Microbubbles in the Pulmonary Artery Generated During Experimental Hepatic Radiofrequency Ablation Is Correlated with Increased Pulmonary Arterial Pressure

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PURPOSE: Microbubbles in hepatic veins during hepatic radiofrequency (RF) ablation is a well-known observation. In this experimental study, we examined the association between microbubbles in the pulmonary artery and alterations in mean pulmonary arterial pressure (MPAP) during hepatic RF ablation with a perfusion electrode system.

MATERIALS AND METHODS: Sixteen domestic pigs were included in the study. Twelve animals were randomly assigned to RF ablation with maintained ($n = 6$) or interrupted ($n = 6$) hepatic inflow. Four animals were assigned to a control group where interruption of hepatic inflow but no RF ablation was performed. Microbubbles in the pulmonary artery were recorded by transesophageal echocardiography and scored according to the number of bubbles per heart cycle. Mean pulmonary arterial pressure was continuously registered by a pulmonary artery catheter. The association between the microbubble score and increase in MPAP during ablation was examined using Spearman's rank correlation coefficient.

RESULTS: Echocardiographic recordings were acquired in 9 of 12 animals in the two treatment groups. Microbubbles in the pulmonary artery were present in four animals in each treatment group. Mean pulmonary arterial pressure increased from a baseline value of 17.7 mm Hg ± 2.3 to a maximum value of 29.7 mm Hg ± 7.7 during ablation ($P = .018$). A significant association was found between the microbubble score and increase in MPAP ($P = .001$).

CONCLUSIONS: Microbubbles were detected in the pulmonary artery during hepatic RF ablation both during maintained and interrupted hepatic inflow. A strong association was found between microbubbles in the pulmonary artery and increased MPAP. The clinical implications of our findings are to be determined.

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Abbreviations: CVP = central venous pressure, HR = heart rate, MAP = mean arterial pressure, MPAP = mean pulmonary arterial pressure, PA = pulmonary artery, RF = radiofrequency, RV = right ventricle

RADIOFREQUENCY (RF) ablation is increasingly used for in situ tumor destruction in patients with nonresectable liver tumors (1,2). Increased echogenicity within and surrounding coagulated hepatic tissue is seen at ultrasonography during hepatic RF ablation, which is believed to represent microbubbles of water vapor and other cellular products (3). Intravascular microbubbles have been observed in the hepatic veins and in the right atrium during hepatic RF ablation (4,5). A possible association between microbubbles in the pulmonary circulation generated during hepatic RF ablation and pulmonary arterial pressure has not previously been examined. Increased coagulation volume can be achieved by reduction of hepatic perfusion during ablation by temporary mechanical occlusion of the portal vein and the hepatic artery (Pringle maneuver) (6,7). It is not known if the Pringle maneuver influences the presence of intravascular microbubbles.

The aim of this study was to quantify microbubbles in the pulmonary artery during hepatic RF ablation and to examine whether a relationship exists between microbubbles in the

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pulmonary artery and alterations in pulmonary arterial pressure. Furthermore, we wanted to examine if the use of the Pringle maneuver influenced the number of microbubbles or pulmonary arterial pressure.

MATERIALS AND METHODS

Study Design

The study protocol was approved by our institutional animal care board. Sixteen domestic pigs with a mean weight of 30.4 kg (SD = 3.3 kg) were included in the study. Twelve animals were randomly assigned to RF ablation during maintained hepatic inflow (group A, $n = 6$) or interrupted hepatic inflow (group B, $n = 6$). Additionally, four animals were assigned to a group where the Pringle maneuver but no RF ablation was performed (control group).

Operative Procedure

After premedication with intramuscular injection of ketamine 15–20 mg/kg (Ketalar; Pfizer, Oslo, Norway), atropine sulfate 1 mg (Atropin; Nycomed Pharma, Oslo, Norway), and azaperone 2–4 mg/kg (Stresnil; Janssen-Cilag, Beerse, Belgium), an intravenous cannula was placed in an ear vein. General anesthesia was induced with intravenous administration of pentobarbital 150–400 mg and morphine 10–30 mg. After endotracheal intubation, anesthesia was maintained with inhaled isoflurane 1%–1.2% in an admixture of oxygen and air. The fraction of inspired oxygen was 0.5. The analgesic effect was supplemented with morphine infusion at 10–20 mg/h. In animals who developed severe systemic hypotension during ablation, 2,000–3,000 mL isotonic crystalloid (Ringer acetate; Fresenius Kabi, Oslo, Norway) and/or inotropic agents (Ephedrine; Nycomed Pharma) were administered after ablation had been completed.

For monitoring of hemodynamic parameters, an arterial catheter was placed in the femoral artery, and a 7.5-F pulmonary artery catheter (CCOmbo 774HF75; Edwards Lifesciences, Irvine, Calif) was introduced via the right external jugular vein and advanced to the pulmonary artery by pressure and waveform analysis. The pulmonary artery catheter was connected to a Vigilance monitor (version 6.2, Edwards Lifesciences). The pressure transducer was placed in the midaxillary line, and the arterial and pulmonal pressures were flushed and zeroed immediately before baseline measurements were obtained. A 134-cm^2 dispersive plate (EZ 344-02; Berchtold, Tuttlingen, Germany) was placed over the right hip. A midline incision with a transverse right subcostal extension was made. The hepatoduodenal ligament containing the hepatic artery, the portal vein, and the bile duct was identified, and a silicone vessel loop (Sterion, Minneapolis, Minn) was passed twice around these structures.

An impedance-controlled RF ablation system (Elektrotom HiTT 106; Berchtold) was used for creating coagulations. It incorporates a generator that delivers alternating current at 375 kHz to a maximum of 1.2 A. The active electrode is 1.7 mm in diameter, with a 15-cm-long shaft incorporating a lumen for saline perfusion. The terminal noninsulated segment of the perfusion electrode is 15 mm in length. A syringe pump (Pilot C; Fresenius Vial, Brezins, France) was used for infusion of isotonic saline through the electrode during ablation. The perfusion electrode was inserted 2 cm into the liver parenchyma between the portal arch and within 1.5 cm of the right portal vein, perpendicular to the vessel. Radio-frequency energy was applied for 1 minute with an effect of 30 W, immediately followed by 8 minutes with 50 W. To prevent bleeding from the needle track, the electrode was activated at 25 W during its withdrawal. In animals randomized to hepatic inflow occlusion, the silicone vessel loop was tightened around the hepatoduodenal ligament 1 minute prior to application of RF energy and released immediately after ablation had been completed for a total duration of 10 minutes. In the control group, hepatic inflow was occluded for 10 minutes in all animals, without insertion of an ablation electrode into the liver. All animals were euthanized 4 days after ablation.

Echocardiographic Recordings

Transesophageal recordings were obtained by a Vivid 7 echocardiograph with a 5-MHz phased-array multiplane transesophageal probe (GE Vingmed Ultrasound, Horten, Norway). The pulse repetition frequency was set to 0.5–1.0 kHz, with a frame rate of 77 per second ± 5. A short-axis view was modified to optimize the view of the right ventricle and pulmonary artery. Prior to registration, 10 mL saline was rapidly injected in the superior vena cava, and visualization of the corresponding microbubbles was used to verify that the structures investigated were in fact the right ventricle and the pulmonary artery. If these bubbles could not be visualized prior to the ablation procedure, the recording was considered not technically acceptable. Echocardiographic recordings commenced 2 minutes prior to ablation and continued 1 minute after the end of ablation. Recordings were obtained each minute and stored digitally as cineloops for subsequent off-line analysis. The number of microbubbles in the pulmonary artery was scored from 0 to 3 as modified from Eftedal and Brubakk (8) (**Table 1**).

Table 1
Microbubble Score

Microbubble Score	Microbubbles per Heart Cycle
0	None
1	1–5
2	5–50
3	>50

Note.—The number of microbubbles observed in the pulmonary artery during RF ablation by transesophageal echocardiography was scored from 0 to 3 as modified from Eftedal and Brubakk (8).

Registration of Hemodynamic Parameters

Heart rate (HR), mean arterial pressure (MAP), mean pulmonary arterial pressure (MPAP), and central venous pressure (CVP) were recorded every 5 seconds by data collection software (ICUpilot; CMA Microdialysis AB, Solna, Sweden) and stored on a personal computer. Data were continuously recorded prior to ablation, during ablation, and 10 minutes after ablation had been completed, or for the control group 10 minutes after hepatic inflow had been reestablished.