with a cancer-free margin, which is thought to be equivalent to a limited hepatic resection. This preliminary study suggests that thoracoscopic MCT might be a new, less invasive option providing a cure for HCC in segments VII and VIII in patients with advanced liver cirrhosis and severe complications.

Key words: *Hepatocellular carcinoma, Microwave coagulation therapy, Thoracoscopic operation*

Hepatocellular carcinoma (HCC) is one of the most common fatal malignancies in Southeast Asia and South Africa^{1,8)}. Hepatic resection has been developed as the most reliable procedure for long-term, tumor-free survival^{3,7)}. The morbidity and the mortality in hepatic resection have decreased with improvements in surgical techniques and perioperative management. However, most of the patients in Japan with HCC suffer from hepatic dysfunction due to chronic hepatitis or liver cirrhosis, and hepatic resection is not always a feasible option for patients with advanced liver cirrhosis and severe complications. Percutaneous ethanol injection (PEI)^{2,14)} and transcatheter arterial embolization (TAE)^{4,6)} have been widely performed for small initial or recurrent HCCs and unresectable HCCs because of their minimal invasiveness and easy repeatability. However, PEI and TAE are not suitable for complete tumor ablation because of the residual viable tumor cells in and around the tumor after these treatments^{12,14,17)}. Microwave coagulation therapy

(MCT) was introduced by Saitu et al as a new therapeutic option for 21 patients with small HCCs less than 5 cm in diameter⁹⁾ and its advantage is homogenous coagulation of the tumor. Recently MCT has been performed via a laparoscopic^{11,18)} and percutaneous route¹³⁾. Thoracoscopic MCT is a new therapeutic approach for HCC in segments VII and VIII, which allows minimal access to the tumor and complete tumor ablation.

The purpose of this report was to discuss the usefulness of thoracoscopic MCT as a new therapeutic approach for HCCs in segments VII and VIII.

PATIENTS AND METHODS

Background of the patients who underwent thoracoscopic MCT

We performed thoracoscopic MCT on 4 patients (MCT group) who had malignant liver tumors. Three of the four patients (Nos.1, 3, 4) had severe complications, including a dissecting aortic aneurysm, advanced liver cirrhosis and hemophil-

Table 1. Cases of thoracoscopic MCT

No.	Age Sex	Location Tumor size	Diagnosis	Indication	ICGR15 (%)	Complications before operation
1	61M	S8 30mm	HCC Poorly diff.	residual tumor after PMCT	13.9%	dissecting aortic aneurysm pulmonary fibrosis left renal atrophy
2	72F	S8 15mm	HCC Mod. diff.	insufficient image by US exam	-	post radiation therapy partial resection of left lung by VATS
3	60M	S8 25mm	HCC Well diff.	poor hepatic function	54.0%	advanced liver cirrhosis
4	64M	S8 28mm	HCC Well diff.	disorder of blood coagulation	17.1%	hemophilia A

ICGR 15: Indocyanin green retention at 15 min

Table 2. Clinical features of the patients

	MCT group (n=4)	Hx group (n=10)	T-test
Age	64.8	64.9	N.S.
Sex (M:F)	3:1	8:2	N.S.
Tumor size (mm)	24.5±6.7	28.6±8.5	N.S.
ICGR15%	24.2±11.3	17.7±10.9	N.S.
PT (%)	70.0±24.0	72.9±16.7	N.S.
T.Bil (ml/dl)	0.9±0.3	0.8±0.32	N.S.
ATS (IU/L)	35.8±14.0	49.8±16.0	N.S.
ALB (g/dl)	3.3±0.9	3.8±0.4	N.S.
ChE (IU/L)	221.5±129.8	288.7±68.8	N.S.

ICGR 15: indocyanin green retention at 15 min

PT: prothrombin time, ALB: albumin, ChE: cholinesterase, T. Bil: total bilirubin

ia A. One patient (No.2) had received radiation therapy for cancer of the tongue and a partial resection of the left lung by video assisted thoracic surgery (VATS) for lung metastasis. Surgical resection is the most reliable procedure for liver tumors, but it was thought to be too invasive for these patients. Moreover, other less invasive options, such as PEI or percutaneous microwave coagulation therapy (PMCT) which are performed by an ultrasonographic (US)-guide, were not suitable due to the subdiaphragmatic location of the tumor. Therefore, we performed thoracoscopic MCT as a less invasive option for complete tumor ablation (Table 1).

Tumor sizes ranged from 15mm to 30mm and were diagnosed as HCC by US, CT and hepatic angiography. A histological diagnosis was performed by an intraoperative needle biopsy of the tumor. The final histological diagnosis was a well differentiated type of HCC in 2 patients (Nos.3, 4), a moderately differentiated type in one (No.2) and a poorly differentiated type in one patient (No.1).

Patients with an S8-limited resection of the liver (Hx-group)

Intraoperative data (operation time, intraoper-

ative blood loss) and post operative hepatic functions (changes of T.Bil, AST level) in the patients undergoing thoracoscopic MCT were compared with a S8-limited resection group (N=10) in whom hepatectomy was performed during the same period. Statistical analysis was performed using the Student's t-test.

Table 2 shows the backgrounds of the patients in the MCT group and in the S8-limited resection group (Hx group). There were no significant differences in age, sex and preoperative hepatic function (ICG retention rate, prothrombin time, T.Bil, AST, ALT, ALB, CH-E).

Surgical Technique

After institution of anesthesia, the patients were intubated with a double-lumen endotracheal tube and placed in the left lateral decubitus position. A 2.0 cm incision was made along the posterior-axillary line in the seventh intercostal space. After single-lung ventilation was instituted, a trocar 11-mm in diameter (Autosuture Surgiport; United States Surgical Corp, Norwalk, CT) was introduced into the thoracic cavity. A wide-angle, zero-degree thoracoscope with an operating port was introduced through this trocar, and explo-

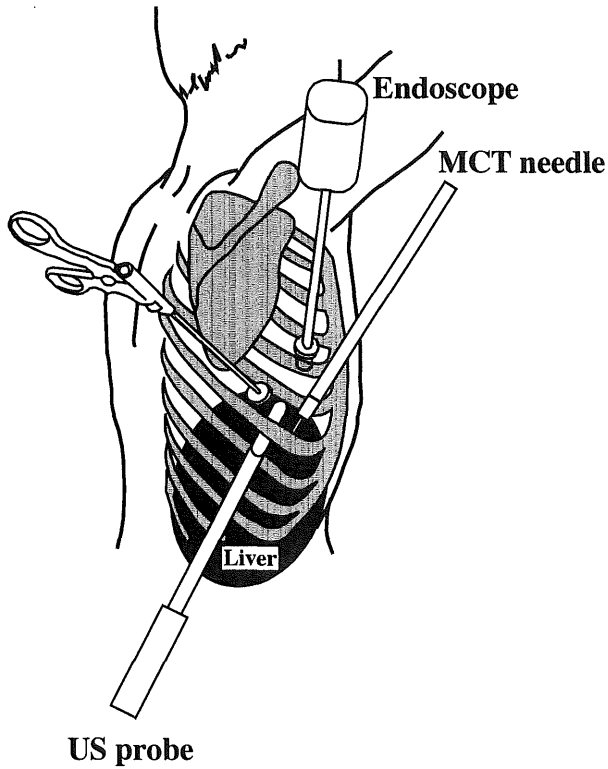


Fig. 1. Operative procedure of thoracoscopic MCT

ration of the thoracic cavity was performed. A second trocar was introduced through the fourth intercostal space along the mid-axillary line. A thoracoscope was introduced through this trocar and a 7.5 MHz laparoscopic US-probe (UST-5521-7.5, Aroka Co. Ltd., Japan) was introduced through the seventh intercostal trocar (Fig. 1). The site and extent of the tumor and its relationship to the hepatic vessels were evaluated by trans-diaphragmatic intraoperative thoracoscopic ultrasonography and the coagulation area was marked on the diaphragm by an electrocautery knife (Fig. 2-A). A third trocar for the microwave electrode was introduced through the fifth intercostal space, in most cases along a posterior-axillary line so as to insert it straight above the tumor. When the tumor size was less than 2.5cm, we performed thoracoscopic MCT trans-diaphragmatically, but when the tumor size was more than 2.5cm, we dissected the diaphragm and the thoracoscopic MCT was performed directly from the hepatic surface. Dissection of the diaphragm was performed carefully with regard to haemostasis and lymphorrhoea in the patients with liver cirrhosis (Fig. 2-B). An endoscopic stapler or harmonic scalpel was beneficial in preventing postoperative bleeding and lymphorrhoea from the cut surface of the diaphragm. Intraoperative laparoscopic

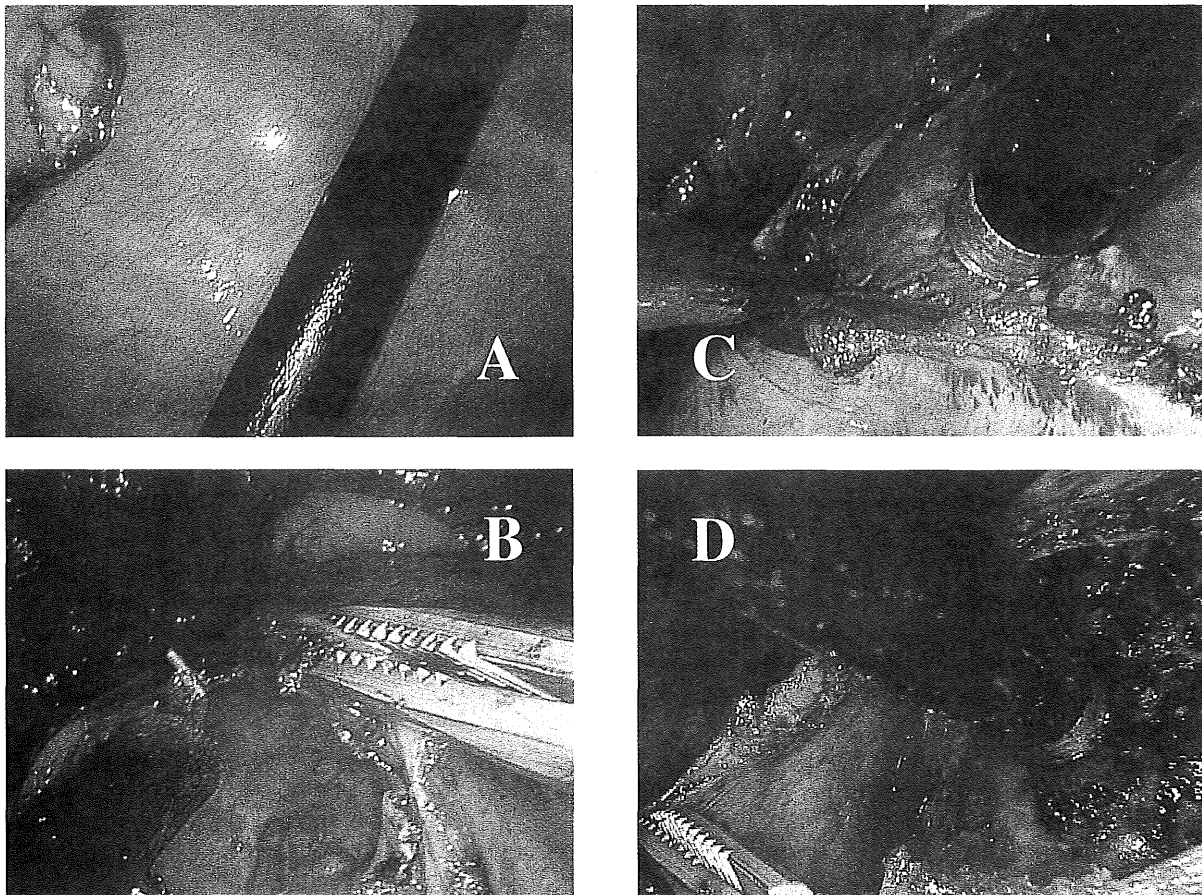


Fig. 2. Intraoperative findings of thoracoscopic MCT

ultrasonography was performed again directly from the hepatic surface and the coagulation area was marked over 10mm outside the edge of the tumor on the hepatic surface. We selected a suitable needle length among the three types of microwave electrode (the length of the needles were 2, 3, 4.5 cm). The coagulation area was irradiated with microwaves (80W, 60 sec) at intervals of 1.0 cm (Fig. 2-C, D). After microwave coagulation, haemostasis was confirmed by careful observation of the coagulated hepatic surface. The right subphrenic space was washed with 37.0°C warm saline and the dissected diaphragm was closed with an endoscopic interrupted suture using 3-0 absorbable strings. A single 20F chest tube was inserted into the intra-thoracic space and the procedure was terminated after closure of the trocar sites in two layers.

RESULTS

Intraoperative data

Table 3 shows the intraoperative data of the patients in the MCT group, which were compared with the patients in the Hx-group. The operation time for thoracoscopic MCT ranged from 150 min to 230 min (mean: 197.5±42.5 min) and no significant difference was observed between these two groups. The amount of intraoperative blood loss was negligible (mean: 30.1g) in the thoracoscopic MCT group and a significant difference was observed between the two groups ($p<0.05$).

Table 3. Perioperative data

	MCT group (N=4)	Hx group (N=10)
Operation time (min)	197±42.5	234.7±49.1
Intraoperative blood loss (g)	30.0±14.1	320.2±321.6

Postoperative course

All patients in the MCT group recovered rapidly to preoperative conditions. Oral intake was started on the first to the third day and the chest tube was removed on the second to the fifth day after operation. There were no severe complications such as postoperative bleeding, bile leakage or liver abscess. A middle grade fever elevation was observed in two patients (Nos.3, 4) for one week and pleural effusion was observed in one patient (No.4). These complications recovered conservatively.

Changes of AST and T.Bil level

Fig. 3 shows the changes after operation in the serum AST (AST) and serum total bilirubin (T.Bil) levels in the patients who underwent thoracoscopic MCT. The AST levels increased on the first day, ranging from 181 to 338 IU/L (mean: 256 IU/L) and were parallel to the degree of microwave irra-

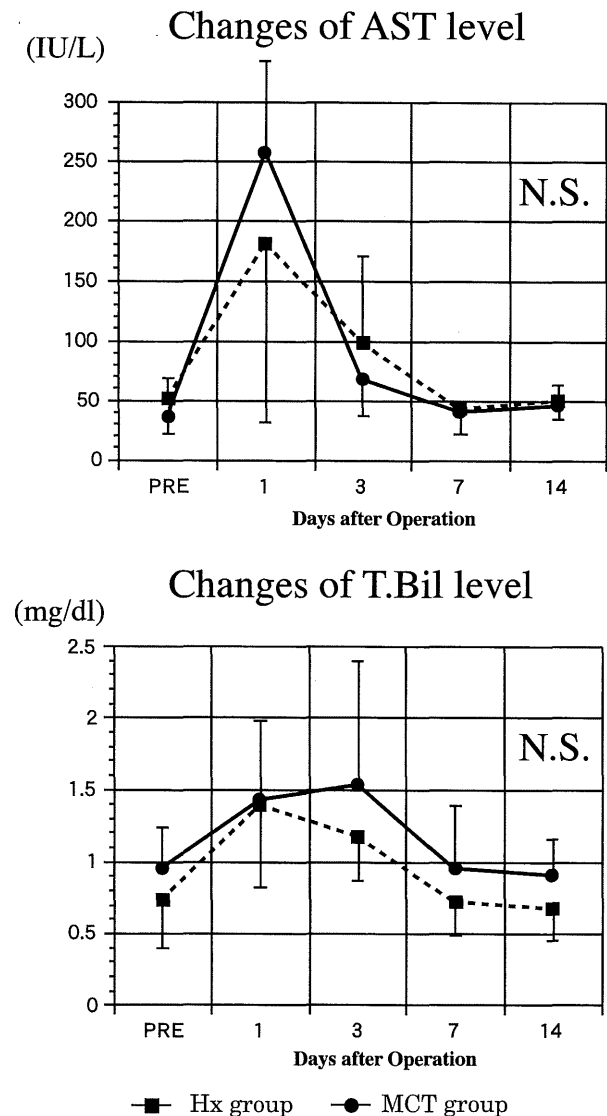


Fig. 3. Comparison of AST and T.Bil levels between Hx group and MCT group

diation. There was no significant difference between the MCT group and Hx-group with respect to the increase in AST levels, and this returned to normal levels on the third day in all patients. The T.Bil levels changed less than 2.0 mg/dl in 3 of 4 patients. In only one patient with advanced liver cirrhosis, T.Bil increased to 2.6 mg/dl on the third day and returned to the normal value on the 14th day after operation.

CT examination before and after MCT

Fig.4-A shows the CT image before thoracoscopic MCT. The tumor was detected as a low-density area in the right subphrenic lesion of the liver and was emphasized by enhanced CT. Fig.4-B shows the CT image after treatment. The tumor changed to a lower density area with surrounding liver parenchyma and was not emphasised by enhanced CT. These findings indicated that the tumor had been completely changed to coagulation necrotizing tissue by MCT with a sufficient surgical margin.

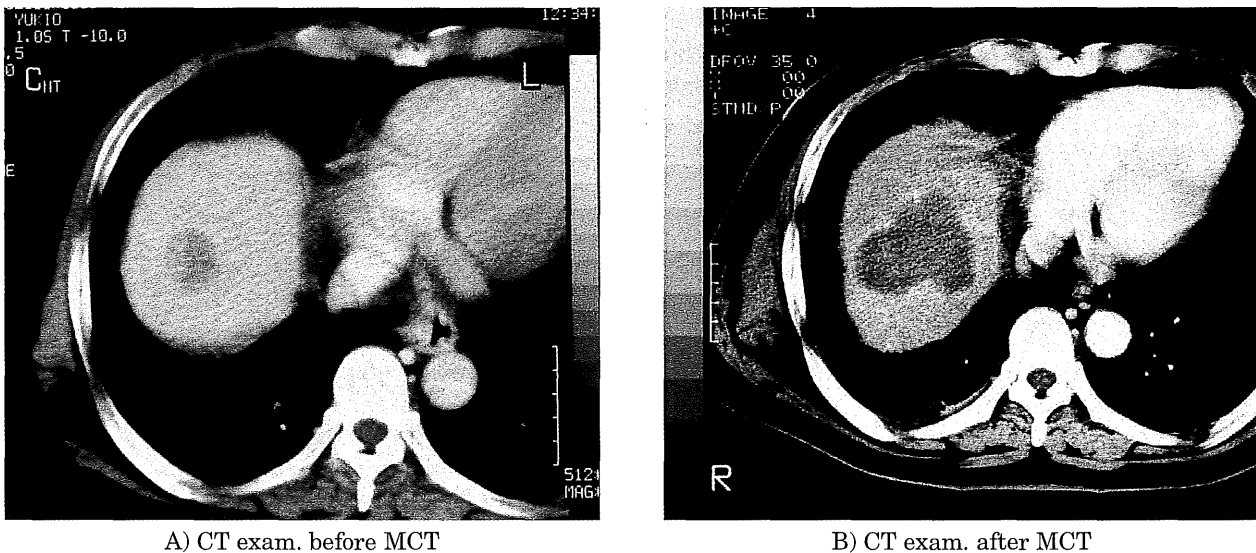


Fig. 4. CT examinations before and after thoracoscopic MCT

Early prognosis after MCT

Median hospitalization was 22 days (range: 14 to 36 days). Follow-up was completed in all patients and ranged from 5 to 10 months (median: 6 months). serum α -fetoprotein level was increased in 2 patients (Nos. 3,4) before MCT and decreased to normal ($<20\text{ng/ml}$) after MCT. No recurrence has been observed in any of the patients.

DISCUSSION

There are many options for the treatment of HCC, such as hepatic resection, PEI, TAE, and MCT. Surgical resection is the most reliable procedure in terms of tumor ablation and a good long-term, tumor-free survival^{6,7}. However, there are some disadvantages including the surgical risk and its invasiveness. For these reasons, surgical resection is not a feasible option for patients who have a poor hepatic function reserve due to advanced liver cirrhosis or who have severe complications.

PEI and TAE are widely performed, alone or in combination, for the initial treatment of patients with poor hepatic function reserve or for recurrent unresectable HCCs. The advantages of PEI are its safety, easy repeatability and minimal invasiveness. However, PEI has some disadvantages, including insufficient tumor necrosis because of inhomogenous distribution of the ethanol into the tumor and liver parenchyma, and local recurrence after treatment^{9,11,14}. TAE is sometimes effective for the main tumor, but not effective for cancer cells in the fibrous capsule of the tumor or small metastatic nodules around the main tumor³.

MCT is a new therapeutic option for HCC recently developed in Japan. The characteristics are homogenous coagulation of the tumor with the surrounding liver parenchyma^{5,17}. Microwave coagulation was initially developed as an instrument

for haemostasis or coagulation of a dissecting surgical stump during hepatic resection^{5,15}. MCT was first reported by Saitu et al as a therapeutic treatment for HCC. They reported that 21 patients with HCC nodules less than 5 cm were treated by MCT and had a good prognosis without local recurrence or severe complications¹⁴. In recent years, MCT has been performed via a laparoscopic^{12,16} or percutaneous route¹⁸. Seki et al first reported PMCT with 18 HCC patients, who had single HCC nodules less than 2 cm in diameter. They reported no local recurrence and no complications after this treatment. The advantage of PMCT is complete tumor ablation inside the coagulation area, and PMCT is a feasible option for patients with small HCCs and a poor hepatic function reserve¹⁸.

However, there are some problems with MCT for tumors in segments VII and VIII. MCT for these lesions are difficult to perform via a laparotomy, or via a laparoscopic method without mobilization of the liver. Furthermore, the percutaneous route is not suitable for complete tumor ablation of the HCCs in these lesions because they are sometimes invisible by external ultrasonography and there is a long distance from the puncture point to the tumor with the result that it is difficult to perform an accurate puncture and complete tumor ablation.

Thoracoscopic MCT is a new therapeutic approach for HCCs in segments VII and VIII. A thoracoscopic approach allows minimal access to the tumor in segments VII and VIII without mobilizing the liver and accurate tumor ablation, including sufficient liver parenchyma around the tumor by laparoscopic ultrasonography transdiaphragmatically or directly from the liver surface¹². The outstanding advantage is the flexible management of MCT. Under thoracoscopic MCT, the coagulation area can be adjusted to the size

and location of the tumor, so that complete tumor ablation can be performed, even for tumors more than 2cm in diameter or for multi-nodular types of HCC.

In this study, we estimated the coagulation area by an enhanced CT scan after the thoracoscopic MCT. The postoperative CT showed complete tumor ablation with a sufficient tumor-free margin, and the necrotic area caused by MCT was thought to be equivalent to a limited hepatic resection.

Another outstanding advantage of thoracoscopic MCT is its mild invasiveness. In this study, we observed a transient increase in the AST levels in the early period after MCT, which might be due to the remaining necrotic tissue in the liver caused by MCT. However, in spite of poor hepatic function and/or severe complications, the hepatic functions rapidly returned to the preoperative value. Patients were able to start oral intake on the next day after MCT and recovered to preoperative conditions within a week. The mild invasiveness of thoracoscopic MCT seems to be due to the following reasons: 1) MCT could be performed without the mobilization of the liver. 2) There was no warm ischemic damage of the liver due to the hepatic vascular occlusion. 3) The intraoperative blood loss was minimal. 4) The thoracoscopic route had no influence upon the intra-abdominal organs. 5) Patients had minimal wound pain after MCT.

On the other hand, there are some problems with thoracoscopic MCT, as follows. 1) The thoracic route is difficult to perform on patients with severe adhesion of the right thoracic cavity and a severe pulmonary function disorder. Thoracoscopic MCT was not indicated for the patients with these complications. 2) Microwave irradiation produces H₂O-gas in the hepatic parenchyma which prevents real-time sonographic monitoring of the coagulated area. With regard to this point, color doppler ultra-sonography may be useful in detecting the coagulation area.

In this preliminary study, the follow-up periods after MCT were too short to estimate the local curability and long-term prognosis. However, Yamanaka et al reported that the crude and disease-free survival rates for a laparoscopic or open MCT group were comparable to those for a wedge resection group¹⁶⁾, and similar results may be expected from thoracoscopic MCT.

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