Computed Tomography-guided Radiofrequency Ablation for Sub-diaphragm Hepatocellular Carcinoma: Safety and Efficacy of Inducing an Artificial Pneumothorax

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We retrospectively evaluated the safety and efficacy of artificial pneumothorax induction to perform computed tomography (CT)-guided radiofrequency ablation (RFA) for sub-diaphragm hepatocellular carcinomas (HCCs). From June 2008 to October 2010 at our institution, 19 HCCs (16 patients) were treated using CT-guided RFA after artificial pneumothorax induction. A 23-G needle was inserted into the liver surface at a site of 2 connected pleurae without lung tissue. After a small amount of air was injected, the pleural space widened, creating a small pneumothorax. Additional air was insufflated via a newly inserted 18-G cannula to raise the lung away from the planned puncture line for RFA. The electrode was then advanced transthoracically. Ablation was performed using a cool-tip electrode with manual impedance control mode. The injected air was then aspirated as much as possible. Artificial pneumothorax was successfully induced in all cases. The average total volume of injected air in each case was 238ml. No artificial pneumothorax-related complication occurred; lung injury occurred in one case during RF electrode insertion. No local progression occurred during follow-up. Recurring HCCs were observed in eight patients. Artificial pneumothorax induction is safe and effective for CT-guided RFA of sub-diaphragm HCCs, which are difficult to locate on US.

Key words: hepatocellular carcinoma, liver, radiofrequency ablation, CT fluoroscopy, artificial pneumothorax

Liver radiofrequency ablation (RFA) is widely accepted as a successful, locally controlled treatment for hepatocellular carcinoma (HCC). RFA is usually performed under ultrasonography (US) guidance. However, US is not always effective; an example is its sometimes-inadequate detection of sub-diaphragm HCCs. RFA for subphrenic HCC has proven difficult to perform successfully because of the reported risks of local progression following the procedure [1, 2]. Many novel techniques have been developed to improve the efficacy of RFA for subphrenic HCC. Some of the methods being investigated are artificial pleural effusion, artificial ascites, a trans-thoracic approach under computed tomography (CT) guidance, and thoracoscopic or laparoscopic approaches [3–11]. Generally, the choice of treatment method depends on the preference of the medical professional or the institution according to, for example, the ease and availability of CT or general anesthesia.

In the case of CT-guided RFA, the use of artificial pneumothorax can be considered a beneficial approach. Our results indicate that artificial pneumothorax induction is a safe and effective method for treating sub-diaphragm HCCs using CT-guided RFA.

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pleural effusion is challenging because it depends on the patient's body position during the procedure. The transthoracic approach with lung penetration frequently results in a pneumothorax [7–9] and may even cause an air embolism [12–14]. To minimize complications following the procedure, we have performed CT-guided liver RFA after inducing an artificial pneumothorax. The purpose of the present study was to retrospectively evaluate the safety and efficacy of the artificial pneumothorax induced during liver RFA.

**Patients and Methods**

From June 2008 to October 2010, 32 patients were treated at our institution using CT-guided liver RFA, because of the restricted efficacy of US for the detection of sub-diaphragm HCCs. Of these patients, 19 HCCs in 16 patients were treated using CT-guided RFA with an induced artificial pneumothorax. An artificial pneumothorax was induced when the lung was on the puncture line. The patient characteristics are summarized in Table 1. The locations of the HCCs treated using CT-guided RFA were as follows: segment 1 for two HCCs, segment 4 for three HCCs, segment 7 for five HCCs, and segment 8 for nine HCCs. The median diameter of the HCCs was 16mm (range 10–44mm). Overt pleural adhesion was considered a contraindication in the patients with a history of lung surgery, chronic lung inflammation, or pleurodesis because in such cases, it might not be possible to induce an artificial pneumothorax.

If the tumor was not visible by plain CT, transarterial chemoembolization was performed several days before the liver RFA in conventional fashion using lipiodol. Lipiodol accumulation inside the HCC was helpful to achieve accurate penetration under CT fluoroscopic guidance. The body position of the patient during the procedure depended on the tumor location, in order to successfully raise the base of the lung using an artificial pneumothorax. The supine position was chosen when the tumor was located in the anterior segment; the prone position when the tumor was in the posterior segment, and the lateral decubitus position when the tumor was on the lateral side of the liver.

Artificial pneumothorax was introduced in 2 steps. First, a 23-G needle was inserted under CT fluoroscopic guidance into the liver surface at a location of two connected pleurae, where no lung tissue was present. If the needle tip was located in the thoracic space, a small amount of air (20–100ml) could separate the pleural layers.

**Table 1 Patient characteristics**

<table>
<thead>
<tr>
<th>Patient No. Age/sex</th>
<th>Location (segment)</th>
<th>Tumor size (mm)</th>
<th>Air volume (ml)</th>
<th>Complication</th>
<th>Follow-up (month)</th>
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<tr>
<td>1. 76M</td>
<td>supine</td>
<td>15</td>
<td>100</td>
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<tr>
<td>2. 62M</td>
<td>supine</td>
<td>17</td>
<td>200</td>
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<td>25</td>
</tr>
<tr>
<td>3. 77M</td>
<td>supine</td>
<td>15</td>
<td>30</td>
<td>no</td>
<td>22</td>
</tr>
<tr>
<td>4. 74F</td>
<td>supine</td>
<td>18</td>
<td>200</td>
<td>no</td>
<td>21</td>
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<td>15</td>
<td>150</td>
<td>no</td>
<td>19</td>
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<tr>
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<td>50</td>
<td>no</td>
<td>18</td>
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<tr>
<td>7. 72F</td>
<td>supine</td>
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<td>150</td>
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<td>17</td>
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<td>16</td>
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<td>supine</td>
<td>17</td>
<td>600</td>
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<td>3</td>
</tr>
</tbody>
</table>

*Patient 7 underwent RFA twice. Two HCCs were treated at first ablation.
** A lung injury occurred during the RF electrode insertion.
rate the contacting pleurae, creating the small artificially induced pneumothorax. Next, an 18-G cannula (Surflo; Terumo, Tokyo, Japan) with a side hole was introduced into this space. Additional air was insuf-flated until the base of the lung was raised above the planned puncture route for the RFA (Fig. 1). The electrode was then inserted transthoracically, without penetrating the lung. After liver ablation, the injected air was aspirated as much as possible.

RFA was performed under local anesthesia, using a Cool-tip™ electrode (Valleylab, Boulder, CO, USA). In all cases, the insertion of the electrode was performed using CT fluoroscopic guidance (Somatom Sensation-16 scanner; Siemens Medical Systems, Erlangen, Germany). The conditions of the CT fluoroscopy were 100kV and 30mAs. After the insertion of the electrode, a 1-mm collimation CT scan was obtained. The electrode position was characterized in three directions: axial, coronal, and sagittal. The RF energy was applied using an impedance-controlled algorithm. The puncture tract was ablated following the removal of the electrode, and a chest radiogram was obtained 2h after the procedure and then again the next morning to check for the presence of a pneumothorax. Local progression or the development of new HCCs was monitored using CT or magnetic resonance imaging (MRI) every 3 months after the procedure. Our institutional review board permitted this retrospective study.

Results

The artificial pneumothorax was successfully induced in all 16 patients. Pleural adhesion was not observed in any of the patients. The median injected air volume was 200ml (range 30–600ml). Following the induction of the artificial pneumothorax, no complications, such as a decrease of blood oxygen saturation or hemorrhage, were recorded. At the end of each procedure, almost all of the injected air was successfully aspirated through the 18-G cannula with a side hole.

The procedure was performed in the supine position in 11 patients (64.7%), in the lateral position in 3 patients (17.6%), and in the prone position in 3 patients (17.6%). In one patients, RFA with the artificial pneumothorax was performed twice to treat a second, newly developed HCC. Each artificial pneumothorax was successfully induced (twice in the same patient), and no pleural adhesion was observed.

In all cases, the RFA was completed transthoracically without penetrating the lung. In 14 cases (82.4%), the lung was moved away successfully from the puncture route on the axial CT view (Fig. 2). In 3 cases (17.6%), the base of the lung did not move away fully. In this instance, the puncture site was shifted to the caudal side. The electrode was then inserted below the base of the lung in order to avoid lung penetration, and the RFA was completed successfully.

Fig. 1 The method used to induce an artificial pneumothorax. A, White dots are puncture guides placed on the body surface. The puncture point is near the cost phrenic angle, where no lung tissue is present; B, After local anesthesia is administered using a 23-G needle, and a small amount of air is injected from the same needle. If the needle tip catches the thoracic cavity, injected air spreads into the thorax; C, A small artificial pneumothorax can be induced following an injection of 20–100ml of air. An 18-G cannula is then introduced under CT fluoroscopic guidance. Additional air is injected until the base of the lung is raised above the level of the tumor.
Among these three tumors, which were located in segment 7 or 1, lung damage occurred in one case during the electrode insertion. A long RF electrode (20 cm) was used because the tumor was deeply located. In this case, the electrode could not be inserted under CT fluoroscopic guidance because of the narrow gantry space and the lateral position of the patient. A 20-cm-long electrode was used only in this case. By the time the electrode tip had been observed using CT fluoroscopy, the electrode had already injured the base of the lung. The puncture site was moved further to the caudal side, and the RFA was completed without penetrating the lung. A small pneumothorax occurred after the procedure but did not require chest tube placement. Other complications such as hemorrhage or infection were not observed.

Follow-up CT or MRI examinations were performed periodically, with a median follow-up period of 9.5 months (range 3–28 months). Local progression did not occur, but the development of new HCCs was reported in eight patients (50%).

Discussion

Liver RFA is usually performed under US guidance because of its convenience. However, US cannot always locate HCCs, particularly sub-diaphragm HCCs. New methods are required to increase the success rate of these procedures. Artificial pleural effusion has been reported to be a useful method [3, 4], in which a 5% glucose sterile solution is injected into the pleural cavity using a Veress needle (a blunt-tipped needle) with the patient in a semi-sitting position until the tumor is located. This method is useful to treat
obscured subphrenic HCCs, but is not performed in every institution.

Another method was also reported: CT-guided RFA with lung penetration. This method resulted in frequent pneumothoraces (38–71% of cases). In 0–29% of the procedures performed in this manner, chest tube placement is required [7–9]. Double penetration of the visceral pleurae can frequently cause complications, and lung penetration may cause an air embolism. The frequency of air embolism has been reported to be 0.07% [12] and more recently, 0.4% [13]. If possible, avoidance of lung penetration is preferred, because there is no effective way of protecting against an air embolism, which can sometimes be fatal [14].

Thoracoscopy- or laparoscopy-assisted liver RFA is a more invasive procedure, requiring general anesthesia [10, 11]. At our institute, CT can be conveniently used to guide interventional procedures. We thus consider the use of CT-guided liver RFA with an induced artificial pneumothorax a less invasive option in the treatment of HCCs previously undetected on US.

Air can be introduced into the thorax in several ways. A blunt-tipped needle is advanced to the lung to penetrate the thoracic cavity [15]. However, even a blunt-tipped needle can lead to lung damage in cases of pleural adhesion. On the other hand, our method uses a needle puncture at the bottom of the thoracic cavity where no lung tissue exists, in order to prevent lung injury. CT cannot visualize the thoracic cavity at the level of the liver surface, but the thoracic cavity can be punctured by advancing the needle tip to the surface of the diaphragm. If the needle tip is positioned inside the thorax, injected air spreads into the thorax and separates the 2 parietal pleurae, which can then be detected using CT. If the needle tip is positioned outside the thorax, injected air remains near the needle tip. If the needle tip is positioned inside the abdominal cavity, injected air spreads along the liver surface. The thoracic cavity can be observed following the adjustment of the needle tip under CT fluoroscopic guidance.

After the induction of a small artificial pneumothorax, another 18-G cannula with side hole is advanced into the thorax. Additional air is injected thorough the coaxial needle until the lung tissue is raised above the tumor level. An injection of 400 ml of air can elevate the lung in 82% of cases in this study. As the width of the lung is thinner at the bottom of the thoracic cavity, the base of the lung can be raised by a small volume of air injection. However, injected air gradually spreads upward, and the lung is not lifted even if the volume of injected air has increased. Therefore, the injection of air is discontinued after approx. 500 ml of air, and the insertion of the electrode is performed from a lower level to prevent lung injury. Insertion of the electrode was completed in all of the present cases, but pneumothorax occurred in only one patient during the electrode insertion, in which sufficient elevation of the lower lobe was not obtained. It might be difficult
to lift the lower lobe sufficiently because the volume of lung parenchyma is higher in the lower lobe.

Injected air can spread into the independent portion in the thorax, and thus the patient position strongly affects the distribution of the injected air. In the present patient series, the position of the patient during the procedure was determined according to the tumor location; if the tumor was in segment 4, the patient was in the supine position. If the tumor was in segment 7, the patient was in the prone position.

Our convenient and low-cost method for inducing an artificial pneumothorax does not require any special equipment, such as a needle with a protective sheath. Injected air can be aspirated following the RFA procedure via an 18-G cannula with a side hole. If a side hole is not present, the needle tip can easily be obstructed so that injected air cannot be aspirated sufficiently.

We conducted a literature review by searching the PubMed database. The search was performed using the keywords “liver” and “radiofrequency ablation” and “pneumothorax”. For the years from 2001 to 2015, there is only one report of liver RFA with the induction of an artificial pneumothorax [16]. In that report, the artificial pneumothorax was induced using an epidural kit. The needle was injected by applying positive pressure using a syringe plunger. When the needle tip was inside the thoracic cavity, the syringe pressure decreased. The induction of an artificial pneumothorax was successful in all cases, without complications. However, a needle insertion toward the lung may cause lung injury. Our way of introducing an artificial pneumothorax may be safer because we puncture the thoracic cavity at the bottom where no lung tissue exists. In the present study, the mean injected air volume was 566 ml (range 200–800 ml). The injected air volume and the treatment effects of RFA were similar to those in our cases.

An artificial pneumothorax is used in other procedures such as lung RFA and mediastinal tumor biopsies [15, 17, 18]. In those studies, an artificial pneumothorax could not be induced in 2 cases because of pleural adhesion. A history of thoracic surgery or radiation therapy is an obstacle for the induction of an artificial pneumothorax. Solomon et al. reported that 750 ml of air injected into the thoracic cavity caused a decrease in saturated oxygenation [15]. In contrast, 2,000 ml of injected air did not cause any complications during a mediastinal biopsy [17, 18]. The air injection should be performed carefully, paying special attention to the risk of dyspnea or circulatory changes. Unlike mediastinal biopsies, liver RFAs can be performed with smaller volumes of injected air, because the lung tissue can easily be raised above the level of the thoracic base.

We observed that, by our method, subphrenic HCCs were well controlled using RFA, and local progression was not reported during the follow-up period. Therefore, sub-diaphragm HCCs can be successfully treated with a low complication rate by inducing an artificial pneumothorax. However, we observed that newly developed HCCs did occur in other parts of the liver in half of the cases in the present study.

We should also highlight the potential limitations of the present study. First, the patient population was small (n = 16). Because pleural adhesion cannot be judged clearly before the procedure, artificial pneumothoraces may not be induced in some cases. In addition, this study was retrospective. Prospective clinical studies are needed to further evaluate the usefulness of this procedure.

In conclusion, subphrenic HCCs can be treated effectively using CT-guided liver RFA by inducing an artificial pneumothorax. Artificial pneumothoraces were induced in all cases without complications. The induction of an artificial pneumothorax is a safe and effective method to minimize the complications of CT-guided liver RFA to treat subphrenic HCCs.

References


