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Cost-effectiveness of Multiparametric MRI in 800 Men Submitted to Repeat Prostate Biopsy: Results of a Public Health Model

PIETRO PEPE[1], GABRIELE PEPE[1], LUDOVICA PEPE[1], ANTONIO GARUFI[2], GIAN DOMENICO PRIOLO[2] and MICHELE PENNISI[1]

[1]*Urology Unit and* [2]*Imaging Department - Cannizzaro Hospital, Catania, Italy*

Abstract. *Background/Aim: To evaluate the cost-effectiveness of multiparametric magnetic imaging resonance (mpMRI) in men submitted to repeat saturation prostate biopsy (SPBx). Materials and Methods: From January 2011 to June 2017, 800 men underwent repeat SPBx; the cost-effectiveness of mpMRI if used as a 'triage test' to avoid unnecessary repeat prostate biopsy was retrospectively calculated using the Italian Public National Health System Day Service. Results: SPBx vs. MRI fusion targeted biopsy diagnosed 215 (89.5%) vs. 184 (76.6%) out of 240, respectively. The overall cost of the 800 prostate biopsies was 138,221 €; the use of mpMRI as triage test would have spared 364/800 procedures, equivalent to 60,905 € (44% of the entire cost), whilst missing 15/205 (7.3%) cases of clinically significant cancer. Conclusion: mpMRI used as a triage test could reduce the need for prostate biopsies by about 45%, thereby improving cost-effectiveness, however, patients should be informed of the false-negative rate associated with mpMRI.*

Prostate cancer (PCa) is the most common tumor with more more than 360,000 deaths per year (1); on the other hand, the risk of overdiagnosis for screening protocols is 50% (2). In recent years, multiparametric magnetic resonance imaging (mpMRI) has been recommended for the diagnosis of clinically significant PCa (3) in men who are candidates for repeat prostate biopsy (4-8) in order to reduce the risk of overtreatment. Moreover, mpMRI has been suggested as 'triage test' at initial biopsy to improve the cost-effectiveness of prostate biopsy. In fact, the cost of care is a major focus from a health policy perspective (9-13); PCa care cost is expected to increase 27-42% between 2010 and 2020, with the single largest driver being ongoing care for prostate cancer (14). In this respect, mpMRI alone appears valuable and cost-effective, especially in men with prior negative biopsy and a suspicion of prostate cancer (8, 15).

In our study, the cost-effectiveness of mpMRI in terms of spared unnecessary biopsies was retrospectively evaluated in men submitted to repeat saturation prostate biopsy.

Correspondence to: Dr. Pietro Pepe, Urology Unit - Cannizzaro Hospital, Via Messina 829, Catania, Italy. Tel: +39 957263285, Fax: +39 957263259, e-mail: piepepe@hotmail.com

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Patients and Methods

From January 2011 to June 2017, 800 men (median age=62 years; range=47-78 years) with negative digital rectal examination underwent repeat saturation transperineal prostate biopsy (SPBx) for the persistent suspicion of cancer [increasing or persistently elevated PSA value]. Informed consent was obtained from all individual participants included in the study. Ten days before SPBx, all the patients underwent pelvic mpMRI; SPBx (median of 30 cores; range=28-34 cores) was performed transperineally using a GE Logiq P6 ecograph (General Electric; Milwaukee, WI, USA) supplied with a bi-planar trans-rectal probe (5-7.5 MHz) using a tru-cut 18 gauge needle (Bard; Covington, GA, USA) under sedation and antibiotic prophylaxis (16). All mpMRI examinations were performed using a 3.0 Tesla scanner (ACHIEVA 3T; Philips Healthcare, Best, the Netherlands) equipped with surface 16-channel phased-array coil placed around the pelvic area with the patient in the supine position; multi-planar turbo spin-echo T2-weighted, axial diffusion weighted imaging, axial dynamic contrast enhanced MRI and spectroscopy were performed for each patient. The mpMRI lesions characterized by a Prostate Imaging-Reporting and Data System (PI-RADS) score of 4 or more were considered suspicious for cancer (7, 17). Two radiologists blinded to pre-imaging clinical parameters evaluated the mpMRI data separately and independently. In the presence of mpMRI lesions suggestive of cancer, cognitive transperineal fusion biopsy or mpMRI/transrectal ultrasound (TRUS) *vs.* transperineal fusion guided-biopsies (four cores for each procedure) were added to SPBx using a GE Logiq E9 and Hitachi 70 Arietta ecograph (Hitachi Medico, Chiba, Japan), respectively (7, 18) (Table I). The GE Logiq E9 and Hitachi Arietta 70 platforms allowed processing of a software-based rigid registration of pelvic mpMRI and TRUS (end-fire probe and biplanar probe, respectively)

Table I. *Detection rate for prostate cancer (PCa) by performing saturation prostate biopsy vs. multiparametric magnetic imaging resonance/transrectal ultrasound (mpMRI/TRUS) fusion biopsy.*

		PCa Clinically significant	
Prostate biopsy	Overall	Detected	Missed
Overall: 800 biopsies	240 (100%)	205/240 (85.4%)	35/240 (24.6%)
mpMRI/TRUS fusion biopsy*	184 (76.6%)	169 (82.4%)	15/56 (26.8%)
Saturation biopsy	215 (89.5%)	195 (81.2%)	20/25 (80%)

*Prostate Imaging-Reporting and Data System ≥4.

Table II. *Cost-effectiveness of multiparametri magnetic resonance imaging (mpMRI) used as 'triage test' to avoid unnecessary repeat prostate biopsy: Results of a public health model (Day Service).*

Day Service procedure	No. of cases	Cost of single biopsy (€)	Overall cost (€)
Histology: Normal parenchyma	560	135.60	84,728
Histology: PCa	240	190.40	53,493
Biopsies avoided negative mpMRI (PI-RADS ≤3)	364	135.60/190.40	60,905
Overall biopsies	800	-	138,221

PCa: Prostate cancer; Prostate Imaging-Reporting and Data System.

by the use of a fusion device; moreover, an electromagnetic tracking system showed the needle localization.

The accuracy of mpMRI and MRI/TRUS fusion biopsy in diagnosing clinically significant PCa (Gleason score >6, greatest percentage of cancer >50% and more than two positive cores) was evaluated (3). In addition the cost-effectiveness of mpMRI used as *triage test* in order to avoid unnecessary repeat prostate biopsy was calculated; the overall cost of prostate biopsy was retrospectively calculated using the public health Day Service (19) model (the estimated price refers to the year 2017). The procedure allowed free hospital access for the patient including the execution of the needed diagnostic and therapeutic procedures: blood examinations, cardiac assessment, mpMRI, SPBx combined with mpMRI/TRUS targeted fusion biopsy, and histological specimen.

The Italian National Health System Day Service established the overall cost of a prostate biopsy as between 135.6 *vs*. 190.4 € in diagnosis of normal parenchyma *vs*. PCa, respectively; moreover, in selected cases (based on income) the patient paid an additional sum of 46.10 €.

Results

The median PSA was 8.6 ng/ml (range=4.5-26 ng/ml); mpMRI was positive (PI-RADS ≥4) in 380/800 (47.5%) patients. None had significant complications from prostate biopsy that needed hospital admission; moreover, the mpMRI procedure was well tolerated and successfully performed in all cases. A T1c PCa was found in 240/800 (30%) patients and normal parenchyma in the remaining 560 (70%). SPBx *vs*. mpMRI/TRUS fusion targeted biopsy diagnosed 215 (89.5%) *vs*. 184 (76.6%) out of 240 PCa, respectively; in detail, SPBx missed 25 (10.5%) suggestive as being clinically significant PCa *vs*. 56 (23.4%) by mpMRI/TRUS fusion biopsy in 20 (80%) and 15 (26.8%) cases, respectively (Table I). In addition, mpMRI/TRUS fusion biopsy diagnosed eight (3.3%) cases of anterior zone PCa missed by SPBx. Diagnostic accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of mpMRI/TRUS fusion biopsy in diagnosing PCa were 80.3, 81.0, 80.0, 63.1 and 88.3%, respectively; mpMRI had a false-positive of 36.8% (140/380 cases) and false-negative rate of 23.3% (56/380) cases.

The overall cost of the 800 prostate biopsies calculated using the Day Service model was 138,221 € (Table II); the use of mpMRI as a triage test would have spared 364/800 (45.5% of the cases) procedures, equivalent to 60,905 € (44% of the entire cost), whilst missing 15/205 (7.3%) cases of clinically significant PCa.

Discussion

Prostate biopsy constitutes a significant outlay of healthcare resources; in the United States more than 1.3 million prostate biopsies are performed annually at a price ranging from $500

to $4,000 (20); if more than half of these biopsies are negative, there is the opportunity to save healthcare costs by avoiding these procedures. Complications from prostate biopsy are similarly expensive and methods to reduce their incidence may be cost-effective (16, 21); the risk of sepsis with its associated costs (*i.e.* hospitalization, antibiotic therapy) in men submitted to transrectal biopsy is between 2% and 3.5%. In addition, the overall health spending of prostate biopsy should include the cost of health personnel, medical instruments, surgical theatre (when used) and the follow-up of clinically insignificant PCa (active surveillance) and the related overtreatment of definitive therapy (erectile dysfunction and urinary incontinence in up to 75% and 48% of patients, respectively, 5-10 years after surgery) (22).

Multiparametric MRI is increasingly being recommended for the diagnosis of clinically significant PCa in men who are candidates for repeat prostate biopsy for persistent suspicion of PCa (7). An alternative approach is to begin with mpMRI to determine which patients need a biopsy and, in those who need it, how it might best be conducted (13, 23). Recent studies have reported encouraging results on the performance of mpMRI to optimize cost-effectiveness of prostate biopsy procedures. In the Prostate MR Imaging Study (PROMIS), the largest accuracy study on the use of mpMRI in candidates for initial prostate biopsy (13), the authors concluded that mpMRI is cost effective as the first test for the diagnosis of PCa, when followed by an MRI/TRUS targeted biopsy in men in whom the mpMRI suggests a suspicion of clinically significant PCa and a second standard prostate biopsy if no clinically significant PCa is found. Recently, Pahwa *et al*. showed that mpMRI followed by targeted MR-guided biopsy in naive men is cost-effective compared with the standard prostate biopsy strategy for the detection of clinically significant PCa (23).

Although, mpMRI improves the cost-effective of prostate biopsy, the false-negative rate of mpMRI (about 20% of the cases) in diagnosing clinically significant PCa should be take into consideration in the clinical management of patients (4, 7); in this respect, the use of a risk calculator that includes mpMRI plus more clinical parameters (age, familiality for PCa, initial or repeat biopsy, PSA values and its kinetics, and genetic markers) could better define the risk of clinically significant PCa for each patient (24).

Regarding our results, some considerations should be made. Firstly, the study was retrospective; secondly mpMRI accuracy was evaluated using biopsy specimens and not the entire prostate gland. Thirdly, we do not know if the presence of a mpMRI PIRADS ≥4 (140 cases) in men with negative prostate biopsy was indicative of false-positive results or missed PCa; at the same time, it is unknown if delayed diagnosis of PCa missed by mpMRI could be responsible for a worse prognosis. Finally, the cost-effectiveness of prostate biopsy procedure was underestimated because the total cost including personnel, surgical theatre and degradation of the instruments was not calculated; in fact, the true cost of the procedure performed in a private health setting should be doubled or tripled in comparison with the public Day Service model.

In conclusion, mpMRI is mandatory in order to improve the accuracy of repeat prostate biopsy in diagnosing clinically significant PCa; if used as triage test, mpMRI could significantly reduce the number of unnecessary repeat prostate biopsies (by about 45%) improving the cost-effectiveness. However, at the same time, patients should be informed of the false-negative rate associated with mpMRI.

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