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SURGICAL ENDOSCOPY
and Other Interventional Techniques

The physiologic effect of the pneumoperitoneum on radiofrequency ablation

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Abstract
Background: Radiofrequency ablation (RFA) is gaining widespread acceptance as a safe and effective method for liver tumor ablation. Complete tumor ablation is essential for the success of the procedure. Multiple modalities have been explored in an effort to increase the size of the lesion created by RFA. The purpose of this study was to determine the physiologic effects of the pneumoperitoneum on RFA lesion size.
Methods: A total of 32 RFA lesions were created in eight pigs. After the induction of anesthesia, pneumoperitoneums of 2, 12, and 24 mmHg were established sequentially in each animal. After an equilibration period of 2 min, RF was administered with a constant saline-infused (0.9%) needle at 25 W for 3 min. In subsequent and complementary experiments, both before and during RF administration at each intraperitoneal pressure (IPP), Doppler flow was measured by laparoscopic ultrasound in the portal vein and hepatic artery while blood pressure was monitored by a femoral arterial line. The animals were then killed humanely and the livers were harvested. Measurements were taken in three dimensions of the ablated areas, and the volume was calculated. Statistical analyses were performed using analysis of variance (ANOVA) and repeated measures test.
Results: The average volumes of the lesions (in cm^3) were 3.1 $\pm$ 1.8, 5.2 $\pm$ 1.7, and 6.7 $\pm$ 3.3 for IPP of 2, 12 and 24 mmHg, respectively; there was a significant difference between the area of lesion at an IPP of 2 mmHg and an IPP of 24 mmHg ($p < 0.05$). Blood flow in the portal vein also decreased significantly from 1.8 $\pm$ 0.6, 0.98 $\pm$ 0.5, and 0.43 $\pm$ 0.2 at IPP of 2, 12, and 24 mmHg, respectively ($p < 0.001$). Hepatic artery blood flow and peripheral blood pressure did not change significantly in the respective IPP groups.
Conclusions: This study indicates that the volume of liver ablated by RF can be increased by augmenting the IPP. Our data support the theory that a decrease in portal blood flow results in decreased heat dissipation during RFA. The laparoscopic approach to RFA offers the advantage of allowing control of the IPP, which may result in a larger volume of ablated tissue per treatment than can be achieved with the percutaneous technique. These preliminary data on normal hepatic tissue must be confirmed clinically in the setting of hepatic tumors.

Key words: Radiofrequency ablation (RFA) — Pneumoperitoneum — Liver tumors — Intraperitoneal pressure — Hepatic blood flow — Laparoscopy

Radiofrequency ablation (RFA) is a locally applied technique that offers a promising treatment for nonresectable liver tumors. It involves the use of high-frequency alternating current to create frictional heating of the tissue surrounding the electrode; the tissue then undergoes desiccation and coagulative necrosis. When used for the ablation of liver metastases, it has proved to be an effective method with very few side effects [4]. Thus, RFA provides an important alternative treatment for patients who are not candidates for surgical resection of liver tumors due to tumor size, location, and number, or comorbid disease.

Complete tumor ablation is essential for the success of any local treatment of liver tumors. One of the factors that has limited the use of RFA is the size of the lesion that is created. Therefore, recent developments in RFA have focused on attempts to find a way to create larger areas of ablation, so as to ensure the total destruction of the tumor. One of the factors that influences the size of the ablation area is hepatic perfusion. The vascular supply of the liver provides a heat sink that decreases the extent of the area of ablation. One way to mitigate this effect is to decrease the blood flow to the liver. Decrease

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Table 1. Doppler flow vs increasing IPP

	Intraperitoneal pressure		
	2 mmHg	12 mmHg	24 mmHg
Mean lesion volume (cm^3)	$3.1^a \pm 1.8$	5.2 ± 1.7	$6.7^a \pm 3.3$
Hepatic artery flow (Hz)	4.1 ± 1.1	3.8 ± 1.0	3.8 ± 1.1
Portal vein flow (Hz)	$1.8^b \pm 0.6$	$0.98^b \pm 0.5$	$0.43^b \pm 0.2$
Blood pressure	114/62	119/68	123/61

Values are ± SE
[a] $p < 0.05$
[b] $p < 0.001$

in the hepatic blood flow is usually accomplished by the Pringle maneuver, which allows a more rapid conduction of the current and creates a larger area of necrosis. As a result of the increased emphasis on minimal invasiveness and the expansion of the applications of laparoscopy to RFA, the Pringle maneuver, which increases the time needed for the dissection, while still feasible, is not generally performed during laparoscopic RFA. At the same time, studies have shown that the creation of a pneumoperitoneum alone results in a decrease in liver perfusion [9, 10]. Therefore, when the technique of RFA is performed laparoscopically, the reduction in blood flow may have an effect on the size of the ablated lesions.

RFA can be performed percutaneously, by laparoscopy, or by laparotomy. Compared to the percutaneous method laparoscopy offers the advantages of better visualization, increased detection of tumors via the use of intraoperative ultrasound, and the protection of adjacent structures. Recent studies have confirmed the efficacy of RFA performed via the laparoscopic approach [7, 18, 19]. However, the physiologic effects on the RFA of creating a pneumoperitoneum are not well understood. Other studies using laparoscopy have shown that blood flow in the liver decreases due to increased intraabdominal pressure. A decrease in hepatic blood flow is also known to increase the size of RF-ablated lesions due to a reduction in the heat sink created by the vascularization. Given these facts, it seems possible that the creation of a pneumoperitoneum would alter hepatic blood flow enough to affect the size of the ablated area created by the application of RF. Therefore, we designed an experiment to study the physiologic effects of different intraperitoneal pressures (IPP) on the efficacy of RFA.

Materials and methods

We used a saline-infused system with a 375-kHz generator (Berchtold) that produced a maximum 60 W of power through a 1.2-mm insulated needle. The active electrode needle has several micro boreholes that allow the passage of physiologic saline into the surrounding tissue. The flow is supplied by an injection pump via infusion tubing and was set to infuse at a rate of 60 ml/h. The saline helps to prevent desiccation and acts as a liquid electrode to propagate the heating of the tissue.

Eight anesthetized 35–40-kg pigs were used in this protocol. In each pig, IV fluid of normal saline (0.9%) was administered at a rate of 100 cc/h throughout the experiment. A grounding pad was placed on the back of the pig, next to the spine. After the induction of anesthesia, two 12-mm trocars were placed, one in the supraumbilical position for the endoscope and the other in the left lateral position for the laparoscopic ultrasound. Then pneumoperitoneums with insufflation pressures of 2, 12, and 24 mmHg were established sequentially in each animal. The RF electrode was introduced percutaneously under direct laparoscopic vision.

After an equilibration period of 5 min at each IPP, RF was applied with a constant saline-infused (0.9%) needle at 25 W for 3 min under laparoscopic ultrasound guidance. If impedance levels were unacceptable, the treatment was arrested for 10 sec and then restarted. In subsequent and complementary experiments, both before and during RF administration at each pressure, Doppler flow was measured in the portal vein and hepatic artery using a laparoscopic Doppler probe while blood pressure was monitored by an arterial line. The animal was then killed humanely and the liver harvested.

Measurements were taken in three dimensions of the ablated areas, and their estimated volumes were calculated. The volume was calculated using the following formula: $4/3\ \pi \times (\text{radius } 1) \times (\text{radius } 2) \times (\text{radius } 3)$. Statistical analysis was performed using analysis of variance (ANOVA) and repeated-measure tests.

In this experiment, we used a saline-infused electrode. RF works such that the current created by the RF electrode creates frictional heating of the surrounding tissue, which serves to further propagate the heat to the surrounding tissue. Once the tissue has reached a temperature of ≥50°C, the proteins denature and the tissue undergoes coagulative necrosis. Therefore, it is the tissue ions themselves that propagate the energy and determine the efficacy of the treatment. If the tissue becomes desiccated, it is no longer able to conduct the current needed to heat and eventually ablate the tissue.

Results

Eight pigs were used and 32 lesions were successfully created at $n = 11$ for each pressure of 2 and 12 mmHg and $n = 10$ for a pressure of 24 mmHg. There were no complications during the procedures. The average volume of the lesions increased with increasing IPP. The difference in the lesion volumes created between 2 and 24 mmHg was significant ($p < 0.05$). Although the difference between the volumes of the lesions created between 2 and 12 mmHg showed a trend toward increase, it approached, but did not reach, significance ($p = 0.056$). Doppler flow in the portal vein decreased significantly with increasing IPP (Table 1). ANOVA analysis yielded and F value of 26 with $p < 0.001$. Further analysis with Fisher's PLSD revealed a significant difference between each group. There was no statistical difference in the blood flow in the hepatic artery or in the systolic or diastolic blood pressure at each IPP.

Discussion

Our results indicate that, as compared to low intraperitoneal pressures (2 mmHg), the area of ablation created by RFA increases with increased pneumoperitoneal pressures. Furthermore, this effect appears to be secondary to the decrease in portal vein blood flow that was observed concomitantly with the increase in intraabdominal pressure. The portal blood flow decreased by ≤ 76% between the highest and lowest pressures, although the blood flow in the hepatic artery was not significantly decreased. This finding is consistent with other studies [1, 3, 6]. Other research has confirmed that blood flow exerts a strongly negative influence on lesion size [14].

Our experiment was performed in vivo with normal livers; therefore, it may be questioned whether this effect has clinical significance for the treatment of hepatic tumors. However, both experimental and clinical studies have documented increased areas of ablation after the interruption of hepatic blood flow [4, 11, 14, 15]. Hepatic adenocarcinoma metastases tend to have reduced blood flow as compared to normal liver tissue. Whether (or not) the reduction in the portal blood flow due to the presence of a pneumoperitoneum would increase the effectiveness of RFA in clinical tumor ablation is a matter of debate. However, it should affect the surrounding rim of normal hepatic tissue, which also needs to be ablated to ensure negative margins.

Another factor that would alter the effectiveness of the RF application is the location of the treated area in relation to neighboring vessels [8]. The vascular flow of a tumor is critical to its response to increased temperature [13]. In our study, the lesions were placed randomly in locations throughout the liver, avoiding major vascular or biliary structures, which were visualized via ultrasound. However, the effect of diminished blood flow may be more or less pronounced in lesions adjacent to the larger vessels. In subsequent studies, it may be of value to assess the degree of the effect relative, to the ablated area's proximity to major vascular structures and to determine whether there is a minimal distance from the vessels beyond which the effects of pneumoperitoneal pressure are no longer seen.

Overall, the volumes of our lesions were significantly smaller than those previously reported when other electrodes were used in other studies [1, 3, 5, 16, 17]. This finding may reflect the reduced time of application and the low wattage used. Whereas most studies use a treatment time of ≥5 min, we restricted our treatments to 3 min. The power level we used (30 W) was also below that recommended for most treatments of liver tumors (≥50 W). The goal of our study, however, was not to maximize the size of the lesions created but rather to define the effect of the pneumoperitoneum on the ablation size. Our time and wattage parameters were based on previous studies done in our laboratory that showed this combination yielded the most consistent results for this type of electrode.

The clinical significance of this study must be viewed in light of the fact that the lesions created at 12 mmHg (or the pressure normally used during laparoscopic interventions) approached but did not achieve significance compared to those lesions created at 2 mmHg. However, this finding does indicate that when RFA is performed percutaneously or by laparotomy, it may take longer to ablate areas of the same size as those treated under the same conditions when RFA is performed by laparoscopy. However, this has not been evident in the clinical studies reported thus far. In addition, it would be difficult to perform a controlled study to measure such a parameter.

Currently, RFA is performed by either percutaneous, laparoscopic, or open techniques, each of which has its advantages. The percutaneous approach offers the possibility of using only local anesthesia and can therefore be applied for patients who are otherwise not candidates for surgical intervention. The advantages of performing either laparoscopy or laparotomy include the ability to visualize the lesions and the use of intraoperative ultrasound. Intraoperative ultrasound has been shown to increase sensitivity in detecting hepatic lesions. The advantage of intraoperative ultrasound cannot be underestimated, since some studies report 38% of patients to have lesions previously undiagnosed by preoperative evaluation [12, 20]. In addition, it is reported that the use of laparoscopy alone to stage liver tumors has increased by ≤12% the number of patients found to have extrahepatic spread of disease that was previously undetected by preoperative imaging studies [2]. Other potential advantages include the protection of adjacent structures, the control of hemorrhage, more accurate placement of the probe, and the ability to perform a Pringle maneuver. The placement of the RF probe seems to be as accurate when it is placed laparoscopically as when it is placed in open surgery [16]. Laparoscopy has all of the advantages of laparotomy but with the added benefits of a minimally invasive procedure. In addition, our study now indicates that there may be an additional advantage—that of decreased hepatic blood flow resulting from the establishment of a pneumoperitoneum, which may translate into decreased ablation time. Therefore, it seems that laparoscopy may prove to be the ideal technique.

In conclusion, our study demonstrates that the creation of a pneumoperitoneum does have a physiologic effect on the size of the area ablated by RF, which seems to be secondary to a decrease in portal vein blood flow. This lends support for the choice of laparoscopy as the preferred method for RFA for liver tumors application. Further studies are warranted to determine the optimal pressure of the pneumoperitoneum for laparoscopic RFA.

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