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The national-wide incidence of prostate-specific antigen testing trend for a decade in Korea by age group

Young Hwii Ko[1], Kwon-Chan Roh[2], Byung Hoon Kim[3]

[1]Department of Urology, College of Medicine, Yeungnam University, Daegu, [2]Medical R&D Service Design Center, College of Medicine, Yeungnam University, Daegu, [3]Department of Urology, School of Medicine, Keimyung University, Daegu, Korea

Purpose: To document nationwide serum prostate-specific antigen (PSA) testing trends over the past decade and to investigate the impact of testing on prostate cancer (PCa) detection.

Materials and Methods: Using annual National Health Insurance Service of Korea data for the period 2006 to 2016, PSA testing rates were investigated for men aged ≥40 years by decade, and associations between test rates and registered PCa cases were analyzed.

Results: During the study period, the incidence of PCa increased about threefold (4,415 in 2006 to 15,046 in 2016). PCa incidences increased with age ($p<0.001$) and about 60% of cases were over 70 years old. Despite a fourfold increase in PSA testing (246,911 in 2006 to 937,548 in 2016), the average exposure rate among all men was only 7.27% in 2016, and the mean number of repeat tests for those that did not develop PCa during the study period was 2.9. PSA test rates increased with age and in 2016 were 1.65% for those in their 40s, 4.90% for those in their 50s, 12.0% for those in their 60s, 19.2% for those in their 70s, and 21.6% for those aged ≥80. Regardless of the age groups, a significant association was found between PSA test numbers and the detection of PCas.

Conclusions: In contrast to the soaring incidence of PCa especially in those aged over 70 years who have a more frequent chance for PSA testing triggered by concomitant voiding symptoms, low exposure in general and among relatively younger men favors a countrywide screening policy.

Keywords: Prostate cancer; Prostate-specific antigen; Screening

INTRODUCTION

The incidence of prostate cancer (PCa) in Korea and other Asian countries has dramatically increased over the last decade. Since 2002, when PCa was first reported to be the 5th most common malignant disease among Korean males, its incidence has consistently increased. In 2016 it became the 4th most commonly developing male malignancy disease. In the most recent report (2019), PCa was the 3rd most prevalent cancer among Korean men, and 2nd most common among men over 65 years old [1]. Notably, this increase seems not to improve social awareness on prostate-specific antigen (PSA) testing given recent dominantly negative survey outcomes on it [2], which can be largely attributed to the

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Corresponding Author: Young Hwii Ko https://orcid.org/0000-0002-9150-4292
Department of Urology, College of Medicine, Yeungnam University, 170 Hyeonchung-ro, Nam-gu, Daegu 42415, Korea
TEL: +82-53-620-3695, FAX: +82-53-627-5535, E-mail: urokyh@naver.com

absence of a nationwide screening policy.

PSA testing plays a pivotal role in the detection of PCa, given that the majority of contemporary PCa cases exhibit only ambiguous male lower urinary tract symptoms, which more frequently originate from concomitant benign prostate hyperplasia (BPH). However, randomized clinical trials (RCTs) on PSA screening in Western countries conducted a decade ago demonstrated debatable survival benefit [3,4], which subsequently became the rationale presented by the US Preventive Services Task Force (USPSTF) for recommending withdrawal of PSA screening for the US population in 2012 [5]. Even so, the macroscopic consequences of screening could be quite different between countries presumably due to different PSA testing rates and genetic influences on the incidence of PCa. These differences between countries raise the question as to how contemporary Western guidelines on PSA screening, so strongly influenced by statements from the USPSTF, apply to Asian populations faced with increasing PCa incidences. Thus, we documented national-wide trends of serum PSA testing over a recent decade and investigated the impact of testing on PCa detection rates.

MATERIALS AND METHODS

1. Data source

The data used in the present study were obtained from the National Health Insurance Service (NHIS) of Korea, which covers approximately 98% of the population and provides universal health coverage. The Korean NHIS database includes almost all medical data, including diagnostic codes, procedures, and outcomes (deaths), and also provides sociodemographic information such as age, health insurance premiums, and residential area. However, the current version of NHIS does not provide information on the biological aggressiveness of cancers, serum PSA levels, tumor stages, or pathologic grades. In the present study, all personal identification numbers were encrypted before data processing to comply with the privacy guidelines of the Health Insurance Portability and Accountability Act, and study procedures and ethical aspects were approved beforehand by our Institutional Review Board (approval number: YUMC-2019-11-012-002).

To expand the study period and provide a detailed projection on PCa incidence and cancer-specific mortality trends in Korea, additional national-wide data were separately obtained from the Statistics Korea site on the incidence and specific mortality rates of PCa per 100,000 men from 1999 to 2018 [6].

2. Study design and subjects

Male subjects aged ≥40 years that underwent PSA testing from 2006 through 2016 were identified. Patients newly diagnosed with PCa and registered in the NHIS with an ICD-10 code of C61 or V193/194 each year during the study period, were also investigated. The PSA test codes utilized in this study were B5490, C4280, C7428. The primary endpoints of this study were (1) PSA testing rates for those aged ≥40 years and (2) the association between those that received a PSA testing and newly registered PCa cases on an annual basis and in their 40s, 50s, 60s, 70s, or 80s and over, given the higher reported incidences of PCa among the elderly in Asia [7,8].

3. Statistical analysis

The Student's t-test was used to determine the significances of differences between group characteristics and outcomes 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. Correlation analysis was used to determine the associations between PSA test numbers and numbers that developed PCa, and the Cochran Armitage trend test was used to compare differences in outcomes between ages. Two-sided p-values of <0.05 were considered statistically significant. The statistical analysis was performed using SAS software (SAS Institute, Cary, NC, USA).

RESULTS

1. Numbers of prostate cancer cases during the study period 2006–2016

The numbers of NHIS registered PCa cases increased about threefold from 4,415 in 2006 to 15,046 in 2016 and increased significantly with age (Cochran Armitage trend test, p<0.001). PCa was most detected in those aged ≥80 years every year (Table 1).

2. Prostate cancer incidences and cancer-specific mortality rates by NHIS data

For the period 1999 to 2018, the incidence of PCa increased during the second decade by about 10 times as compared with the first from 3.1 to 29.0 PCa cases per 100,000 men. PCa-associated mortality showed a 4-fold of increase and age-standardized mortality remained constant after a small peak in 2007 (Fig. 1). Among the registered PCa patients, over half of them were aged ≥70 years (Fig. 2). In 2018, 90.5% of them were ≥60 years, 57.8% were ≥70 years, 35.4% were ≥75 years. Aged between 55–69 years occupies

Table 1. Incidences of registered prostate cancer (PCa) by year in the six age groups

Year	Category	Total	Age group				
			40s	50s	60s	70s	Over 80s
2006	Detected PCa	4,415 (0.046)	60 (0.001)	417 (0.015)	1,626 (0.095)	1,739 (0.225)	573 (0.284)
	Population (≥40 y)	9,686,975	4,293,362	2,702,636	1,717,421	771,738	201,818
2007	Detected PCa	6,944 (0.069)	97 (0.002)	568 (0.020)	2,213 (0.125)	2,980 (0.358)	1,086 (0.510)
	Population (≥40 y)	9,999,912	4,333,766	2,851,682	1,769,337	832,057	213,070
2008	Detected PCa	8,041 (0.078)	95 (0.002)	690 (0.023)	2,582 (0.141)	3,393 (0.380)	1,281 (0.565)
	Population (≥40 y)	10,337,914	4,377,870	3,002,131	1,837,226	893,794	226,893
2009	Detected PCa	9,162 (0.086)	125 (0.003)	843 (0.027)	2,846 (0.150)	3,980 (0.414)	1,368 (0.561)
	Population (≥40 y)	10,694,580	4,424,693	3,170,224	1,894,727	961,242	243,694
2010	Detected PCa	10,180 (0.092)	188 (0.004)	994 (0.030)	3,141 (0.161)	4,343 (0.423)	1,514 (0.579)
	Population (≥40 y)	11,039,633	4,434,091	3,369,420	1,946,828	1,027,907	261,387
2011	Detected PCa	10,653 (0.094)	123 (0.003)	916 (0.026)	3,142 (0.158)	4,833 (0.441)	1,639 (0.588)
	Population (≥40 y)	11,386,232	4,435,055	3,592,137	1,983,827	1,096,507	278,706
2012	Detected PCa	11,264 (0.096)	133 (0.003)	1,005 (0.027)	3,308 (0.163)	4,996 (0.422)	1,822 (0.606)
	Population (≥40 y)	11,723,878	4,437,927	3,776,653	2,025,529	1,183,270	300,499
2013	Detected PCa	12,393 (0.103)	193 (0.004)	1,204 (0.031)	3,584 (0.171)	5,466 (0.434)	1,946 (0.594)
	Population (≥40 y)	12,042,751	4,452,694	3,909,234	2,094,829	1,258,609	327,385
2014	Detected PCa	12,793 (0.104)	160 (0.004)	1,204 (0.030)	3,748 (0.170)	5,492 (0.421)	2,189 (0.608)
	Population (≥40 y)	12,354,915	4,474,484	4,020,937	2,194,268	1,305,432	359,794
2015	Detected PCa	13,033 (0.103)	153 (0.003)	1,227 (0.030)	3,884 (0.166)	5,400 (0.404)	2,369 (0.595)
	Population (≥40 y)	12,635,426	4,459,325	4,097,255	2,342,576	1,337,821	398,449
2016	Detected PCa	15,046 (0.117)	207 (0.005)	1,350 (0.039)	4,396 (0.176)	6,369 (0.465)	2,724 (0.619)
	Population (≥40 y)	12,886,340	4,418,589	4,155,589	2,502,779	1,369,560	439,823

Values are presented as number (%) or number only.

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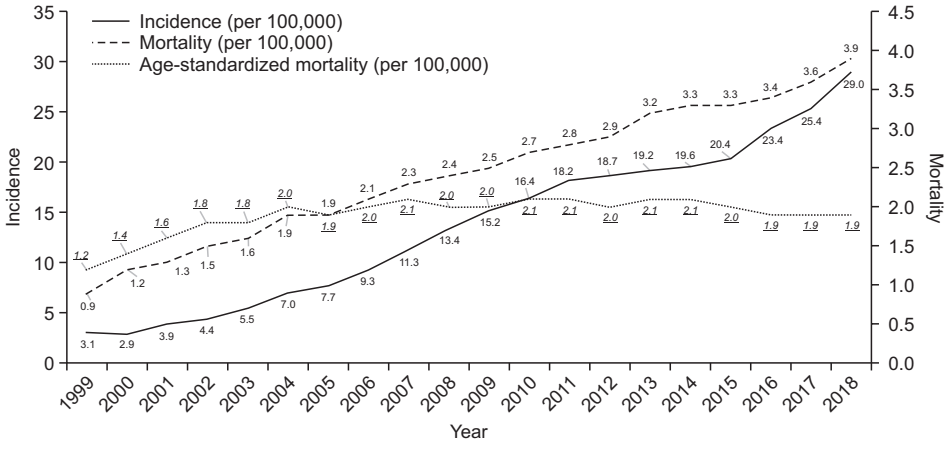

Fig. 1. Annual incidences and mortality rates of prostate cancer registered in National Health Insurance Service (NHIS) of Korea (1999–2018).

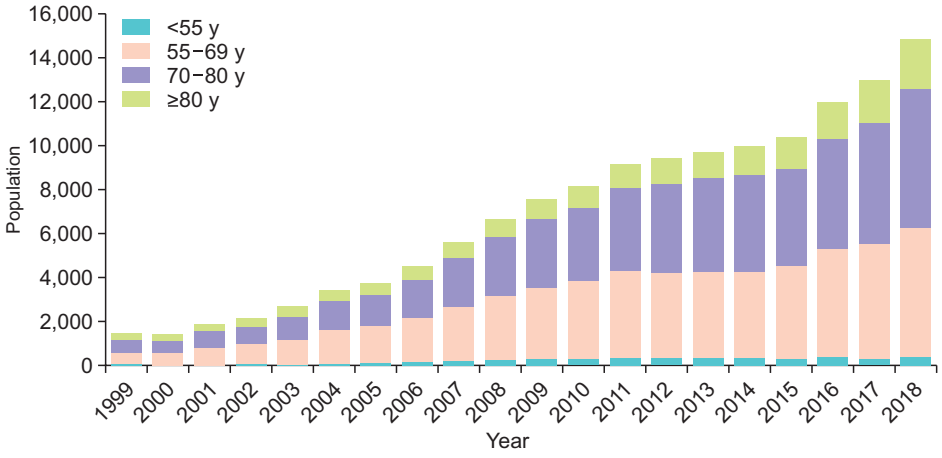

Fig. 2. Annual incidence of prostate cancer by age group.

39.6% of them.

3. Prostate-specific antigen testing rates during 2006–2016

PSA testing numbers increased about fourfold from 246,911 in 2006 to 937,548 in 2016. Numbers continuously increased on an annual basis during the research period, but the test rate for the whole male population aged ≥40 years was only 7.28% in 2016 (Table 2). During the study period, the PSA tests were performed 2.9 times/individual on average; those registered as having developed PCa were excluded. In 2016, PSA testing rates significantly increased with age, that is, from 1.65% for those in their 40s, 4.90% for those in their 50s, 12.0% for those in their 60s, 19.2% for those in their 70s, to 21.6% for those aged ≥80 years (Cochran Armitage trend test, p<0.001). Regardless of age groups, a significant association was found between PSA testing numbers and the detection of PCas over the study period (Table 3).

DISCUSSION

The socioeconomic benefits of PSA screening in the general population remain a topic of debate. Two representative RCTs on large populations in the US [3] and Europe [4] produced contrary results regarding the effect of PSA screening on PCa survival rates, even though PCa was the most common malignant disease among the male population and a leading cause of death in both areas. Since the publication of these RCTs, their conflicting results and negative recommendations regarding the need for screening have long deterred the use of PSA testing in general populations [5]. However, given the distinctive epidemiologic and racial background of PCa, the most serious consequence of these Western-based prohibitive guidelines is the negative impact they have had on the establishment of screening policies for men living in other countries that might benefit.

In 2000, PCa became the 10th most common malignant disease among Korean males [9]. Despite the rapid increase in its incidence over the last two decades especially among the elderly population, social perceptions of the risks posed by PCa have lagged reality because PCa is just the 6th most common cancer nationwide, which in turn has diminished the perceived usefulness of PSA testing as a screening strategy. Currently, the PSA testing is not included in regular

Table 2. Serum prostate-specific antigen (PSA) test rates by year in the six age groups

Year	Category	Total	Age group				
			40s	50s	60s	70s	Over 80s
2006	Men with PSA test	246,911 (2.549)	22,309 (0.520)	59,939 (2.218)	85,115 (4.956)	61,817 (8.011)	17,731 (8.786)
	Population (≥40 y)	9,686,975	4,293,362	2,702,636	1,717,421	771,738	201,818
2007	Men with PSA test	312,888 (3.129)	32,032 (0.739)	76,476 (2.682)	105,637 (5.970)	76,376 (9.179)	22,367 (10.497)
	Population (≥40 y)	9,999,912	4,333,766	2,851,682	1,769,337	832,057	213,070
2008	Men with PSA test	479,046 (4.634)	49,002 (1.119)	120,265 (4.006)	159,922 (8.705)	116,491 (13.033)	33,366 (14.706)
	Population (≥40 y)	10,337,914	4,377,870	3,002,131	1,837,226	893,794	226,893
2009	Men with PSA test	571,643 (5.345)	57,776 (1.306)	146,424 (4.619)	187,875 (9.916)	138,931 (14.453)	40,637 (16.675)
	Population (≥40 y)	10,694,580	4,424,693	3,170,224	1,894,727	961,242	243,694
2010	Men with PSA test	631,417 (5.720)	60,815 (1.372)	165,455 (4.910)	202,810 (10.417)	156,966 (15.270)	45,371 (17.358)
	Population (≥40 y)	11,039,633	4,434,091	3,369,420	1,946,828	1,027,907	261,387
2011	Men with PSA test	700,040 (6.148)	63,949 (1.442)	177,734 (4.948)	221,419 (11.161)	182,857 (16.676)	54,081 (19.404)
	Population (≥40 y)	11,386,232	4,435,055	3,592,137	1,983,827	1,096,507	278,706
2012	Men with PSA test	755,372 (6.443)	67,523 (1.522)	190,584 (5.046)	237,082 (11.705)	199,180 (16.833)	61,003 (20.301)
	Population (≥40 y)	11,723,878	4,437,927	3,776,653	2,025,529	1,183,270	300,499
2013	Men with PSA test	801,241 (6.653)	67,949 (1.526)	194,925 (4.986)	254,260 (12.138)	215,448 (17.118)	68,659 (20.972)
	Population (≥40 y)	12,042,751	4,452,694	3,909,234	2,094,829	1,258,609	327,385
2014	Men with PSA test	831,495 (6.730)	70,133 (1.567)	195,618 (4.865)	267,307 (12.182)	222,746 (17.063)	75,691 (21.037)
	Population (≥40 y)	12,354,915	4,474,484	4,020,937	2,194,268	1,305,432	359,794
2015	Men with PSA test	863,782 (6.836)	69,845 (1.566)	195,801 (4.779)	277,502 (11.846)	236,259 (17.660)	84,375 (21.176)
	Population (≥40 y)	12,635,426	4,459,325	4,097,255	2,342,576	1,337,821	398,449
2016	Men with PSA test	937,548 (7.276)	73,053 (1.653)	203,853 (4.906)	302,065 (12.069)	263,233 (19.220)	95,344 (21.677)
	Population (≥40 y)	12,886,340	4,418,589	4,155,589	2,502,779	1,369,560	439,823

Values are presented as number (%) or number only.

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Table 3. Associations between numbers of prostate-specific antigen tests and prostate cancer (PCa) cases detected in the six age groups

Category	Correlation coefficient	p-value
Total PCa registered	0.986	<0.00001
PCa detected age group		
40s	0.839	0.00124
50s	0.983	<0.00001
60s	0.982	<0.00001
70s	0.984	<0.00001
80s	0.962	<0.00001

checkups in Korea, which contrasts with the inclusions of tests for other common male malignant diseases such as lung, stomach, colon, and liver cancer, which were the 1st, 2nd, 3rd, and 5th most prevalent malignant diseases among Korean males in 2019 [1]. Therefore, this study was undertaken to investigate the actual rate of PSA testing in Korea over the last decade, during which PCa has become the 4th most common male cancer, and yet, PSA screening strategy has attracted minimal interest in the general population [2].

The present study produced several interesting findings that deserve to be emphasized. First, when PCa patients were divided into age groups, the rate of PCa development was greatest among those in their 70s. On average, 90% of PCa cases registered during the study period were aged ≥60 years and one-third of them were aged ≥75 years. In other words, PCa in Korea has become a disease of elderly and super-elderly males, which explains the presence of a plateau in the age-standardized PCa mortality since 2007 even though almost 4 times increased of the unadjusted cancer-specific mortality in the last two decades as shown in Fig. 2. Because the incidence of PCa is projected to increase in parallel with societal aging, PCa is set to become a major health care issue for elderly Korean men. Indeed, in 2016, PCa became the most common male cancer in Japan and affected about 70% of the contracted population aged over 75 years [7]. Furthermore, a western study also showed that the prevalence of incidental PCa in an autopsy setting was 30% among men between 30 and 69 years of age and 75% among those aged ≥70 [10]. Another unique characteristic of PCa is that it appears to be more aggressive in the elderly. Studies indicate that subjects ≥70 develop diseases of higher grade and stage [11,12]. In the same context, older patients have been reported to have higher risks of biochemical recurrence, distant metastasis, and disease-specific death [11-13]. Therefore, given the limited life span of these men and the unfavorable characteristics of PCa, decisions need to be made regarding proper screening and management protocols. Data available suggest the adoption of a screening policy given rapid societal aging, which runs contrary to USPSTF recommendations in 2012 despite opening slots of PSA screening for the explained individuals aged between 55 to 69 years by the revision in 2018 [14]. Even by following this recent amendment, this particular age group occupies below 40% of the Korean NHIS data, missing the majority of patients with PCa in 2018.

Second, although increases in the incidence of PCa are driven by the elderly, their younger counterparts in Korea are largely unaware of the merits of PSA testing. The present study demonstrates that the elderly have a greater opportunity to be PSA tested. In 2016, about 20% of Korean males over their 70s had a PSA test, which represented a marked increase as compared with about 8% tested in 2006. Nevertheless, the overall PSA test rate of 7.27% in 2016 was significantly lower than those in Western countries. Although it is difficult to compare PSA screening test rates between countries, a PLCO (Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial) study carried out in the US reported that over 90% of men in a 'usual care' arm underwent some type of PSA testing in 2009 [15]. In another US study, 75% of men aged ≥50 had been PSA tested, and 54% of the 75% reported up-to-date PSA screening [16]. Similarly, a Japanese hospital-based cohort study reported that 73.5% of PCa patients aged 55 to 69 years were detected by PSA screening in 2013 [17]. However, in Korea only about a quarter of those diagnosed with PCa were found to have undergone PSA testing before receiving a pathologic diagnosis during 2008 to 2016 [18]. In 2004, only 15% of Korean men over 50 years reported having been screened during the previous 2 years [19]. Given the expanding incidence and prevalence of PCa in Asian countries, the outcomes of our study indicate regular PSA testing is of clinical relevance for Korean males.

The authors are well aware of the limitations of this study. First, Korean NHIS data does not currently provide basic information on PCa risk stratification, such as information on PSA serum levels, clinical stages, or Gleason scores or grades. Thus, we were unable to differentiate significant disease from indolent PCa. The majority of RCTs on the efficacy of PSA testing have consistently reported a significant decrease in the incidence of advanced PCa and an increase in the incidence of localized disease, which reflects the probability of low-risk dominantly screening by this strategy [20]. However, concerns over the over-diagnosis and over-treatment of insignificant PCa should be weighted with the concerns on consistently reported aggressive nature of disease among the Korean males [21-23]. Second, because the current version of NHIS did not contain data on patients

that had undergone PSA testing at a private, non-insured health check-up, some of those included in the analysis as non-screened may have been properly tested. 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 2021 [24] and the elderly-driven prevalence PCa in Korea as shown in Fig. 2, the omission of these private PSA testing data is unlikely to have substantially affected our results. Also, the reported disparity of PSA testing among Korean males with different socioeconomic statuses should be considered [25]. Third, the current version of the NHIS does not contain information on cancer-specific survival, and because screening for malignant diseases aims to improve cancer-specific survival, this data should be corrected in some other way to support the case for public PSA screening. However, considering that the reported average disease duration for registered PCa patients is less than 5 years currently [1], this period might not be sufficient to expect a prolongation of survival in PCa by applying PSA screening among the Korean male population.

CONCLUSIONS

In contrast to the soaring incidence of PCa especially in those aged over 70 years who have a more frequent chance for PSA testing triggered by the concomitant BPH-induced symptoms, low exposure in general and among relatively younger men implies a probability of disease under-detection given the asymptomatic nature of PCa. The elderly/super-elderly driven prevalence revealed from the Korea NHIS data and uneven nature of PSA testing by the lack of screening favors the establishment of countrywide policy which enables expanding the implementation of PSA testing.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHORS' CONTRIBUTIONS

Research conception and design: Young Hwii Ko. Data acquisition: Young Hwii Ko. Statistical analysis: Young Hwii Ko and Byung Hoon Kim. Data analysis and interpretation: Young Hwii Ko and Kwon-Chan Roh. Drafting of the manuscript: Young Hwii Ko. Critical revision of the manuscript: Byung Hoon Kim. Obtaining funding: Young Hwii Ko. Administrative, technical, or material support: Kwon-Chan Roh. Supervision: Kwon-Chan Roh. Approval of the final manuscript: Byung Hoon Kim.

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