



ORIGINAL ARTICLE

The Incidence of Prostate-Specific Antigen Test in a Country With a Limited Social Perception of Prostate Cancer 2006–2016: Disparities Manifested by Residential Area

Young Hwii Ko¹, Byung Hoon Kim²

¹Department of Urology, College of Medicine, Yeungnam University, Daegu, Korea

²Department of Urology, School of Medicine, Keimyung University, Daegu, Korea

Purpose: To trace the incidence of serum prostate-specific antigen (PSA) tests by the residential areas of Korea, where social awareness on prostate cancer (PCa) is limited due to the absence of a public screening.

Materials and Methods: From Korean national health insurance data, the number of men older than 40 years who performed PSA testing without PCa or before the enrollment on the national registry during 2006–2016 was identified, then its association with the incidence of PCa were analyzed by a residential area categorized into metropolitan, urban, and rural area.

Results: PSA testing was performed more in the metropolitan area in 2006–2008, but performed the most prevalently in the rural area since 2010. Among the 17 administrative districts, the most PSA-tested district was Jeollabuk-do (9.36%) in 2016, which was Seoul (2.85%) in 2006. The mean repetition number of PSA tests during 11 years of the study period was highest among the inhabitant of Seoul (3.25 times, $p < 0.0001$), followed by Gwangju (2.98 times), another metropolitan city. The mean repetition number of PSA tests during the study decade was in the order of metropolitan area (2.97 times), rural area (2.83 times), and urban area (2.75 times, $p < 0.0001$). In every year, however, the incidence of PCa was the highest in a rural area, where had the oldest mean age.

Conclusions: Despite a recent increase of PSA screening and diagnosis of PCa especially in the rural area, the opportunity of repeated testing was presented more to the inhabitant of a metropolitan area.

Key Words: Prostate cancer, PSA screening, Incidence

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Corresponding author:

Young Hwii Ko

Email: urokyh@naver.com

<https://orcid.org/0000-0002-9150-4292>

INTRODUCTION

Because the incidence of prostate cancer (PCa) in Korea currently is led by its spread among the elderly population, it is projected to increase significantly in parallel with the accelerating trend of societal aging.^{1,2} In the detection of PCa, serum prostate-specific antigen (PSA) testing plays a pivotal

role, given that the majority of contemporary PCa does not manifest any specific symptoms besides ambiguous male lower urinary tract symptoms that originated more frequently from the concomitant benign prostate hyperplasia. Therefore, the most serious consequence of current Western-based prohibitive guidelines on the PSA test, particularly for the elderly in Korea, is that their negative



impact on the establishment of screening policy for the men who may benefit from the PSA test, given this distinctive epidemiologic background on the PCa.

As with other Asian countries,³ the incidence of PCa in Korea is rapidly increasing in the last decade. Since 2002, when PCa was firstly reported as the 5th most commonly developing male malignant disease, the incidence of PCa has kept increasing jumping one spot to the 4th from 2016. In the most updated report (2019), PCa became the 3rd prevalent cancer among the Korean male, and 2nd most common cancer especially in the aged men over 65 years old,⁴ despite a limited social awareness dominantly caused by the absence of a nation-driven public screening policy influenced by contemporary western recommendations.

Given the age-related increasing incidence of PCa along with the national-wide trend of aging which has been manifested more remarkably in a rural than an urban area, we traced the incidence of serum PSA testing by the residential areas of Korea and investigated its impact on the detection of PCa.

MATERIALS AND METHODS

1. Data Source and Study Subjects

Data used in this study were obtained from the National Health Insurance Review and Assessment Service of Korea (NHIS), which covers approximately 98% of its population and provides universal health coverage. The Korean NHIS database includes almost all medical data, including diagnostic codes, procedures, and outcomes (deaths), and it also includes sociodemographic information such as age, health insurance premiums, and residential area. All personal identification numbers are encrypted before data processing to comply with the privacy guidelines of the Health Insurance Portability and

Accountability Act. All study procedures and ethical aspects were approved by the Yeungnam University Hospital Institutional Review Board (approval number: YUMC-2019-11-012-002).

From the NHIS data, male subjects older than 40 years who performed the PSA test from 2006 through 2016 were identified. The PSA test code utilized in this study was B5490, C4280, C7428, and the tests performed just before 3 months, and after the registration into NHIS as C61 were excluded. Patients who were newly diagnosed with PCa and registered in the NHIS with an International Statistical Classification of Diseases, 10th revision code of C61, as well as V193/194 each year between the study periods, were also investigated.

2. Study Design and Endpoints

Currently, Korea consists of 17 administrative districts categorized into (1) Seoul, the capital city, (2) 6 metropolitan cities including Incheon, Daejeon, Daegu, Gwangju, Ulsan, and Busan, (3) Sejong special self-governing city (a planned city as an administrative capital), (4) 8 provinces including Gyeonggi-do, Gangwon-do, Chungcheongbuk-do, Chungcheongnam-do, Jeollabuk-do, Jeollanam-do, Gyeongsanbuk-do, Gyeongsangnam-do, and (5) Jeju self-governing province. We simply categorized these 17 districts into 3 residential areas based on the current population including (1) metropolitan area (Seoul, 6 metropolitan cities, and Gyeonggi-do province), (2) urban area (all the other administrative cities population more than 50,000), (3) rural area (the rest administrative districts including gun/eup/myeon). Considering a reported association between the incidence of PCa and aging, the mean age of each residential area was investigated from annual statistics in Korea.

The primary endpoints of this study were (1) to determine the prevalence of PSA test by the residential area, and (2) to identify an association

between the implementation of PSA test and the newly registered PCa by the residential area, given the reported disparities in the prevalence of PCa, based on age and the socioeconomic status.⁵

3. Statistical Analysis

To compare the characteristics and outcomes between each group, Student t-test was used for continuous variables, and the chi-square test was used for binary and categorical variables. Cancer incidence rates were calculated per 1,000 person-years. To determine the association between the PSA test and the development of PCa, correlation analysis was utilized. Two-sided p-values of <0.05 were considered to be statistically significant. All statistical analyses were performed using SAS ver. 9.4 software (SAS Institute Inc., Cary, NC, USA).

RESULTS

1. The Difference of PSA Incidence by the Residential Area 2006–2016

The incidence of the PSA test across 3 residential areas was significantly different, which was performed highest in the metropolitan area between 2006 and 2008 (p<0.001) (Table 1). Though it was carried out the most prevalently in a rural area since 2010, the incidence of PSA tests was consistently increased across all 3 residential areas without a recession from 2.41%–2.56% in 2006 to 7.20%–7.52% in 2016 (Fig. 1).

A significant difference was also observed in the PSA testing incidence among the 17 administrative districts except for Sejong city (a newly built administrative city), which is about double fold in the most frequently performed district of Jeollabuk-do (9.36%) than the least frequently performed district of Jeju self-governing province (4.31%) in 2016 (Fig. 2). The most PSA-tested district was

Table 1. The incidence of serum prostate-specific antigen (PSA) test in each year by the residential area

Year	Total			Metropolitan			Urban			Rural			p-value
	Men with PSA test	Population (≥40 yr)	PSA test %	Men with PSA test	Population (≥40 yr)	PSA test %	Men with PSA test	Population (≥40 yr)	PSA test %	Men with PSA test	Population (≥40 yr)	PSA test %	
2006	246,848	9,686,975	2.54	167,598	6,463,012	2.59	52,228	2,171,171	2.41	26,952	1,052,789	2.56	<0.001
2007	312,818	9,999,912	3.12	212,303	6,687,169	3.17	68,471	2,241,586	3.05	31,981	1,071,155	2.99	<0.001
2008	478,973	10,337,914	4.63	325,742	6,926,493	4.70	104,079	2,319,192	4.49	48,992	1,092,226	4.49	<0.001
2009	571,582	10,694,580	5.34	383,894	7,178,261	5.35	127,868	2,401,349	5.32	59,705	1,114,966	5.35	0.329
2010	631,357	11,039,633	5.71	424,128	7,422,385	5.71	140,582	2,480,595	5.67	66,529	1,136,653	5.85	<0.001
2011	699,978	11,386,232	6.14	470,610	7,664,185	6.14	156,799	2,561,763	6.12	72,330	1,160,283	6.23	<0.001
2012	755,308	11,723,878	6.44	506,015	7,897,031	6.41	174,369	2,703,462	6.45	74,648	1,123,382	6.64	<0.001
2013	801,191	12,042,751	6.65	536,280	8,115,561	6.61	187,092	2,782,995	6.72	77,596	1,144,196	6.78	<0.001
2014	831,434	12,354,915	6.72	556,644	8,324,992	6.69	194,725	2,901,653	6.71	79,858	1,128,269	7.08	<0.001
2015	863,727	12,635,426	6.83	577,705	8,506,683	6.79	206,004	2,981,226	6.91	79,951	1,147,515	6.97	<0.001
2016	937,494	12,886,340	7.27	623,557	8,665,405	7.20	226,383	3,056,316	7.41	87,536	1,164,618	7.52	<0.001

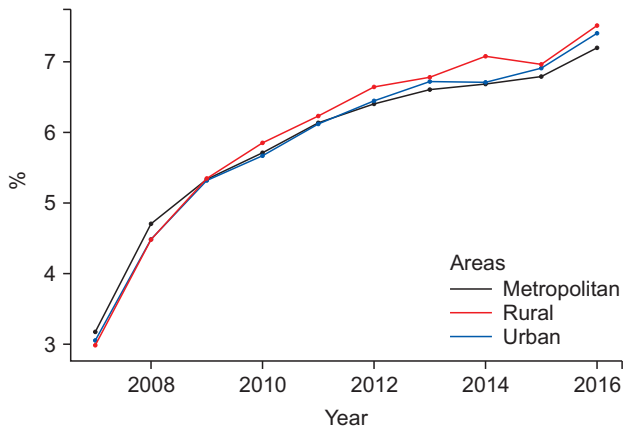


Fig. 1. The incidence of serum prostate-specific antigen test in each year by the residential area.

Jeollabuk-do in 2016, which also was Seoul in 2006.

The mean repetition number of PSA tests during 11 years of the study period was highest among the inhabitant of Seoul (3.25 times, $p < 0.0001$), where is a sole district more than 3 repeated tests were performed on average. The mean repetition number of PSA tests during the study decade was in the order of metropolitan area (2.97 times), rural area (2.83 times), and urban area (2.75 times, $p < 0.0001$).

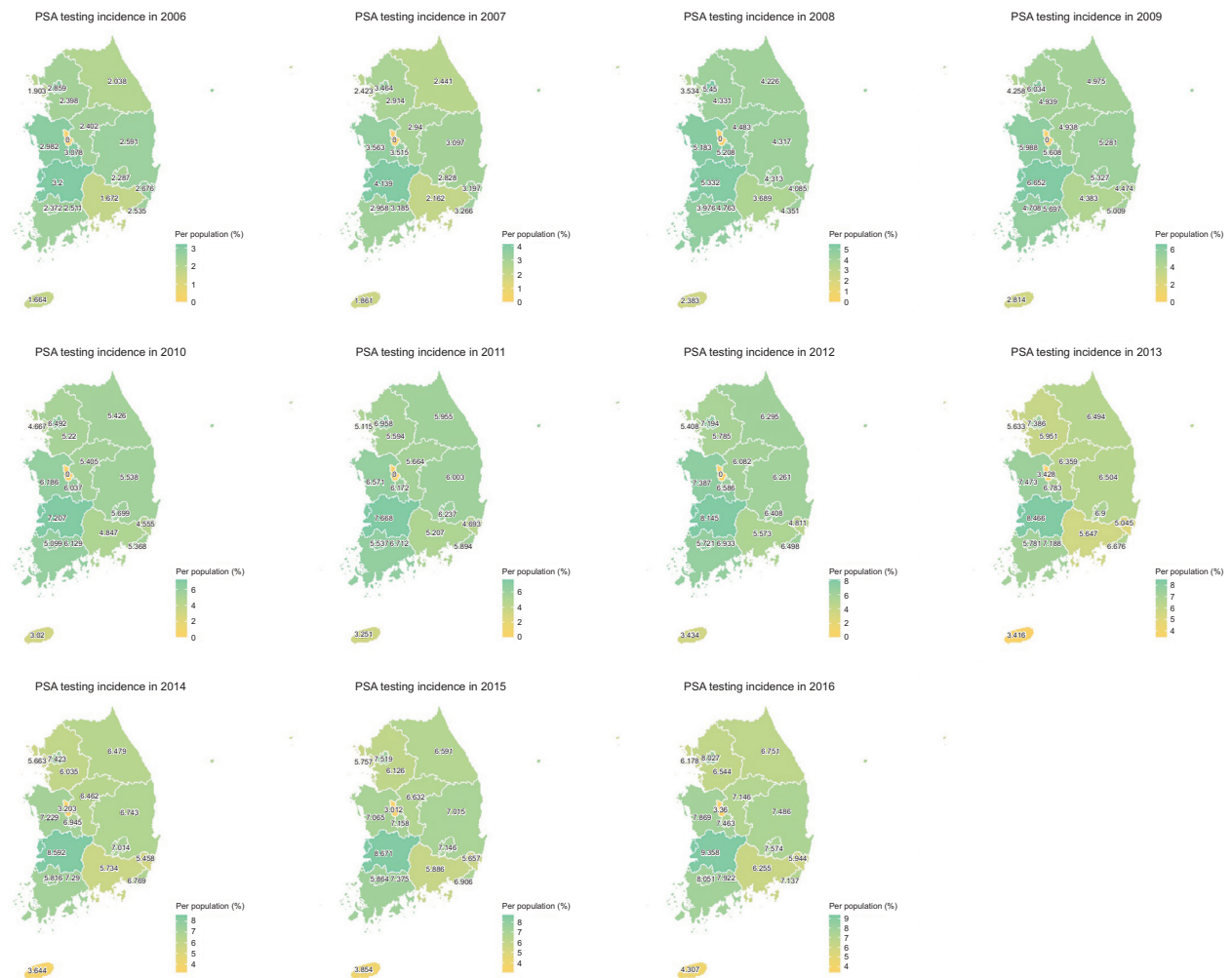


Fig. 2. The incidence of serum prostate-specific antigen test in each year by the 17 administrative districts.

2. The Difference of PCa Incidence by the Residential Area 2006–2016

During the research period, the incidence of NHIS registered PCa increased about threefold from 4,425 in 2006 to 15,043 in 2016 (Table 2). In 2016, the most prevalent PCa district was Jeollanam-do, which was Seoul in 2006 (Fig. 3). In every year, the incidence of PCa was the highest in a rural area (Fig. 4), where had the oldest mean age (Table 3).

DISCUSSION

The ultimate aim of a population-based screening strategy is to promote cancer-specific survival. About the benefit from the mass screening policy based on PSA, however, there is still controversy particularly since 2012,^{6,7} when the US Preventive Study Task Force (USPSTF) recommended the ban of PSA screening for the mass population mainly due to the lack of positive evidence on the prolonging the survival by applying it to the screening, rather generating overdiagnosis and overtreatment on so-called an insignificant disease.⁸ Even though USPSTF modified their original recommendations in 2018, opening slots of PSA screening for the explained individuals aged between 55 to 69 years,⁹ the macroscopic consequence of accepting a specific screening strategy can be quite different in each country, based on the exposure rate to the PSA testing and manifestation of racial differences in PCa incidence. In this point, how the contemporary Western guidelines on PSA screening that are strongly affected by the statements from the USPSTF apply to Korean males' remains unclear, when one considers the lack of data on the frequency of PSA testing and distinctive difference in the proportion of the aged population among the newly diagnosed PCa in Korea.

Nowadays, the majority of PCa was found in the non-metastatic stage, mainly due to the enhanced

Table 2. The incidence of registered prostate cancer (PCa) in each year by the residential area

Year	Total			Metropolitan (PCa %)			Urban (PCa %)			Rural (PCa %)			p-value
	Detected PCa	Population (≥40 yr)	PCa %	Detected PCa	Population (≥40 yr)	PCa %	Detected PCa	Population (≥40 yr)	PCa %	Detected PCa	Population (≥40 yr)	PCa %	
2006	4,425	9,686,975	0.04	-	6,463,012	0	-	2,171,171	0	-	1,052,789	0	<0.001
2007	6,941	9,999,912	0.06	4,599	6,687,169	0.07	1,641	2,241,586	0.07	943	1,071,155	0.09	<0.001
2008	8,041	10,337,914	0.07	5,248	6,926,493	0.08	1,835	2,319,192	0.08	1,016	1,092,226	0.09	<0.001
2009	9,158	10,694,580	0.08	5,954	7,178,261	0.08	2,039	2,401,349	0.08	1,227	1,114,966	0.11	<0.001
2010	10,179	11,039,633	0.09	6,528	7,422,385	0.09	2,364	2,480,595	0.10	1,332	1,136,653	0.12	<0.001
2011	10,651	11,386,232	0.09	6,940	7,664,185	0.09	2,389	2,561,763	0.09	1,377	1,160,283	0.12	<0.001
2012	11,261	11,723,878	0.09	7,249	7,897,031	0.09	2,565	2,703,462	0.09	1,476	1,123,382	0.13	<0.001
2013	12,390	12,042,751	0.10	7,986	8,115,561	0.10	2,952	2,782,995	0.11	1,480	1,144,196	0.13	<0.001
2014	12,790	12,354,915	0.10	8,199	8,324,992	0.10	3,006	2,901,653	0.10	1,617	1,128,269	0.14	<0.001
2015	13,030	12,635,426	0.10	8,470	8,506,683	0.10	3,104	2,981,226	0.10	1,491	1,147,515	0.13	<0.001
2016	15,043	12,886,340	0.11	9,749	8,665,405	0.11	3,571	3,056,316	0.12	1,766	1,164,618	0.15	<0.001

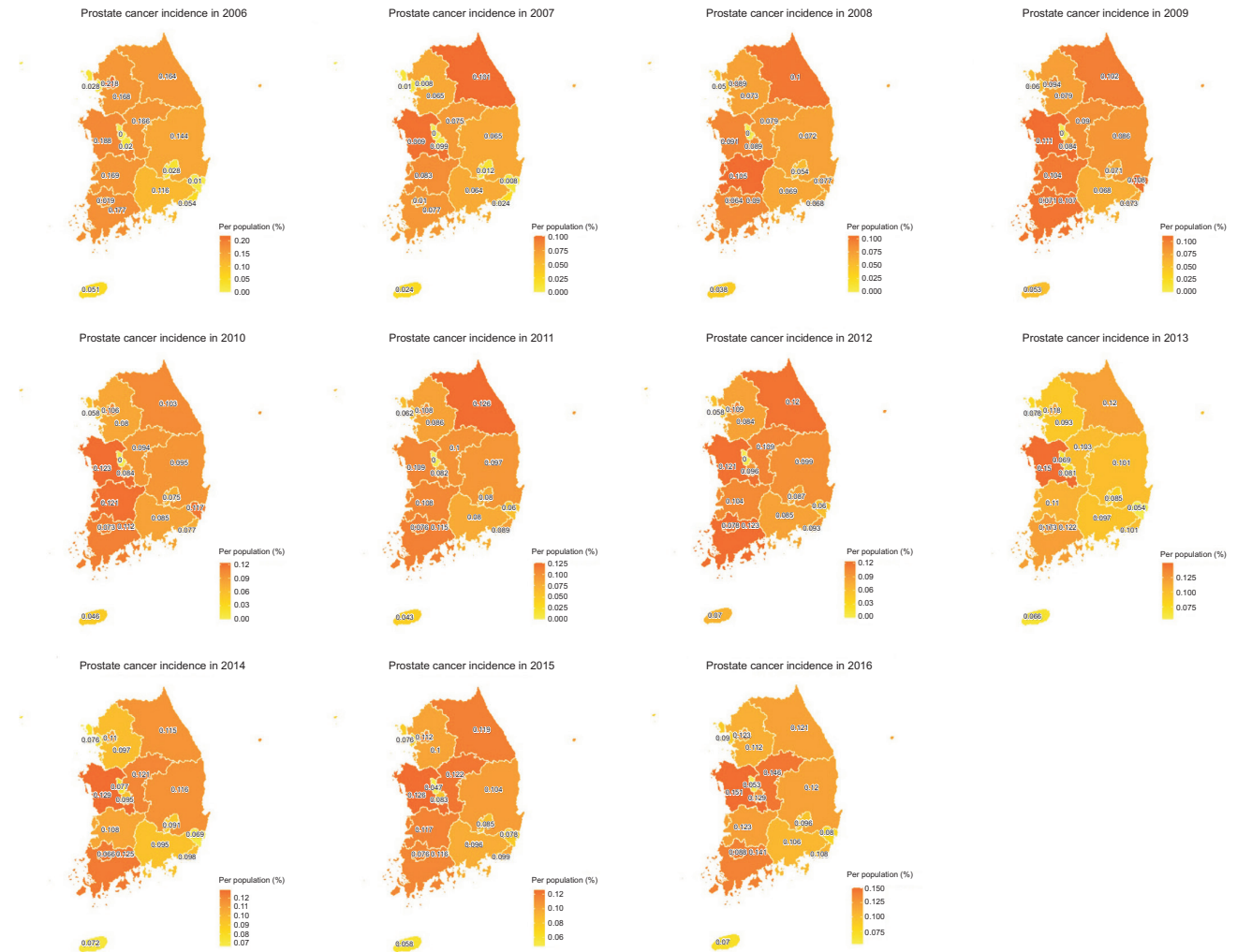


Fig. 3. The incidence of registered prostate cancer in each year by the 17 administrative districts.

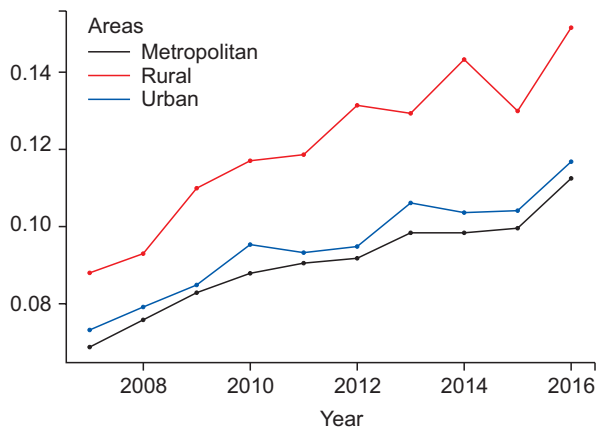


Fig. 4. The incidence of prostate cancer in each year by the residential area.

public awareness of the prostatic disease that often develops in the aging male, along with the increased detection by PSA testing. As a result, the incidence of PCa in Korea increased dramatically, more than 12 times just within a couple of decades by the most updated national-wide cancer registry (1,258 in 2000 vs. 14,857 in 2018), even in the absence of a regular check-up policy on PCa in contrast to other prevalent malignant diseases such as lung, stomach, colon, and liver cancer, that currently is the 1st, 2nd, and 5th prevalent male cancer in Korea.⁴ As with other Asian countries, the peculiar characteristic in the epidemiologic feature of PCa is that it primarily encroaches on

Table 3. Comparison of the preoperative questionnaire and uroflowmetry according to *de novo* overactive bladder after radical prostatectomy

Year	Mean age					Incidence of PSA test					Incidence of PCa				
	Total	Metro politian	Urban	Rural	Total	p-value	Total	Metro politian	Urban	Rural	p-value	Total	Metro politian	Urban	Rural
2006	64.6	64.07	64.96	67.24	<0.001	2.55	2.59	2.41	2.56	<0.001	0.16	0.17	0.14	0.19	<0.001
2007	64.28	63.72	64.62	67.27	<0.001	3.13	3.17	3.05	2.99	<0.001	0.07	0.07	0.07	0.09	<0.001
2008	64.14	63.62	64.43	66.96	<0.001	4.63	4.7	4.49	4.49	<0.001	0.08	0.08	0.08	0.09	<0.001
2009	64.18	63.72	64.29	66.93	<0.001	5.34	5.35	5.32	5.35	0.3285	0.09	0.08	0.08	0.11	<0.001
2010	64.37	63.89	64.54	67.08	<0.001	5.72	5.71	5.67	5.85	<0.001	0.09	0.09	0.1	0.12	<0.001
2011	64.73	64.27	64.86	67.42	<0.001	6.15	6.14	6.12	6.23	<0.001	0.09	0.09	0.09	0.12	<0.001
2012	64.97	64.54	65.1	67.6	<0.001	6.44	6.41	6.45	6.64	<0.001	0.1	0.09	0.09	0.13	<0.001
2013	65.62	64.97	65.45	67.96	<0.001	6.65	6.61	6.72	6.78	<0.001	0.1	0.1	0.11	0.13	<0.001
2014	66.01	65.22	65.74	68.13	<0.001	6.73	6.69	6.71	7.08	<0.001	0.1	0.1	0.1	0.14	<0.001
2015	66.28	65.61	66.13	68.5	<0.001	6.84	6.79	6.91	6.97	<0.001	0.1	0.1	0.1	0.13	<0.001
2016	67.02	65.91	66.33	68.79	<0.001	7.27	7.2	7.41	7.52	<0.001	0.12	0.11	0.12	0.15	<0.001

Values are presented as percentage.
PSA: prostate-specific antigen, PCa: prostate cancer.

the elderly with age-related increasing incidence rates.^{1,2} Therefore, considering the prominent trend of social again in the rural area than urban or metropolitan counterparts, we are going to contrast the incidence of PSA across these residential areas from this study.

Several interesting findings that deserve to be emphasized were observed from this study. First, the investigated PSA incidence of 7.27% among those aged over 40 years from this study shown in Table 1 was significantly lower than that from other countries. In a PLCO (Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial) study carried out in the US, they reported that over 90% of men in the ‘usual care’ arm underwent some degree of PSA testing in 2009.⁶ In 2005, it has been reported that about 40% of those aged over 50 years in the US had at least one PSA test in the prior year.¹⁰ A Japanese hospital-based cohort study reported that 73.5% of PCa patients aged 55–69 years were detected by PSA screening in 2014,¹¹ but in Korea, about a quarter of diagnosed PCa had repeated PSA test before the diagnosis in the recent decade.¹²

Second, despite a similarly increasing exposure rate to the PSA test across all residential areas among the Korean male, the repeated screening opportunity was focused on the inhabitant of a metropolitan area. The value of a single session of PSA test as a screening modality has been investigated by several recent trials, but they consistently failed to demonstrate a similar clinical relevance as serial check-ups had.^{13,14} Thus, the ideal screening strategy has to be designed to provide serial check-ups by repeated PSA tests. From this point of view, the relatively lower interval of repeated test of rural area (2.83 times on average during 11 years) in comparison to the inhabitant of a metropolitan area (3.25 times in Seoul, 2.97 times on average from metropolitan area) deserves to be addressed. Given the maintained trend of the highest incidence of PCa in a rural area than

the other areas, this disparity by the residential area should be reconsidered from the viewpoint of equality, in the accessibility of medical services.

The authors are well aware of the limitations of this study. First, the current version of the Korean NHIS data does not provide basic information on risk stratification of PCa, including the serum level of PSA, clinical stage, and Gleason score or grade. Thus, we cannot identify the significant disease among the indolent PCa in this analysis. While the majority of randomized clinical trials on the efficacy of the PSA test as a screening tool for PCa demonstrated a significant decrease in the incidence of advanced disease, which reflects the probability of low-risk PCa dominantly screened by this strategy.¹⁵ However, concerns over the overdiagnosis and overtreatment of insignificant PCa should be weighted with the concerns on consistently reported aggressive nature of disease among the Korean males.¹⁶⁻¹⁸ Second, because the current version of NHIS did not allow to capture the patients who previously had PSA testing performed through a private, noninsured health check-up, some of the nonscreened groups in this study may have proper PSA screening in the real world. The number of those with PSA testing by the private sector was unknown due to the absence of a national-wide counting system. However, given the current reported average retirement age of 51.2 years from their longest employment among the Korean male in 2021¹⁹ and the elderly-driven prevalence PCa in Korea as shown in Table 3, the omission of these private PSA testing data is unlikely to have substantially affected our results, especially for the inhabitant of rural area. Third, although associations between the residential area, the mean age, the incidence of PSA and PCa were identified from this study, a causal relationship was not clear from the observational study design. Furthermore, the variables which allow being investigated by the current version of NHIS look

superficial to extract a solid conclusion. Thus, these results should be considered as hypothesis-generating and will spur further investigations into PSA screening in societies with limited social awareness of the disease.

CONCLUSIONS

Despite a recent increase of PSA screening and diagnosis of PCa especially in the rural area driven by a larger proportion of the aged population, the opportunity of repeated testing was presented more frequently to the inhabitant of a metropolitan area. Given the relatively low exposure rate to the PSA test regardless of the residential areas in general and the uneven nature of PSA testing by the lack of screening, these outcomes propose the clinical relevance for the establishment of countrywide policy which enables expanding the implementation of PSA testing, in a country with rapidly growing PCa incidence.

NOTES

- Conflicts of interest: No potential conflict of interest relevant to this article was reported.

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- ORCID

Young Hwii Ko: <https://orcid.org/0000-0002-9150-4292>

Byung Hoon Kim: <https://orcid.org/0000-0001-5272-6362>

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