Unnecessary Imaging for the Staging of Low-Risk Prostate Cancer Is Common

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OBJECTIVE
International evidence-based best practice guidelines discourage routine imaging for staging purposes in low-risk patients with newly diagnosed prostate cancer. We quantified the rate of overuse of preoperative imaging procedures in a referral cohort of low-risk patients.

MATERIAL AND METHODS
An institutional database comprised of all patients undergoing robotic-assisted laparoscopic prostatectomy was queried for “low-risk” patients between May 2005 and January 2010. “Low-risk” was defined by the most inclusive criteria for imaging recommendations: prostate-specific antigen ≤10 ng/mL and Gleason score ≤6. We defined staging imaging as a bone scan, computed tomography (CT) of the pelvis or endorectal magnetic resonance imaging performed after the diagnosis of prostate cancer and before prostatectomy for the indication of “prostate cancer.” Six-hundred seventy-seven patients were identified as having low-risk disease and comprised our study population.

RESULTS
Of the 677 patients identified as low risk, 328 (48%) underwent at least one preoperative imaging procedure despite the guideline recommendations. Two-hundred two of 677 (30%) patients were administered at least 2 of the 3 modalities, and 18/677 (3%) patients received all 3 imaging examinations before prostatectomy. Suspicious results from the CT (7/265%, 2.7%) or bone scan (21/241%, 8.7%) resulted in 27 patients undergoing additional radiographic imaging, none of which resulted in suspicious lesions requiring intervention or biopsy.

CONCLUSIONS
Despite international evidence-based guidelines for the staging of newly diagnosed prostate cancer patients, many urologists continue to refer low-risk patients for unnecessary imaging studies. This may place the patient at increased risk from radiation or contrast exposure and places an unnecessary financial burden on the patient and health care system.

More than 90% of prostate cancer patients are diagnosed with clinically localized disease, making the routine use of radiographic staging largely unnecessary. With the exception of the small percentage of patients who present with very high prostate-specific antigen (PSA) (i.e., >20 ng/mL) or Gleason scores ≥8, the rates of positivity of cross-sectional or radionuclide imaging is exceptionally low. Further, the low positive predictive value of the examinations within this clinical cohort rarely result in clinically meaningful diagnoses, more often leading to additional unnecessary tests and worry after false-positive or suspicious results. Not only do these examinations subject the patient to increased financial and time burdens, but the exposure to excess radiation and contrast agents is not without its own inherent risks.

Multiple international evidence-based guidelines from societies involved in the treatment of men with prostate cancer, including the American Urological Association (AUA), European Association of Urology, National Cancer Center Network, and American College of Radiology (ACR), discourage routine imaging of “low-risk” patients. Although the definition of “low-risk” differs slightly among these groups (Table 1), even the most inclusive guideline (the ACR) does not recommend imaging patients with a biopsy Gleason sum of ≤6 and a PSA ≤10 ng/mL.

Despite these recommendations, we have noticed that many of our low-risk patients continue to receive preoperative staging studies before referral to our institution. To quantify the overuse of preoperative imaging, we reviewed the records of all patients undergoing robotic-assisted laparoscopic prostatectomy (RALP) in whom staging imaging was deemed unnecessary by all guidelines released since 2000. We assessed the results of the imaging, as well as additional tests performed to further evaluate suspicious findings on initial staging, and correlated these results with histopathologic findings. In addition, we calculated the financial costs associated with these imaging procedures.
MATERIALS AND METHODS

We queried an institutional review board–approved database comprised of all patients undergoing RALP between May 2005 and January 2010 for low-risk patients, defined as those with a PSA \( \leq 10 \text{ ng/mL} \) and biopsy Gleason sum \( \leq 6 \). These criteria represent those who would not qualify for the most inclusive criteria for staging recommendations, those established by the ACR. We excluded any patients who received imaging studies ordered as part of an external research protocol, or for clinical reasons other than cancer staging. International patients who received preoperative workup outside the United States were excluded from our analysis. Six-hundred seventy-seven patients met these criteria for low-risk disease and comprised our study population.

Patient records were reviewed to identify the rates of computed tomography (CT), bone scans, and endorectal-coil MRI (erMRI) ordered for the purpose of staging after the diagnosis of prostate cancer and before surgical intervention for the indication of “prostate cancer” (ICD9 185.0). The ordering physician was classified as either the referring urologist or the primary surgeon. Original radiologic reports were obtained and reclassified in a blinded fashion as negative, suspicious, or positive. We further noted any additional imaging or procedures that patients underwent to investigate suspicious findings on the initial imaging evaluation.

In addition to the RALP, all patients underwent bilateral pelvic lymphadenectomy of the obturator fossa, and pathologic outcomes were recorded. Preoperative and pathologic characteristics of patients undergoing RALP were calculated using means for continuous variables and proportions for categorical variables. These characteristics were calculated separately for those who underwent imaging and those who did not. Significance of differences was defined as \( P < .05 \) and was calculated using t-tests for continuous variables and chi-square tests for categorical variables. All tests were two-sided. Analyses were conducted using SPSS version 17.0 (SPSS, Inc., Chicago, IL).

RESULTS

From the 677 patients identified as low risk on preoperative evaluation, 328 (48%) patients underwent at least one preoperative imaging procedure (Fig. 1). One-hundred eight of 677 patients received only a single imaging examination, of whom 53 patients were evaluated by CT, 27 by erMRI, and 28 by bone scan. Two-hundred two patients were administered 2 of the 3 modalities, most commonly CT and bone scan in 56% (187/328). Eighteen patients received all 3 imaging examinations before prostatectomy. Of the 264 CT examinations ordered, 254 (96%) were read as negative (Fig. 2). Pelvic lymphadenopathy was radiographically diagnosed in 7 patients, all of whom were N0 on final pathology. Among the 241 bone scans performed, 220 (91%) were interpreted as negative and 21 (8.7%) were read as suspicious for bone metastases. Referring urologists ordered 254/264 (96%)
of the CT examinations and 236/241 (98%) of bone scans.

Suspicious results from the CT or bone scan resulted in 27 patients undergoing additional radiographic imaging. Ten patients underwent an additional CT of the chest, 3 patients received an MRI of the spine, and 2 patients had an additional CT of the abdomen and pelvis. Other imaging studies included an MRI imaging of the adrenals, positron emission tomography scan, MRI of the abdomen, abdominal ultrasound, CT urogram, head CT, and plain radiographic evaluation of the shoulders, head, ribs, leg, or sternum.

Preoperative and histopathologic characteristics were generally favorable among patients with low-risk disease (Table 2). Most baseline characteristics were similar between those who were imaged and those who were not, with the exception of clinical stage. The low-risk patients undergoing imaging were more likely to have a palpable nodule on digital rectal examination, as 13% of the imaged patients were clinical stage T2(a), compared with 6% of those who were not imaged ($P = .005$). On final pathology, 94% (635/677) of patients in the low-risk cohort had organ-confined disease. Extraprostatic extension and seminal vesicle invasion were present in 44/677 (6%) and 3/677 (0.4%) patients, respectively. No patients had positive lymph nodes on pathologic evaluation. There were no differences in the proportions of pathologic stage or grade between those who were imaged and those who were not. In addition, there were no differences in the rates of positive surgical margins and biochemical recurrence between patients who were imaged and those who were not. When stratified by the type of imaging examination performed, there were no significant differences between the groups in terms of preoperative or histopathologic characteristics.

**COMMENT**

The goal of imaging prostate cancer patients preoperatively is to detect occult locoregionally advanced or distant metastatic disease that would alter the primary treatment plan. To recommend routine staging, 3 requirements must be met. First, a positive finding must affect treatment decisions. Second, there must be a significant prevalence of occult advanced disease in the population to be staged to make routine screening worthwhile. Finally, the imaging test must be sensitive enough to reliably detect occult disease. In the patient with screen-detected, clinically localized prostate cancer, it is rare that these requirements are met; indeed, it is common that all 3 of these requirements are absent.

To help physicians sort through the data regarding these issues and decide which patients should undergo staging, international evidenced-based guidelines have been established from all major societies involved in the treatment of men with prostate cancer (Table 1). Although not identical, all of the guidelines suggest that patients diagnosed with very-low-risk prostate cancer do not need to undergo imaging examinations. The recommendations proposed by the ACR have the most inclusive guidelines for the use of imaging studies to stage newly diagnosed prostate cancer ($\text{PSA} > 10 \text{ ng/mL}$ and Gleason score $> 6$) and were thus chosen to be our definition for inclusion in our study.$^8$

We found that nearly half (48%, 328/677) of our low-risk patients underwent some form of imaging that was not recommended by evidenced-based guidelines. Suspicious or positive findings resulted in 27 patients

<table>
<thead>
<tr>
<th>Table 2. Preoperative and histopathologic characteristics</th>
<th>All Low-risk Patients (PSA &lt; 10 and Gleason 6)</th>
<th>Imaged?</th>
<th>No</th>
<th>Yes</th>
<th>P Value</th>
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<tr>
<td>Number of patients</td>
<td>677</td>
<td></td>
<td>349</td>
<td>328</td>
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<tr>
<td>Age, mean</td>
<td>58.2</td>
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<td>PSA, mean</td>
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<td>4.74</td>
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<td>Clinical T1c, %</td>
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<td>94</td>
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<td>Clinical T2a, %</td>
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<td>5.8</td>
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<td>Prostate weight, mean (g)</td>
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<td>51.8</td>
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<td>pT2</td>
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<td>pT3/4</td>
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<td>3 + 4 = 7</td>
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<td>44</td>
<td>52</td>
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<tr>
<td>4 + 3 = 7</td>
<td>4.9</td>
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<td>8–10</td>
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<td>Extracapsular extension, %</td>
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<td>5.6</td>
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<td>Seminal vesicle invasion, %</td>
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<td>Focal (&lt;2 mm)</td>
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<td>3.5</td>
<td>3.4</td>
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<td>Biochemical recurrence, %</td>
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<td>.50</td>
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<td>Median follow-up, mo</td>
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<td>16.5</td>
<td>12.4</td>
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</table>

Statistical test used: t-tests for continuous variables and chi-square tests for categorical variables.
undergoing 29 additional radiographic tests to further evaluate the suspicious findings. None of these examinations demonstrated metastases or intervention-changing diagnoses.

Presumably, the bone scans were ordered to assess for skeletal metastases. Evidence of distant metastasis would likely impact our decision to recommend patients for prostatectomy, but the prevalence of metastasis in a low-risk group of patients is extremely low and the bone scan is not sensitive enough to detect micrometastases. A meta-analysis of 23 trials found that only 2.3% of patients with a PSA <10 ng/mL at diagnosis had a positive bone scan.4 None of the patients in our study had skeletal metastatic disease, although 8.7% of the bone scans were positive and necessitated further imaging.

CT is often used to evaluate for pelvic lymphadenopathy, because some urologists will forgo local treatment in favor of systemic therapy in patients with documented nodal metastasis. However, similar to the bone scan, the CT lacks sensitivity to accurately make this diagnosis. The prevalence of detectable lymphadenopathy in low-risk patients is estimated to be <5%, with an even lower incidence of true nodal metastasis.5,10 In the same meta-analysis discussed previously, 5 studies found that CT accurately identified lymphadenopathy in zero of 1290 patients with a PSA <20 ng/mL.4 In fact, the likelihood of nodal metastases is so low in our study population that the American Urological Association PSA, Best Practice Statement suggests that pathologic staging by lymphadenectomy is not necessary.6 Even if lymphadenopathy were accurately detected, it might not affect treatment decisions. Because some evidence exists to suggest that patients with node-positive disease achieve a survival benefit by lymphadenectomy,11,12 we do not consider a CT finding of lymphadenopathy to be a contraindication for prostatectomy.

The overuse of imaging examinations may be harmful to patients. A recent study by Smith-Bindman et al discovered that the median effective dose of multiphase abdomen-pelvis CT scan is 32 mSv. At that dose, the authors concluded that 1 in every 660 60-year-old men undergoing a multiphase abdomen-pelvis CT scan will develop cancer from the procedure.13 According to the Life Span Study cohort of atomic bomb survivors, exposure to 32 mSv significantly increases the relative risk for developing cancer.14 In addition to the radiation from the initial imaging tests, suspicious findings on original studies led 27 patients to incur the additional radiation exposure of follow-up studies, all of which were ultimately negative. Risks of contrast exposure, specifically contrast-induced nephropathy and nephrogenic systemic fibrosis, must also be considered.15,16

Previous studies have examined the usage rate of various imaging modalities in patients diagnosed with prostate cancer. A survey of 1500 urologists in 1997 revealed that 52% of respondents stated that they ordered bone scans in all prostate cancer cases and 29% ordered CT scans regardless of PSA values.17 In an analysis of the CaPSURE database, Cooperberg et al reported that after 1997%, 23% of low-risk prostate cancer patients received some form of imaging staging test.18 Most recently, a study examining the use of imaging in Medicare patients with cancer revealed that the rate of imaging among prostate cancer patients increased every year from 1999 to 2006. The annualized rate of increases over this time for CT, MRI, and nuclear medicine studies was 4.6%, 6.2%, and 2.5%, respectively.19 Although this was not stratified by risk group, the contemporaneous downward stage migration of prostate cancer suggests declining utility of these studies in the population as a whole.

This superfluous imaging also has serious economic implications. For a CT scan of the abdomen and pelvis with and without contrast, a radionuclide bone scan and an erMRI, our institution charges $1480, $512, and $2500, respectively. Medicare reimburses $976.98, $299.01, and $823.32, respectively.20 Thus, the 328 patients who underwent imaging examinations before prostatectomy resulted in an excess charge of $644,392. To put this in perspective, the Medicare surgeons’ fee for a RALP and the global follow-up is $1995.45. The surgeon’s treatment of the 328 patients would thus have been reimbursed a total of $654,507, nearly an identical amount to that spent on unnecessary imaging. Extrapolating our findings to the country as a whole, it is clear that such overimaging results in millions of wasted dollars.

The focus on the cost-sensitive incorporation of evidence-based medicine has never been more acute. Considering that the evidenced-based guidelines are widely distributed and accepted, it is useful to consider the possible reasons for such overuse. One possibility for the high rate of overimaging is that urologists order diagnostic tests out of clinical habit rather than attention to current guidelines and recommendations. Perhaps the subtle differences between imaging recommendations may confuse physicians about who should receive staging imaging. An argument can be made that the numerous guidelines for prostate cancer have resulted in a certain gray area of staging recommendations for a “medium-risk” patient. However, all guidelines have identified a subset of low-risk patients in whom imaging studies are not required. We specifically designed this study to avoid patients in the gray zone, focusing instead on patients who were universally classified as low risk, in whom no disagreement over recommendations exists.

Perhaps the persistent overuse of imaging is because physicians are practicing defensive medicine. Unfortunately, there is no searchable database of malpractice claims brought against physicians to assess whether any urologists have been successfully sued for failure to image such patients. In our study, 96% of CT examinations and 98% of bone scans were ordered by the referring urologist. However, there was a small percentage of patients in whom we ordered the examinations. We thus acknowledge that other factors exist that may encourage a urol-
ogist to order imaging tests, because we were motivated to order unnecessary imaging ourselves. One such factor may be the presence of a palpable nodule, because more patients with clinical T2a disease underwent imaging, although this only represented 13% of the imaged cohort. Clinicians may also have a financial incentive to refer this group of low-risk patients for diagnostic testing, because some urologists have office-based CT scanners or ownership interests in local imaging centers. Finally, as patients become better educated and involved in their own care, it is possible that they are inquiring about the use of various imaging techniques and demanding them. Discussing the abundance of information about prostate cancer and helping patients navigate the numerous staging options is often a lengthy, time-consuming conversation. It may be easier for a physician to simply order a test to mollify a patient than spend the necessary time educating him about why certain tests are unnecessary.

Our study has several limitations. It is a single-institution, retrospective review of referred patients, with much of the data derived from outside institutions before referral. It is possible that some low-risk patients imaged by their primary urologist may have been diagnosed with metastatic disease and not referred. As such, we do not know the true “denominator” of our study, although historical data would suggest that the frequency of this outcome is exceptionally low. The practice and imaging patterns in our referral base may not be generalizable to other communities. Indeed, previous studies have identified the rates of routine imaging in our area as the highest in the country.21 In addition, because all of our patients were referred externally for surgical care, it is unclear whether our patients were treated differently than those managed locally or referred for another treatment modality.

A recent editorial in the New England Journal of Medicine discussed the need for a physician-directed approach to health care cost savings. For each medical specialty, it proposed creating a “Top Five” list of expensive diagnostic tests or treatments commonly ordered that have been shown by current evidence not to provide meaningful benefit to a certain subset of patients.22 As illustrated by our study, the current imaging practices in patients diagnosed with low-risk prostate cancer could certainly be on this list for urology.

CONCLUSIONS

Despite the prevalence of international evidenced-based imaging guidelines for radiographic staging of newly diagnosed prostate cancer, many urologists continue to refer low-risk prostate cancer patients for unnecessary imaging studies. Forty-eight percent of low-risk patients in our referral-based practice received staging evaluations with imaging procedures deemed unnecessary by all clinical practice guidelines. This practice places unnecessary financial burdens and possible health risks on both the patient and health care system.

References