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Original article

Cost-effectiveness of multiparametric magnetic resonance imaging and targeted biopsy in diagnosing prostate cancer

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Abstract

Introduction: Transrectal ultrasound-guided biopsy (TRUSGB) is the recommended approach to diagnose prostate cancer (PCa). Overdiagnosis and sampling errors represent major limitations. Magnetic resonance imaging (MRI)-targeted biopsy (MRTB) detects higher proportion of significant PCa and reduces diagnosis of insignificant PCa. Costs prevent MRTB from becoming the new standard in PCa diagnosis. The present study aimed at assessing whether added costs of MRI outweigh benefits of MRTB in a cost-utility model.

Materials and methods: A Markov model was developed to estimate quality-adjusted life-year gained (QALY) and costs for 2 strategies (the standard 12-core TRUSGB strategy and the MRTB strategy) over 5, 10, 15, and 20 years. MRI was used as triage test in biopsy-naive men with clinical suspicion of PCa. The model takes into account probability of men harboring PCa, diagnostic accuracy of both procedures, and probability of being assigned to various treatment options. Direct medical costs based on health care system perspective were included.

Results: Following standard TRUSGB pathway, calculated cumulative effects at 5, 10, 15, and 20 years were 4.25, 7.17, 9.03, and 10.09 QALY, respectively. Cumulative effects in MRTB pathway were 4.29, 7.26, 9.17, and 10.26 QALY, correspondingly. Costs related to TRUSGB strategy were $8,027, $11,406, $14,883, and $17,587 at 5, 10, 15, and 20 years, respectively, as compared with $7,231, $10,450, $13,267, and $15,400 for the MRTB strategy. At 5, 10, 15, and 20 years, MRTB was the established dominant strategy.

Conclusions: Incorporation of MRI and MRTB in PCa diagnosis and management represents a cost-effective measure at 5, 10, 15, and 20 years after initial diagnosis.

Keywords: Prostate cancer; MRI; Targeted biopsy; Cost-effectiveness

1. Introduction

The adoption of widespread prostate-specific antigen screening has led to increased early-stage, localized prostate cancer (PCa) detection with a controversial effect on mortality [1,2]. Although radical treatments such as surgery or radiation therapy (RT) have shown excellent oncological outcomes in intermediate-risk PCa [3], evidence suggests that these treatments do not result in increased survival in men with low-grade low-volume disease [4]. Rather, the treatment-related side effects outweigh the benefits in this group of patients [5]. Thus, efforts are made to reduce overdiagnosis and overtreatment of insignificant PCa.

An option to achieve this goal would be to use multiparametric magnetic resonance imaging (mpMRI) and magnetic resonance imaging (MRI)-targeted biopsy (MRTB) instead of random transrectal ultrasound-guided biopsy (TRUSGB), which is limited by uncertainty and random effect as the operator cannot visualize the tumor. TRUSGB has several other important limitations, such as low overall cancer detection rate (ranging from 20%−50% depending on the number of cores), overdiagnosis of clinically insignificant disease in up to 50% of men screened on an individual basis [5], and undersampling of

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the anterior/apical region of the prostate, which may lead to missed cancer diagnosis in up to 18% of men with suspected PCa [6].

To address this lack of sensitivity and specificity of TRUSGB, the use of MRI has proven useful. MRI has the ability to precisely detect significant PCa while avoiding the detection of insignificant ones [7]. If a tumor is identified, MRTB is more likely to detect cancer with fewer cores [7,8]. Reduced costs, infection rates, and patient's discomfort represent potential benefits of using fewer cores. Moreover, MRTB is shown to accurately correlate with radical prostatectomy (RP) specimens in experienced centers [9] and has been shown to reflect the true Gleason score of the tumor, thus allowing for a better risk stratification and treatment allocation at the time of diagnosis [10]. To date, the most widely used technique for MRTB is the so-called "cognitive targeting." The cognitive approach requires the urologist to review the MRI separately and cognitively register the location of the lesion on ultrasound (US) images of the prostate to aim the needle toward the appropriate target [11]. Although limited by their costs, logistic requirement, and length of procedure, 2 other approaches are available: "in-bore targeting" is achieved with the use of MRI compatible biopsy material, the biopsy being performed during the MRI, and "fusion targeting," which uses specific software that allows for fusion of the MRI with the real-time US images [6]. Superiority of one approach over the others remains to be demonstrated [6,12].

Despite all the potential advantages, MRTB is not yet considered as standard but rather as an adjunct to TRUSGB [11]. Lack of standardization in reading and reporting MRI results [13], subjective variability due to learning curve effects, costs related to MRI [14], and fear of missing significant PCa by performing only MRGTB have hampered its wider diffusion. The present study aims at assessing whether the added initial costs related to MRI are balanced with the benefits of MRI-cognitive targeted biopsy in a cost-utility model.

2. Materials and methods

2.1. Modeling assumptions

A Markov model with Monte Carlo microsimulations [15] was constructed to determine incremental cost-effectiveness ratio (ICER) and health-economic effect of incorporating MRTB in the process of diagnosing PCa. An ICER threshold up to $50,000 per quality-adjusted life-year gained (QALY) was adopted [16]. Our model was built with a 5-, 10-, 15-, and 20-year time horizon.

The present model was based on a prospective study from Pokorny et al. [8,13,17]. In our model, 2 strategies were compared: the standard 12-core TRUSGB strategy and the MRTB strategy (Fig. 1), in which biopsy-naive men with clinical suspicion of PCa (based on digital rectal examination and prostate-specific antigen [PSA] values 4−10 μg/l) undergo a "triage" MRI upfront. The MRI was considered "positive" if a lesion was identified and attributed PIRADS 3 to 5 score. Specific rates from literature and base assumptions used to derive transition probabilities of the Markov model are summarized in Table 1. Costs derived from a typical Canadian setting are shown in Table 2. The models were built using TreeAge Pro 2013 (Release 13.1.1.0, TreeAge Software Inc.).

2.2. Health states in the model

The Markov model [15] is a health states transition model, which started at the initiation of each diagnostic testing strategy, TRUSGB and MRTB, as described earlier. A cycle length of 1 year was used. The model measured the incidence of PCa detected as low or intermediate and high risk, disease recurrences, progression, and PCa-related and non-PCa-related death within the 5-, 10-, 15-, and 20-year period for all patients. It comprises 10 health states. Health states and transitions between these are presented in Fig. 1. Patients can remain in the same state for more than 1 Markov cycle. The effectiveness measure (outcome) considered in the analysis was the quality-adjusted life-years gained, i.e., overall survival weighted with the specific health state utilities.

2.3. State-transition probabilities and rates

Results of the clinical trial [8] were used to identify rate of MRTB after MRI, rate of positive biopsy on TRUSGB strategy, as well as distribution of cancer in low- and intermediate/high-risk groups (Table 1). Several other studies have been used to derive the rate of false negative for MRTB and TRUSGB [7,14,18], and the 1-year probabilities of remission/recurrence after curative treatment [19] or active surveillance (AS) [20,21], of developing metastatic PCa and castration-resistant PCa (CRPC) [22,23], of PCa-related death or death from other causes (based on disease-free survival, progression-free survival, and overall and disease-specific survival) [14,23–26]. Furthermore, several assumptions have been made using published literature and expert opinion on the treatment stratification by risk groups. In the low-risk cohort, 15% were assumed to undergo AS and 85% were assumed to receive initial treatments [27,28]. Patients on AS were assumed to receive a delayed treatment at an annual probability of 0.08 for first 2 years, 0.04 for 3 to 5 years, and 0.02 for 5 to 10 years [29].

2.4. Utilities

A 0.92 utility was taken into account for remission after curative-intent treatment for low-risk group or intermediate-high-risk group. The corresponding values for relapse state and metastatic/CRPC state were 0.78 and 0.45, respectively [26].