Utility of Contrast-Enhanced Ultrasound (CEUS) in Hepatocellular Carcinoma Surveillance in Fontan-Associated Liver Disease

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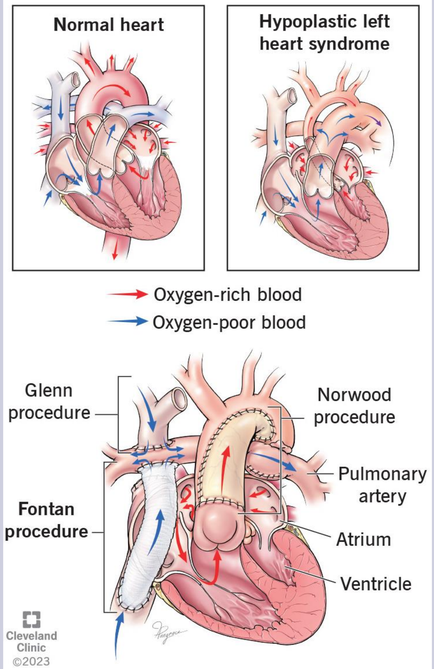
Fontan-Associated Liver Disease (FALD)

- Patients with congenital heart disease (CHD) or univentricular physiology undergo Fontan procedure and have diversion of systemic venous return to the pulmonary artery
- Fontan physiology can lead to chronic hepatic venous congestion and decreased cardiac output causing progressive hepatic fibrosis known as FALD
- FALD is associated with increased risk of hepatocellular carcinoma (HCC)



Fontan Physiology-Associated Lesions

- **Nodular Regenerative Hyperplasia (NRH):** benign, diffuse, hyperplastic hepatic lesions that form nodules without the development of fibrosis
- **Focal Nodular Hyperplasia (FNH):** benign hyperplastic hepatic lesion (may be single or multiple) with a central scar and no fibrosis
- Benign lesions can erroneously demonstrate suspicious features on conventional CT/MR imaging

Society Guidelines

- No Fontan-specific guidelines
- Current recommendations for other patient populations at risk of developing HCC: surveillance and screening with biannual alpha-fetoprotein (AFP) and diagnostic abdominal imaging

Limitations with Current Imaging Modalities

- Negative impact of cumulative radiation risk of CT in young patient population
- High cost of MR and limitations due to cardiac post-surgical changes and implanted metal hardware with pacemakers (connected or isolated)
- Standard ultrasound may not visualize focal lesions seen with FALD
- CEUS is typically used as diagnostic tool *after* a focal lesion is identified

A Novel Use of Contrast-Enhanced Ultrasound

- **Purpose:** Introduce the use of CEUS as a means of screening, surveillance, and diagnostic characterization of focal lesions in post-Fontan patients
- **Methods:**
  - Retrospective case series of 10 post-Fontan patients at tertiary medical center
  - Patients underwent concomitant non-contrast liver ultrasound and CEUS between February 2020 and October 2024
  - Reviewed data from prior imaging studies, including CT and MR imaging
  - Lesions were identified and monitored for stability over two years in order to be characterized as benign in accordance with AASLD criteria

Results

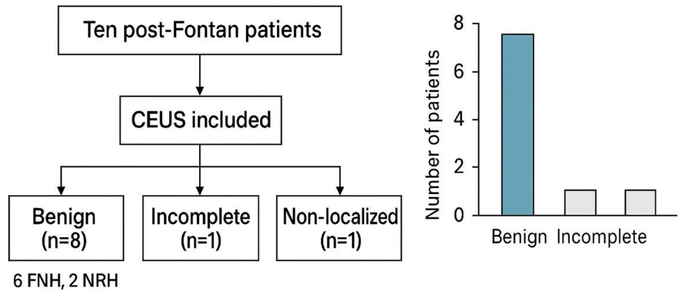


Figure: *10 post-Fontan patients underwent HCC screening with both standard US and CEUS to screen for HCC*

- Patients with known lesions were aged between 22 to 38 years old at the time of CEUS (mean age: 29.8); median age of Fontan procedure was 3 years old
- CEUS classified hepatic lesions as benign in 8 of 10 patients (6 FNH, 2 NRH)
  - All 8 cases had confirmed benign lesions
  - 7 of 10 cases had confirmatory CT triple phase indicating NRH/FNH
  - Follow up MRI was recommended in all cases to rule out malignancy
- 2 cases of difficult visualization with CEUS
  - One unable to localize lesion; one incomplete characterization of lesion
- No evidence of HCC was detected in this small series study

CT Triple Phase versus CEUS Imaging

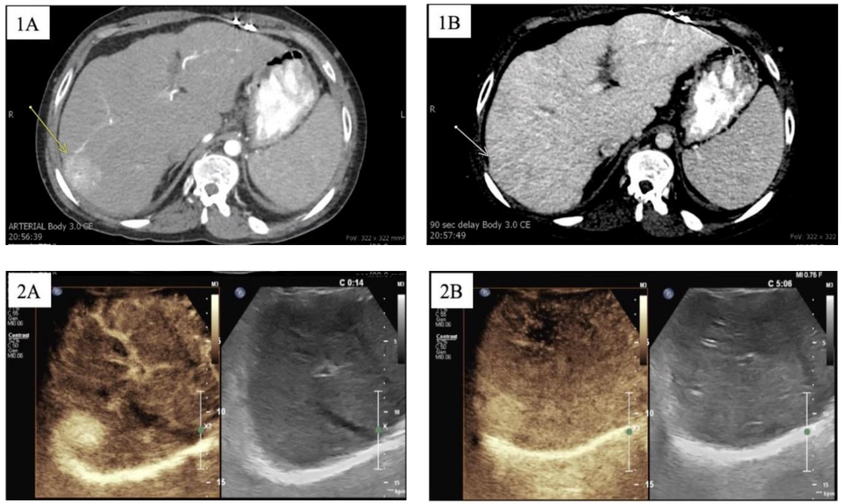


Figure: *Comparison between CT Triple Phase and CEUS in post-Fontan patients*

(1A) Surveillance imaging of post-Fontan patient that demonstrates a lesion/observation with non-rim arterial phase enhancement (APHE) on the later arterial phase in segment VII
(1B) Portal venous phase imaging demonstrates subtle washout of contrast making this lesion/observation suspicious for HCC
(2) Contrast-enhanced ultrasound (CEUS) performed demonstrating arterially hyper-enhancing lesion **(2A)** without washout at 4 minutes **(2B)**. CEUS is able to further classify the lesion as a benign Fontan-related FNH-like lesion

Study Conclusions

- This is a novel use of contrast-enhanced ultrasound as a surveillance method, as it is typically used in specific lesion characterization *after* identification
- CEUS can potentially be used as a safe surveillance method for HCC in the management of post-Fontan patients without the risks/challenges of standard CT and MR imaging
- Larger-scale studies validating the role of CEUS in post-Fontan patients should be conducted to validate CEUS as a safe and efficient surveillance method