Opportunistic Osteoporosis Screening: Addition of Quantitative CT Bone Mineral Density Evaluation to CT Colonography

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Abstract

Purpose: For patients undergoing CT colonography (CTC), the screening presents an opportunity for concurrent osteoporosis screening, without increasing radiation exposure or the time involved for the patient, using proximal femur quantitative CT-CT x-ray absorptiometry (QCT-CTXA).

Methods: This cohort included 129 women and 112 men (mean age: 60.1 ± 8.2 years; range: 50–95 years) who underwent CTC between March 2013 and September 2014. Areal bone mineral density (BMD; g/cm^2), and resultant left femoral neck T-score, was prospectively measured on the supine CT series. QCT results were reported with the CTC. Chart review evaluated whether the patients were eligible for BMD screening according to guidelines from the US Preventive Services Task Force and the National Osteoporosis Foundation guidelines; whether they had undergone prior BMD testing; and whether QCT results changed patient management.

Results: Overall, 68.0% (164 of 241) of patients from this cohort had not previously undergone BMD screening. According to the National Osteoporosis Foundation guidelines, 44.0% (106 of 241) of patients were eligible for screening. T-scores within the osteopenic and osteoporotic range were detected in 32.3% (78 of 241) and 5.0% (12 of 241) of patients, respectively. Of these patients with low BMD, 66.7% (60 of 90) either had not previously undergone screening or were eligible for BMD testing. Reporting of QCT-CTXA T-scores altered management in 9 patients (3.7%) who had low BMD.

Conclusions: Maximizing the pre-existing value from imaging studies is crucial in the current era of health care reform. We demonstrate that colorectal and osteoporosis screening can be combined at CT examination, adding clinical and likely economic value.

Key Words: Screening, CT colonography, osteoporosis, bone mineral density

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INTRODUCTION

Osteoporosis is a common condition, affecting >10 million people in the United States, and it is associated with a lifetime fracture risk of approximately 50% in women and approximately 20% in men [1,2]. Osteoporosis-related fractures affect quality and quantity of life, with hip fractures in particular associated with high morbidity and mortality [3,4] Despite these risks, and the availability of proven treatments to reduce fractures, osteoporosis is underdiagnosed and therefore undertreated in the United States [5-7]. The reasons for underdiagnosis are multifactorial and include non-adherence to screening guidelines, with approximately one-half of female Medicare beneficiaries having never been screened. In addition, guidelines are conflicting: US Preventive Services Task Force (USPSTF) guidelines state that screening of men is of undetermined benefit, owing predominantly to an insufficiency of data and to resource costs [7-9].

Abdominal CT scans obtained for other indications can be used in an opportunistic fashion to screen for osteoporosis, without substantial additional cost [10-12]. The most pertinent measurement for opportunistic screening is bone mineral density (BMD) at the femoral neck, because it can be used in conjunction with the World Health Organization (WHO) Fracture Risk

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Assessment Tool (FRAX™), to estimate fracture risk and guide treatment. Previous work has documented that quantitative CT-CT x-ray absorptiometry (QCT-CTXA) at the time of CT colonography (CTC) is equivalent to standard dual x-ray absorptiometry (DXA) in identifying low BMD [13].

Given the significant overlap of the patient population undergoing CTC, with those at risk for low BMD, adding CTXA evaluation to CTC could increase identification of patients who are at increased fracture risk, with minimal additional cost. To this end, we have added femoral neck CTXA BMD evaluation to CTC screening in our clinical practice. The purpose of this study was to evaluate the clinical impact of this practice, including the detection of patients with previously unrecognized low BMD. A secondary endpoint was determining whether this identification of low BMD had an effect on patient management.

METHODS

Patient Cohort

The University of Wisconsin Health Sciences Institutional Review Board approved this HIPAA-compliant retrospective study. The need for obtaining signed informed consent was waived for this retrospective analysis. Beginning in March 2013, all patients undergoing CTC, at 2 (of 7) clinical sites with a phantom available, underwent CTXA BMD assessment as part of their extracolonic evaluation. All patients aged >50 years who had clinical CTXA BMD assessment at the time of CTC, between March 2013 and September 2014, were identified. Patients who were referred from outside the institution were excluded from analysis, owing to the limited information available in the electronic medical record. The final study cohort consisted of 241 patients (129 women, 112 men), ranging in age from 50 to 95 years, with a mean (standard deviation [SD]) age of 60.1 (8.2) years at the time of CTC.

CT Acquisition

Multidetector CT (MDCT) scanning for standard CTC screening was performed using the low-dose technique. Immediately before MDCT imaging, the colon is distended with carbon dioxide, using a continuous, automated, low-pressure delivery system. Noncontrast supine and prone MDCT acquisitions of the abdomen and pelvis were obtained using 16- or 64-detector scanners (GE Healthcare, Waukesha, Wisconsin), with 1.25-mm collimation, a 120 kVp, and a low-dose, modulated, tube-current technique (noise index: 50 mA; range: 30-300 mA). Images are reconstructed using a standard soft-tissue algorithm, with 1.25-mm slice thickness at 1-mm intervals. For extracolonic evaluation (including BMD), the supine series is reconstructed as well, with a 5-mm slice thickness at 3-mm intervals. Each patient had a QCT calibration phantom on the CT table, centered at the hips (Fig. 1), to allow Hounsfield-unit calibration for BMD measurement.

CT X-Ray Absorptiometry Image Analysis

The procedure for QCT hip BMD acquisition has been described previously [13]. Briefly, CTC volume images were sampled using SlicePick software (Mindways Software, Inc, Austin, Texas), to produce a simulated projection anteroposterior image, to locate the femoral head and lesser trochanter, in the same way as with a localizer.

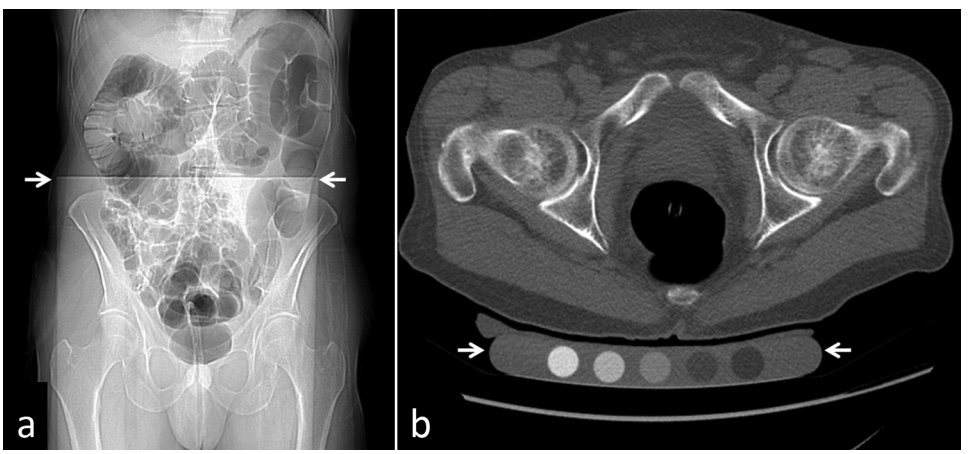

Fig 1. (a) CT scout image depicting phantom (top of phantom at *white arrows*) underneath patient. (b) Axial CT image depicting phantom (between *white arrows*) underneath patient.

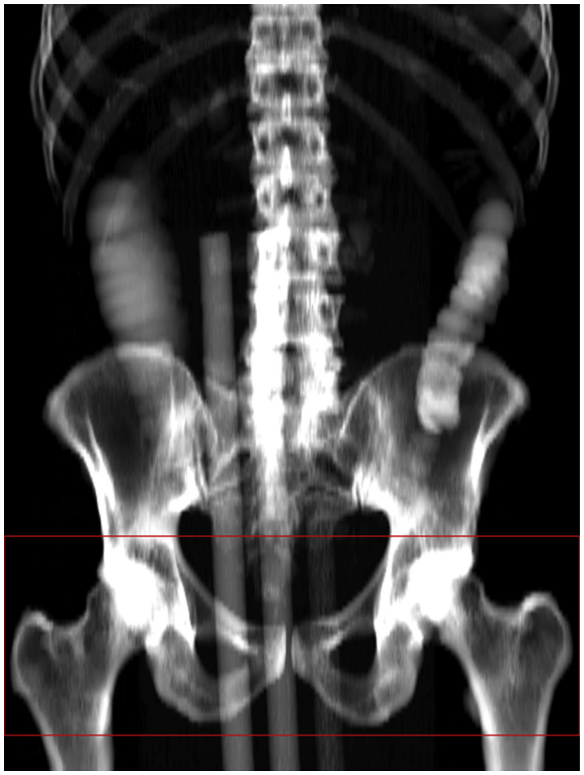

Fig 2. Simulated projection image used for localization. Localization region is defined between the *red lines*.

A contiguous set of slices covering this region was chosen for BMD analysis (Fig. 2).

The QCT-derived areal BMD was determined using CTXA Hip software, version 5.0 (Mindways Software, Inc, Austin, Texas), according to manufacturer directions. This process has been described in detail elsewhere [14]. Regions of interest (ROIs) similar to those used in DXA devices (Hologic Inc, Bedford, Massachusetts) for proximal femur analysis (total hip, femoral neck, intertrochanter, and trochanter) were identified automatically, by the software, on the projected image (Fig. 3). The left hip was chosen for analysis (n = 240), unless the femoral shaft was found to be inadequately imaged for the entire lesser trochanter to be analyzed, in which case the right hip was chosen (n = 1).

The automatically identified ROIs were visually checked by dedicated CT technologists, to verify that the lower extent of the intertrochanteric ROI was set at the lower junction of the lesser trochanter and the femoral shaft, and that the femoral neck axis and femoral neck ROI position were appropriate. The ROIs were adjusted by the technologists as required, with verification of the final selection by the physician interpreting the CTC, to determine need for repeat analysis. Final resultant areal BMD (g/cm^2) data were stored in the QCT Pro database (Mindways Software, Inc), for export as text files. Femoral neck T-scores were calculated using the CTXA (Mindways Software Inc) reference database. The results were prospectively reported, along with colorectal and other extracolonic findings, such as abdominal aortic aneurysm screening.

Chart Review

Patient electronic medical records were reviewed by a single investigator (TZ), at a median of 9 months (range: 2-19 months) after reporting of the T-score from CTXA. The date of prior BMD evaluation, eligibility for screening according to USPSTF or National Osteoporosis Foundation guidelines [8,9], and management decisions made based on BMD results were recorded.

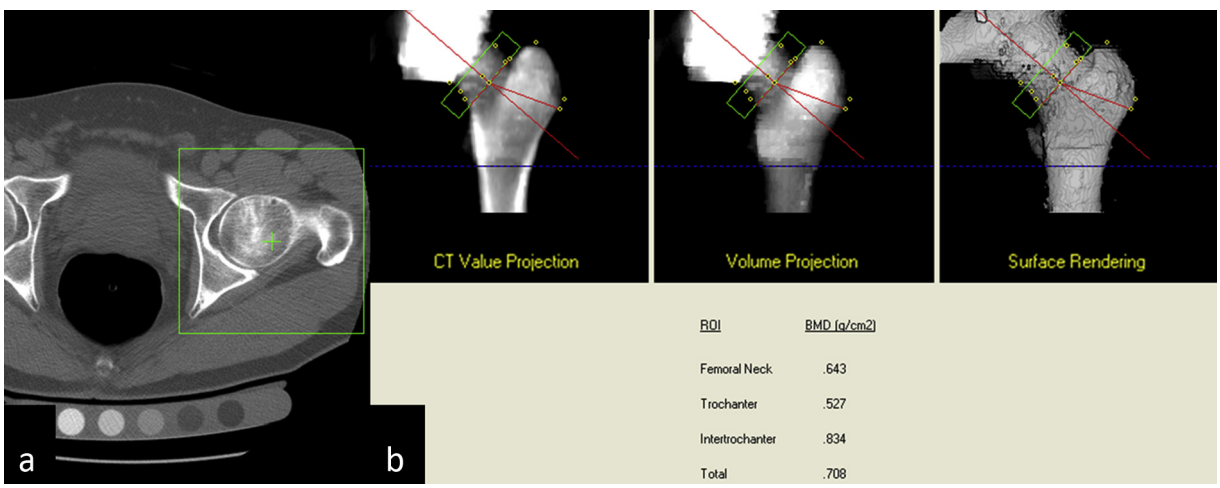

Fig 3. (a) The *green box* is utilized to select the hip for automated analysis. (b) *Green boxes* define the femoral neck for BMD determination. BMD = bone mineral density; ROI = region of interest.

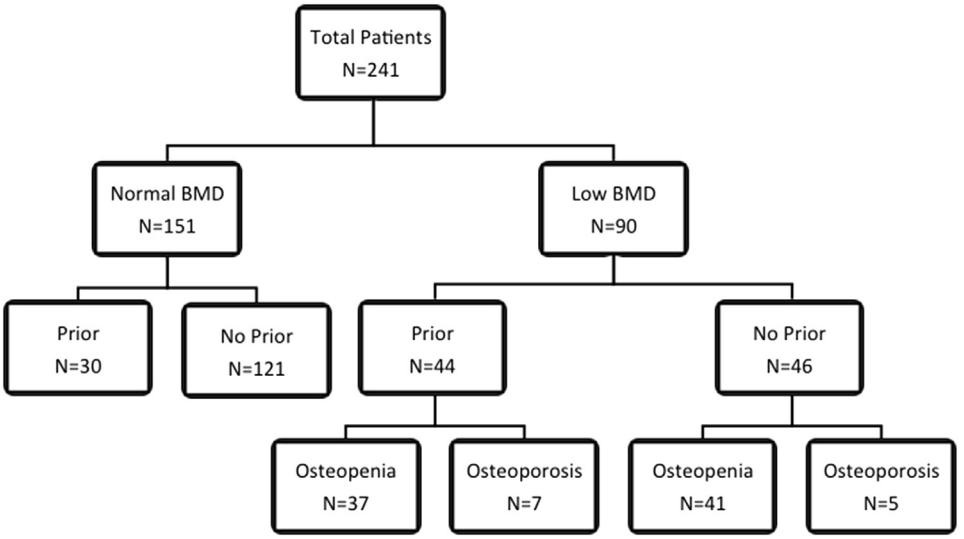

Fig 4. Patient cohort breakdown: "Low BMD" patients are those who are osteopenic (defined as T-score ≤ -1.0) or osteoporotic (defined as T-score ≤ -2.5).

RESULTS

Prevalence of Low BMD

The patient population is outlined in Figure 4. Of the study cohort, 37.3% (90 of 241) had low BMD, with 32.3% (78 of 241) classified as osteopenic, and 5.0% (12 of 241) as osteoporotic. Female patients had low BMD 48.8% (63 of 129) of the time, with 43.4% (56 of 129) classified as osteopenic, and 5.4% (7 of 129) as osteoporotic. For male patients, 24.1% (27 of 112) had low BMD, with 19.6% (22 of 112) classified as osteopenic, and 4.5% (5 of 112) as osteoporotic. For patients aged >65 years, 50.9% (28 of 55) had low BMD, with 41.8% (23 of 55) osteopenic, and 9.1% (5 of 55) osteoporotic. Patients aged ≤64 years had low BMD 33.3% (62 of 186) of the time, with 29.6% (55 of 186) osteopenic, and 3.8% (7 of 186) osteoporotic.

Eligibility for Screening

According to USPSTF guidelines, 39.8% (96 of 241) of patients were eligible for screening, which was 74.4% (96 of 129) of the female cohort. Criteria for eligibility included: being female and being aged >65 years, for 29 patients; and having an estimated risk, determined using the WHO FRAX™, greater than that of a 65-year-old woman (estimated 10-year risk: 9.3%), for 67 patients. When National Osteoporosis Foundation guidelines were used, which advocate screening of men aged ≥70 years, an additional 10 men were eligible for screening, yielding 44.0% (106 of 241) of the population, and 8.9% (10 of 112) of the male cohort. Of the patients eligible for screening, 32.1% (34 of 106) had not previously undergone screening.

Detection of Low BMD

Of the patients with low BMD detected at CTC, 48.9% (44 of 90) had not previously undergone screening. An additional 14 patients were eligible for repeat screening. The reported low BMD resulted in: 1 patient starting bisphosphonate treatment; 1 patient beginning calcium and vitamin-D supplementation; and 4 patients having follow-up DXA evaluation. An additional 3 patients with normal BMD were eligible for follow-up DXA evaluation, which was cancelled because of the CTXA evaluation. In total, patient management was altered in 9 patients (3.7%), owing to the opportunistic BMD evaluation at the time of CTC.

Case Examples

A 55-year-old man who had undergone a negative CTC in 2008 has a 5-year follow-up CTC in 2013. The patient is a smoker, but healthy, and therefore would not meet current guidelines for BMD screening. CTXA was performed as an add-on to CTC, with a resultant T-score of −1.9, in the osteopenic range. The patient began calcium and vitamin-D supplementation and received a nutrition consultation.

A 59-year-old healthy woman who underwent CTC in 2006, owing to an incomplete colonoscopy, was overdue for repeat CTC in 2014. She had undergone DXA, in 2011, which demonstrated osteopenia, with a left femoral neck T-score of −2.4. No specific plan for BMD

re-evaluation was noted in the chart. CTXA was performed as an add-on to CTC, with a resultant T-score of −2.7. Due to the diagnosis of osteoporosis, alendronate therapy was initiated, with follow-up DXA scheduled for 1 year later.

DISCUSSION

CTXA is a useful addition to CTC as it allows for simultaneous BMD screening in appropriate patients without an additional study and in addition can identify those with low BMD who do not meet current screening guidelines. The addition of CTXA to a CTC examination requires minimal change to the workflow, because the processing required can be efficiently performed by CT technologists after a short training period, during which the interpreting physician performs visual quality control. The CTXA results can be reported by inputting the BMD, the T-score, and the WHO classification into a template. In addition, this study suggests that CTXA can alter patient management.

Increasing rates of BMD screening fills a clinical need: Previous studies have demonstrated adherence rates to screening guidelines of 12% to 56% across groups, and 19% to 97% among individual physicians [15,16]. Although providers and patients who adhere to screening recommendations for colon cancer and polyps might be presumed to adhere to those for osteoporosis, 32.1% of the patients for whom BMD screening was indicated in this study had not undergone screening. In addition, this low-cost addition to CTC could potentially expand BMD screening guidelines, although further research into the cost−benefit balance is needed first. Addition of BMD evaluation in this cohort did help identify patients with low BMD who would have otherwise gone undetected: Approximately one-half of these patients had never been screened.

The greatest potential of this study is to improve osteoporosis detection in men. The most recent USPSTF guidelines give an "I" rating to osteoporosis screening in men, meaning the evidence is insufficient to support screening. In the rationale for this rating, the USPSTF concedes that BMD testing in men could prevent a substantial fracture burden, whereas opportunity cost is cited as the only harm. This opportunity cost is determined by the substantial number of additional DXA scanners that would be required to screen the male population who would benefit [8]. The addition of CTXA to CTC stands to decrease this opportunity cost of screening males, many of whom would otherwise go unscreened. The cost-effectiveness of this approach is beyond the scope of this manuscript, but is a potential area for future investigation.

Bone mineral density screening is part of a growing list of extracolonic screening opportunities available at the time of CTC. The detection of abdominal aortic aneurysms, as well as extracolonic cancers, is a known benefit of CTC [17,18], and is a cost-effective use of resources [19]. Other opportunities for "value added" at CTC include: screening for nonalcoholic fatty liver disease, via liver attenuation, measurement of visceral fat, and quantification of abdominal aortic calcification [20-22].

Measuring lumbar spine attenuation has been proposed as another way to screen for osteoporosis at both CTC and routine CT [10,11]. However, this method requires additional time, without providing additional economic incentive, which could limit its adoption. Comparatively, CTXA is a postprocessing technique that requires only dedicated software and minimal technologist and radiologist time; it is eligible for an add-on charge as well, which could increase its adoption.

An area of future investigation is to evaluate the effect of offering CTXA with CT examinations performed for any indication on adherence to BMD screening guidelines. Awareness of the problem of osteoporosis would need to increase within the abdominal radiology community to make this offering effective. The scans that allow coexistent screening are predominantly those of the abdomen and pelvis; yet, previous work [23] has demonstrated that vertebral body compression fractures are missed in up to 84% of cases on these examinations, if sagittal reconstruction is not specifically reviewed.

In addition, although noncontrast examinations have shown a correlation with DXA, and therefore would be reasonable to use for screening [11], data are still needed to determine whether the same is true for contrast-enhanced studies. Early work [24] has demonstrated that CT enterography examinations with biomechanical image analysis can predict low BMD in patients with inflammatory bowel disease. Further work is needed to validate CTXA as a screening modality with contrast-enhanced CT. Recently, a newer version of the QCT software (Mindways Software, Inc) that does not require prospective placement of the phantom under the patient was approved by the FDA, potentially allowing for wider adoption of the opportunistic CT screening approach.

This study has several limitations, most notably that the population was limited to those undergoing CTC. However, this patient population overlaps extensively with patients for whom screening is recommended, and the radiologists performing CTC are already of the screening mindset, making this an appropriate group of physicians for early adoption. An additional limitation is

that the study is retrospective, so follow-up action on BMD reporting was limited to chart review. Action relating to BMD reporting may have been taken outside our health care system, and therefore not documented in our electronic medical record.

A further limitation is that we did not actively advertise availability of this screening to referring providers. This limitation may account for the low rate of altered patient management despite the high prevalence of abnormal results. A prospective trial that involved direct follow-up with patients would allow for a more accurate evaluation of the effects of adding CTXA to CTC. Finally, given the short follow-up time, no evaluation can be made of fracture rates for those screened in this fashion. Again, a prospective trial comparing those who undergo CTXA at CTC with those who undergo either optical colonoscopy or CTC without CTXA would allow for a more robust evaluation.

In summary, adding CTXA to CTC adds value by increasing the number of patients screened who are not within current screening guidelines, and detecting those with osteoporosis. Intervention within this patient population could reduce the rate of fractures and the associated socioeconomic impact. In addition, normal BMD evaluation results at CTC could reduce the need for DXA screening. This opportunistic screening is performed with minimal cost and could replace DXA for initial screening evaluation in selected populations.

TAKE-HOME POINTS

- Patients with osteoporosis are currently underscreened and underdiagnosed.
- CTXA BMD evaluation is an easy addition to a CTC program.
- Opportunistic BMD screening at CT can increase screening rates and identify low BMD in those not otherwise eligible for screening.

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