Role of Colour Doppler Ultrasonography (CDUS) in patients undergone Orthotopic Liver Transplantation (OLT) with diagnosis of Primary Nonfunction (PNF)

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Purpose

Liver transplantation is the treatment of choice in patients with end-stage liver disease. [1] Liver transplantation has been performed in an increasing number of patients with liver dysfunction due to chronic liver disease and acute liver failure [2].

The survival rates of transplant patients have constantly increased, thanks to improved surgical technique, availability of more suitable immunosuppressive drugs and more effective clinical and imaging postoperative surveillance [3].

Early graft dysfunction could have a major impact on the prognosis and clinical outcome after liver transplantation (LTX). Incidence of graft dysfunction is up to 27% after deceased-donor LTX. Graft function is influenced by multiple factors, including organ quality, ischemia time, graft reperfusion, and immunological matching. Thus, graft failure is an extremely multifactorial condition.

Primary nonfunction (PNF) is defined as an aggravated form of reperfusion injury resulting in irreversible graft failure without detectable technical or immunological problems. It is the most common cause of early graft loss and the most common reason for early retransplantation. Early retransplant is the only therapy for PNF [4], infact without retransplantation, death will occur early in the post-transplant period due to sepsis, irreversible brain injury, and multiple organ system failures [1].

The incidence of PNF is reported to be between 1.8% and 14% of all liver transplants [4].

The diagnosis of PNF is made when a graft fails to demonstrate evidence of initial function following transplantation without any technical or immunological causes. Diagnosis of graft failure is based on clinical and laboratory evaluations of the recipient: rapidly rising transaminases, absence of bile production, severe liver-related coagulation deficit, hypoglycemia, high lactate levels, and hepatic hemodynamic instability.

At pathological evaluation in liver biopsy was found cytolysis and coagulative necrosis.

Risk factors associated with its occurrence and short-term outcome have been discussed, but the actual reasons for PNF are still largely unknown [5], however, prolonged cold ischemia times, female donor gender, increased donor age, donor intensive care unit (ICU) stay, livers from donation after cardiac death (DCD) donors, prolonged operating room time during the transplant procedure, fatty changes in the liver graft, reduced graft size, and renal insufficiency in recipient have been implicated as risk factors [4].

The purpose of post-OLT imaging monitoring is to provide an early diagnosis of vascular complications (thrombosis, stenosis and dilatation of the hepatic artery, portal vein and vena cava), biliary complications (fistulas, intrahepatic and anastomotic strictures, abscess formation and lithiasis), and collections.
Modern follow-up protocols involve colour Doppler ultrasonography (CDUS) as a first-line modality. This is a noninvasive, inexpensive modality that is easily performed at the patient’s bedside in the intensive care unit (ICU) and provides qualitative and quantitative morphological and functional information [3].

The aim of our study is to assess the role of CDUS in transplanted patients who required retransplantation for PNF.
Methods and Materials

From January 2001 to July 2010, 457 patients underwent OLT at the Policlinico of Modena.

Our retrospective study included 21 PNF cases in 20 patients, 15 male and 5 female, ranging in age from 18 to 67 years (median was 47.05).

We retrospectively evaluated all CDUS examinations performed between liver transplantation and re-transplantation, in particular we analyzed patency of hepatic artery (resistive index [RI], systolic acceleration time [SAT], patency of portal vein (peak systolic velocity [PSV], flow direction) and patency of suprahepatic veins with flow phasicity. Any CDUS anomaly identified according to the literature was described.

All liver transplants were performed in an orthotopic fashion, with piggy-back technique and without veno-venous bypass.

All patients with clinical diagnosis of PNF underwent retransplantation. Median time between 1st and 2nd transplant (in 1 patient also time between 2nd and 3rd transplants) was 7 days (range, 1-23). The clinical PNF diagnosis was confirmed at patological-anatomy evaluation in all cases.

When a graft fails to demonstrate evidence of initial function following transplantation, without any technical or immunological causes, the condition was diagnosed as PNF. Graft (liver) function was evaluated by biochemical testing: aspartate aminotransferase (AST), alanine aminotransferase (ALT), pseudocholinesterase (CHE), lactate dehydrogenase (LDH), lactate, bilirubin, prothrombin time, activated thromboplastin time (aPTT), international normalized ratio (INR) and fibrinogen.

Other possible causes of early graft failure (technical, immunological, infectious, etc) were excluded after reviewing the clinical course, operative findings, pathology reports, radiologic findings, laboratory data, and autopsy findings.

CDUS in patients transplanted was performed using an Acuson Sequoia scanner equipped with a 5-2-MHz convex-array transducer (Siemens, Erlangen, Germany) located in the Radiology department, and a portable Megas CVX ultrasound system with a 4-2-MHz convex-array transducer (Esaote, Genoa, Italy) located at the patient's bedside in the ICU, in operative room, in intensive therapy unit within 6 hours from surgery and daily during the first week of ICU stay.

A baseline US study was usually performed to assess liver morphology, echostructure, presence of parenchymal focal lesions, peri-liver and intra-abdominal collections and significant ectasia of intra and extra-hepatic bile ducts. Then a CDUS study of vascular anastomosis was performed: hepatic artery, portal vein and suprahepatic veins. First we
identified the portal vein and detected the flow direction. Then we studied Doppler trace morphology and Pulsed Doppler US, performed using a 30°- 60° angle of insonation to measure peak velocity of portal flow, which usually has monophasic pattern.

Presence of intraluminal echogenic material, reversed flow direction and total absence of color Doppler signal in the portal vein were considered pathognomonic signs of thrombosis. Next step was to identify the hepatic artery at the hilum, through the color-signal analysis and if multiple anastomoses were present, the study of arterial vessels was performed by sampling the proper, right and left hepatic arteries.

Then we analyzed the systolic-diastolic modulation of hepatic artery using pulsed Doppler, and calculated RI using an automatic software or manually identifying two points: the peak systolic one and the end diastolic one.

We considered normal an RI value between 0.5 and 0.85 [6]. Values outside this range required close monitoring until normalization of RI or other imaging modality study (CT). In case of RI alteration, SAT was also considered, which normally is inferior to 0.08 sec. Association of pathological values of SAT and RI was considered suspected of thrombosis.

Finally we verified presence of supra-hepatic venous drainage and analyzed type of pattern that can be monophasic, biphasic or triphasic.

When CDUS shows vascular or parenchyma alteration patients were studied with other diagnostic modality: CT or MRI.
Results

In the period from transplantation to re-transplantation in all patients, CDUS showed portal vein patency with physiologic flow direction.

Peak velocity of portal flow resulted in a range of values from 15 to 142 cm / sec with a mean value of 53.65 cm / sec.

In all patients, CDUS allowed to correctly visualize main liver arteries. Doppler study showed a regular systo-diastolic modulation with normal SAT value.

RI ranged from 0.34 to 0.97 with an average value of 0.69.

In all cases, CDUS permitted to identify supra hepatic veins and to assess patency of the venous drainage and the proper hepatic venous flow.

The most frequent pattern of supra hepatic venous drainage was biphasic.
Fig. 0: Male, 56 years old, in 2nd day post-OLT, with evidence of initial liver failure, presents portal vein patency, physiologic flow with peak systolic velocity of 85 cm/sec, measured with a 50° # angle, normal systo-diastolic modulation of hepatic artery and RI of 0,64(Fig.2). Suprahepatic venous drainage presents triphasic pattern(Fig.3). No significant ectasia of intra and extra-hepatic bile ducts is present.

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Fig. 0: Male, 61 years old, in 2nd day post-OLT with evidence of initial liver failure, presents portal vein patency, physiologic flow with peak systolic velocity of 56 cm/sec, measured with a 34° angle, high systolic peak of hepatic artery and increased RI of 0.86(Fig.5). SAT is normal (0.047 s)(Fig.6). Suprahepatic venous drainage presents monophasic pattern(Fig.7). No significant ectasia of intra and extra-hepatic bile ducts is present.

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Fig. 0: Same patient 2 days after: CDUS exam shows normalization of systo-diastolic modulation and RI value (0.65).

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Conclusion

No significant abnormalities in CDUS parameter (average RI, average velocity, vascular patency and flow modulation axis) were found in all patients.

CDUS resulted to be an accurate method to study major vascular anastomosis in post-OLT patients and to avoid invasive exams in the immediate post-operative period after OLT.

In all cases patency of the portal vein and physiologic direction of portal flow was assessed. High variability of portal flow in post-OLT was frequently found between different patients and often in the same patient. This is caused by hepatic portal flow hemodynamic which needs time to settle because of collateral circulation, already present before OLT.

High variability about RI values was shown by CDUS in different patients. In early post-OLT is often possible to find an increase rate of RI which depends on reduction of diastolic phase due to several factors. As described by Garcia-Criado [6] it is related to abnormalities in the arterial vascularization caused by normal variation in intrahepatic resistance post-OLT.

In all cases, SAT was normal and was found to be a very important parameter for a correct interpretation of RI variations in early post-OLT.

In 4 cases RI was transitory <0.55 with normal SAT and it normalized in the sequent period because of changes in systemic hemodynamic.

In all cases CDUS demostrated physiologic venous drainage which presented variable patterns depending on elapsed time since transplantation. The most frequent type of pattern was biphasic.

In all patients CDUS proved to be an easy and repeatable technique that can be performed at the patient’s bedside, able to exclude major vascular complications due to liver non-function. Variations were all comparable to normal changes usually present in post-OLT.
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