

Utility of Bone Scan in Pre-Liver Transplant Work-Up of Patients with hepatocellular carcinoma

Ahmed Alqarni¹, Monther Kabbani¹, Faisal Abaalkhail^{1,2}, Alicia Chorley¹, Hany Elbeshbeshy¹, Waleed Al-Hamoudi^{1,3}, Saleh Alabbad¹, Mark Stuarduvant¹, Mohammad Alsofayan¹, Wael Al-Kattan², Baderaldeen Ahmed¹, Mohamed Al Sebayer¹, HussienElsiesy^{1,2*}

¹Liver Transplantation, King Faisal Specialist Hospital & Research Center

²Alfaisal University

³Gastroenterology, King Saud University, Riyadh, Saudi Arabia

Received: October 2, 2016; Accepted: November 30, 2016; Published: January 14, 2017

*Corresponding author: Hussien Elsiesy, King Faisal Specialist Hospital & Research Center and Department of Liver transplantation, Altakhasusi Street, Riyadh, 11211, Saudi Arabia, Tel: +966114647272; E-mail: helsiesy@gmail.com

Abstract

Background and Aims: Our program utilizes bone scan routinely as part of liver transplant (LT) evaluation of patients with hepatocellular carcinoma (HCC). The aim of this study is to evaluate the utility of bone scan in the pre-transplant workup.

Methods: This is a retrospective chart review of our LT database from January 2011 to December 2014 of all patients with HCC who had LT. Collected data include age, gender, etiology of liver disease, imaging (CT or MRI), bone scan, explants tissue pathology, type of transplant and transplant outcome.

Results: During the study period, 275 LTs were performed. Fifty-two patients had HCC, of whom 34 underwent bone scan. The average age was 58(22-72), and 20 patients were males. The etiology of liver disease was hepatitis C (21 patients), cryptogenic cirrhosis (7 patients) and HBV (6 patients). Sixteen patients had HCC within the Milan criteria, 12 within University of California at San Francisco (UCSF) criteria, and 6 patients were beyond the UCSF criteria. Twenty four patients underwent Living donor liver transplantation (LDLT), whereas 10 patients underwent Deceased donor liver transplantation (DDLT). Of the 34 patients, 1 patient had positive suspicious bone scan (2.9%). The remaining 33 patients had negative bone scan (97%). One patient within UCSF criteria had false positive bone scan (negative PET-CT and no recurrence after liver transplant).

Conclusions: Bone scan has low utility in patients with HCC within the Milan criteria and should not be routinely used as part of the liver transplant workup.

Key Words: Bone scan; Hepatocellular carcinoma; Bone metastases; Liver transplantation

Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver tumor accounts for over 80% [1, 2] and the burden of this devastating disease is expected to increase. HCC is the second leading cause of cancer-related death worldwide [3]. Incidence rates are not uniform across different geographical regions, but

vary in accordance with the frequency of risk factors [4]. Each year, approximately 750,000 new cases are diagnosed, risk factors include pre-existing infection with hepatitis B or C viruses and cirrhosis [5, 6].

The diagnosis of HCC in our study was made based on radiological criteria according to the AASLD guidelines [7, 8].

Bone metastases (BM) are rare in patients with early-stage hepatocellular carcinoma (HCC) [9]. In some centers, liver transplantation (LT) policies require patients with HCC to undergo bone scans.

Bone scintigraphy was performed using a dual-head gamma camera equipped with general-purpose collimators. Anterior and posterior whole-body images were acquired approximately 3 hours after intravenous administration of 925 MBq 99mTc-hydroxymethane diphosphonate (HDP). Additional static planar images were acquired at the discretion of the attending nuclear physician. The results of each bone scan were classified as follows: (i) positive for metastases (defined as focal uptake of the radiotracer in non-physiologic locations that could not be explained by other conditions, such as trauma, known degenerative diseases, or inflammation); (ii) negative for metastases (physiologic uptake alone or uptake with a distribution consistent with recent trauma or known degenerative diseases); or (iii) suspicious for BM (increased uptake in non-physiologic locations without characteristics of metastases, such as isolated focal uptake) [10].

Our program utilizes bone scan routinely in the pre-transplant evaluation of patients with hepatocellular carcinoma (HCC). The aim of our study is to evaluate the utility of bone scan in the setting of the pre-transplant liver workup in HCC patient.

Method

This is a retrospective chart review of our liver transplant (LT) database of all patients with HCC who underwent bone

scan prior to liver transplantation. From January 2011 to December 2014, 275 LTs were performed, including 183 LDLTs and 92 DDLTs. Fifty-two patients had HCC, of whom bone scan was performed on 34 patients. The data collected include the following: age, gender, etiology of liver disease, tumor size and number on CT or MRI, bone scan results, explant tissue analysis, type of transplant [living donor (LDLT) versus deceased donor (DDLT)] and transplant outcome. Patients within Milan criteria received a MELD exception of 22 on cadaveric waiting list, patients within UCSF criteria were allowed to undergo LDLT, and patients beyond UCSF criteria received liver transplantation only if they were successfully down staged using loco-regional therapy.

Results

During the study period, 275 LTs were performed, including 183 LDLTs and 92 DDLTs. Fifty-two patients had HCC, of whom bone scan was performed in 34 patients. The average age was 58 (22-72), and 20 patients were males. The etiology of liver disease was hepatitis C (21 patients), cryptogenic cirrhosis (7 patients), and HBV (6 patients). The median follow up was 38 months. Sixteen patients had HCC within Milan criteria and 12 patients within University of California at San Francisco criteria (UCSF), and 6 patients were beyond UCSF criteria. Twenty-four patients underwent LDLT, whereas 10 patients underwent DDLT (Figure 1).

Of the 34 patients, 33 patients had negative bone scan. One patient with suspicious positive bone scan had negative PET scan and no clinical evidence of bone metastases on follow up and she still alive. she was 61 years old with NASH and MRI report showed liver cirrhosis with two HCC both located in segment 4A one 3.4cm x 2.7cm and the second HCC 1.4cm x 1.6cm within UCSF criteria, she was underwent living-related liver transplant (Right Lobe) and histopathology showed moderately differentiated, hepatocellular carcinoma largest focus measures 3cm in maximum dimension, no vascular invasion, uninvolved liver shows macro and micro liver cirrhosis, vascular resection margins are free of tumor (Table 1).

The explant showed well differentiated HCC in 16 patients, moderately differentiated HCC in 10 patients, poorly differentiated in 1 patient, combined HCC & cholangiocarcinoma in 1 patient and complete necrosis after the loco-regional therapy in 6 patients.

Three patients died, one within UCSF criteria and two beyond UCSF criteria, two due to hepatic artery thrombosis and one due to sepsis and multi organ failure.

Discussion

Technetium-99m methylene diphosphonate (Tc-99m MDP) bone scintigraphy (BS) has been widely used to detect skeletal metastasis in practice. The advantage of BS lies in its ability to effectively survey the entire skeletal system in a single scan, which takes only a short period of time [11].

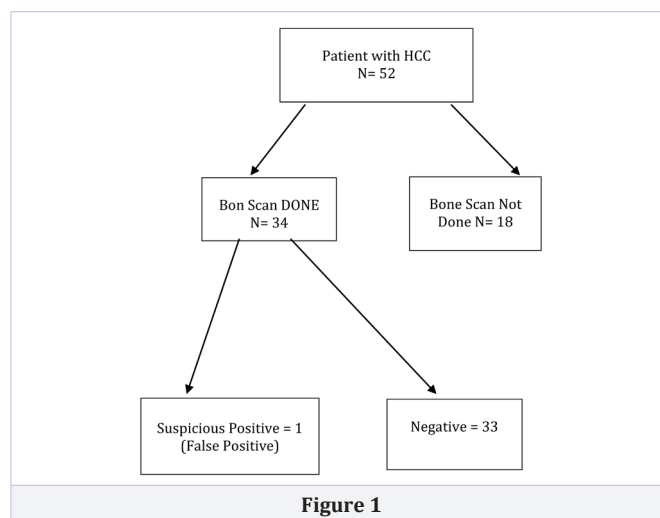


Table 1: Bone Scan result in relation to tumor size.

PATIENTS	MILAN	UCSF	Beyond UCSF
Total	16	12	6
Positive	0	1	0
Negative	16	11	6
Percentage	0%	8%	0%

Once a diagnosis of HCC has been confirmed, disease staging is essential for treatment selection [1]. Curative treatments, such as resection or liver transplantation (LT), are offered to patients with early stage tumors according to the Barcelona Clinic Liver Cancer Group (BCLC) classification [1], that is, patients with a single lesion <5 cm or up to three lesions ≤3 cm without macrovascular invasion. These criteria, known as the Milan criteria [12], identify a group of patients with HCC who may experience good disease-free survival after LT and outcomes comparable to those of patients receiving LT for other indications. Therefore, the majority of transplantation programs use these criteria

For selection of patients with HCC. The Milan criteria are used as part of our policy for selection of patients with HCC as candidates for LT. To identify possible subclinical metastases, our program requires that all patients with HCC undergo computed tomography (CT) of the chest and a bone scan to be included on the LT waiting list. However, the recommendation to screen for metastasis in patients with early-stage HCC as a requirement for inclusion on the LT waiting list is not evidence-based. Recently, some research groups investigated the frequency of bone metastases (BM) and the utility of bone scans (BSs) in the pre-LT assessment of this patient population [13, 14]. These studies showed that, in view of the low frequency of metastases, BSs should only be performed in this setting in patients with clinical signs or symptoms indicative of bone metastasis. Rodríguez S, et al. [15], Koneru et al. [16] and Witjes et al. [14] also concluded that BSs are not cost-effective and do not improve selection of LT candidates.

We report our experience in evaluating the role of bone scan in detecting HCC bone metastases in pre-liver transplant patients and find that our results are in agreement with other reports evaluating the role of bone scan in patients with HCC.

We have shown that bone scan has no utility in patients with HCC within Milan criteria and should not be routinely used as part of the liver transplant work-up.

Conclusion

We have shown that bone scan has low utility in patients with HCC within Milan criteria and should not be routinely used as part of the liver transplant work-up.

References

1. Hegab B, Abdelfattah MR, Azzam A, Mohamed H, Al Hamoudi W, Alkhail FA, et al. Day-of-surgery rejection of donors in living donor liver transplantation. *World journal of hepatology*. 2012;4(11):299-304. doi: 10.4254/wjh.v4.i11.299.
2. Mittal S, El-Serag HB. Epidemiology of hepatocellular carcinoma: consider the population. *J Clin Gastroenterol*. 2013;S2-6. doi: 10.1097/MCG.0b013e3182872f29.
3. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015;136(5):359-386. doi: 10.1002/ijc.29210.
4. Silva MF, Sherman M. Criteria for liver transplantation for HCC: what should the limits be? *J Hepatol*. 55(5):1137-1147. doi: 10.1016/j.jhep.2011.05.012.
5. Dmitrewski J, El-Gazzaz G, McMaster P. Hepatocellular cancer: resection or transplantation. *J HepatobiliaryPancreat Surg*. 1998;5(1):18-23.
6. Fattovich G. Progression of hepatitis B and C to hepatocellular carcinoma in Western countries. *Hepatogastroenterology*. 1998;Suppl 3:1206-1213.
7. Bruix J, Sherman M. Management of hepatocellular carcinoma. *Hepatology*. 2005;42(5):1208-1236.
8. Song DS, Bae SH. Changes of guidelines diagnosing hepatocellular carcinoma during the last ten-year period. *Clin Mol Hepatol*. 2012;18(3):258-267.
9. Kanda M, Tateishi R, Yoshida H, Sato T, Masuzaki R, Ohki T, et al. Extrahepatic metastasis of hepatocellular carcinoma: incidence and risk factors. *Liver international : official journal of the International Association for the Study of the Liver*. 2008;28(9):1256-1263. doi: 10.1111/j.1478-3231.2008.01864.x.
10. Krasnow AZ, Hellman RS, Timins ME, Collier BD, Anderson T, Isitman AT. Diagnostic bone scanning in oncology. *Semin Nucl Med*. 1997;27(2):107-41.
11. Lee KH, Park JM, Yoon JK, Koh KC, Paik SW, Kim BT. Bone scintigraphy of skeletal metastasis in hepatoma patients treated by TAE. *Hepatogastroenterology*. 2003;50(54):1983-1986.
12. Mazzaferro V, Regalia E, Doci R, Andreola S, Pulvirenti A, Bozzetti F, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. *N Engl J Med*. 1996;334(11):693-699.
13. Sheth H, Javed SS, Hilson AJ, BuscombeJR, Davidson BR. Radioisotope bone scans in the preoperative staging of hepatopancreatobiliary cancer. *Br J Surg*. 2004;92(2):203-207.
14. Witjes CD, Verhoef C, Kwekkeboom DJ, Dwarkasing RS, de Man RA, Ijzermans JN. Is bone scintigraphy indicated in surgical work-up for hepatocellular carcinoma patients? *J Surg Res*. 2013;181(2):256-261. doi: 10.1016/j.jss.2012.07.013.
15. Rodriguez S, Balbinotto Neto G, Kiss G, Brandao A. Cost-effectiveness of whole-body bone scans in the pre-liver transplant assessment of patients with hepatocellular carcinoma in Southern Brazil. *Clin Transplant*. 2016;30(4):399-406. doi: 10.1111/ctr.12699.
16. Koneru B, Teperman LW, Manzarbeitia C, Facciuto M, Cho K, Reich D, et al. A multicenter evaluation of utility of chest computed tomography and bone scans in liver transplant candidates with stages I and II hepatoma. *Ann Surg*. 2005;241(4):622-628.