

INCIDENTAL FINDING OF DELAYED KIDNEY EXTRACTION DURING ROUTINE TC99-MDP BONE SCAN IN HEALTHY YOUNG ADULTS DOES NOT PREDICT KIDNEY DYSFUNCTION - HISTORICAL COHORT ANALYSIS

Guy Verhovsky MD*¹ and Azik Hoffman MD MHA²

*¹IDF Medical Corps, Israel

²Urology department, University Health Network, Toronto, Ontario, Canada.

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Abstract

Purpose: To assess clinical impact of randomly diagnosed delayed renal extraction of Tc99-MDP in healthy young adults, and the ability of bone scintigraphy to predict similar finding on renal ultrasound.

Methods: 158 healthy with no previous renal abnormalities with delayed tracer extraction on late phase images acquisition were included. All patients were evaluated for previous medical conditions, underwent renal ULS and were followed routinely for urological conditions. Relations were assessed using chi2 test and concurrently univariate statistical analysis. Pearson correlation test and spearman test were used to analyze strength and direction of connections.

Results: Bone scintigraphy revealed 12 (7%) cases of hydronephrosis, 5 of them not identified on U/S, which revealed 17 (9%) cases. Ureters dilatation was suspected in 9 (5%) cases of bone scintigraphy. Five cases of hydro-ureteronephrosis were identified on bone scintigraphy and ULS. Only hydronephrosis and / or ureters dilatation predicted similar finding on renal ULS ($P < 0.05$). Bone scintigraphy readily reveals ectopic or small kidney. All cases of delayed isotope extraction after 3 hours and normal ULS suffered neither clinical signs nor renal function deterioration during follow up.

Conclusions: Bone scintigraphy findings in addition to delayed isotope extraction after 3 hours may require additional urological workup in order to diagnose clinically significant cases. Additional renal ULS can add to workup accuracy. Patients without previous urological history, with only delayed isotope extraction and no concurrent renal ULS finding will not suffer renal function deterioration, nor develop clinical urological symptoms on medium term follow up.

INTRODUCTION

Technetium bone scan (Tc^{99m} - MDP) is the gold standard diagnostic procedure in management of complicated bone stress fracture in the Israeli Medical Corp and in clinical diagnosis of military and sports injuries. Soldiers are referred to this examination due to typical complains such as tibial or femoral pain regional pain after a period of strenuous physical activity (1). Tc^{99m} MDP is introduced intravenously and is released freely through the intra

vascular space, and distributed rapidly into the extracellular space. Three hours after the injection of the isotope, its concentration in the tissue is proportional to the concentration of tissues calcium, and is uptaken in the areas of fracture and infection. Scan results may display a high range of non-osseous findings. Tc^{99} -MDP may be absorbed in the soft tissue and may be detected in kidney parenchyma. This renal accumulation may indicate full or partial obstruction of the urinary tract or abnormal renal function. Renal accumulation may also represent delay in the isotope secretion from the kidneys with mild hydronephrosis without clinically significant finding in children. In those cases, strict clinical surveillance is recommended (2). There is paucity of data regarding incidence of similar finding in healthy adolescents and adults with no previously known history of renal disease or anatomic abnormality.

The IDF Medical Corps performs roughly 3500 bone scans annually. The most common coincidental urinary tract observations are tracer retention in kidney parenchyma, urinary collecting system and structural anomalies, which are observed in about 15% of the cases. Also, urinary tract obstructions in post- mortem procedures are relatively common, reported in 3.5% of population (3). Similar findings are reported in about 2% of children, probably representing congenital urinary tract anomalies. Delayed secretion or clearing of the isotope detected in a routine imaging in asymptomatic individual with no known asymptomatic renal congenital or acquired condition usually represent delay in secretion from the parenchyma, partial obstruction of the uretero-pelvic junction (UPJ) or uretero-vesicle junction (UVJ) obstruction. Both conditions can easily be discriminated on the bone scan. However, there are no guidelines regarding the proper urological workup following such a random bone scan finding in healthy young individuals. The aim of this study is to describe the phenomena and identify factors that may require further investigation in order to prevent future renal damage.

MATERIALS & METHODS

950 patients with incidental renal Tc^{99} - MDP retention bone scintigraphy were identified in our database during 2010 to 2014. Patients age was 18 to 26 years. Patients with known previous renal conditions (such as congenital UPJ obstruction), previous known renal or collecting system surgery or renal diseases were excluded. Kidney estimated glomerular filtration rate (eGFR) was calculated according to MDRD formula (4). 158 patients with delayed tracer extraction on late phase images acquisition (3 hours post isotope injection) who completed renal ultrasound after bone scintigraphy were included in our data.

Whole body bone scintigraphy was performed according to the Society of Nuclear Medicine procedure guidelines (5). The radiopharmaceutical Tc^{99} - MDP was administered intravenously using an indwelling catheter. The average activity administered for bone scintigraphy by a single intravenous injection was 500 MBq (300-740 MBq) (8-20 mCi). The organ which received the largest radiation was the bone. Planar anterior and posterior images of the axial skeleton were acquired in two phases: Blood pool (tissue) phase (immediately after injection and within 10 minutes) and delayed (skeletal) phase (approximately 3 hours after the injection). Patients were well-hydrated and instructed to drink water liberally and were asked to void frequently during the interval between injection and delayed imaging. Patients were also asked to void immediately prior to the late phase imaging. Kidneys or bladder abnormalities were reported as tracer uptake in the kidney (focal or diffuse), location and morphology of the kidneys and ureters (if noted) and retention of tracer in the kidneys ureters or bladder. additional delayed images (6-24 hour) were not obtained.

Following bone scintigraphy, renal U/S was performed. Degree of hydronephrosis was reported according to Society of pediatric urology grading system (6). Ureters dilatation was reported when measuring >4 mm in diameter. Patients with suspected finding on ULS were referred to urologist for further investigation. All patients were followed (median: 29 months, range 14-60) for development of renal stones, urinary tract infections and renal colic symptoms. The research was approved by the IDF Medical Corps Institutional Review Board.

Statistical analysis – Relation between imaging studies and co-morbidities were assessed using χ^2 test. Relations between Tc^{99} - MDP bone scintigraphy finding and abnormal finding on ULS were assessed using univariate and multivariate statistical analysis. Pearson correlation test and spearman test were used to analyze connection and to indicate direction of connection. Statistical analysis was performed using SPSS 21 ©.

RESULTS

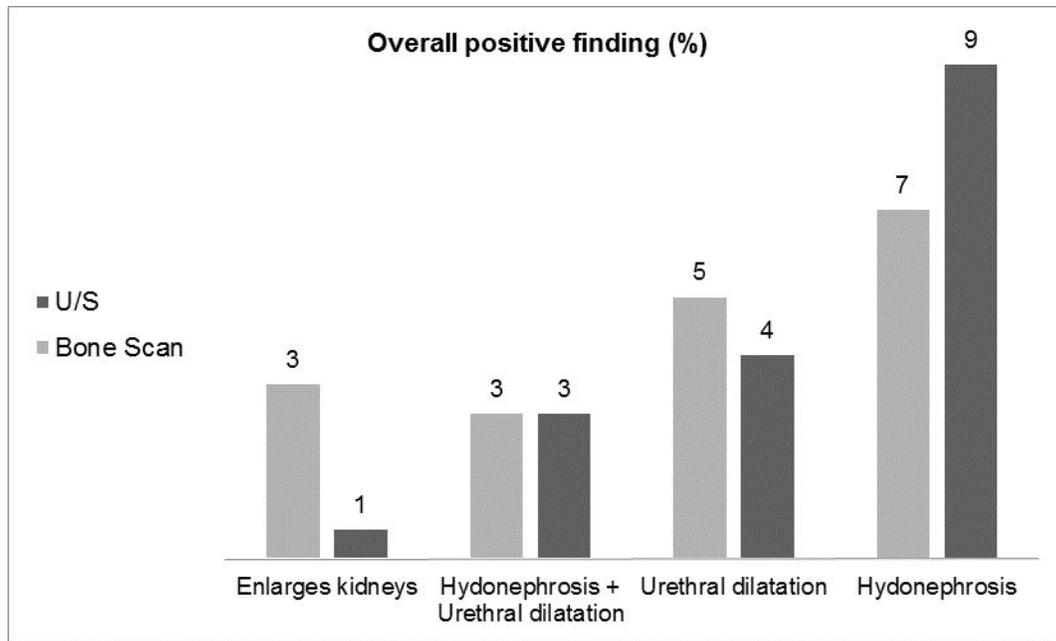
Group characteristics of patients with and without ULS finding are summarized in *Table 1*:

Table 1. Group characteristics

	Positive finding on ULS	Negative finding on ULS
Median age at scan, years (Inter- percentile range)	20 (19.75 – 21)	20 (19 – 21)
Male, No. (%)	17 (61%)	98 (69.5%)
Female, No. (%)	11 (39%)	43 (30.5%)
Previous medical condition, Yes (%)	3 (0.5%)	8 (5%)
Median Height, cm (Inter- percentile range)	168 (160 – 175)	170 (164 – 175)
Median GFR, ml/ Kg/ min (inter percentile range)	100 (112 – 83)	104 (126 – 80)
Side (Rt / Lt / Bil) %	33 / 30 / 36	42 / 24 / 34

Similar cumulative percentages of positive findings were detected in ULS and bone scintigraphy (17% and 18%), although bone scintigraphy revealed more patients with enlarged kidneys (3% vs. 1%), while ULS diagnosed more cases of hydronephrosis (9% vs. 7%), as illustrated in **figure 1**.

figure 1. Overall positive findings



Bone scintigraphy revealed 12 (7%) patients with unilateral hydronephrosis, 5 of them not indentified on U/S, which revealed 17 (9%) cases. Ureters dilatation was suspected in 9 (5%) patients on bone scintigraphy, 4 not detected on U/S. All five cases of hydro-ureteronephrosis were identified on bone scintigraphy and U/S. All other remaining patients included in the data were reported to have delayed isotope extraction (3 hours following isotope injection) with no other pathologies on both bone scintigraphy and U/S. Hydronephrosis grades was higher in patient not reporting other medical conditions (P=0.056, not shown in a figure). Bone scintigraphy also reported 6 (3%) cases of enlarged kidney, only one of them was confirmed on U/S.

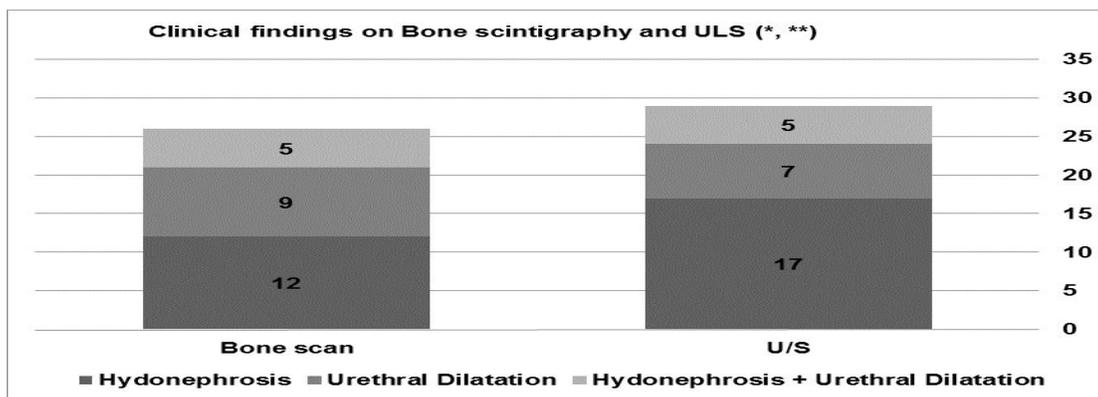


Figure 2. Cumulative absolute number of patients

** Positive finding on Bone scan was predictive of finding on concurrent U/S ($P < 0.05$)

As illustrated on **figure 2**, although bone scintigraphy and U/L produce similar results, some patients who were diagnosed on U/S were overlooked by bone scintigraphy. Hydronephrosis with or without ureter dilatation on bone scintigraphy was shown to correlate with similar finding on renal U/S ($P < 0.05$). Unrelated other co-morbidities (e.g. hypertension, low back pain) were found to be predictive of randomly finding ureteronephrosis on bone scintigraphy (relative risk: 7.9, 1.3- 46) and U/S (relative risk: 3.68, 0.8- 15). However, no statistically significant change in renal function (estimated Glomerular filtration rate) was noticed during follow up.

DISCUSSION

Previously published data suggested that bone scintigraphy using Tc^{99m} -MDP could effectively predict renal function (estimated glomerular filtration rate and renal patterns of extraction) when compared to Tc^{99m} -DTPA characteristics (7). Renogram patterns were categorized grossly into the following four patterns: Standard pattern (T_{max} is less than five minutes and renal excretion is prompt), delayed pattern (slow renal excretion regardless of T_{max}), Obstructive pattern (T_{max} occurs at the end of the present time), and Hypo-functioning pattern (renal washout parallels the cardiac blood pool on the background). However, subject population included hospitalized in-patients evaluated for bone metastasis and other serious medical conditions, as high prevalence of hydronephrosis was reported (15 out of 35 patients). Our study population is unique in this matter, since it describes for the first time healthy young population with no previously known renal disease, and assesses the ability of Tc^{99m} -MDP bone scan to locate such conditions. Moreover, since routine ultrasound can effectively locate renal and collecting system abnormalities in all ages (2, 8), high rates of correlation between Tc^{99m} -MDP bone scintigraphy and renal ultrasound implies that bone scintigraphy is able to diagnose previously undetected renal abnormalities in young healthy adults. Interestingly, the most prevalent diagnosis reported in previously published studies addressing incidental finding on renal imaging was obstructed kidney, followed by small kidney and vesico-ureteral reflux (2, 8). Similarly, our data revealed most commonly some degree of renal obstruction, but also 16 previously undiagnosed patients with small and / or ectopic kidneys, and no new case of vesico-ureteral reflux. This probably represents the natural prevalence of asymptomatic inborn or early childhood renal abnormalities.

A recently published AUA update regarding assessment and management of incidentally detected unilateral hydronephrosis in adults suggests that asymptomatic patients without evidence of obstruction on renography (kidney elimination half-time < 10 min) or equivocal finding (half-time of 10 to 20 min) usually do not require intervention (2). On univariate analysis, we found no variable that could predict significant finding on U/S in healthy subjects who had suspected finding on bone scintigraphy. However, high degree of correlation was noted between hydronephrosis, ureters dilatation or both on bone scintigraphy and U/S, acknowledging that bone scan can, other than effectively predicting kidney GFR, also predict anatomical kidney abnormalities of location and shape or hydro-ureteronephrosis. Moreover, in cases of hydro-ureteronephrosis, bone scintigraphy readily identified and predicted the same finding on confirmatory U/S. Such cases should be further evaluated since it may indicate substantial renal and collecting system abnormalities (2).

Enlarged kidneys were diagnosed in 6 cases (3%) on bone scintigraphy. Only one of them was seen on U/S, probably due to lack of accuracy in determining the renal zone of interest when evaluating bone scintigraphy, especially when concurrent hydronephrosis is present. Therefore, the presence or lack of such finding could not be assessed on bone scintigraphy only.

We did not perform formal nuclear renography to compare to bone scintigraphy in all patients, in order to reduce unnecessary ionizing radiation exposure. In 5 patients with high degree of hydronephrosis or hydro-ureteronephrosis renal scan was performed, and revealed delayed isotope extraction following furosamide administration, correlating with high grade obstruction. We also did not evaluate late (> 3 hours) bone scintigraphy scans. Late scan may result

in a higher target-to-background ratio and permit better evaluation of renal pelvis if obscured on the routine (2-5 hours) images. 6 to 24-hours delayed imaging may be particularly helpful in patients with renal insufficiency or peripheral circulatory disorders and those with urinary retention.

In conclusion, Bone scintigraphy readily reveals delayed isotope extraction in young healthy adults. Only minority of those cases have clinically significant impact. Additional findings on bone scintigraphy (hydronephrosis, ureteral dilatation or both) may support the need for additional urological workup, such as renal U/S, which can add important structural information. Patients without previous urological history, with only delayed isotope extraction and no renal U/S finding will not suffer renal function deterioration, nor develop clinical symptoms on medium term follow up.

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