Prospective analysis of value of contrast-enhanced sonography during biopsies of focal liver masses

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Aim

To compare complication and success rates between two methods of ultrasound guidance for biopsy of liver lesions, contrast-enhanced and our current protocol without contrast.

Rationale

As a major oncology and hepatology center, we perform about 3-5 guided biopsies for liver tumors weekly. Ultrasound is the preferred modality for imaging biopsies due to its ability to visualize and position the biopsy needle in real time with high accuracy and safety, is nonionizing, and is quicker compared to other techniques, especially CT-guided biopsies. The failure rate of ultrasound guided liver biopsies (including cases where biopsy was declined to be performed due to lack of lesion visibility) is about 10%. By comparison, in our practice genotyping of metastatic tumors, with multiple core biopsies, is often requested for entry into oncology trials, and failure of tumor genotyping after biopsy is estimated to be about 30% (1).

Recently, the first ultrasound contrast agent was FDA-approved for characterization of liver lesions [sulfur hexafluoride lipid-type A microspheres (Lumason, Bracco Diagnostics, Monroe Township, NJ)] (2). The microbubble agent is deemed safe, including in cardiac failure patients and those with chronic airway obstruction (3, 4). Injecting microbubbles may allow better visualization of lesions and adjacent vasculature by enhancing the microvasculature and adjacent vessels and potentially reduce incidence of failed biopsy or bleeding complications. In addition, determination of necrotic regions in a lesion may allow better direction of biopsy (5, 6).

Yet there is limited literature on the use of ultrasound contrast agents for improving targeted liver biopsies (7, 8). We intend to prospectively assess the non-diagnostic biopsy and complication rates in a group of patients who undergo contrast-enhanced ultrasonography (CEUS) using microbubbles at the time of biopsy. We will then compare the results from this group with the failure and complication rate from a control group of patients undergoing the standard US-guided biopsy procedure. Over 12 months we expect to perform approximately 200 biopsies. Power analysis suggests that 125 patients in both contrast-enhanced sonography and control groups, each, are required. We should be able to enroll sufficient patients in 18 months.

Performance site

University Hospital
Methodist Hospital

Patient selection

Inclusion criteria

1. Males and females
2. Age 18 years or greater
3. Scheduled to undergo liver biopsy with ultrasound guidance at a performance site

Exclusion criterion

1. Liver biopsy is not intended to obtain tissue from a specific lesion
2. Known or suspected cardiac shunt
3. History of hypersensitivity to any active or inactive ingredients in Lumason

Methods

A radiology investigator will identify all qualifying potential subjects scheduled for liver biopsy at a performance site. On arrival at the performance site, a radiology investigator will, in a room away from other patients or staff, explain the study to the potential subject, answer any questions, and seek written informed consent. The potential subject will be given a copy of the consent to read to prior to consenting. If consent is granted, the patient will undergo either CEUS-guided biopsy (even dates, e.g., October 2) or standard US-guided biopsy (odd dates, e.g., October 3). For CEUS patients, Lumason (25 mg lipid type A lyophilized powder + 60.7 mg seulfur hexafluoride, in 5 mL saline) will be injected intravenously into the antecubital fossa immediately prior to US imaging, and then biopsy will be performed using standard technique, referring to the CEUS images. For control patients, US and biopsy will be performed per the standard protocol at the performance site, without the use of Lumason.

For each patient group, we will determine the complication rate associated with the procedure. Complication will be defined as 1) bleeding seen on post-biopsy CT or US, 2) drop in hemoglobin of more than 1.5 g/dL within one week after biopsy, or 3) need for hepatic artery embolization. We will also assess the success rate of biopsy for each patient group. Success will be defined as the biopsy sample being sufficient for histological diagnosis and/or complete genotyping.

Data safety monitoring will be performed quarterly by the study team. We will monitor accrual, complication rates, any other study-related issues, and any literature published that may impact the study.

Enrollment

As this is a pilot study to determine how complication rates and diagnosis rates compare between a new technology (CEUS) and our standard protocol, and little pertinent data currently exists, we have no good basis to do power and sample size calculations. The planned enrollment of 125 patients in each arm is based on patient volume over a reasonable study period (18 months) and internal funding considerations (cost of Lumason, not charged to the patient) We will seek approval for 300 patients to ensure at least 125 in each arm.

Resources/Budget

This project will be internally funded, and a budget is under development. The patient will not be responsible for any study costs (results evaluation, the contrast agent, or its injection) but will be responsible for all other costs associated with standard protocol US-guided biopsy of the liver.

References

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