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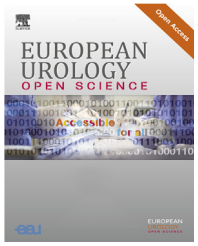

European Association of Urology

Brief Correspondence

Rates of Positive Abdominal Computed Tomography and Bone Scan Findings Among Men with Cambridge Prognostic Group 4 or 5 prostate cancer: A Nationwide Registry Study

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Abstract

European and American guidelines recommend abdominal computed tomography (CT) and bone scans for staging of high-risk prostate cancer (PC). To improve clinical risk stratification of nonmetastatic PC a new, five-tier risk classification system has been developed, the Cambridge Prognostic Groups (CPG), in which "high-risk" PC is divided into favourable CPG 4 and unfavourable CPG 5. We used the National Prostate Cancer Register of Sweden (NPCR) to define the rates of positive CT and bone scan findings among men with CPG 4 or 5 cancer. Among men with CPG 4 and prostate-specific antigen (PSA) <50 ng/ml, only 3.6% (95% confidence interval 2.9–4.5%) of the CT scans showed regional lymph-node metastasis (N1M0), while 6.2% (95% confidence interval 5.4–7.0%) of the bone scans were positive. Rates for both were higher in the subgroups with PSA 50–99 ng/ml (10% and 15%) and with CPG 5 disease. The low positivity rate questions routine use of CT for men with CPG 4 cancer and PSA <50 ng/ml, particularly considering the poor sensitivity and specificity for detection of lymph node metastasis. The positivity rate was higher for bone scans, and as current clinical practice relies on trials using bone scans for staging (eg, to define low- versus high-volume metastatic disease), continued routine use of bone scans seems justified.

Patient summary: Our analysis of data from the National Prostate Cancer Register of Sweden showed that for men with favourable high-risk prostate cancer (Cambridge Prognostic Group 4), the rate of positive computed tomography (CT) scans was low. This result suggests that CT scans may not be necessary for detecting cancer spread in men with Cambridge Prognostic Group 4 prostate cancer.

Nonmetastatic prostate cancer (PC) is usually curable with surgery or radiotherapy, whereas men with metastatic PC need multimodal treatment [1]. Accurate staging is therefore essential for optimising treatment. European and American guidelines recommend computed tomography (CT) of the abdomen and a bone scan for patients with high-risk PC [1,2]. However, the sensitivity, specificity, and positive predictive value of these imaging modalities are

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poor [3], particularly for CT in detecting lymph node metastasis [4].

To improve the clinical risk stratification of PC, a new, five-tier classification system has been developed, the Cambridge Prognostic Groups (CPG) [5], in which the traditional high-risk group is divided in more favourable CPG 4 and unfavourable CPG 5. CPG is now recommended by the UK National Institute for Health and Care Excellence.

The aim of this study was to determine whether diagnostic outcomes of CT and bone scans warrant their routine use for men with CPG 4 PC or if these investigations may be omitted.

Aggregated data were retrieved from the National Prostate Cancer Register of Sweden (NPCR) by the Swedish Prostate Cancer Guidelines group. The use of these anonymous data did not require ethical approval. The NPCR captures 98% of all diagnosed PCs in Sweden [6]. We analysed data for all men who were diagnosed between June 2014 and December 2019 with high-risk PC (stage T3 and/or Gleason score 8–10 and/or prostate-specific antigen [PSA] $\geq$20 ng/ml), PSA <100 ng/ml, and a registered result for a bone and/or CT scan. Variables extracted from the NCPR were PSA value at diagnosis, clinical local tumour stage (T1–4), Gleason score, and scan results. The disease was subcategorised as CPG 4 or CPG 5. CPG 4 is defined as either Gleason score 8, PSA >20 ng/ml, or T3 as the only high-risk feature. CPG5 is defined as any of Gleason score 9–10 or T4, or any combination of Gleason score 8, PSA >20 ng/ml, or stage T3 [5].

The outcome measure was percentages of N1 and M1 disease with confidence intervals (CIs), as registered in the NPCR. For analysis of N1 disease on CT scans, only patients with M0 disease were included, as the presence of regional lymph node metastasis rarely affects the clinical management of patients with M1 disease. Since the prevalence of metastasis increases with higher PSA values, the proportion of positive scans was also analysed after excluding men with PSA >50 ng/ml from the CPG 4 group. This PSA cutoff was chosen as it has long been used by the NPCR. No other PSA cutoff point was analysed.

A total of 9399 men with high-risk PC and PSA <100 ng/ml had a bone scan. Of these, 3810 (41%) had CPG 4 and 6219 (59%) had CPG 5 disease. The bone scan was positive (M1 disease) in 262 men (6.9%, 95% CI 6.1–7.7%) with CPG 4 and 1254 (20%, 95% CI 19–21%) with CPG 5 disease. The bone scan was positive for 47/317 men (15%, 95% CI 11–19%) with CPG 4 PC and PSA of 50–99 ng/ml. The percentage of positive bone scans among the remaining 3493 men with CPG 4 PC and PSA <50 ng/ml was 6.1% (95% CI 5.4–7.0%).

Analysis of the CT data included 4884 men with M0 disease and PSA <100 ng/ml, of whom 2266 (46%) met the CPG 4 criteria. Among men with CPG 4 disease, 91 of the CT scans (4.0%, 95% CI 3.2–4.9%) categorised the disease as N1. The percentage of N1 cases in the CPG 5 group was 14% (95% CI 16–22%). Of the 146 men with CPG 4 PC and PSA of 50–99 ng/ml, 14 (9.6%, 95% CI 5.3–15.6%) had N1 disease. Excluding these 146 men from the CPG 4 group left 3.6% (95% CI 2.9–4.5%) of the remaining men with N1 disease according to CT imaging.

This nationwide register study showed that the current standard procedures for staging—a bone scan plus an abdominal CT scan—detect metastases in only a small proportion of men with CPG 4 (“favourable high-risk”) PC. Only 4% of the abdominal CT scans for men with M0 disease showed regional lymph node metastases (N1). This low positivity rate in combination with the low sensitivity and positive predictive value seriously questions the routine use of abdominal CT imaging for this patient group, at least for those with PSA <50 ng/ml (almost 10% of men with PSA of 50–99 ng/ml had a positive scan). Omission of routine CT imaging for patients with CPG 4 disease would reduce the number of CT scans by one-third among men with high-risk disease (CPG 4 or 5) and PSA <50 ng/ml. The percentage of positive bone scans was higher (6%), and as detection of bone metastasis affects treatment plans more than enlarged regional lymph nodes do, continued use of bone scans seems to be justified.

An attractive alternative to defining the indication for staging by risk groups is to use nomograms that allow individualised estimation of a patient’s risk of metastasis [7]. Prostate-specific membrane antigen (PSMA) positron emission tomography (PET)/CT has higher sensitivity and specificity than CT plus a bone scan for detecting PC metastasis. PSMA PET/CT may eventually become the standard for PC staging, but its use is limited because of capacity shortages and costs. Moreover, as current clinical practice relies on trials the use of bone scans for staging (eg, to define low- versus high-volume metastatic disease), bone scans may be used even when PSMA PET/CT is available [8].

Our findings are in agreement with previous studies. Thurtle and associates [9] reported a positive bone scan in 5.8% of men with CPG 4 and 13.7% of men with CPG 5 disease when the local stage was defined by magnetic resonance imaging (MRI). Hofman and co-workers reported a CT positivity rate of 6.6% for nodal disease in men with high-risk PC. We were unable to find any study reporting the proportion of positive CT scans for men with CPG 4 disease.

Strengths of our study include the nationwide, population-based design and the large number of scan results included. The study has some limitations. In particular, the local tumour stage was based on digital rectal examination and tumour grade was not based on MRI-targeted biopsies.

Author contributions: Ola Bratt had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Bratt, Gnanapragasam.
Acquisition of data: Bratt.
Analysis and interpretation of data: Bratt, Stenman, Abrahamsson, Redsäter, Gnanapragasam.
Drafting of the manuscript: Abrahamsson, Redsäter, Stenman.
Critical revision of the manuscript for important intellectual content: Bratt, Stenman, Abrahamsson, Redsäter, Gnanapragasam.
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