CLINICAL STUDY

Elevated Lung Shunt Fraction as a Prognostic Indicator for Disease Progression and Metastasis in Hepatocellular Carcinoma

Tyler Sandow, MD, Daniel DeVun, MD, Paul Gulotta, MD, Humberto Bohorquez, MD, and David Kirsch, MD

ABSTRACT

Purpose: To evaluate lung shunt fraction (LSF) as an early predictor for local disease progression or the development of metastatic disease.

Materials and Methods: Retrospective analysis was performed on 52 patients with hepatocellular carcinoma who underwent preradioembolization assessment, including the calculation of LSF. Comparison of preprocedural and postprocedural surveillance imaging was performed. Mean patient age was 67 years (range, 50–88 y), with a mean surveillance of 245 days (range, 24–871 d). Statistical analysis was conducted to assess the relationship between LSF and local disease progression or development of new metastatic disease.

Results: In patients in whom metastatic disease developed during routine surveillance, the mean LSF was almost double that in patients in whom no metastasis developed (18.3% vs 9.3%; $P = .001$). Patients with elevated LSFs were also more likely to show intrahepatic disease progression (15.6% vs 8.5%; $P = .003$). LSFs $< 8\%$ corresponded to negative predictive values of 74% for local disease progression and 95% for development of metastasis, signaling a better prognosis. Of pretreatment variables examined (age, sex, previous treatment with disease progression, lesion size, lesion number, LSF, α-fetoprotein level, and portal vein thrombus), only LSF was an independent predictor for new metastasis (odds ratio [OR] = 1.2; $P = .01$). LSF (OR = 1.2; $P = .03$) and progression after previous treatment (OR = 4.7; $P = .04$) were independent predictors for local progression.

Conclusions: As local disease progression and metastatic disease were more likely to occur in patients with elevated LSFs, LSF may be the most sensitive predictor for local disease progression and new metastatic disease.

ABBREVIATIONS

AFP = α- fetoprotein, CI = confidence interval, HCC = hepatocellular carcinoma, LSF = lung shunt fraction, MAA = macroaggregated albumin, OR = odds ratio, SPECT = single-photon emission computed tomography

Hepatocellular carcinoma (HCC) is the most common form of primary hepatic malignancy and has increased in incidence and associated mortality during the past several decades, with greater than 750,000 new cases diagnosed each year (1,2). The diagnosis of HCC portends a very poor prognosis with limited systemic therapeutic options (3–5). Currently, the only curative therapies remain surgical resection and transplantation (4,6).

Recurrence of HCC after transplantation remains a dreaded complication seen in as many as 20% of patients (7). Nearly all cases of recurrent HCC after transplantation showed vascular invasion in the native liver at the time of explantation (8). Intratumoral shunts from vascular invasion may provide conduits for circulating tumor cells to reach distant sites (9). This arteriovenous shunting could allow blood and circulating tumor cells to bypass the capillary bed to implant at distant sites without being

From the Departments of Radiology (T.S., D.D., P.G., D.K.) and Transplant Surgery (H.B.), Ochsner Clinic Foundation, New Orleans, Louisiana; and University of Queensland School of Medicine, Ochsner Clinical School (D.D., P.G., H.B., D.K.), New Orleans, Louisiana. Received October 20, 2015; final revision received December 29, 2015; accepted January 6, 2016. Address correspondence to D.D., Department of Radiology, Ochsner Clinic Foundation, 1514 Jefferson Hwy., New Orleans, LA 70121; E-mail: ddevun@ochsner.org

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filtered by the hepatic parenchyma, contributing to future metastatic disease (10,11).

The evaluation of lung shunt fraction (LSF) is routinely performed before selective hepatic artery radioembolization therapy. LSF is characterized by the amount of radioactive particles that bypass the hepatic capillary bed and reach the pulmonary circulation (11). This quantitative assessment is performed by injecting technetium-99m (^{99m}Tc)–labeled macroaggregated albumin (MAA) via the main hepatic artery and calculating the radioactive counts in the lungs divided by the radioactive counts in the lungs and liver combined (11). The LSF is used in association with other factors to determine the total dose that can be administered safely without contributing to significant radiation pneumonitis (11). Using data from the routine assessment of LSF before radioembolization, the present study's purpose is to evaluate for a possible correlation between LSF and the future development of local disease progression or metastatic disease in patients with HCC.

MATERIALS AND METHODS

Study Cohort

After obtaining institutional review board approval, a retrospective analysis was conducted that included patients with HCC who were evaluated for selective hepatic artery radioembolization from November 2009 to March 2015. A total of 82 preradioembolization evaluations were performed in patients with the diagnosis of HCC during this time period. The diagnosis of HCC was made with imaging findings based on Organ Procurement and Transplant Network class 5 imaging guidelines (12) and/or tissue sampling in all patients. The study included all patients with HCC who underwent preradioembolization hepatic angiography with available preprocedural and postprocedural cross-sectional imaging. Twenty-nine patients were excluded from the study because of a lack of sufficient preprocedural or postprocedural cross-sectional imaging, secondary to the large referral nature of the institution. The choice of radioembolization versus alternative therapies was determined during a multidisciplinary liver conference before intervention and was based on patient performance status, previous transarterial chemoembolization treatment success, tumor characteristics, and stage of disease. Patients with diffuse liver involvement, poor tumor response to chemoembolization, and/or portal vein thrombus/tumor thrombus were considered for radioembolization with yttrium-90 (^{90}Y) instead of chemoembolization (Fig 1).

Technique

Preradioembolization hepatic angiography included a mapping study to evaluate the hepatic vasculature. Selective embolization of the gastroduodenal artery as well as other arterial branches was performed to prevent nontarget embolization during subsequent radioembolization treatment. Before the conclusion of the mapping study, radioactive ^{99m}Tc-labeled MAA was injected into the main hepatic artery or proximal left or right hepatic artery to assess LSF. Following the injection of radioactive particles, the patient was transferred to the nuclear medicine department, and single-projection anterior planar images were obtained with γ-camera scintigraphy. The LSF was calculated for all patients as the total lung count divided by the sum of the total lung and liver counts. The number was reported as a percentage in the nuclear medicine report.

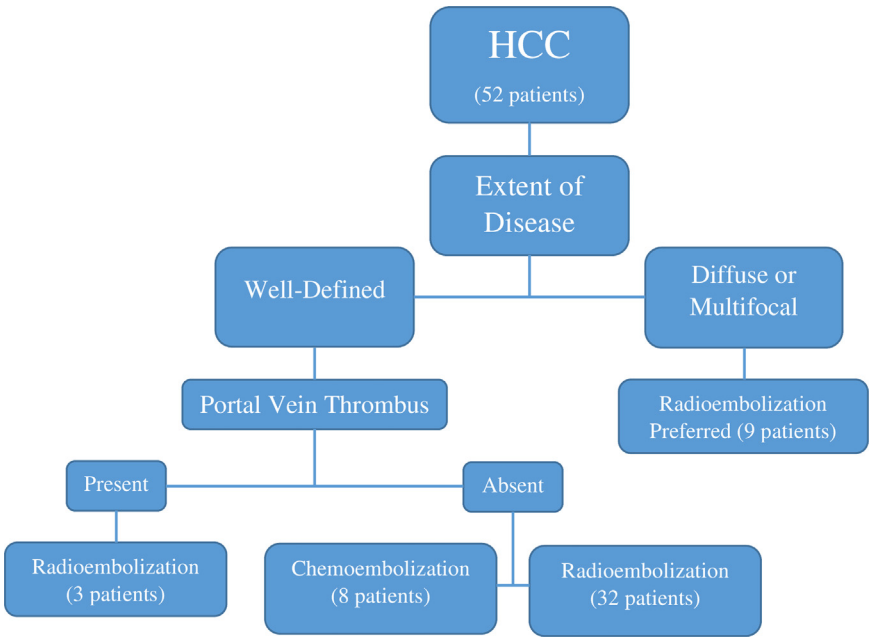

Figure 1. Flowchart for transarterial therapy selection.