VIA MEDICA

Nuclear Medicine Review 2004
Vol. 7, No. 1, pp. 21–25

ISSN 1506–9680

Original

# Single injection hepatic radionuclide angiography and hepatobiliary scintigraphy in the evaluation of liver transplant function

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[Received 28 II 2003; Accepted 02 III 2004]

## Abstract

BACKGROUND: The aim of the study was the evaluation of the perfusion, morphology and biliary three patency of liver transplants employing two radionuclide methods.
MATERIAL AND METHODS: The study was performed on 10 controls and 10 patients after an orthotopic transplantation (up to two years). „First pass" dynamic acquisition was performed with a scintillation camera, after a bolus injection of 360 MBq 99mTc-diethyl- IDA, (60 frames/60s), continued by a 59 minute (1 frame/min) slower dynamic study. From the liver and kidney activity during the „first pass" study, the hepatic perfusion index (HPI) was calculated using slope-analysis. Hepatobiliary scintigrams obtained during second phase of the study were analyzed for morphology, and parenchymal and hepatobiliary TA curves were generated and analyzed according to the time to maximal activity (Tmax) and the time to half of maximum activity (T/2).
RESULTS: In comparison to the controls (HPI, X = 0.64.5 ± ± 0.05%) portal perfusion had slightly (X = 0.68 ± 0.04%), but not significantly ($p > 0.05$) increased. In 3 patients, the biliary phase of hepatobiliary scintigraphy showed an increased accumulation of the radiopharmaceutical in the left (n = 1) or right (n = 2) hepatic duct. The uptake of the radiopharmaceutical (Tmax, X = 18.5 ± 2.9 min) was slightly, but not significantly ($p > 0.05$) delayed in comparison to the controls (X = 14.2 ± ± 3.4 min), while excretion was significantly ($p < 0.05$) prolonged (X = 59.5 ± 12.1 min) (X = 34.2 ± 4.1 min). Intrahepatic bile flow was insignificantly ($p > 0.05$) prolonged (X = 31.3 ± 3.7 min) in comparison to the controls (X = 25.7 ± ± 3.5 min) while extrahepatic bile flow was high, significantly ($p < 0.01$) prolonged (X = 89.0 ± 14.3 min) than physiological one (X = 45.0 ± ± 7.2 min).
CONCLUSIONS: Radionuclide methods are noninvasive, sensitive and valuable in monitoring liver transplants.
**Key words: radionuclide angiography, hepatobiliary scintigraphy, nuclear medicine techniques, liver transplant**

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## Introduction

The aim of the study was the evaluation of the perfusion, morphology and biliary three patiency of liver transplants employing two radionuclide methods. Considering the rising number of institutions that perform liver transplantation, there is an increasing demand for both structural and functional investigation of the vascular and biliary system by hepatobiliary scintigraphy whether it is orthotopic, heterotopic, auxiliary [1–3] or transplantation in children [4, 5]. Although there is a need for pre-operative assessment of the donor and recipient liver [6] (including a liver-spleen scan for liver volume, a multiple gated acquisition cardiac scan or thallium study, a bone scan and a quantitative ventilation perfusion scan for hepatopulmonary syndrome) the main role of these investigations is employed in the postoperative period, when there is a higher possibilty of problems with vascular and biliary anastomoses, rejection, infections and bile leaks which can be detected by hepatobiliary studies [7]. It is especially important to be able to distinguish intra from extrahepatic cholestasis [8], which is possible by using various analyses of the data from a hepatobiliary TA curve [9, 10]. The studies are non-invasive and can be performed readily at the bedside in the intensive care unit [11].

The aim is the evaluation of the perfusion, morphology and biliary three patiency of liver transplants employing two radionuclide methods.

## Material and methods

The study was performed on 10 controls and 10 patients after an orthotopic transplantation (up to two years). „First pass" dynamic acquisition was performed with a scintillation camera, after a bolus injection of 360 MBq 99mTc-diethyl- IDA, (60 frames/60 s), continued by a 59 minute (1 frame/min) slower dynamic study. From the liver and kidney activity during the „first pass" study, HPI was calculated using slope-analysis [12]. Hepatobiliary scintigrams obtained during the second phase of the study were analyzed for morphology, parenchymal and hepatobiliary TA curves were generated and analyzed according to the time when maximal activity (Tmax) and the time to half of the maximum activity (T/2) was achieved.

The mean value (X), standard deviation (SD), coefficient of variation (CV%) were calculated and a T-test was performed.

## Results

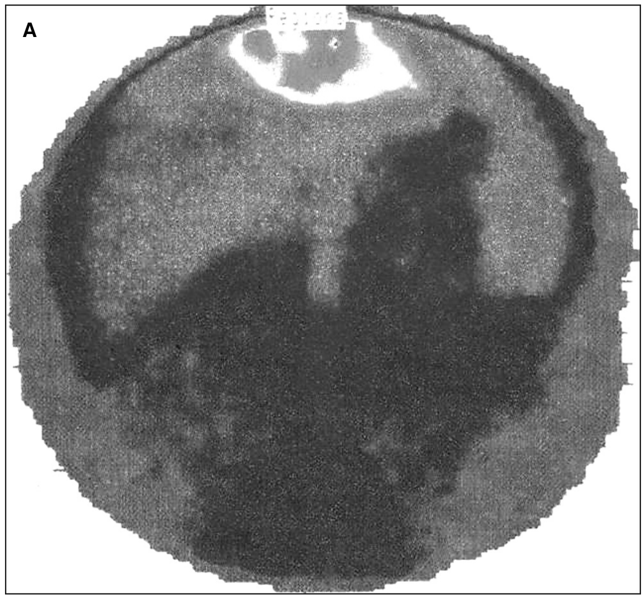
During the vascular phase of the study, liver perfusion was uniform (Fig. 1A). In comparison to the controls, where the hepatic perfusion index (HPI), reflecting portal inflow to the liver was X = 0.64.5 ± 0.05%, portal perfusion was slightly (X = 0.68 ± ± 0.04%), but not significantly ($p > 0.05$), increased (Fig. 1B).

During the parenchymal phase of the study, distribution of the radiopharmaceutical was uniform (Fig. 2A).

In 3 patients, the biliary phase of the hepatobiliary scintigraphy showed an increased accumulation of radiopharmaceutical in the left (n = 1) or right (n = 2) hepatic duct (Fig. 2B). The uptake of the radiopharmaceutical estimated from the data from the liver TA curve (Tmax, X = 18.5 ± 2.9 min) was slightly, but not significantly ($p > 0.05$) delayed in comparison to the controls (X = 14.2 ± 3.4 min), while excretion was significantly ($p < < 0.05$) prolonged (X = 59.5 ± 12.1 min) than physiological one (X = 34.2 ± 4.1 min). The intrahepatic bile flow estimated from the bile duct TA curve was insignificantly ($p > 0.05$) prolonged (X = 31.3 ± 3.7 min) in comparison to the controls (X = 25.7 ± 3.5 min) while extra-hepatic bile flow was high, significantly ($p < 0.01$) prolonged (X = 89.0 ± 14.3 min) than physiological (one (X = 45.0 ± 7.2 min) (Fig. 2C).

## Discussion

In all of our patients, the vascular phase passed without any disturbances. There was uniform vascularisation in the entire liver tissue, without sites of hypo- or hyper-perfusion, while the analysis of the data from the liver vascular TA curve showed almost the same ratio between the arterial and portal phase as in the controls. In general, vascular complications may involve the hepatic artery, hepatic veins or the portal vein. Hepatic arterial occlusion results in focal areas of diminished or absent radiopharmaceutical agent uptake in the allograft [13, 14]. Similar focal defects may be due to other causes, such as abscesses, haematomas or bilomas. However, if there is no infarction or complete loss of allograft perfusion, hepatobiliary imaging may demonstrate nonspecific hepatocyte dysfunction characterized by impaired extraction of the IDA agent and prolonged circulation in the blood pool [15, 16]. This is the reason why, in this study, hepatic radionuclide



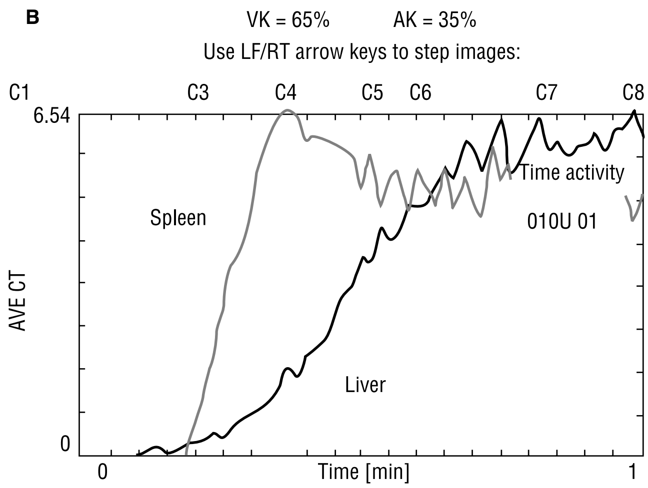
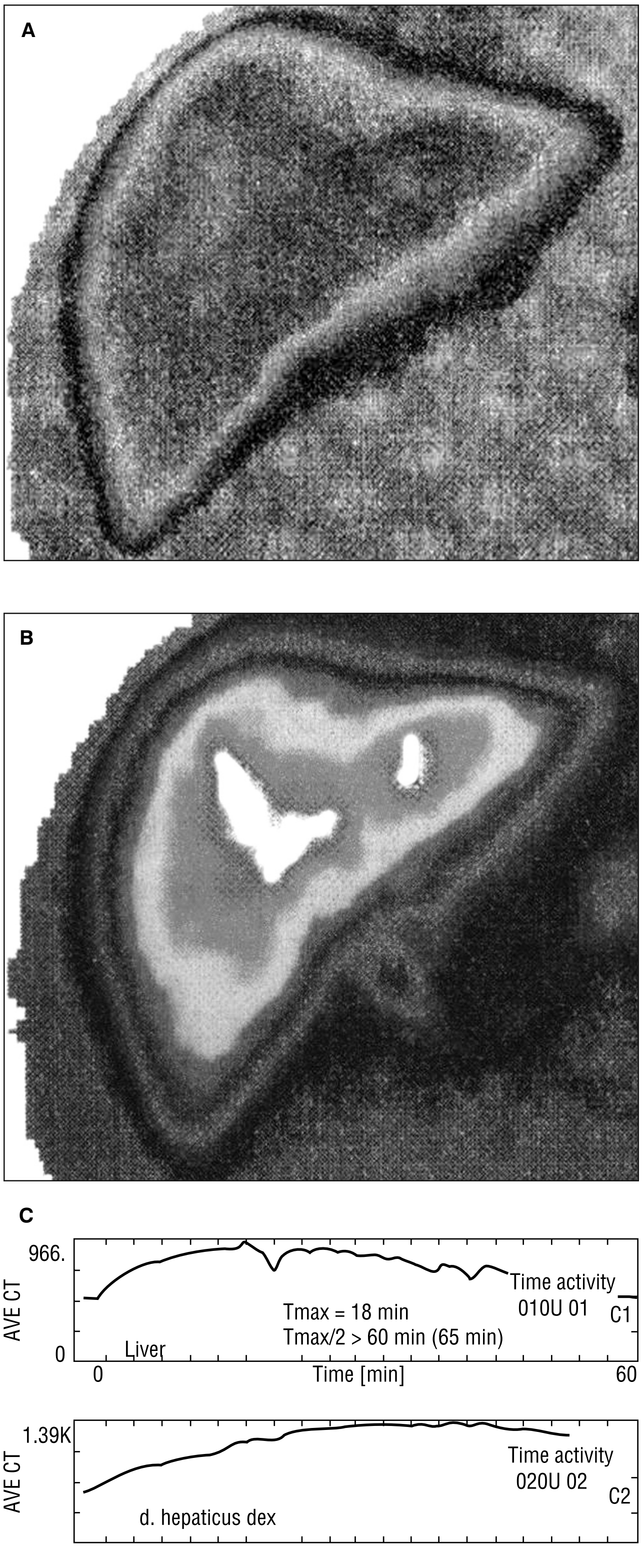




**Figure 1.A.** Composite scintigram (60 s): "first pass" study point out the uniform liver perfusion, without focal defects; **B.** ROI analyses: according to the time when the maximal values are registered on the splenic TA curve (grey), it is possible to determine , using slope analyses, the relative distribution betwen the arterial and portal supply on the liver TA curve (black). The values are physiological (HPI = 0.65).




**Figures 2.A.** Static scintigram in the 8[th] min: uniform distribution of the radiopharmaceutical during parenchymal phase; **B.** Static scintigram in the 30[th] min (biliary phase): retention of the radiopharmaceutical in the left and more intense in right hepatic duct, with decreased activity in ductus hepaticus communis and ductus choledochus. Activity is visible in the small intestine; **C.** C1 — hepatic curve: slightly impaired uptake and prolonged excretion of the rf. from the hepatocytes; C2 — curve from right hepatic duct and hilus region: slightly impaired intrahepatic and very impaired extrahepatic bile flow.

angiography was performed, so that the lack of the arterial phase could be clearly visualized, as well as of the portal phase if the thrombosis existed. Hepatic vein obstruction should have the same scintigraphic appearance as in Budd-Chiarri syndrome, i.e. with caudate lobe hypertrophy [17] either in the sequential or composite image of the first or the second part of the study.

In the biliary phase of our study, extrahepatic with consecutive intrahepatic cholestasis was observed in most of the patients, which might be explained by the fact that orthotopic liver transplantation results in markedly impaired hepatocellular uptake and biliary secretion of organic anions, as well as significantly reduced bile acid synthesis, which, in addition, diminishes bile secretion of the graft [18]. Apart from this, in all our patients choledocho-choledocho-anastomosis was performed on the narrow bile ducts (none of the patients had widened bile ducts due to some sort of cholestasis), which additionally influenced the slower bile flow. Partial obstruction can be identified by an abrupt decline in activity from one segment of the duct to the next [19, 20], while in complete obstruction, activity accumulates proximally to the obstruction, with no activity in the gut for 24 hours [21]. Using the data from the time activity curves, it is sometimes possible to distinguish intra from extrahepatic obstruction, which is very important with regards to therapy.

According to Kim et al. [22] the diagnostic sensitivity and specificity of hepatobiliary scintigraphy for biliary obstruction were 93% (100% for segmental, 83% for total) and 88% (35/40), respectively. He claims that hepatobiliary scintigraphy is an accurate diagnostic modality in the evaluation of biliary complications after adult-to-adult living donor liver transplantation, although it has limitations as a means of differential diagnosis of non-biliary complications which is in accordance with our results. Kurzawinski et al. [23] proved that the sensitivity and specificity of scintigraphy for the detection of biliary stricture was 62 and 64 per cent respectively. This study suggests that scintigraphy is a useful screening test for biliary complications after orthotopic liver transplantation, while endoscopic retrograde cholangiography is only necessary if the hepatobiliary scintigraphy is abnormal. In contrast to our results, according to Ekman et al [24], the difference in clearance rate of $^{99m}$Tc-diethyl-iodo-HIDA from the blood between healthy controls and liver transplant patients was highly significant ($p < 0.01$), corresponding to the clinical condition of the two groups. They concluded that the clearance rate of the above-mentioned radiopharmaceutical, based on a simple measurement from the time-activity curve derived from a blood pool region of interest, is a reliable test of liver function. Brunot et al. [25] demonstrated a close correlation between early biopsy results and perfusion indices in patients with a liver graft as well as uptake parameters determined by hepatobiliary scintigraphy. According to Westra [26], in the interpretation of hepatobiliary scintigraphy findings, as well as other modalities, familiarity with normal graft appearance, as influenced by various surgical and technical factors, and knowledge of the underlying condition of the patient and the clinical course of postoperative complications are crucial for a correct interpretation of the findings from imaging studies. Gelfand [27] claims that parameters that were useful in predicting an adverse outcome were a failure to visualize excreted radiopharmaceutical at or beyond the biliary anastomosis on a study performed within 24 hours after the transplant, and a persistent or increasing delay in the time of the visualization of excreted radiopharmaceutical.

Abnormalities in liver uptake and excretion were seen in rejections, but they were also seen in patients who remained well without rejection or parenchymal disease. Significant biliary leaks were identified in the three cases in which they were known to be present. In liver transplant recipients, hepatobiliary imaging is useful in predicting graft survival and identifying biliary leaks. Kanegawa [28] reported that although it is difficult to distinguish between infection and rejection, hepatobiliary scintigraphy may be useful in evaluating transplanted liver function in rejection. Engeler [29] claimed that the majority of scintigrams demonstrated normal uptake (60/ /75, 80%) and delayed excretion (65/76, 85%), which was most marked immediately after transplantation. These findings suggest that $^{99m}$Tc-DISIDA scintigraphy can differentiate between transplants with and without rejection/cholestasis but not between rejection and cholestasis. If $^{99m}$Tc-DISIDA excretion is normal, rejection and cholestasis are unlikely. According to Mochizuki [30], the sensitivity, specificity and accuracy were 100, 100, 100% for ectravasation and 80, 100, 98% for obstruction, respectively. Hepatobiliary scintigraphy appears to be an accurate means of detecting biliary leak and obstruction associated with the transplanted liver. According to Kuni [31], hepatobiliary scintigraphy results suggest that scintigraphy can distinguish intrahepatic cholestasis from pure hepatocyte damage. Using this method, it is possible to detect bile leakage [32–35], patency of biliary-enteric anastomosis [36–38], hepatocyte disfunction [39] or rejection [40], but we did not have any such cases, in our study.

In the absence of radiopharmaceuticals for the detection of infection such as $^{99m}$Tc-HM PAO, $^{111}$In WBC, $^{67}$Ga-citrate, $^{99m}$Tc-ciprofloxacin on the hepatobiliary scintigraphy, infection should be presented by prolonged blood pool activity and diminished hepatocyte uptake and excretion of the IDA agent and may be indistinguishable from rejection [15]. However if the abscess communicates with biliary tree, radioactivity fills it slowly [18].

## Conclusions

Radionuclide methods are noninvasive, sensitive and valuable in the monitoring of liver transplants.

The following four clinical situations were assessed by hepatobiliary scans: early graft function; rejection episodes; vascular complications; and biliary-tract problems. Nuclear medicine has an important and valuable role in the postoperative monitoring of patients after liver transplantation. The studies are non-invasive and can be performed readily at the bedside in the intensive care unit.

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