Safety and utility of transjugular liver biopsy in hematopoietic stem cell transplant patients

Poster No.: C-1096
Congress: ECR 2012
Type: Scientific Exhibit
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Keywords: Interventional non-vascular, Catheter venography, Fluoroscopy, Venous access, Biopsy, Haematologic diseases, Transplantation, Liver
DOI: 10.1594/ecr2012/C-1096

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50,417 hematopoietic stem cell transplants (HSCT) were performed worldwide in 2006 (1) and the number of patients receiving transplants from unrelated donors is expected to double in the next 5 years (2). Graft-versus-host disease (GVHD) of the liver and hepatic veno-occlusive disease (VOD) are unique complications of HSCT and are among the leading causes of morbidity and mortality in HSCT recipients. The morbidity rate can be up to 80% of patients and is responsible for 4-14% of deaths (3).

Despite HLA identity between a patient and donor, about 40% of recipients of HLA-identical grafts develop GVHD and the liver is involved in 50% of these cases. Histologically hepatic GVHD presents as lymphocytic infiltration of the portal areas, pericholangitis, endothelial injury, and bile-duct destruction.

VOD is characterized clinically by the triad of hepatomegaly, ascites/weight gain and jaundice. It develops secondary to high dose cytoreductive therapy in patients who have a particular susceptibility leading to endothelial injury in sinusoids and small hepatic venules with consequent activation of the coagulation cascade and clot formation resulting in obliteration of hepatic venules.

These diseases can mimic other complications of HSCT, such as infection, hemorrhage, and hepatotoxicity with cholestasis, but GVHD and VOD require specific treatment. Early treatment improves the probability of treatment success. Therefore, timely and accurate diagnosis is essential. When the diagnosis is unclear based on the clinical picture, liver biopsy is required. Even with typical clinical presentation biopsy may be necessary. According to the study of Esposito et al. 14 out of 21 HSCT patients had different pathologic diagnosis than what was clinically suspected (4).

Liver biopsy can be obtained with both percutaneous or transjugular approach. However, many HSCT patients are at risk for bleeding secondary to thrombocytopenia and/or coagulopathy and many has ascites, which presents a relative contraindication to the percutaneous approach. Therefore, HSCT patients are commonly referred to transjugular liver biopsy.

The purpose of our study was to assess the safety and utility of transjugular liver biopsy in this high-risk patient population.
Methods and Materials

We retrospectively reviewed and analyzed the medical records of 348 consecutive patients who underwent transjugular liver biopsy between 1/1/2005 and 8/31/2011 at the Brigham and Women's Hospital/Dana-Farber Cancer Institute which is one of the largest volume HSCT center in the United States. This included a total of 378 transjugular liver biopsies performed by a single team of interventional radiologists using the same technique and the Cook Liver Access and Biopsy set with a 19 gauge core biopsy needle. 166 out of the 378 procedures were performed in 141 HSTC patients. All biopsy samples were immediately placed in a sterile cup containing formalin and sent to the Pathology Department of the Brigham and Women's Hospital for further processing and histological analysis. Data collected from patients’ computerized medical records included a retrospective review of charts, reports of the transjugular liver biopsy procedures, laboratory values and pathology reports of the biopsy specimens. Complication was defined as an adverse event that occurred as a direct result of the liver biopsy. This study was approved by the Institutional Review Board of the Brigham and Women's Hospital.
Results

During our study period 166 out of the 378 procedures were performed in 141 HSTC patients. The HSTC patients underwent transjugular liver biopsy included 87 males and 54 females with the average age of 45.3 years. 57 patients had platelet transfusion before the procedure; the platelet count in these patients before the transfusion was 24.9 ± 12.7. The final pre-procedural platelet count including all patients was 114.7 ± 89.0 (n=165, one patient had no available platelet count data in our electronic medical record). The pre-procedural INR was 1.3 ± 0.4 (n=159) and PTT was 37.0 ± 13.7 (n=150). The patients had elevated liver function tests (ALT 378.9 ± 57.3, n=166; AST: 331.3 ± 78.5, n=166; ALP: 342.9 ± 26.3, n=166; Tbili: 7.8 ± 0.726, n=166).

One to ten biopsy samples were obtained per patient (4.4±1.6). The technical success was 99.4%, there was one failed biopsy due to patient agitation. Pathologic analysis of the biopsy samples led to a diagnosis in 98.2% (there were 3 non-diagnostic samples). The histologic diagnosis was GVHD in 88 patients, VOD in 31 patients, VOD+GVHD in 13 patients and other (steatohepatitis, drug toxicity,etc.) in 34 patients.

The porto-systemic venous gradient was significantly higher in the VOD group (Fig. 1 on page 6). The postprocedural hematocrit level (30.6 ± 5.2, n=149) obtained within 24 hours after the procedure was not significantly different compared to the preprocedural value (31.3 ± 5.5, n=166).

There were 3 major complications (1.8%); one patient developed arterio-biliary fistula which required embolization, one patient suffered subcapsular and intraperitoneal hemorrhage leading to death, and one patient required blood transfusion within 24 hrs after the procedure due to 4 units of hematocrit drop.

Two examples of major complications:

Patient #1

52-year-old female status post HSCT with relapsed non-Hodgkin's lymphoma and abnormal liver function tests. The patient underwent transjugular liver biopsy and 10 days later she presented to ER with sharp right upper quadrant pain, nausea and vomiting. Abdominal MR showed gallstones, enlarged gallbladder with mild periportal edema and increased signal intensity surrounding the portal triads. Therefore, she underwent laparoscopic cholecystectomy and pathology showed chronic cholecystitis. Two weeks after the surgery she presented to the ER with intense epigastric pain, nausea and vomiting and elevated lipase and amylase. CT scan of the abdomen and pelvis showed
acute pancreatitis, intra and extrahepatic biliary ductal dilation with high density debris in the common bile duct and ascites (Fig. 2 on page 6). ERCP was performed which revealed a clot protruding from the papilla and multiple filling defects within a mildly dilated common bile duct representing clot. These findings were consistent with hemobilia leading to obstructive clots within the bile ducts causing jaundice and pancreatitis. Abdominal MRA showed filling of the biliary tree with contrast in the arterial phase (Fig. 3 on page 7) She was referred for angiography which confirmed the arterio-biliary fistula and was successfully treated with coil embolization (Fig. 4 on page 8).

**Patient #2**

50-year-old woman with myelodysplastic syndrome status post HSCT with skin GVHD and elevated LFTs. The patient underwent transjugular liver biopsy. Her pre-procedure hematocrit was 25.5. Next morning she complained of pain in her right shoulder and abdomen. Hematocrit was rechecked and was 30. A few hours later, a code was called, the patient was unresponsive. She kept a pulse throughout the code and was alert to stimulus. Subsequently, she was transferred to the ICU. Upon arrival, she was initially alert and oriented, but soon after was unable to maintain her blood pressure and went into a PEA arrest. Hematocrit was 11.7 after the code. A repeat check revealed hematocrit of 7. A bedside right upper quadrant ultrasound showed a subcapsular hematoma and moderate amount of intraabdominal fluid (Fig. 5 on page 9). Despite extensive resuscitation efforts she died in hypovolemic shock.
Fig. 1: Porto-systemic venous gradient in hematopoietic stem cell transplant patients.

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Fig. 2: CT scan of the abdomen and pelvis shows acute pancreatitis, intra and extrahepatic biliary ductal dilation with high density debris in the common bile duct (arrows) and ascites.

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Fig. 3: Abdominal MRA shows contrast filling of the hepatic artery (solid white arrow) and biliary tree (open white arrow).

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**Fig. 4:** Left image shows a right hepatic angiogram demonstrating filling of the biliary tree with contrast via an arterio-biliary fistula. Right image shows a post-embolization right hepatic angiogram of the same patient with no communication between the right hepatic artery and the biliary tree.

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Fig. 5: Right upper quadrant ultrasound shows a hyperechoic perihepatic subcapsular collection consistent with hematoma.

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Conclusion

According to our knowledge this is the first study including more than 30 patients to review the safety and utility of transjugular liver biopsy in HSCT recipients. Prior low scale studies demonstrated very high complication rates of transjugular liver biopsy in HSCT patients. Oshrine et al. (5) reported 80% (4 out of 5 patients) rate of major complications of transjugular liver biopsy in pediatric HSCT patients and Chahal et al. (6) reported 11% (3 out of 27 patients) rate of major complications in adult HSCT patients. Our retrospective study analyzing 166 procedures performed on 141 HSTC patients suggests that transjugular liver biopsy is a safe procedure that provides important information for the clinical and therapeutic management of this high-risk patient population. In addition, measurement of porto-hepatic venous gradient during the procedure can support the diagnosis and according to prior data may be helpful to determine prognosis in patients with VOD. A corrected hepatic sinusoidal pressure greater than 10 mmHg was shown to be 52% sensitive and 91% specific for VOD, and the prognosis was poor when pressure exceeds 20 mmHg (7).
References


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