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ORIGINAL ARTICLE

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A Cost-Benefit Comparison of Biparametric Magnetic Resonance Imaging Versus Conventional Prostate Cancer Screening

Jung Sik Huh, Kyung Kgi Park

Department of Urology, School of Medicine, Jeju National University, Jeju, Korea

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Corresponding author:
Kyung Kgi Park
Department of Urology, Jeju National University Hospital, School of Medicine, Jeju National University, 15 Aran 13-gil, Jeju 63241, Korea
Email: urology.park@gmail.com
https://orcid.org/0000-0001-9807-1461

Purpose: : This study aimed to compare the cost-effectiveness and feasibility of biparametric magnetic resonance imaging (bp MRI) for prostate cancer screening to prostate-specific antigen (PSA)-based screening.

Materials and Methods: We retrospectively reviewed the data from 602 men who had PSA-based prostate cancer screening between July 2014 and April 2017 and 621 men who underwent bp MRI-based prostate cancer screening between May 2017 and December 2020. Of them, 467 men with Prostate Imaging Reporting and Data System scores of 3 or higher underwent magnetic resonance imaging/ultrasound fusion transrectal biopsy and random transrectal prostate biopsy. The remaining 154 patients underwent random prostate biopsies only. Patient demographics, digital rectal examination, staging, PSA level, PSA density, bp MRI findings associated with prostate cancer detection on biopsy, admission rate for complications after prostate biopsy, and associated medical costs were analyzed.

Results: Prebiopsy demographics were comparable. The MRI-based screening had a higher prostate cancer detection rate (62.7%) than conventional screening (45.1%). Biparametric MRI was more sensitive for clinically significant prostate cancer (csPCa) (40.6% vs. 23.5%). In 154 men who lacked a targetable prostate lesion, 47 and 14 patients (9.1%) had insignificant and significant prostate cancer, respectively. None of the patients had more than Gleason 8 (4+4). MRI-based screening costs more than conventional screening. However, the cost of detecting csPCa can be reduced by 49.4% (United States dollar [USD] 14,883.5 vs. USD 7,355.0).

Conclusions: MRI-based screening is sensitive for csPCa and is cost-effective. It can also reduce unnecessary biopsies to detect insignificant prostate cancer.

Key Words: Cost-benefit analysis, Magnetic resonance imaging, Prostate-specific antigen

INTRODUCTION

Biparametric magnetic resonance imaging (bp MRI) can be used for screening patients with suspected prostate cancer, and its usefulness and merits have been demonstrated in many studies [1, 2]. High positive and negative predictive values of bp MRI/ultrasound (bp MRI/US) fusion biopsy in men according to their Prostate Imaging Reporting and Data System (PI-RADS) score have also been documented [3].

Prostate-specific antigen (PSA) levels and digital rectal examination (DRE) are easy and inexpensive methods recommended for prostate cancer screening [4, 5]. However, this method has some limitations in identifying significant prostate cancers [6, 7].

MRI-based screening and MRI/US fusion biopsy were superior to conventional methods in screening for significant prostate cancer [8]. However, multiparametric MRI (mp MRI) is time-consuming, expensive, and potentially harmful because of the use of nephrotoxic contrast agents. Therefore, some authors recommend bp MRI with no contrast agents and fewer phases than mp MRI. Noncontrast bp MRI maintained good sensitivity and specificity in identifying clinically significant prostate cancer [9]. However, a detailed cost analysis of bp MRI is lacking, despite numerous effectiveness reports.

Therefore, in this study, we compared conventional (PSA and DRE alone) and bp MRI (bp MRI, PSA, and DRE) screening methods for prostate cancer based on efficacy and overall costs.

MATERIALS AND METHODS

1. Patients

We have conducted this study in accordance with the principles of the Declaration of Helsinki. The Institutional Review Board (IRB) of Jeju National University Hospital (IRB number: 2016-06-012) waived the requirement of informed content as our research was based on retrospective review.

A total of 1223 men with a PSA level >3.5 ng/mL or palpable nodule on a DRE assessed between July 2014 and December 2020 were enrolled in the study. From July 2014 to April 2017, 602 patients who underwent systemic biopsy without prebiopsy were recruited to the conventional screening group. From May 2017 to December 2020, 621 patients who underwent a prebiopsy bp MRI and systemic and/or targeted biopsy with ultrasound fusion were assigned to the bp MRI screening group. Of these 621 patients, 467 underwent systemic and targeted biopsy because of having PI-RADS scores >3. All patients underwent prostate biopsy at a single institution. A total of 598 patients with initial benign diagnoses were followed up until December 2020, and the diagnosis of prostate cancer was confirmed through subsequent biopsy. Patients were excluded if they had received 5-α reductase inhibitors within 3 months of biopsy or underwent prostate biopsy at another hospital.

2. Biopsy Protocol

All anticoagulant therapies were discontinued 7 days before the prostate biopsy. Bowel preparation was done on the night prior to the biopsy. Prophylactic oral ciprofloxacin (500 mg) was administered once daily, 30 minutes before and 2 days after the biopsy procedure. For the procedure, patients were placed in the left lateral decubitus position. Intrarectal lidocaine jelly was injected, and the periprostatic area was infiltrated with local anesthetic (5 mL of 2% lidocaine). A spring-driven 18-gauge needle core biopsy gun (Max Core Biopsy; BARD, Covington, GA, USA) was used. Ultrasound imaging was utilized to guide the systematic core biopsy and 3 core targeted MRI/US fusion biopsies, all performed by a urologist (KKP) with over 10 years of experience with prostate biopsies and 5 years' experience with MRI/US fusion biopsies.

MRI/US fusion-targeted biopsies were performed based on the PI-RADS (version 2) information provided by bp MRI. On suspicious lesions with a PI-RADS score of 3, we performed 10–12 core systemic biopsies after 3 core targeted biopsies. However, if the patient had a score below 3, only a systemic biopsy was done.

3. MRI Protocol

MRI was performed using a 3T MRI system (Intera Achieva; Philips Medical Systems, Best, Netherlands) with a pelvic phased-array coil before prostate biopsy. The imaging protocol included T2-weighted turbo spin-echo and diffusion-weighted (DW) imaging. T2-weighted turbo spin-echo images were acquired in 3 orthogonal planes. DW images were obtained using the single-shot echo-planar imaging technique with b values 2 of 0 and 500 s/mm. Apparent diffusion coefficient DW maps were automatically constructed pixel by pixel.

4. Image Analysis

Two radiologists (JSL and BSK) with 6 and 13 years of experience in interpreting prostate MRI results reviewed all images. Both radiologists had 5 years of experience in PI-RADS (version 2) scoring. They conducted a consensus

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review of the bp MRI images obtained from all patients to identify regions with the target lesion and the PI-RADS score of the lesion. In case of more than one suspicious lesion, they recommended targeting both lesions using MRI/US fusion biopsy.

5. MRI-Ultrasound Fusion Protocol

We performed MRI/US fusion-guided biopsy under electromagnetic (EM) tracking of suspicious lesions identified on MRI. An EM field generator (Northern Digital Inc., Waterloo, ON, Canada) was placed above the pelvis, which allowed real-time tracking of a custom biopsy probe embedded with a passive EM tracking sensor (Traxtal Inc., A Philips Healthcare Co., Toronto, ON, Canada). MRI T2 axial and/or DW images were then loaded into a Philips/PercuNav system (Royal Philips Electronics, Amsterdam, The Netherlands). We manually matched the apex of the prostate on T2-weighted axial MR prostate imaging and a transrectal US image and then matched the verumontanum and bladder neck of the images. Finally, the images were fused using embedded fusion software (PercuNav), which enabled the identification of the target lesion in the suspected areas described in the MRI report on real-time transrectal ultrasound axial images.

6. Pathology

We recorded the number and locations of positive cores and the Gleason scores of each positive core. Prostate cancers with a Gleason score sum of 6 and low-volume Gleason 3+4 (i.e., <5% of any core containing Gleason 4 cancer) were defined as clinically insignificant prostate cancer.

7. Statistical Analysis

Patient characteristics of the conventional and bp MRI-based screening groups were comparatively analyzed. The Student t-test was performed using Prism 5.1 D (GraphPad Software Inc., San Diego, CA, USA). All tests were 2-tailed and $p<0.05$ was considered significant.

8. Cost Evaluation

Costs incurred during prostate cancer screening through the diagnostic, prebiopsy, and postbiopsy 30-day window were obtained from the patient files and defined by payment amounts. We included all costs associated with each prostate biopsy screening service (e.g., all line items per claim for prostate biopsy and/or imaging). We obtained the sum of the patient responsibility payment amount from the outpatient file over the diagnostic/peribiopsy period to calculate the costs for each patient. These payment variables included imaging, laboratory tests, medication, admission, and biopsy fees. The clinically significant detection rate of prostate cancer was set as a benefit of each screening method and their formula is as follows: mean medical cost per person×total number of biopsied men/clinically significant prostate cancer (csPCa) detection rate.

RESULTS

The prebiopsy demographics of both groups were comparable. More cases were detected in the MRI-based screening group (62.7%) than in the conventional screening group (45.1%). The MRI-based screening group (40.6%) also detected more clinically significant prostate cancer than the conventional screening group (23.5%). In patients who had systemic biopsy only in the absence of targetable lesions, 93 were confirmed to be without cancer, 47 had insignificant prostate cancer, and 14 (9.1%) had significant prostate cancer. None of the patients had more than Gleason 8 (4+4).

Of the 331 patients with benign results on conventional biopsy, 59 (17.8%) eventually received a csPCa diagnosis with repeat systemic biopsy within the follow-up period. In the MRI-based screening group, none of the 267 patients with benign disease at initial fusion or random prostate biopsy had prostate cancer during the mean 2.4 years of follow-up.

Patients were required to spend an average of United States dollar (USD) 581 and USD 641 with conventional and MRI-based screening methods, respectively. This cost per patient was accounted for. The conventional screening group had the largest expenditure for random biopsy, followed by pre-examination and medication expenditures. As more biopsies were performed, more patients were rehospitalized because of

complications; therefore, the third was a complication-related expenditure. The MRI/US fusion biopsy group also spent the most on prostate biopsy, followed by MRI. However, the cost of prostate biopsy remained lower in the MRI group. The number of patients hospitalized for complications was fewer in the MRI group, resulting in reduced complication-related expenditures. The medical costs involved in the detection of 1% of patients with csPCa in the target screening population were USD 14,881 and USD 7,354 for conventional and MRI-based screening, respectively, totaling a cost reduction of approximately 49.4%. However, the cost increased to USD 11,429 in the group where only random biopsies were performed for nondetectable lesions in the prebiopsy MRI (Table 1). The cost included checking the serum PSA level, performing each prostate biopsy, admission, readmission for treating prostate biopsy-related complications, and undergoing MRI, especially in the bp MRI-based screening group (Table 2). Despite the increased cost of bp MRI, the

Table 1. Comparison between the 2 screening methods

Characteristic	Conventional screening	MRI-based screening		p-value
	Random bx	MRI/US fusion bx	Random bx	
Total number of enrolled men	602	621		
Number of biopsied men	602	467	154	
Age (yr)	66.13±8.57	67.8±8.23	64.8±8.76	0.98
PSA level (ng/mL)	7.09±12.34	8.09±10.92	6.52±9.76	0.78
Prostate volume (mL)	44.95±27.18	40.47±20.45	48.98±22.43	0.45
PSAD (ng/mL/mL)	0.15±0.21	0.20±0.24	0.13±0.19	0.92
DRE				0.98
No palpable nodule	519 (86.2)	369	154	
Palpable nodule	83 (13.7)	98	0	
Biopsy Gleason score				0.51
No cancer	331	174	93	
Gleason 6 (3+3)	100	87	32	
Gleason 7 (3+4) low volume	30	15	15	
Gleason 7 (3+4) high volume	71	31	7	
Gleason 7 (4+3)	47	51	7	
Gleason ≥8 (4+4)	35	108	0	
csPCa detection	142 (23.5)	190 (40.7)	14 (9.1)	0.01*
Overall PCa detection	271 (45.1)	293 (62.6)	61 (39.6)	0.01*
Re-admission rate for complication	24 (3.9)	17 (3.6)	6 (3.9)	0.45
Mean medical cost per 1% of detection rate for csPCa (USD)	14,881.95	7,354.96	11,429.68	0.01*
Mean medical cost per person (USD)	580.94	641.61	675.39	0.89

Values are presented as number (%) or mean±standard deviation.

MRI, magnetic resonance imaging; Bx, biopsy; US, ultrasound; PSA, prostate-specific antigen; PSAD, prostate-specific antigen density; DRE, digital rectal examination; csPCa, clinically significant prostate cancer; PCa, prostate cancer; USD, United State dollar.

*p<0.05, statistically significant differences.

Table 2. The financial details for each biopsy method

Variable	Cost per item (USD)	No. of random bx	Total cost for random bx	No. of fusion bx	Total cost for fusion bx
PSA	24	602	14,345	621	14,798
DRE	7	602	4,297	621	4,433
Fusion biopsy-related medical fee	289		0	467	134,932
Prebiopsy lab test and medication fee	180	602	108,645	467	84,281
Biparametric MRI fee	202	0	0	621	125,505
Systemic biopsy-related medical fee	289	602	173,938	0	0
Mean admission for biopsy-related complication	2,021	24	48,504	17	34,358
Total cost	-	-	349,729	-	398,306
Cost per person	-	-	581	-	641

USD, United State dollar; Bx, biopsy; PSA, prostate-specific antigen; DRE, digital rectal examination; MRI, magnetic resonance imaging.

*USD 1 = 1,237 Korean won; all financial data from our institution; α: admission for biopsy-related complication, range: USD 1,374.45–4,285.23.

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expenditure significantly reduced compared with that in the conventional screening group. This is because of a reduction in the costs of performing a biopsy and/or rehospitalization for managing associated complications since the MRI-based screening group does not require biopsies.

DISCUSSION

To monitor prostate cancer in men with urinary tract symptoms in a urologic clinic, clinicians initially test serum PSA levels and perform a DRE. When necessary, prostate biopsy is done to confirm prostate cancer. However, transrectal prostate biopsy is associated with the risk of infection, hematuria, and pain during the procedure [10-12]. Hence, estimating the possibility of clinically significant prostate cancer is essential before performing a biopsy to reduce the number of unnecessary biopsies. To achieve this, we evaluated the feasibility of prebiopsy bp MRI-based screening in terms of total direct cost and cancer detection rate compared with that of the conventional method, including PSA and DRE.

Our findings suggest that bp MRI-based prostate cancer screening effectively diagnosed clinically significant prostate cancer using fewer diagnostic biopsy cores than conventional PSA-based screening. This decreased the number of biopsy-related complications without significantly increasing the average cost per person and demonstrated cost-effectiveness in this retrospective case-control study.

The widespread use of PSA testing can reduce mortality [13]. In 2012, the US Preventive Services Task Force (USPSTF) recommended against nonselective PSA screening [14]. As a result, many clinicians do not perform routine PSA testing. Thus, the previously decreased prostate cancer mortality in the 2 decades since the introduction of PSA has not been maintained, and the incidence of advanced prostate cancer and cancer-related mortality has increased since 2012 [15]. In 2017, the USPSTF reinstated its previous recommendations [16].

Clinical tools are essential in the screening of significant prostate cancer before performing a prostate biopsy. Multiparametric MRI has shown high sensitivity and specificity for the identification of clinically significant prostate cancer [17]. Some authors have reported the usefulness of MRI as a screening tool and prebiopsy discriminator [18]. However, mp MRI is time-consuming, expensive, and potentially harmful with the use of nephrotoxic contrast. Therefore, some authors recommend noncontrast bp MRI and fewer phases than mp MRI. Noncontrast bp MRI maintained good sensitivity and specificity in screening for clinically significant prostate cancer.

Biparametric MRI has shown diagnostic accuracy; its cancer detection rates are comparable to those of mp MRI with reduced cost, study time, and contrast-associated risk [2, 19, 20].

Transrectal prostate biopsy carries a risk of postbiopsy sepsis. It can increase healthcare costs and biopsy-related mortality. Gross et al. [21] reported that 2%–5% of biopsies led to sepsis, and in terms of financial aspects, the estimated direct cost of sepsis after prostate biopsy, adjusted for inflation, ranged from USD 8,672 to USD 19,100 per patient. Moreover, hospitalization due to biopsy complications was reported to cost an average of USD 2,021. This price was calculated as the highest medical expenditure among the costs charged for biopsy, but it was a mean 85% decreased complication-related cost compared to the results of the study of Gross et al. [21]. However, if these costs increase, the cost-benefit ratio will be greater in the fusion biopsy group. Not only should biopsies be fewer in number to achieve a much better outcome regarding postoperative complications, but reducing the number of unnecessary biopsies reduces the total cost of screening. In this study, patients in the MRI group underwent bp MRI before the biopsy to identify significant prostate cancer, and 154 patients (24.7%) were excluded if clinically significant prostate cancer was suspected. In the conventional group, of 602 patients with high PSA levels, 461 (76.6%) had no clinically significant cancer. In the MRI-based screening group, 276 of 467 patients (44.4 %) who had more than PI-RADS 3 also had benign or insignificant cancer. However, this rate was significantly lower than that in the conventional group. Owing to the relatively low sample size in this study, the readmission rate was not significantly different between the 2 groups.

Although bp MRI-based prostate cancer screening had an additional cost of bp MRI compared to the conventional groups, the average cost per person was not significantly

higher because of the low number of biopsies, which reduced the overall cost.

Boesen et al. [22] also reported a bp MRI as a triage test in 1,020 biopsy-naive men with suspected prostate cancer. A total of 305 men (30%) could avoid biopsy because of low-suspicion bp MRI findings, and significant prostate cancer diagnoses were improved by 11% (396 in the bp group vs. 351 men in the conventional group; p<0.001). However, they did not discuss the financial implications of using prebiopsy bp MRI. Additional and complementary tests to improve diagnostic results should consider their increased cost. We believe that an efficient health policy is cost-effective. Thus, we can recommend the bp MRI as a triage test to patients and insurance companies. Despite using additional bp MRI in this study, the average cost per person did not substantially increase.

As suggested by Thompson et al. [17], prebiopsy mp MRI can aid in various aspects of prostate cancer diagnosis and management. It can be used in screening as a triage test, serve as the image set for fusion ultrasound biopsy, and help distinguish capsule invasion in intermediate- to high-risk diseases to support treatment decisions and guide selection for planning active surveillance These merits complement each other.

The key element is that the reduction in complications from biopsy reduces the overall cost of screening. Certain authors have suggested that freehand transperineal biopsy may be recommended under perineal local anesthesia to reduce the risk of infection [23, 24]. However, cost-related studies and well-designed RCTs are insufficient [25].

Biparametric MRI has T2-and DW images, but no dynamic contrast images. bp MRI also has multiple sectional images, such as axial, sagittal, and coronal images. Some authors have argued that bp MRI with axial sectional imaging alone may be comparable to conventional bp MRI [26]. Thus, the cost of MRI can also be reduced. We consider these methods promising triage tests to identify significant prostate cancer before the biopsy. However, multi-institutional prospective studies are required to confirm their feasibility.

This study has limitations. First, prostate biopsy-related costs may vary by country. As such, our data may not necessarily be representative across all health systems. Nevertheless, our results are expected to form a baseline model that will likely prompt similar beneficial patterns of time savings and cost-effectiveness in other health systems. Second, we believe that this retrospective study will be required multi-institutional prospective studies because these results were arised from retrospective and small sample sized study subjects.

CONCLUSIONS

In terms of cost-effectiveness, bp MRI is feasible tool with identify the clinically significant prostate cancer and a triage test can discriminate more significant prostate cancer in patients than conventional methods with substantial cost benefits. However, to overcome lack of this study, further prospective study should be needed to clarify the effectiveness of this screening method.

NOTES

- Conflicts of Interest: The authors have nothing to disclose.
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- ORCID
Jung Sik Huh: https://orcid.org/0000-0003-2767-4390
Kyung Kgi Park: https://orcid.org/0000-0001-9807-1461

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