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Quantifying downstream impact of inappropriate staging imaging in a cohort of veterans with low- and intermediate-risk incident prostate cancer

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Abstract

Introduction: According to current National Comprehensive Cancer Network guidelines, routine imagining for staging low-risk prostate cancer is not recommended. However, extensive overuse of guideline-discordant imaging continues to persist. Incidental findings are common on imaging and little is known about the optimal management. Rates of incidental findings vs. false positive diagnosis from inappropriate imaging are poorly understood and have yet to be quantified for low- and intermediate-risk prostate cancer patients.

Objective: To determine the frequency of positive radiologic findings in patients with low- and intermediate-risk prostate cancer during initial staging at VA New York Harbor Healthcare System.

Methods: We retrospectively reviewed all low- and intermediate-risk prostate cancer patients' medical records from the VA New York Harbor Healthcare System for diagnosis from 2005 to 2015. We reviewed each individual's prebiopsy prostate specific antigen (PSA), Gleason score, and clinical stage. We also determined if imaging obtained yielded a false positive, incidental finding, or if metastatic disease occurred within the 6 months following initial diagnosis.

Results: There were 414 men, who were classified as low- to intermediate-risk prostate cancer and underwent inappropriate staging imaging of 4,306 men diagnosed with prostate cancer. Of these 414 men, 178 (43%) had additional follow-up imaging for positive findings. We calculated an incidental finding rate of 10% and a false positive rate of 38% for patients. Five (1%) patients had metastatic disease.

Conclusion: Despite guideline recommendations, imaging overuse remains an issue for low-intermediate-risk prostate cancer patients. The false positive rate found in this analysis is alarmingly high at 38%. This use of scans is burdensome to the healthcare system and patient. This study highlights the frequency of inappropriate imaging and its negative consequences.

Keywords: Prostate cancer; Staging imaging; False positives; Incidental findings

1. Introduction

Prostate cancer is the most commonly diagnosed solid organ malignancy in men in the United States. Since the advent of prostate specific antigen (PSA) screening and subsequent stage migration, the overwhelming majority of men with incident prostate cancer present with localized disease [1,2]. This trend has made obsolete the routine use of

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advanced imaging to stage all incident prostate cancer [3,4]. Instead, multiple professional societies have published clear guidelines to identify those patients who are at high risk for metastatic disease and thus, need imaging during an initial staging work up, with the American Society of Clinical Oncology identifying imaging for those at low risk as a top 5 opportunity to reduce cost and improve care [5–7]. Despite these recommendations, the use of guideline-discordant imaging among men with low- and intermediate-risk prostate cancer remains high in the United States [8–10].

Guideline-discordant computed tomography (CT) scans, magnetic resonance imaging (MRI), and whole-body bone scans (BS) have repercussions. Incidental findings or incidentalomas are common on imaging, but little is known about their frequency or significance [11]. False positives on imaging tests promote subsequent follow-up imaging and place patients at risk for unnecessary medical testing and radiation exposure. Rates of incidental findings and false positive diagnoses downstream from an initial inappropriate imaging study are poorly understood and have yet to be quantified for low- and intermediate-risk prostate cancer patients.

We sought to determine the frequency of positive staging imaging findings among patients with newly diagnosed low- and intermediate-risk prostate cancer who underwent guideline-discordant imaging during initial staging workup. To do this, we obtained data from the national Veterans Affairs (VA) database and then performed retrospective chart review at our local institution. Our findings will generate improved understanding of the downstream imaging resulting from inappropriate prostate cancer staging. The data may ultimately serve as critical inputs to a cost-effectiveness model, which would determine costs resulting from positive tests. The results of this study will be of great interest to individual decision makers, both patients and physicians, and to policy makers seeking to improve the value of healthcare.

2. Materials and methods

After Institutional Review Board (IRB) approval was obtained, we performed a retrospective chart review of men with incident prostate cancer at the VA New York Harbor Healthcare System. Cohort members were identified using the VA Corporate Data Warehouse (CDW), in which patient information on cancer diagnoses, staging, treatment, and outcome are maintained in a HIPAA-compliant and secure archive.

Inclusion criteria for the retrospective cohort were all low- and intermediate-risk prostate cancer patients diagnosed in the years 2005 to 2015 within the VA's New York Harbor Healthcare System who had at least 1 guideline-discordant imaging test (CT, BS, or MRI) during their initial staging workup (within 6 months of initial diagnosis). Patient-risk level was determined based on National Comprehensive Cancer Network prostate cancer guidelines corresponding to the year of diagnosis [12]. The National Comprehensive Cancer Network risk stratification for low-, intermediate-, and high-risk prostate cancer is based on clinical stage from digital rectal exam, Gleason grade from prostate biopsy, and PSA. Low-risk prostate cancer was defined as clinical stage T1-T2a, Gleason score ≤6, and PSA <10 ng/ml. Intermediate risk was defined as stage T2b-T2c or Gleason score ≤7 or PSA <10 to 20 ng/ml, and high risk as T3a or Gleason score 8 to 10 or PSA >20 ng/ml. From January 2004 to May 2007 guidelines considered CT/MRI appropriate if a patient was clinical stage ≥ T2b or PSA >10 or Gleason >3+4. From June 2007 to June 2015 CT/MRI was considered appropriate if a patient was clinical stage ≥T2b or PSA > 10 or Gleason >4+3. Bone scan was appropriate for stage T1 with PSA level >20 mg/mL, stage T2 with PSA level >10 mg/mL, or for stage ≥T3 or/and Gleason >4+3 or bony symptoms [12]. Imaging that occurred outside of the 6-month period after diagnosis was not considered. Imaging for radiation planning, prostate cancer risk stratification for active surveillance or extraprostatic extension, or treatment purposes were not considered guideline-discordant and as such these patients were excluded. To ensure data completeness, patients with less than 1 year of VA activity prior to diagnosis date were also excluded. No member of our cohort advanced to high-risk disease status during the 6-month study period.

Chart review was performed to classify the findings from guideline-discordant imaging results. Positive findings were classified as false positives, incidental findings, or metastatic disease (i.e., true positive). Detailed definitions of each of these classifications are below. We also tabulated the number of follow-up imaging tests performed subsequent to abnormal findings. We conducted individual chart review of order comments and notes to confirm that scans were ordered for staging purposes and that men who received CT scans for radiation planning were excluded. Additional chart review was performed to determine the clinical relevance of any significant findings when providers recommended imaging or procedures subsequent to the receipt of positive-staging imaging.

2.1. Description of variables

Our outcome of interest was the category of initial and follow-up imaging results. These could be normal (i.e., negative), false positive, incidental finding, or metastatic disease. These definitions are based on widely held definitions in the radiologic community [11].

Normal: The patient had imaging for cancer staging purposes, and there were no abnormal findings. No further follow-up imaging was recommended or executed.

False-positive: The patient had imaging for cancer staging purposes, and the findings were positive. Follow-up imaging may or may not have been conducted with the results below.

1. No imaging was conducted and the patient was treated for localized prostate cancer.
2. Follow-up imaging was obtained for the described abnormality and the lesion was determined by the radiologist or treating physician to be benign.

Incidental finding: The patient had imaging for cancer staging purposes, and there was an incidentally discovered mass or lesion unrelated to prostate cancer for which the interpreting radiologist recommended follow-up imaging or intervention [13]. Follow-up imaging or intervention may or may not have been conducted.

Metastatic disease: Imaging findings of advanced prostate cancer on CT, BS, or MRI were found to be true positives, including gross extracapsular disease, nodal metastatic disease, and/or visceral metastatic disease.

Covariates included age, race, prebiopsy PSA, Gleason score, initial treatment type, and clinical stage at diagnosis.

3. Results

We identified 4,306 men diagnosed with incident low- or intermediate-risk prostate cancer from 2005 to 2015 at the VA's New York Harbor Healthcare System. Of those, 927 underwent inappropriate staging imaging within 6 months of initial prostate cancer diagnosis. We excluded 513 men for 1 of the following: men who did not have complete clinical records with at least 1 year of clinical history at the VA, men with pretreatment CT scans who underwent subsequent radiation, and men who underwent imaging tests for indications other than prostate cancer staging, as these are appropriate justifications for imaging. Following these exclusions, 414 men comprised our final cohort (Table 1).

Among our cohort of 414, 379 (92%) men had a BS, 274 (66%) had a CT, and 9 (2%) had an abdominal/pelvic MRI. The median number of total staging and follow-up imaging tests per patient was 2 (range, 1–6). Our cohort of 414 received a total of 662 staging imaging tests. Of these 662 staging studies, 67 (10%) had incidental findings, 252 (38%) had false positives, 2 (<1%) had both incidental finding and a false positive, and 336 (51%) were normal (Table 2). Only 5 (1%) men had imaging findings consistent with metastatic prostate cancer. Of these 5, 1 had pelvic lymphadenopathy, 3 had osseous metastases, and 1 had lung metastases.

In our cohort of 414, 282 (68%) men had at least 1 abnormal finding. Of these, 178 (43% of the full cohort) underwent follow-up imaging as a result of the findings from their initial guideline-discordant staging test, with 18 men receiving more than 1 follow-up imaging test. Most often this entailed a plain film X-ray for 151 men, followed by 12 men who received CT scans, 9 who underwent abdominal/pelvic MRI, and 6 various tests (ultrasound, BS, cystoscopy, and renal scan). Based on the follow-up studies of these 178 men, 174 (98%) men had no evidence of metastatic disease, and 4 (2%) were confirmed as having metastatic disease.

Table 1
Patients with incident prostate cancer undergoing guideline-discordant staging imaging

Total patients	414
Age	No (%)
40–49	6 (1)
50–59	79 (19)
60–69	186 (45)
70–79	118 (29)
80+	25 (6)
Race	
African American	262 (63)
Caucasian	145 (35)
Other/missing	7 (2)
Clinical Stage	
1A	1 (0.2)
1C	373 (90)
2 (Otherwise unspecified)	2 (0.5)
2A	14 (3)
2B	5 (1)
2C	19 (5)
PSA at diagnosis	
<10	367 (89)
10–20	47 (11)
>20	0
Gleason score	
6	165 (40)
7	249 (60)
First treatment	
Radiation	246 (59)
Radical prostatectomy	109 (26)
Active surveillance/WW	22 (5)
Focal therapy	3 (1)
LTFU/unknown	34 (8)

LTFU = lost to follow-up, WW = watchful waiting.

Abnormal BS findings were classified according to location. Of 379 BS performed, 238 men (63%) had abnormal BS. Of these, 130 (55%) had axial lesions, 39 (16%) had appendicular lesions, 60 (25%) had both axial and appendicular lesions, and 9 (4%) had soft tissue lesions. Findings for all 379 BS performed were classified as 141 (37%) normal, 225 (59%) false positives, 9 (2%) incidental findings, and 4 patients (1%) having metastatic disease (Table 2).

Of the 274 total staging CT scans, 187 (68%) were normal and 87 (32%) were abnormal. Among the abnormal findings, 26 (30%) were deemed false positives, 58 (67%) incidental findings, 2 (2%) had false positive and incidental finding, and 1 (1%) of metastatic disease (Table 2). Four patients underwent procedures for incidental findings, including a negative cystoscopy, partial cystectomy for invasive bladder cancer, hemi-thyroidectomy for thyroid cancer, and endovascular repair of abdominal aortic aneurysm.

Abdominal/pelvic MRIs were obtained on 9 men, 1 man had abnormal findings that were further classified as a false positive.

Table 2
Imaging findings among men with incident prostate cancer undergoing guideline-discordant staging imaging

	Bone scan	CT	MRI (abd/pelvic)	Total
Staging imaging studies	379	274	9	662[a]
Normal findings	141 (37)	187 (68)	8 (89)	336 (51)
False positives	225 (59)	26 (9)	1 (11)	252 (38)
Incidental findings	9 (2)	58 (21)	0	67 (10)
Metastatic disease	4 (1)	1 (0.4)	0	5 (1)
Incidental finding and false positive	0	2 (0.7)	0	2 (0.3)

[a] Some patients had more than 1 staging imaging test, thus, total staging images (662) is greater than cohort size (414).

4. Discussion

In this study, we determined the downstream outcomes of guideline-discordant imaging tests ordered to stage low- and intermediate-risk prostate cancers. We discovered a very high rate of false positive results and incidental findings. Follow-up of these off-target findings rarely revealed a significant discovery but did add a significant number of additional tests, a median of 2 per patient. Only 1% of these men had findings indicating metastatic disease. These findings suggest that large number of men undergo needless tests during their initial workup of which the only result is more testing.

Additionally, our study confirms the well-documented low specificity of BS. Traditionally, the use of BS has been for the detection of osseous metastases. There is a lack of specificity for the detection of bone metastasis, with reports of sensitivities and specificity ranging from 51% to 83% and 57% to 82%, respectively [14−16]. Small bone marrow-based metastases with no associated dense osteoblastic response may not be identifiable and nonmalignant skeletal disease may cause focal uptake of bone specific tracers, often requiring further correlative imaging. This poor accuracy was confirmed in our study, with 63% of BS having a positive finding where further imaging was recommended. Of those positive scans, only 4 had follow-up imaging confirming metastatic disease.

An alarming 178 men out of 414 were exposed to additional imaging. These follow-up studies also likely indicate further waiting for referrals, inconveniences with more visits to the hospital, anxiety of an unknown diagnosis, exposure to radiation in the case of CT/Radiograph, and financial burden to the patients and healthcare system. One recent study of the SEER-Medicare population estimated an annual cost of $9,300,000 of unindicated staging imaging, with an additional $2,000,000 for downstream imaging in the low- and intermediate-risk patient population [17]. Given the inaccuracy of planar BS, newer imaging hybrid techniques have risen in popularity but have not yet replaced former modalities in guidelines [12]. These may 1 day become the preferable staging imaging test, but are currently only investigational.

While BS findings often result in false positives, CT scans are notorious for the discovery of incidentally revealed clinically silent findings such as cysts, vascular abnormalities, or tumors. The overall rate of incidental findings is reported to be as high as 31% for abdominal CT [18]. In studies reviewing staging imaging for prostate cancer, clinically significant findings on CT range from 6.7% to 20.6 % [19,20]. In our current study, we found a 21% rate of clinically significant incidental findings on CT in the low-risk prostate cancer population. There were 2 synchronous malignancies identified on staging CT that required intervention. These results are similar to a study by McEvoy, which assessed the diagnostic yield of abdominal sequences in MR staging for all prostate cancer patients. They found an incidental rate of 21%, with half of these patients requiring further investigations, and ultimately 5% underwent surgery for an unexpected malignancy [21]. They concluded that routine abdominal MR sequences were of very low yield in routine prostate cancer screening and should only be reserved for high-risk cases. In evaluating all abdominal imaging, Ozsoy et al. identified a low prevalence of 1.25% of incidental cancer found on imaging, mainly renal cancers [22]. The significance of these findings depends on the particular patient and their overall health status.

We found a high rate of incidental findings in our cohort. We must consider what is the sensible management of information that nobody asked for and who is responsible. Radiology literature cites ethical issues with the detection of incidentalomas as these can side track the focus off the primary malignancy, may be perceived as a source of generating business for radiologists, and may not be covered by insurance [23]. A factor further complicating the matter of incidental findings is that there exists significant variation in recommendations by radiologists for further management. Previously, there was a paucity of literature to guide management. Since 2010, white paper guidelines now focus body radiologists to base their recommendations on clinical judgment for relevant findings. More recent white papers are narrowed to organ systems for more discrete recommendations [24]. Another concern is the lack of documented follow-up for incidental findings, a finding we observed as well, with 37% of patients with an abnormal finding not undergoing any further imaging [11]. While the ordering physician may have deemed many of those findings insignificant, focused recommendations in radiology reports could avoid uncertainties and overuse of resources. Regardless of the imaging test of choice, incidental findings will continue to challenge physicians.

Our study has several important strengths and limitations. The strengths of this case series come from the completeness

and quality of the data since all patients in our cohort received care in veterans health administration (VHA). We were able to follow patients for 1 year or greater to determine what further interventions or tests an imaging finding incurred. This is the first report to characterize both false positives and incidental findings in the low- to intermediate-risk prostate cancer population showing meager clinical utility of staging imaging in this context. The study is limited by its inability to account for physician judgment or other patient variables that may explain individual cases of guideline-discordant imaging and follow-up studies. We are also limited by an inability to determine whether findings were actionable and how they may have altered clinical management. Moreover, this study was conducted among a cohort from 1 urban VA facility. Veteran populations generally differ demographically from the general population. Because of this, these results may not be fully generalizable. Even in this narrow population this is an important and useful study because it attempts to quantify a source of downstream, sometimes hidden, costs of inappropriate staging imaging which remains an ongoing problem in prostate cancer healthcare delivery.

5. Conclusion

Despite clear, longstanding guideline recommendations, guideline-discordant staging imaging remains a significant issue for low- and intermediate-risk prostate cancer patients. The yield of such guideline-discordant studies in finding metastatic prostate cancer is vanishingly small (1%) and the rate of other findings which require workup, 38% false positives and 10% incidental findings, is quite significant. Guideline-discordant use of imaging is burdensome to the healthcare system and patient. Future studies can use such data to perform cost-effectiveness analyses to optimize imaging recommendations and to design disincentives for guideline-discordant ordering.

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