

1 **TRANSJUGULAR LIVER BIOPSY: RESULTS OF 97 PATIENTS**

2 **Running Title: *Results of TJLB***

3 **ABSTRACT**

4 **Aim:** To evaluate the feasibility and efficacy of transjugular liver biopsies in patients  
5 ~~with contraindicated percutaneous biopsy in whom percutaneous biopsy is~~  
6 ~~contraindicated.~~

7 **Method:** Between June 2005 and April 2010, 97 patients who admitted for transjugular  
8 liver biopsy were enrolled in **this** retrospective study. All liver biopsies were obtained  
9 ~~with the use of an~~ **using an** 18 gauge Quick-Core liver biopsy and biopsy set through the  
10 right hepatic vein via the internal jugular vein. Clinical indication, histopathological  
11 diagnosis, and complications were noted.

12 **Results:** Primary technical success was achieved in 93 (95.8%) patients. Hepatic veins  
13 could not be catheterized and opacified in two patients and in the remaining two patients  
14 the veins could be opacified and catheterized but we were not able to pass the biopsy  
15 needle into the hepatic vein because of the acute angle between the inferior vena cava and  
16 hepatic veins. At least two specimens were obtained from each patient. The most of  
17 histopathological diagnosis was cirrhosis. A subcutaneous hematoma around the puncture  
18 side was encountered in one patient.

19 **Conclusion:** Transjugular liver biopsy is a feasible and effective alternative in patients  
20 with contraindication for percutaneous biopsy.

21 **Key Words:** Transjugular liver biopsy; Liver biopsy; Liver cirrhosis.

22

23 **INTRODUCTION**

24 Percutaneous liver biopsy (PLB) is the standard method for the diagnosis and treatment  
25 planning of diffuse parenchymal liver disease<sup>1-4</sup>. Percutaneous liver biopsy is not suitable  
26 for patients with coagulation abnormalities and thrombocytopenia. In this situation,  
27 transjugular liver biopsy (TJLB) is the alternative biopsy method. In the TJLB, the liver  
28 tissue is obtained from ~~within~~ the vascular system ~~it~~ minimizes the risk of bleeding<sup>1,5</sup>.  
29 This biopsy technique also provides the opportunity for ~~meanwhile~~ **simultaneous** hepatic  
30 vein pressure measurement and venographic examination. This study presents our  
31 experience with the Quick-Core biopsy set (Cook, Bloomington, IN) for TJLB in patients  
32 ~~in whom percutaneous liver biopsy is contraindicated.~~ **with contraindicated percutaneous**  
33 **liver biopsy**

#### 34 **METHODS**

35 Between June 2005 and April 2010, a total of 97 patients (66 ~~men~~ **males**, 31 ~~women~~  
36 **females**) with a mean age of 46.74±12.7 years (range: 18-74 years) were included in a  
37 **this** retrospective study. The study group consisted of patients who had contraindications  
38 for PLB because of coagulation abnormalities (PT>16 sec, INR>1.2, PTT>40 sec and  
39 trombocyte count<60.000/cm<sup>3</sup>) with laboratory and clinical findings suggestive for  
40 diffuse liver disease. In 29 patients there was concomitant ~~with~~ gross ascites confirmed  
41 by ultrasound. All patients were informed about the indications and possible risks of the  
42 procedure and written informed consent was obtained from each patient, **receiving** ~~and~~  
43 ~~received~~ approval from the institutional review board. The biopsies were performed in  
44 the angiography suite by two radiologists with the use of digital subtraction angiography  
45 (Philips Integris 5000, Philips Medical Systems, Netherlands) and an ultrasound (Toshiba  
46 Nemio 20, Toshiba Medical Systems, Japan) machine.

47 All patients lied down in supine position with pillow placed under their shoulder. The  
48 procedure was performed under local anesthesia with continuous **monitoring**  
49 ~~monitorization of the patient.~~

50 The venous structures including internal jugular vein (IJV), hepatic veins and inferior  
51 vena cava (IVC) were assessed by ultrasound prior to the procedure to confirm the  
52 patency. All biopsies were performed through the right IJV under sterile conditions. For  
53 procedure, right IJV was punctured by 18 G needle under ultrasound guidance. Then, a  
54 0.035 inch J tipped guide-wire was ~~inserted~~ **introduced** through the needle, and a 7 F  
55 short vascular sheath was placed into the IJV over the wire. A 5 F multipurpose catheter  
56 was inserted into the right hepatic vein through this sheath. **Then,** ~~After this,~~ a  
57 venography was performed to confirm the catheter position. When the catheter position is  
58 **was** satisfactory, 0.035 inch super stiff Amplatz guide-wire (Boston Scientific) was  
59 placed into the right hepatic vein through the catheter. The biopsy set (Cook,  
60 Bloomington, IN) was sent to the right hepatic vein over the stiff guide wire. The biopsy  
61 site was adjusted with the use of ~~the~~ arrow placed on the outer part of the metallic  
62 cannula. The preferred biopsy site was anterior part of the right hepatic vein, because the  
63 parenchyma at this site was more than the other parts. Thereafter, biopsy was obtained  
64 with the use of an 18 gauge 60 cm Quick-Core biopsy needle (Figure 1). The number of  
65 needle passes was left to the experience of the radiologist who considered observation of  
66 the gross hepatic tissue specimen obtained. The number of needle ~~passes~~ **passage** times  
67 was noted. All the specimens were sent to the pathology ~~suite~~ **unit** in formalin solution  
68 for histopathological examination. The length and mean number of portal triads per  
69 sample of the material and the pathological diagnosis was noted. After ~~the~~ completion of

70 the procedure a control venography was performed for demonstration of acute  
71 complications. All the procedure related complications were noted.

72 The procedure was completed after ~~pulling out~~ removing the short vascular sheath. This  
73 was done while the patient was sitting and after ~~pulling the~~ removing the sheath ~~out a~~  
74 pressure was applied for five minutes.

75 All patients underwent postprocedural neck and abdomen ultrasound examination for the  
76 possible presence of hematoma and bleeding. Patients were ~~taken~~ kept in the hospital for  
77 24 hours after the procedure. The clinical observation and abdominal palpation, control  
78 hemoglobin levels were followed up. ~~In case of necessity,~~ Abdominal ultrasound  
79 examination was repeated when necessary.

## 80 RESULTS

81 Technical success was achieved in 93 of 97 (95,8%) patients. In two patients with Budd  
82 Chiari syndrome, hepatic veins could not be catheterized and opacified and in the  
83 remaining two patients, the hepatic veins could be catheterized with the stiff guide wire  
84 but the stiff cannula didn't ~~go~~ advance over the guidewire due to the acute angle between  
85 IVC and hepatic veins (Figure 2). The mean number of needle ~~passes~~ passages required  
86 for each patient was  $2.75 \pm 0.8$  (range=2-7). The sample lengths ranged from 1 to 22 mm  
87 (mean: 6,6 mm). The mean number of portal triads per sample was 7.9 (range: 2-25).  
88 Histopathological diagnosis could be established in 98,9% (92 of 93) of the patients. In  
89 one patient, specimen was lost in the pathology unit. Histopathological diagnosis were  
90 cirrhosis in 32 (34,7%) patients, chronic hepatitis in 24 (26,1%) patients, Wilson's  
91 disease in 1 (1,1%) patient, hemochromatosis in 3 (3.3%) patients, graft versus host  
92 disease in 7 (7,6%) patients, primary biliary cirrhosis in 1 (1,1%) patient, acute

93 cholestatic hepatitis in 6 (6.5%) patients, adenocarcinoma in 1 (1,1%) patient,  
94 myeloproliferative infiltration in 2 (2,2%) patients, hemosiderozis in 1 (1,1%) patient,  
95 and the findings were normal findings in 14 (15,2%) patients. Non-inflammatory  
96 steatosis was accepted in as a normal findings. The histopathological diagnoses of TJLB  
97 are given in Table 1. Local hematoma at the puncture site was seen in 1 (1%) patient. No  
98 additional complications were noted.

## 99 DISCUSSION

100 Percutaneous biopsy is the preferred biopsy technique for the definite diagnosis of diffuse  
101 liver disease. However, when there is a contraindication for PLB such as coagulation  
102 abnormalities, and thrombocytopenia, the mortality and the morbidity of the procedure  
103 increases<sup>6,7</sup>. The most important complications for PLB are intraperitoneal bleeding and  
104 capsular perforation<sup>8</sup>. Transjugular liver biopsy decreases these complications since  
105 capsule is not perforated. Obtaining the biopsy from the anterior part of the right hepatic  
106 vein, since the parenchyma is thicker here, may prevent capsule perforation and thereby  
107 reduce the complication rate. But when the catheter is stugged into the liver parenchyma  
108 and a biopsy is obtained in this position, bleeding may occur. When a bleeding occurs it  
109 may be detected during the procedure on control venography. The catheter should come  
110 as close as possible to the perforation site and gelfoam particles can be used to occlude  
111 the bleeding site<sup>9</sup>. In case of hemobilia or hemoperitoneum after completing the  
112 procedure; blood, blood products, and fresh frozen plasma (10-15 ml/kg) can be used for  
113 treatment. When there is no clinical improvement, hepatic angiography and venography  
114 should be performed and the bleeding site should be embolized if possible<sup>10</sup>. There were  
115 no such complications in our study. Lebrec et al.<sup>11</sup> encountered one fatal intraperitoneal

116 bleeding in 1033 TJLB. Kardache et al.<sup>12</sup> and Bruzzi et al.<sup>13</sup> did not encounter any  
117 complication. Little et al.<sup>14</sup> reported one asymptomatic liver perforation.  
118 Insertion site hematomas and carotico-jugular fistulas are reported complications.  
119 Putting the sheet out, **sitting** while the patient is ~~sitting~~, decreases bleeding complications.  
120 ~~But~~ **However**, when it occurs compression is enough for treatment. When it persists then  
121 endovascular or surgical interventions may be used to treat these complications<sup>15,16</sup>. De  
122 Hoyos et al.<sup>17</sup> reported two severe hematomas and concluded that this was the result of  
123 not using ultrasound. We did not encounter any inadvertent puncture and related  
124 complications in this study, and we advocate that ultrasound should be used to decrease  
125 puncture site complications.

126 The preferred site for TJLB is the right IJV because this approach provides **easy** access to  
127 the right hepatic vein and thereby eliminates cardiac compression and vascular  
128 complications. Therefore we were able to use the right IJV in all 93 patients. But when  
129 the right IJV is tortuous or occluded, left IJV or femoral vein can be used as the access  
130 site<sup>18</sup>. However, the femoral approach needs a different biopsy set. We advocate that both  
131 biopsy set types should be present in angiography suites performing TJLB. Because, we  
132 were failed to get biopsy via jugular vein approach for two patients. If we had the femoral  
133 approach set could have used it.

134 The most reported cause of technical failure in the literature, as it was in our study, was  
135 the inability of hepatic vein catheterization<sup>19,20</sup>. Chevallier et al.<sup>21</sup> altered the cannula  
136 angle of the metallic cannula manually in 8 of 139 patients to get a better access by  
137 adjusting the IVC-hepatic vein angle. Another alternative for adjusting the IVC-hepatic  
138 vein angle is deep inspiration. When the patient inspirates deeply the liver moves

139 inferiorly and so you get may get a better IVC-hepatic vein angle<sup>9</sup>. We tried both  
140 manipulations for two patients but were not successful to access the hepatic vein with the  
141 stiff cannula. Mammen et al.<sup>9</sup> used the transcaval approach in hepatic vein occlusion and  
142 IVC-hepatic vein angle discordance and they reported that this method was safe and  
143 effective.

144 Inability to puncture IJV is the second common reason of technical failure<sup>19</sup>. The use of  
145 ultrasound decreases inappropriate punctures and procedure time<sup>22</sup>. Some authors have  
146 marked the IJV and accessed it through this marking but with this method you may have  
147 inappropriate punctures even with minor movements of the patient<sup>20</sup>. We used “free hand  
148 technique” and all the punctures were without complications. In concordance with our  
149 study, Mammen et al.<sup>9</sup> reported 100% success for IJV puncture under ultrasound  
150 guidance.

151 Bruzzi et al.<sup>13</sup> reported that all the materials they obtained were sufficient for  
152 histopathological diagnosis. But the reported rates of satisfactory material for  
153 histopathological diagnosis differ and the ~~adequateness~~ **sufficiency** of the specimen is  
154 decided with the number of portal spaces. More than 11 portal spaces are classified as  
155 very good; 8-10 is classified as well; 4- 8 are near to optimal; less than 4 are insufficient.  
156 In another study 6-20 portal spaces are accepted to be sufficient but even in this case it  
157 represents only 1/50.000 of the liver<sup>23</sup>. In our series, the mean number of portal triads in  
158 each tissue sample was 8. Our results concur with those of Kardache et al.<sup>12</sup> (eight or  
159 more portal triads) and De Hoyos et al.<sup>17</sup> (6.24± 3.18).

160 The length of ~~the~~ biopsy material is another parameter ~~that determines the~~ determining  
161 quality of the specimen. When the length is more than 2 cm, it is accepted as a good

162 biopsy material<sup>24</sup>. In our study the length of the material ranged from 1 to 22 mm (mean:  
163 6,6 mm). The size of ~~the~~ tissue sample was thought to be small or limited, but a definitive  
164 diagnosis was reached 92 of 93 patients. Evaluation of the size of liver specimen  
165 immediately after biopsy is very important. If the sample was not adequate for the  
166 diagnosis, a new biopsy should be performed in the same session thus reducing the  
167 discomfort and stress for the patient. As well as using this strategy is reducing recurrent  
168 biopsy and uninterruptible results returned from the pathology. So we had not to perform  
169 more than one biopsy for any patient later.

170 In conclusion, this study shows that TJLB is an effective and safe method for patients  
171 with coagulation abnormalities. The use of ultrasound for access site and knowledge of  
172 the maneuvers to get a better hepatico-caval angle may increase the technical success  
173 rate.

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176 **Conflict of interest:** The authors declare that they have no conflict of interest

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241 **Table 1.** Histopathological diagnosis of transjugular liver biopsy

<b>Histopathological diagnosis</b>	<b>n/%</b>
Cirrhosis	32 (34,7%)
Chronic hepatitis	24 (26,1%)
Wilson's disease	1 (1,1%)
Hemochromatosis	3 (3,3%)
Graft versus host disease	7 (7,6%)
Primary biliary cirrhosis	1 (1,1%)
Acute cholestatic hepatitis	6 (6,5%)
Adenocarcinoma	1 (1,1%)
Myeloproliferative infiltration	2 (2,2%)
Hemosiderosis	1 (1,1%)
Normal findings	14 (15,2%)
<b>Total</b>	<b>92</b>

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243

244 **FIGURE LEGENDS**

245 **Fig. 1.** A 23-year-old male with presumptive clinical diagnosis of cirrhosis, with an  
246 international normalized ratio of 1.7. **A.** Venogram of right hepatic vein after catheter  
247 positioning into vein shows normal flow in vein with suitable angulations of vein to  
248 inferior vena cava. **B.** Image shows a 7-F stainless steel trocar (*black arrow*) in the right  
249 hepatic vein, with the semiautomated biopsy needle extended (*white arrows*) just before  
250 obtaining biopsy core specimen.

251 **Fig. 2.** A 57-year-old male patient with an international normalized ratio of 1.8. In this  
252 patient, stiff cannula didn't go over the guide-wire due to acute angle between inferior  
253 vena cava and hepatic vein.

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