EUROPEAN UROLOGY ONCOLOGY XXX (2018) XXX–XXX

available at www.sciencedirect.com
journal homepage: euoncology.europeanurology.com

European Association of Urology

Clinical Utility of Multiparametric Magnetic Resonance Imaging as the First-line Tool for Men with High Clinical Suspicion of Prostate Cancer

Valeria Panebianco[a,*], *Maria C. Valerio*[a], *Alessandro Giuliani*[b], *Martina Pecoraro*[a], *Isabella Ceravolo*[a], *Giovanni Barchetti*[a], *Carlo Catalano*[a], *Anwar R. Padhani*[c]

[a] *Sapienza University of Rome, Rome, Italy;* [b] *Environment and Health Department, Istituto Superiore di Sanità, Rome, Italy;* [c] *Paul Strickland Scanner Centre, Mount Vernon Hospital, Northwood, UK*

Article info

Article history:
Accepted March 20, 2018

Associate Editor:
Alberto Briganti

Keywords:
Clinical utility
Multiparametric magbetic resonance imaging
Prostate cancer
Targeted biopsy
Cost-effectiveness

Abstract

Background: Transrectal ultrasound-guided biopsy (TRUS-Bx) is recommended by the European Urology Association (EAU) as the first diagnostic modality for men at risk of prostate cancer (PCa). Current EAU guidelines reserve the use of multiparametric MRI to target or guide any repeat biopsy (mpMRI-Bx). It remains uncertain if TRUS-Bx is effective as a first strategy in terms of costs, diagnostic performance, time to diagnosis, and triage for individualised therapy.
Objective: To determine the diagnostic and treatment costs and the effectiveness of pathways incorporating mpMRI-Bx compared to TRUS-Bx in men at high risk of PCa.
Design, setting, and participants: A cost and time analysis was performed using data from a randomised single-centre study of 1140 patients (prostate-specific antigen >4 ng/ml) divided into two groups: 570 patients underwent an initial TRUS-Bx and 570 underwent 3-T mpMRI-Bx.
Outcome measurements and statistical analysis: Budget analyses were used to compare the diagnostic strategies using reimbursement data from the Italian National Health Security system. Analyses of reimbursable diagnostic and treatment costs were undertaken separately. Histologic outcomes, pathway diagnostic accuracy, therapy choices, and time to diagnosis were compared.
Results and limitations: The cumulative diagnosis costs were 14.6% greater for the mpMRI-Bx pathway than for the TRUS strategy, and 5.2–6.0% higher for therapy. Diagnostic costs were €228 946 for mpMRI-Bx and €199 750 for TRUS-Bx, and the corresponding therapy costs were €1 912 000 and €1 802 800. The mpMRI-Bx strategy was highly effective in excluding clinically significant disease (Gleason ≥7; sensitivity and negative predictive value both 100%, 95% confidence interval 98–100%). The time to diagnosis was significantly shorter for the mpMRI-Bx (median 4.0 mo interquartile range [IQR] 3–6) than for the TRUS-Bx strategy (median 6 mo, IQR 4–12; $p < 0.001$). Limitations include the lack of data on costs associated with treatment-related complications and follow-up data.
Conclusions: The mpMRI-Bx strategy is effective for diagnosing patients with a clinical suspicion of PCa and provides more accurate diagnosis, with combined diagnosis and therapy costs only moderately higher than for the standard strategy.
Patient summary: It is a matter of debate whether a diagnostic pathway that incorporates multiparametric magnetic resonance imaging (MRI) as the first-line test before performing any type of biopsy in men suspected of having prostate cancer (PCa) is cost-effective. Our analysis of the costs for men suspected of harbouring PCa revealed higher diagnostic costs for the MRI approach, with the benefits of greater diagnostic accuracy. Moreover, the combined diagnostic and treatment costs are only modestly higher whenever the same treatment for all patients is considered.

* Corresponding author. Department of Radiology, Oncology and Pathology, Sapienza University of Rome, Viale del Policlinico 155, Rome 00161, Italy. Tel.: +39 06 4455602.
E-mail address: valeria.panebianco@gmail.com (V. Panebianco).

https://doi.org/10.1016/j.euo.2018.03.008
2588-9311/

1. Introduction

Multiparametric magnetic resonance imaging (mpMRI) of the prostate is currently recommended as a prebiopsy test after a prior negative biopsy [1], but the budgetary implications associated with this strategy are largely unknown. Up to now, all cost modelling studies have used published estimates for mpMRI test performance, projections of patient flows along diagnostic and treatment pathways, and estimates of costs for procedures and treatments rather than real world data for patient flows and reimbursements that can be realised via billing systems.

Using the former approach, de Rooij et al. [2] found that the total costs for a diagnostic strategy with mpMRI-guided or -targeted biopsy (mpMRI-Bx) were almost equal to those for transrectal ultrasound-guided biopsy (TRUS-Bx), with the additional advantages of reductions in overdiagnosis and overtreatment with the MRI strategy, which in turn was projected to improve quality of life. However, both the diagnostic performance and cost utilities data for this analysis came from literature reviews [2]. Mowatt et al. [3] evaluated the cost-effectiveness of using mpMRI in biopsy-negative patients with a high clinical suspicion of prostate cancer (PCa), and showed that under certain circumstances mpMRI-Bx might be cost-effective in comparison to TRUS-Bx. Nonetheless, they used data derived from published studies as inputs into their economic models, so their results are not reflective of what can be reimbursed. Pahwa et al. [4] assessed the cost-effectiveness of mpMRI followed by mpMRI-Bx strategies for detection of PCa in Bx-naïve patients. They found that noncontrast MRI followed by cognitively-guided MRI-Bx was the most cost-effective approach. The 2014 UK National Institute for Health and Care Excellence PCa guidelines also published economic evidence on the use of mpMRI for PCa diagnosis, identifying only one relevant paper relating to German and Austrian health care settings [5]; despite potential limitations, mpMRI was found to be more effective and less costly than the standard TRUS-Bx strategy. Faria et al. recently used information from the diagnostic PROMIS trial [6] to perform a cost-effectiveness model of health outcomes and costs for men referred to any prostate biopsy for PCa. The analysis demonstrated that mpMRI as a first strategy is cost-effective for the diagnosis of clinically significant PCa (csPCa) [7].

Given the limitations of projected patient flows and costs, further studies are required to clarify if the integration of mpMRI into the diagnostic pathway for men with suspected PCa could represent an effective approach in health systems in which reimbursements are realised.

The aim of the present study was to evaluate the budgetary costs of the mpMRI-Bx pathway in the diagnostic evaluation of patients suspected of harbouring PCa. The cost analysis was based on data on patient flows taken from a randomised study by Panebianco et al. [8]. A descriptive cost and effectiveness analysis was undertaken to compare the health care outcomes associated with TRUS-Bx and mpMRI-Bx strategies.

2. Patients and methods

2.1. Patient population

Details of the prospective randomised study have already been published [8]. In brief, a prospective single-centre study was conducted after local ethics committee approval, with all patients giving written informed consent. Consecutive Bx-naïve patients with any performance status and without age limitations were enrolled in the study to compare two competing diagnostic pathways (TRUS-Bx vs mpMRI-Bx). All patients had total prostate-specific antigen (PSA) >4 ng/ml, PSA density (PSAD) >0.15 ng/ml/cm^3, PSA velocity >0.75 ng/ml/yr, and free/total PSA ratio <0.10. All TRUS-Bx procedures were performed using a standard systematic biopsy scheme with 10 to 12 cores. The mpMRI protocol was compliant with Prostate Imaging-Reporting and Data System v.1 [9]. All scans were performed at 3 T using a phased array and an endorectal coil. The following sequences were performed: T2-weighted turbo spin-echo sequences; diffusion-weighted imaging sequences, with exponential *b* values of 0, 500, 1000 and 2000; and dynamic contrast-enhanced T1-weighted sequences with a temporal resolution of 5 s. Further details on the mpMRI protocol are listed in Supplementary Table 1. Indications to biopsy suspicious foci identified on mpMRI were given according to a Likert score (<3, no biopsy deemed necessary; ≥3, targeted biopsy required). Selection criteria for clinically insignificant PCa (ciPCa) eligible for active surveillance (AS) included: Gleason score (GS) 6, clinical stage T1c or T2a, PSA <10 ng/ml, PSAD <0.15 ng/ml/cm^3, and fewer than three positive cores with <50% cancer involvement on each positive core [1]. All PCa that did not satisfy these criteria were considered csPCa. Details of the patient flows in each diagnostic pathway are given in Figs. 1 and 2. Patients who were successfully diagnosed with PCa underwent treatments according to their personal and physician preferences and the European Urology Association guidelines. Treatment details for each diagnostic pathway are presented in Figs. 1 and 2.

Group A (n = 570) first underwent TRUS-Bx (Fig. 1). Of those, 355 patients had negative biopsy results and underwent mpMRI, which revealed that 208 patients had suspicious lesion(s). These patients underwent targeted biopsy (TRUS-TB) and repeat TRUS-Bx, which identified 186 cases of csPCa. Three patients with ciPCa underwent AS. As outlined in Fig. 1, 183 patients underwent radical treatments. All 147 patients with negative mpMRI had saturation TRUS-guided biopsies (TRUS-SB) for pathological verification, from which a diagnosis of ciPCa was obtained in 43 cases; 57 precancerous lesions were also detected (Fig. 1). All 43 patients with ciPCa went onto AS; no radical treatments were undertaken in the MRI-negative group.

Group B (n = 570) had mpMRI first (Fig. 2), which revealed 440 patients with findings that required histologic sampling with TRUS-TB and TRUS-Bx. Any-grade PCa was found in 417 patients (410 had csPCa). Seven patients with ciPCa went onto AS, while the others received radical treatments as indicated in Fig. 2. Of the 23 patients with positive mpMRI and negative biopsies, a verification TRUS-SB was undertaken, with diagnosis of nine cases of csPCa. The treatments that they received are detailed in Fig. 2. All 130 patients with negative mpMRI findings also had negative TRUS-Bx. All 130 then underwent TRUS-SB for verification, which revealed 37 ciPCa cancers and 32 precancerous lesions. All 37 patients with ciPCa underwent AS; patients with precancerous conditions went onto follow-up. No radical treatments were undertaken in the MRI-negative group.

2.2. Reimbursement analysis

A budget analysis was performed to evaluate the two different diagnostic strategies, with computations based on the sets of patients entering the two different pathways. The costs of diagnostic and/or therapeutic procedures were those obtainable through reimbursements from the

Please cite this article in press as: , et al. Clinical Utility of Multiparametric Magnetic Resonance Imaging as the First-line Tool for Men with High Clinical Suspicion of Prostate Cancer. Eur Urol Oncol (2018), https://doi.org/10.1016/j.euo.2018.03.008