# Role of Quantitative Bone Scanning in the Assessment of Bone Turnover in Patients With Charcot Foot

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**OBJECTIVE** — To assess the new quantitative bone scan parameters as markers of Charcot neuroosteoarthropathy (CNO) activity.

**RESEARCH DESIGN AND METHODS** — Forty-two patients with acute ($n = 21$) and nonacute ($n = 21$) CNO underwent quantitative bone scanning. Patients with acute CNO were followed for 3–12 months and bone scans were repeated after treatment. New quantitative parameters were assessed and compared with markers of bone turnover and with skin temperature difference (STD).

**RESULTS** — Significant correlations between quantitative bone scan parameters and bone turnover markers were observed (all $P < 0.05$). These parameters decreased after treatment of CNO, and its reduction to the baseline value correlated with differences of bone turnover markers and STD (all $P < 0.05$).

**CONCLUSIONS** — Our study suggests that bone scanning can be used not only for diagnosis of CNO but also for monitoring disease activity by quantitative bone scan parameters.

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Early morphological diagnosis and evaluation of disease activity play an important role in the management of Charcot neuroosteoarthropathy (CNO) (1–4). In clinical practice, morphological methods (e.g., plain X-rays, computed tomography, magnetic resonance) are useful for anatomical and bone structure information (5); and skin temperature difference (STD) is used for the diagnosis and monitoring of the progression of CNO (4,6). However, they are not specific to the bone-remodelling process and could provide less precise assessment in patients with bilateral CNO, which is seen in 22% of patients with CNO (7). The aim of our study was to define new quantitative bone scan parameters for the assessment of CNO activity in relation to morphological and functional factors.

## RESEARCH DESIGN AND METHODS

— Forty-two diabetic patients from the foot clinic with unilateral CNO, in whom bone scans were performed during a 3-year period, were enrolled into the study. The study was approved by the local ethics committee, and all participants gave written informed consent.

Patients with acute ($n = 21$) and nonacute ($n = 21$) CNO had a bone scan at baseline, and the former were followed up until quiescence, when repeat scans were performed after treatment in the nonacute phase (defined as a reduction of clinical signs [e.g., edema, redness] and STD [temperature difference between the site of maximum deformity and similar site on the contralateral foot] below 2°C). Quantitative bone scan parameters, markers of bone turnover (COOH-terminal telopeptide region of type 1 collagen [1CTP] and bone-specific isoenzyme of alkaline phosphatase [BALP]) and measurement of STD were used for determination of CNO activity in all patients at the beginning of the study. All tests were repeated in the subgroup of patients with acute CNO in the follow-up study when STD decreased below 2°C (mean 24.6 ± 6.8 weeks after treatment).

Quantitative bone scintigraphy was performed following intravenous injection of 740 MBq of technetium-99m methylenediphosphonate. Radionuclide examinations were recorded by a gamma camera and computer system (DST-XL; Sopha Medical Vision International, Buc, France).

The quantitative parameters were calculated by using the following formulas:

$$\mathrm{FWB} = \frac{C_F \times 100}{C_{WB}}$$

where FWB, ratio of foot and whole-body uptake of isotope; $C_F$, count of detected impulses over the affected foot; and $C_{WB}$, count of detected impulses over the whole body (count of impulses over the urinary bladder were excluded);

$$\mathrm{BFV\ (cm/s)} = \frac{D_{BF}(\mathrm{cm})}{T_F - T_B(\mathrm{s})}$$

where BFV, blood flow velocity (speed of isotope flow from aortic bifurcation to the affected foot); $D_{BF}$, distance between aortic bifurcation and ankle; $T_F$, time of activity onset in the ankle region; and $T_B$, time of activity onset in the aortic bifurcation.

1CTP and BALP were measured by radioimmunoassay (Telopeptide 1CTP [$^{125}$I] Kit, Orion Diagnostica, Espoo, Finland; and BALP kit, Tandem-R Ostase, Beckman Coulter, Fullerton, CA). STD was assessed by an infrared thermometer (Sherwood Medical Company, St. Louis, MO) after a 30-min rest (8).

Results were expressed as means ± SD. Statistical analysis was performed using GraphPad Prism version 5.00 for Windows (GraphPad Software, San Diego, CA). Correlation was assessed by lin-

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**Table 1—*Baseline and follow-up demographics and biochemical and radiological parameters in patients with acute and nonacute CNO***

| | Nonacute CNO | Acute CNO | Follow-up* |
|---|---|---|---|
| *n* | 21 | 21 | 21 |
| Age (years) | 52.33 ± 10.63 | 54.29 ± 9.64 | — |
| Sex (M/F) | 12/9 | 13/8 | — |
| Duration of diabetes (years) | 17.10 ± 7.52 | 19.81 ± 10.06 | — |
| Type 2 diabetes | 14 (66.7) | 14 (66.7) | — |
| VPT (V) | 43.67 ± 7.73 | 44.48 ± 8.17 | — |
| A1C (%) | 8.58 ± 1.99 | 8.36 ± 1.55 | 8.21 ± 1.57 |
| 1CTP (μg/l) | 6.95 ± 2.32† | 9.57 ± 4.16 | 7.61 ± 3.55§ |
| BALP (μg/l) | 11.22 ± 2.66† | 15.23 ± 7.90 | 10.82 ± 6.71§ |
| STD (°C) | 1.17 ± 0.46‡ | 3.15 ± 1.22 | 1.09 ± 0.48§ |
| BFV (m/s) | 9.33 ± 3.10† | 11.54 ± 3.70 | 8.11 ± 2.51§ |
| FWB | 3.30 ± 1.44† | 5.20 ± 2.86 | 2.67 ± 1.12§ |

Data are means ± SD or *n* (%) unless otherwise indicated. *Mean follow-up of acute CNO was 24.6 ± 6.8 weeks after treatment. Acute versus nonacute CNO: †$P < 0.05$, ‡$P < 0.001$. Acute versus follow-up group: §$P < 0.001$. VPT, vibration perception threshold.

ear regression analysis and the Pearson's correlation coefficient. A $P$ value <0.05 was considered significant.

**RESULTS** — Patients with acute and nonacute CNO were matched for age, sex, duration of diabetes, and glycemic control (Table 1). Patients with acute CNO had significantly increased parameters of disease activity in comparison with patients with nonacute CNO (Table 1).

In the whole cohort at baseline, significant correlations were observed between FWB and markers of bone turnover (1CTP, BALP: $P < 0.0001$ and $< 0.0004$, respectively), but correlation with STD was not significant. BFV significantly correlated with 1CTP, BALP, and STD ($P < 0.002$, $< 0.03$, and $= 0.02$, respectively). However, only in patients with acute CNO did STD correlate with FWB and BFV ($P < 0.01$).

In addition, there were significant reductions in bone scan parameters, bone turnover markers, and STD after treatment of acute CNO (Table 1). There were also significant correlations between changes from baseline between FWB and 1CTP ($P < 0.002$), BALP ($P < 0.005$), and STD ($P < 0.02$). Similar correlations were also seen for BFV (all $P < 0.05$).

**CONCLUSIONS** — In this study, we have shown that our new quantitative bone scan parameters, FWB and BFV, significantly correlated with bone turnover markers in patients with CNO; but only BFV also correlated with STD in the whole cohort. In patients with acute CNO, we observed significant reduction in bone scan parameters, which correlated with changes in bone turnover markers and STD after treatment.

In a previous study, correlation between STD and the ratio of isotope uptake of the affected and unaffected foot was seen, but correlation between STD and the ratio of isotope uptake of affected foot and ipsilateral tibia was not significant (9). We felt that using the whole-body activity would be a better parameter as the bones in the affected leg could have increased uptake due to increased blood flow to that leg secondary to the Charcot process, which could explain why the above study did not show any difference. However, measuring FWB is independent of blood flow to the ipsilateral leg. In addition, we have shown a direct relationship between FWB and the bone-remodelling process assessed by 1CTP and BALP. Similar results for BFV were also seen, but this parameter is dependent on vascular reactivity, which could be influenced by other factors (e.g., foot infection).

STD was shown to correlate with bone scan parameters (FWB and BFV) at baseline and follow-up in acute CNO. Therefore, STD can be helpful as a bedside clinical indicator of disease activity. However, when the diagnosis is unclear, bone-scanning parameters can be used as an adjunct to diagnosis and monitoring treatment but also in patients with bilateral CNO during follow-up when STD may not be helpful.

There are some limitations to quantitative bone scanning. First, it may not be specific for the diagnosis of CNO; it is dependent on strict observance of standard reference conditions during examination. Finally, repeated bone scans would increase radiation exposure but also have cost implications.

In conclusion, our study points to the potential utility of quantitative bone scanning for diagnosis but probably more importantly for CNO activity monitoring.

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