Urological Science 27 (2016) 208–211

Contents lists available at ScienceDirect

Urological Science

journal homepage: www.urol-sci.com

Original article

The most suitable guidelines for performing bone scans in prostate cancer staging – One southern Taiwan medical center's results

Yen-Man Lu [a], Tsu-Ming Chien [a], Hung-Lung Ke [a, b], Shu-Pin Huang [a, b], Chun-Nung Huang [a, b, *]

[a] Department of Urology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan
[b] Department of Urology, School of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

ARTICLE INFO

Article history:
Received 25 March 2015
Received in revised form
17 June 2015
Accepted 18 June 2015
Available online 27 July 2015

Keywords:
bone metastasis
prostate cancer
prostate-specific antigen

ABSTRACT

Objective: The necessity of bone scans in newly diagnosed prostate cancer patients is still a matter of debate. We attempt to evaluate the validity of currently published guidelines by analyzing bone scan results in newly diagnosed prostate cancer (PCa) patients to determine the optimal staging strategies.
Materials and methods: Between January 2011 and July 2014, there were 362 consecutive newly diagnosed PCa patients at Kaohsiung Medical University Hospital, Kaohsiung, Taiwan. Bone scans were performed for all patients at initial staging. Patients positive for bone metastasis were characterized at diagnosis in terms of age, prostate-specific antigen (PSA) level, Gleason score (GS), and clinical stage. We analyzed the sensitivity and specificity of the American Urological Association (AUA) best practice policy, European Association of Urology guidelines, National Comprehensive Cancer Network guidelines, and the classification and regression tree by Briganti et al for diagnostic performance in predicting bone metastasis.
Results: A total 73 of 362 (20.2%) patients were diagnosed with bone metastasis. Patients positive for metastasis on bone scans had significantly higher PSA levels (median: 196.5 ng/mL, interquartile range: 904.3 vs. median: 18.5 ng/mL, interquartile range: 35.7; $p < 0.001$) and higher GSs (8.5 ± 1.0 vs. 7.0 ± 1.6; $p < 0.001$) than those with negative bone scan results. Pairwise comparisons in receiver operating curve analysis demonstrated that the AUA guidelines had a larger area under the curve than the other guidelines.
Conclusion: The current AUA guidelines for the recommendation of staging bone scans had better prediction and application rates than other guidelines in our patient cohort.

1. Introduction

The prevalence of prostate cancer (PCa) has been increasing in recent years, especially in Asia. Digital rectal examination (DRE) and measurement of prostate-specific antigen (PSA) levels are the most common tools for early screening of PCa. A biopsy is recommended if DRE and/or PSA test results indicate any abnormalities. Upon definitive tissue diagnosis, further treatment strategies are based on the results of cancer staging. Based on the clinical stage, Gleason score (GS), and PSA level, PCa patients can be stratified into low-, intermediate-, and high-risk groups. The initial staging workup is dependent on the risk group. For high-risk PCa patients, further treatment plans are determined based on the presence of distant metastasis. As the most frequent site of distant metastasis from PCa is bone tissue,[1] further bone scan staging is recommended by current published guidelines. Due to some well-studied limitations of bone scans, which are potentially unnecessary for low-risk patients but underused for high-risk patients,[2] the necessity of routine bone scan screening is still a matter of debate. The American Urological Association (AUA) recently recommended the avoidance of bone scans in low-risk patients as their first priority in the national Choosing Wisely program.[3] In addition, the current published guidelines are based on a Western database and previous studies have shown that almost half of the newly diagnosed PCa patients in the USA belong to the low-risk group.[4] Therefore, there has been an increase in active surveillance. However, the proportion of intermediate- and high-risk patients is still high in Asian

* Corresponding author. Department of Urology, Kaohsiung Medical University Hospital, Number 100, Tz-You First Road, Kaohsiung 807, Taiwan.
E-mail address: cnhuang.uro@gmail.com (C.-N. Huang).

http://dx.doi.org/10.1016/j.urols.2015.06.287

countries.[5] Therefore, these guidelines should be applied to Asian patients with caution.[5,6] Here, we evaluated the validity of currently published guidelines by analyzing bone scan results in newly diagnosed PCa patients to determine the optimal staging strategies.

2. Materials and methods

2.1. Patients

Between January 2011 and July 2014, we enrolled 362 consecutive newly diagnosed PCa patients at Kaohsiung Medical University Hospital, Kaohsiung, Taiwan. The present study was supervised by the Institutional Review Board of the Kaohsiung Medical University Hospital. Transrectal ultrasound-guided prostate biopsies were performed based on abnormal DRE or PSA test results. Patients receiving 5-alpha-reductase inhibitor treatment were excluded. A standard 18-gauge biopsy needle was used. There were 12 routine biopsy sites, with additional targeted biopsies for any suspicious lesions. A routine bone scan was performed as part of our conventional workup for newly diagnosed PCa patients.

2.2. Bone scintigraphy

Bone scintigraphy was performed after intravenous injection of 20 mCi (740 MBq) of technetium-99m methylene diphosphonate. Whole body imaging was performed under a large field-of-view gamma camera (Siemens, e.cam, Erlangen, Germany) coupled to a high-resolution collimator. Scans were interpreted by two independent, experienced nuclear medicine physicians. Patients with uncertain bone scan findings underwent further computed tomography or magnetic resonance imaging to confirm the final diagnosis. Patients with positive bone scan results were analyzed for PSA level at diagnosis, clinical stage, and GS.

2.3. Guidelines for bone scan recommendation

We then evaluated the sensitivity and specificity of the AUA best practice policy,[7] European Association of Urology (EAU) guidelines,[8] National Comprehensive Cancer Network (NCCN) guidelines,[9] and the classification and regression tree (CART) by Briganti et al.[10] According to AUA guidelines, patients with poorly differentiated tumors or PSA level > 20 ng/mL were recommended for bone scans.[7] EAU guidelines[8] recommended that patients with GS > 7, locally advanced disease, or PSA level > 10 ng/mL undergo staging bone scans. According to NCCN guidelines,[9] staging bone scans should be performed in patients with GS > 7, clinical stage T3/4, cT1 with PSA level > 20 ng/mL, or cT2 with PSA level > 10 ng/mL. A bone scan should be considered for patients with a GS > 7 or PSA level > 10 ng/mL with a palpable tumor (cT2/3), according to the CART by Briganti et al.[10] A receiver operating characteristics (ROC) curve analysis was used to compute area under the curve (AUC) estimates to compare the different guidelines (Figure 1).

All data are expressed as mean ± standard deviation (median with interquartile range in nonGaussian distribution data). Continuous parameters were assessed using a *t* test or Mann–Whitney–Wilcoxon test. Dichotomous variables were evaluated using a Chi-square analysis to define various patient groups according to variables that significantly correlated with positive bone metastasis findings. Statistical significance was set at $p < 0.05$. SPSS version 20.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses.

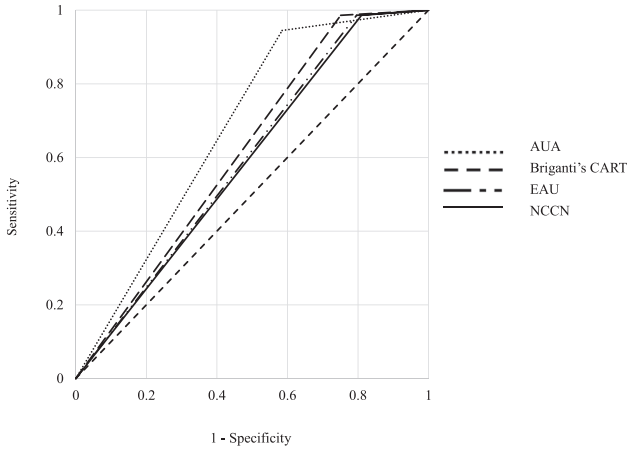

Figure 1. Receiver operating characteristic (ROC) curve analysis for different guidelines. AUA = American Urological Association; CART = classification and regression tree; EAU = European Association of Urology; NCCN = National Comprehensive Cancer Network.

3. Results

The mean patient age was 71.9 ± 8.5 years (range: 48–94 years). The mean PSA level and biopsy GS were 241.1 ± 1082.4 ng/mL and 7.3 ± 1.6, respectively. Of 362 patients, 73 (20.2%) were diagnosed with bone metastasis. Patients with positive bone scan results had a significantly higher PSA level (median: 196.5 ng/mL, interquartile range: 904.3 vs. median: 18.5 ng/mL, interquartile range: 35.7; $p < 0.001$) and a higher GS (8.5 ± 1.0 vs. 7.0 ± 1.6; $p < 0.001$) than those with negative bone scan results (Table 1). Of this subset of patients, PSA levels were ≤ 10 ng/mL in two (2.3%) patients, 10.1–20 ng/mL in four (5.2%) patients, 20.1–50 ng/mL in 12 (14.3%) patients, 50.1–100 ng/mL in 10 (24.4%) patients, and > 100 ng/mL in 45 (60.8%) patients (Figure 2). There were no bone metastases in patients who had a GS < 5. Bone metastasis was found in one (2.6%) patient with a GS of 5, in one (1.6%) patient with a GS of 6, in 13 (16.3%) patients with a GS of 7, in 15 (23.8%) patients with a GS of 8, in 35 (41.2%) patients with a GS of 9, and in eight (57.1%) patients with a GS of 10 (Figure 3).

The number of patients for whom a bone scan was considered according to each set of guidelines was as follows: 238 (65.7%) patients by AUA guidelines, 302 (83.4%) patients by EAU guidelines, 306 (84.5%) patients by NCCN guidelines, and 289 (79.8%) patients by CART by Briganti et al.[10]

The McNemar test demonstrated that there were no differences between the NCCN and EAU guidelines for bone scan recommendations. Other pairwise comparisons showed significantly different suggestions (AUA vs. Briganti, AUA vs. NCCN, AUA vs. EAU, EAU vs. Briganti, NCCN vs. Briganti; all $p < 0.001$). The sensitivity, specificity, and accuracy rate were as follows: 94.5%, 41.5%, and 52.2% for AUA guidelines, 98.6%, 20.4%, and 36.2% for EAU guidelines, 98.6%, 19.0%, and 35.1% for NCCN guidelines, 98.6%, 24.9%, and 39.8% for CART by Briganti et al,[10] respectively. The AUC were 0.630 (95% confidential index: 0.60~0.66) for AUA guidelines, 0.603 for EAU guidelines (95% confidential index: 0.57~0.63), 0.618 (95% confidential index: 0.58~0.64), and 0.604 (95% confidential index: 0.57~0.63) for CART by Briganti et al,[10] respectively. Pairwise comparisons of the ROC curves showed that the AUA guidelines had larger AUC than did the other guidelines. One patient was not recommended by any of the guidelines as requiring a bone scan, but the bone scan showed a bone metastasis result.