The value of three-dimensional transrectal ultrasonography in staging prostate cancer

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INTRODUCTION

Prostate cancer is a major public health issue in the USA and the European Community; it is the second leading cause of cancer death among men in Europe and the USA, representing a significant public health challenge [1]. Radical prostatectomy (RP) is a recognized and well-established treatment option for organ-confined prostate cancer. Accurate staging is critical in managing prostate cancer, and particularly significant for selecting candidates for RP. Undetected extracapsular extension (ECE) of the tumour might result in incomplete tumour excision and increased risk of treatment failure [2].

Current methods for local staging include the DRE, serum PSA level, TRUS, axial CT and endorectal-coil MRI. These methods lack sensitivity and can under-stage up to half of cancers [3]. Conventional TRUS uses two dimensions to visualize the prostate. It has long been thought that any technique that would overcome this spatial limitation would probably result in better staging. TRUS has been used by many investigators to stage prostate cancer, with reports of 50–90% sensitivity [4–8]. In some series, two-dimensional (2D)-TRUS has been found to add little clinically meaningful information over a DRE alone [4–8]. This is inevitably because of the greater interobserver variation and the subjectivity of real-time 2D-TRUS. Therefore, 3D-TRUS has developed through the need for a more accurate, less subjective, relatively inexpensive means of staging prostate cancer [8]. 3D-TRUS can provide ultrasonograms in three planes simultaneously. Apart from the additional information obtained by the third, i.e. the coronal plane, this technique permits precise 3D analyses of relevant anatomical and pathological structures [9–11].

The purpose of the present study was to investigate the value of 3D-TRUS in the local staging of prostate cancer; the findings of 3D-TRUS were correlated with the histopathological staging after RP.

PATIENTS AND METHODS

Between 2000 and 2006, 870 patients had RP at our institution; of this group, 180 were included at random in this prospective study, all being assessed as having clinically localized prostate cancer by a DRE, PSA level, contrast-enhanced CT of the pelvis and/or a bone scan (mean age 63.3 years, range 41–79; mean PSA level 7.9 ng/mL, range 1.25–15). 3D-TRUS staging was used before RP in these patients, by two senior uro-radiologists and interpreted by consensus. The ultrasonographers were unaware of the clinically assessed findings. The final RP was done by a separate group of surgeons.

The system used for 3D-TRUS consisted of a Combison 330 and a Voluson 3D multiplanar endorectal transducer (7.5 + 10 MHz; Kretztechnik AG, Zipf, Austria). Initially, a volume scan of the relevant anatomical region was made, taking 3–4 s, during which both the patient and the physician avoided any movement, to guarantee a flawless scan. Once this scan was obtained, the examination was already completed for the patient. All the TRUS data obtained were collected in a volume image-store. On the monitor of this system, three sections in the horizontal, sagittal and coronal planes, 90° to one another, can be displayed. The coronal image

OBJECTIVE

To use three-dimensional transrectal ultrasonography (3D-TRUS) to reconstruct the prostate, and thus determine its value in staging clinically localized prostate cancer.

PATIENTS AND METHODS

In all, 180 patients with newly diagnosed clinically localized prostate cancer were assessed using 3D-TRUS for staging. TRUS findings were compared with histopathological staging after radical prostatectomy.

RESULTS

Pathological staging of specimens showed extracapsular extension in 69 patients, of whom 53 had pathological capsular perforation and 16 had seminal vesicle invasion. 3D-TRUS identified 58 patients with sites of extracapsular extension with 84% sensitivity, 96% specificity, 94% positive predictive value, 91% negative predictive value and an overall accuracy of 92%. Of the 16 patients with seminal vesicle invasion 14 were identified correctly on 3D-TRUS. Overall the 3D-TRUS staging sensitivity was 84%, specificity 96%, positive predictive value 93%, negative predictive value 91% and accuracy 91%.

CONCLUSIONS

3D-TRUS seems to be an accurate technique for staging localized prostate cancer. If 3D-TRUS indicates locally advanced disease, the probability of capsular perforation or seminal vesicle invasion is very high.

KEYWORDS

prostate, ultrasonography, prostatic neoplasms, staging
is calculated by the computer from the information of the scan. The positions of the individual planes are indicated in the two other planes by reference lines. The three planes can be targeted on any site recorded in the volume scan by means of three position keys [9–11].

Briefly, the TRUS findings that led to the diagnosis of ECE are described. Suspicion of ECE is seen as a disruption of the periprostatic fat layer in association with a hypoechoic lesion. Suspicion of seminal vesicle invasion (SVI) is seen as obliteration of the angle between the SV and the base of the prostate, or continuation of the hypoechoic lesion into the SVs. The interpretation, by consensus, by the two senior uro-radiologists took 3–5 min.

The RP specimens, including prostate, SVs and bilateral pelvic lymph nodes, were examined microscopically after routine preparation by senior uro-pathologists. The prostate was weighted and cut as a whole-mount section at 4-mm intervals. For the pathological reports the 2002 TNM classification was used [3]; the final histopathological staging was compared with 3D-TRUS assessment.

The sensitivity, specificity, positive and negative predictive values (PPV, NPV) and overall accuracy were calculated for the detection of ECE, capsular perforation and SVI on 3D-TRUS.

RESULTS

After a detailed histological evaluation of the prostate specimens, 111 patients had stage pT2 cancer, 69 had pT3 (53 with ECE and 16 with SVI) and none had stage pT4 (Table 1). 3D-TRUS predicted 44 of the 53 sites of tumour infiltration beyond the prostatic capsule. Of the nine sites not detected, six were posterolateral and three were anterior. There were two false-positive predictions of ECE. For the detection of pathological capsular perforation of the tumour, the sensitivity was 82%, specificity 94%, PPV 96%, NPV 79% and accuracy 87% (Table 2).

3D-TRUS accurately staged 14 of 16 patients with SVI, and there were two false-negative predictions of SVI; 11 of the 16 with SVI showed simultaneous ECE, which was correctly diagnosed in 10 of these 11. No false-positive ECE was diagnosed by 3D-TRUS in these patients. For the detection of pathological SVI the sensitivity was 88%, specificity 97%, PPV 88%, NPV 97% and accuracy 96% (Table 2).

Overall, 3D-TRUS assessed 118 patients as having T2 and 62 as having T3 tumours. Therefore, the overall 3D-TRUS staging sensitivity was 84%, specificity 96%, PPV 93%, NPV 91% and accuracy 91% (Table 3); examples of 3D-TRUS images are shown in Figs 1–4.
3D-TRUS IN STAGING PROSTATE CANCER

FIG. 4. 3D-TRUS in a patient with perforation of the prostatic capsule and SV. Infiltration of the right SV (+) and perforation of the right prostatic capsule (*) are marked. The extension of the tumour into the periprostatic tissue and the SV can be best investigated in the coronal plane, which adds important information. H, horizontal plane (right lateral view); S, sagittal plane (view from beneath); C, coronal plane (ventral view).

DISCUSSION

The accurate staging of prostate cancer is critical to managing the disease and selecting candidates for RP [3]; US is constantly developing, and in 1971 Watanabe et al. [12] introduced TRUS as a clinical application for evaluating the prostate. 3D-TRUS for staging in prostate cancer was first described in 1999 by Garg et al. [13]. 3D-TRUS produces a series of sequentially overlaid images, the final result being an image of great resolution and quality. By comparison, 2D-TRUS is a projection of a single image. Despite this, the image acquired using a standard 3D endorectal transducer uses the same grey scale as conventional 2D-TRUS. The diagnosis of prostate cancer is therefore the same as for conventional 2D-TRUS. Areas in the prostate suspicious for cancer are seen as hypoechoic or as glandular asymmetry, while isoechoic lesions will inevitably remain undetected [8].

To our knowledge we are the first group to evaluate 3D-TRUS for staging prostate cancer in a large group of patients. In a pilot study on 36 patients with newly diagnosed clinically localized prostate cancer, Garg et al. [13] used 3D-TRUS with a conventional scanner and no power Doppler US enhancement. They found that 3D-TRUS had an overall staging accuracy of 94%. For local staging, there was 80% sensitivity and 96% specificity with a PPV of 90% and NPV of 96% for detecting ECE. There was a significant improvement in staging accuracy over 2D-TRUS (94% vs 72%; P < 0.05). However, with so few patients, only two had histologically confirmed SVI. The authors noted that the advantage of 3D-TRUS over 2D-TRUS relied entirely on the visibility of prostate cancer on conventional TRUS.

3D-TRUS has been investigated for diagnostic accuracy and staging of prostate cancer. Hamper et al. [14] reported their early experience of 3D-TRUS in 16 men before prostate biopsy; 3D-TRUS allowed better visualization of the gland and focal lesions. These were seen especially on the coronally reconstructed images. 3D-TRUS was better than 2D-TRUS in depicting tumour presence and identifying extra-glandular disease. Because there were so few patients, an accurate statistical analysis was not possible. Further self-directed criticism identified the potential bias in their patient selection and image analysis, as each patient had 2D-TRUS before 3D-TRUS, during which the clinician was aware of the findings of the initial scan. However, they identified the ease of using 3D-TRUS and the ability for the resulting image to be stored for unlimited off-site viewing.

In another study, Sedelaar et al. [4] compared 2D-TRUS with 3D-TRUS for detecting, locating and staging prostate cancer; in 100 patients (half with BPH and half with prostate cancer) they found that 3D-TRUS had a significantly better sensitivity (88% vs 72%) and lower specificity (42% vs 94%) than 2D-TRUS for identifying cancerous lesions. There was no difference between 2D-TRUS and 3D-TRUS for accurate staging. They concluded that although 3D-TRUS had statistically significantly better sensitivity for detecting lesions and lower specificity than 2D-TRUS, 3D-TRUS did not result in a significant clinical improvement in detecting and staging prostate cancer. The reason was that the ability to exactly identify a cancerous lesion was virtually the same for both methods.

With the addition of other clinically relevant information (i.e. PSA level, gland volume and DRE) the false detection of cancerous regions in the BPH group declined by 14%.

In the present study, 3D-TRUS was used to detect local ECE of prostate cancer. The presence of prostate tumour was confirmed beforehand by biopsy. Visualization of the lesion in three planes should allow a better assessment of capsular disruption. Our findings suggest that 3D-TRUS before RP is highly sensitive (84%) for detecting ECE of prostate tumour and has a very high specificity (96%). Suspicion of ECE is seen as a disruption of the periprostatic fat layer in association with a hypoechoic lesion. ECE could be detected with an overall accuracy of 87%. Suspicion of SVI, as obliteration of the angle between the SV and the base of the prostate, or continuation of the hypoechoic lesion into the SVs, had an overall accuracy of 96%.

3D-TRUS was a simple and easy investigation, which did not require special preparation. It is cheap, by contrast with other imaging methods of current interest, especially endorectal MRI [15]. 3D-TRUS is easy to interpret by experts in conventional TRUS. 3D-TRUS has not only the potential for image resolution but also for subsequent interpretation. As an image is stored for off-screen viewing, consensual decisions can be made about the diagnosis and stage, which might reduce the problems of interobserver variability seen with conventional 2D-TRUS. Furthermore, 3D-TRUS is an accurate technique for staging local prostate cancer and provides additional information potentially leading to better selection for RP and a lower incidence of positive surgical margins.

The limitations of conventional grey-scale TRUS in prostate cancer detection are well known. Up to 80% of hypoechoic areas found on TRUS are not cancer. Hypoechoigenicity is not specific and can occur with inflammation, atrophy, hyperplasia, and even normal prostate tissue [16]. In the present study, we used 3D-TRUS not for evaluating intraprostatic tumour but for detecting ECE, which was shown to be easier to distinguish. Furthermore, we did not evaluate how and where the tumour infiltrated beyond the prostatic capsule, only if there was ECE. The location of ECE has a clear influence on the imaging outcome. Anterior cancers might necessitate a separate assessment, as anterior ECE close to the bladder neck is difficult to assess with TRUS.

Moreover, it is known that ECE can be focal (fewer than two microscopic fields) or established (more than two microscopic fields) [17,18]. In the present study only established ECE was correlated with the 3D-TRUS findings. It is unlikely that focal ECE can be seen by 3D-TRUS, unless indirect signs like irregular prostate contours or length of cancer in contact with the capsule are used for suspecting ECE. Another limitation of this study is that the imaging findings were
interpreted by consensus, therefore there was no inter- and intraobserver variability. Furthermore, it was not the aim of the study to compare 2D-TRUS and 3D-TRUS, as there are already several reported studies [4–8]. The development of new US techniques, including power Doppler US, contrast-enhanced, intermittent (flash), tissue-harmonic and pulse-inversion imaging, might improve the ability to detect and stage prostate cancer [7,19].

In conclusion, 3D-TRUS can be used with no problems, and is a simple procedure allowing an exact assessment for staging prostate cancer. Locally confined (≤pT2) and locally advanced (≥pT3) prostate cancer can be differentiated with maximum convenience, reliability and ease. Thus, 3D-TRUS can be considered to guide the decision before a planned RP. If 3D-TRUS indicates locally advanced disease, the probability of capsular perforation or SVI is very high.

CONFLICT OF INTEREST
None declared.

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Abbreviations: 2D, two-dimensional; 3D, three-dimensional; 4D, four-dimensional; NPV, negative predictive value; PPV, positive predictive value.