Original Article

Impact of age and metabolic syndrome-like components on prostate cancer development: a nationwide population-based cohort study

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Background: Because of the contradictory results, more epidemiologic data is needed to determine if metabolic syndrome is a risk factor for developing prostate cancer. This study investigated whether metabolic syndrome-like components affect the incidence of prostate cancer in a Korean population.

Methods: Men over 50 years of age who underwent health examinations in 2009 were followed until December 2015 (n=1,917,430) using National Health Insurance System data. Subjects were divided into three groups according to the number of metabolic syndrome-like components. The predictive accuracy of age for prostate cancer was assessed by the Youden index and multivariate adjusted Cox regression analysis was used to analyze the effect of metabolic syndrome-like components on prostate cancer development.

Results: The risk of prostate cancer increases with age, and the best cutoff age for prostate cancer detection was 62 years (the maximum value of the Youden index). When stratified by the number of metabolic syndrome-like components, the age with the highest Youden index of each group is still 61 or 62 years. In multivariate adjusted Cox regression analysis, there was no statistically significant difference in the incidence rate among the non-component group, the group with 1 or 2 components, and the group with ≥3 components.

Conclusions: The current study found that there was no statistically significant association between metabolic syndrome and prostate cancer development in a Korean population. However, results of this study should be interpreted with consideration due to several limitations including the diversity of definitions of metabolic syndrome components.

Keywords: Metabolic syndrome; prostate cancer; risk factor

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Introduction

Prostate cancer is the second most commonly diagnosed cancer among men worldwide (1). The incidence of prostate cancer has also increased significantly in Korea, and is mainly due to rapid population aging, westernized dietary habits, and increased prostate-specific antigen (PSA) measurements in screening tests (2). Over the past several decades, the prevalence of metabolic syndrome has increased worldwide and has emerged as a public health problem (3). According to recent meta-analyses, westernized dietary patterns such as a greater intake of dietary fat and meat is associated with the incidence of metabolic syndrome (4,5). Additionally, many reports have shown the association between metabolic syndrome and development of various cancers such as colorectal, breast, endometrial, pancreas, and primary liver cancers (6).

In addition to these cancers, metabolic syndrome components could be risk factors for prostate cancer development. However, reports from previous studies about the link between prostate cancer and metabolic syndrome have been inconsistent (7). Although some studies have suggested that metabolic syndrome can increase the risk of developing prostate cancer (8-10), some studies have reported no association or a negative association between metabolic syndrome and prostate cancer (11-13). These inconsistencies have also been observed in the Asian population studies (14).

Because of the contradictory results, more epidemiologic data is needed to determine if metabolic syndrome is a risk factor for developing prostate cancer. Therefore, the objective of this study was to investigate whether metabolic syndrome affects the incidence of prostate cancer in a Korean population based on the National Health Insurance System (NHIS) data. We present the following article in accordance with the STROBE checklist (available at https://dx.doi.org/10.21037/tau-21-249).

Methods

Data base and demographic factors

This study used the NHIS database of Korea to identify patients with prostate cancer between January 2009 and December 2015 (NHIS-2017-1-222) (15). The NHIS database is composed of an eligibility database, medical treatment database, medical care institution database, and health examination database. Patients who were diagnosed with prostate cancer could be identified using diagnostic codes for the medical treatment database.

Information about metabolic syndrome was reported in the health examination database. In this manuscript a metabolic component refers to one of the following five metabolic syndrome-like components: (I) waist circumference ≥90 cm, (II) elevated triglycerides ≥150 mg/dL, (III) reduced HDL cholesterol <40 mg/dL, (IV) systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg, and (V) fasting serum glucose level ≥100 mg/dL. Subjects were divided into three groups according to the number of metabolic syndrome-like components (a non-component group, a group with one or two components, and a group with ≥3 components) to analyze the effect of metabolic syndrome on prostate cancer development.

Lifestyle variables were also included in the health examination database. Smoking status was categorized into non-smokers, ex-smokers, and current smokers. Alcohol consumption status was categorized into four groups: non-drinker, light drinker (1–2 days/week), moderate drinker (3–4 days/week), and heavy drinker (≥5 days/week). Regular exercise over 20 minutes was also categorized into three groups: 0–1 days/week, 2–4 days/week, and ≥5 days/week.

Study population

In Korea, a national health examination is semi-mandatory to local householder, company member and family member over the age of 40 and dependents of member once every 2 years. Therefore, during 1 year, about half of the population over the age of 40 undergo examination. And it is not possible to receive more than two national health examination during 1 year. In this study, male subjects that had undergone a national health examination in 2009 without a previous diagnosis of any cancer were included. Young men under 50 years of age were excluded because of the rare development of prostate cancer in this group. After excluding people with missing metabolic disease data from health examination databases, a total of 1,917,430 men were followed from January 2009 to December 2015 (*Figure 1*). Subjects who the development of prostate cancer did not occur during the follow up period were censored and Cox regression analysis was used for these censored data. Sensitivity analysis was used to handle missing data.

Statistical analysis

SAS software version 9.4 (SAS Institute, Cary, NC, USA) was used for all statistical analyses. Baseline demographic and

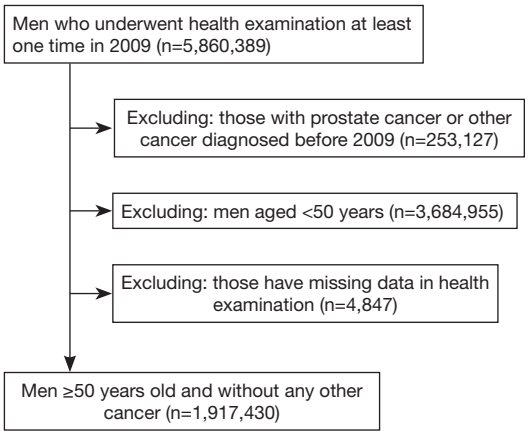

Figure 1 Study design and subject disposition.

clinical characteristics of subjects are presented as number (%). Incidence rate is expressed as the number of newly diagnosed cases of prostate cancer per 100,000 person-years of the follow-up period. One-way ANOVA used to test difference in the incidence rate among the non-component group, the group with 1 or 2 components, and the group with ≥3 components. The predictive accuracy of age for prostate cancer was assessed by calculating the c-index based on the receiver operating characteristics (ROC) curve. The optimum cut-off value was defined as the maximum value of the Youden index. Multivariate adjusted Cox regression analysis was conducted to examine the hazard ratio (HR) and 95% confidence interval (CI) for the development of prostate cancer by metabolic syndrome-like components. Calculations were adjusted for age, alcohol consumption, smoking status, and regular exercise. Statistical significance was considered when the P value was less than 0.05.

Ethical approval

This study protocol was approved by the Institutional Review Board of Bucheon St. Mary's Hospital of Korea (HC20ZISI0062). The study was performed in accordance with the ethical principles of the Declaration of Helsinki (16). Informed consent was waived because anonymous and de-identified information was used for analysis.

Results

Demographic and clinical characteristics according to metabolic disease

Table 1 summarizes the demographic and clinical characteristics of study subjects. Among a total of 1,917,430 participants, 22,584 (1.18%) were diagnosed with prostate cancer, including 3,387 (1.13%) subjects in the non-component group, 13,151 (1.19%) in the group with 1 or 2 components, and 6,046 (1.17%) in the group with ≥3 components. About 85% of the subjects had more than one metabolic syndrome-like component in this cohort. More than half of the subjects had hypertension, followed by hyperlipidemia and diabetes. The numbers of non-, ex-, and current smoker were similar among the groups, and the ratio of non-drunker was highest in the non-component group.

Incidence rate of prostate cancer according to age

Figure 2 shows the incidence rate of prostate cancer according to age. The number of new cases of prostate cancer increased with age. The total incidence rate of prostate cancer increased from 28.07 per 100,000 person-years in the 51-year-old age group to 366.01 per 100,000 person-years in the 75-year-old age group. A similar increasing trend was found when subjects were analyzed by groups, according to the number of metabolic syndrome-like components. There was no statistically significant difference in the incidence rate among the non-component group, the group with 1 or 2 components, and the group with ≥3 components (Table S1).

Age cut-off value for predicting prostate cancer according to metabolic diseases

Sensitivity, specificity, and Youden index for predicting the development of prostate cancer with different age cut-off values are shown in Table S2. The age with the highest Youden index was 62 years for all subjects. The cut-off value for age was identified based on the highest Youden index. When subjects were stratified by the number of metabolic syndrome-like components, the age with the highest Youden index of each group was also 62 years (*Figure 3*).

Risk for prostate cancer according to metabolic diseases when stratified by the number of metabolic diseases

The HRs (95% CI) for prostate cancer according to metabolic syndrome-like components were: 0.992 (0.954–1.031) for the group with 1 or 2 components and 0.974 (0.933–1.018) for the group with ≥3 components in a model adjusted for age, alcohol consumption, smoking status, and regular exercise (*Table 2*). There was no statistically significant difference in the incidence rate among the non-

Table 1 Baseline demographic and clinical characteristics according to metabolic syndrome-like components

Metabolic disease	Non-component	1 or 2 components	≥3 components	Total
No. in population	301,030 (100.00)	1,101,800 (100.00)	514,600 (100.00)	1,917,430
No. of diagnosed prostate cancers	3,387 (1.13)	13,151 (1.19)	6,046 (1.17)	22,584
Age, years				
50–54	109,428 (36.35)	350,969 (31.85)	161,137 (31.31)	621,533
55–59	60,838 (20.21)	222,893 (20.23)	108,289 (21.04)	392,020
60–64	53,612 (17.81)	208,056 (18.88)	101,231 (19.67)	362,899
65–69	34,890 (11.59)	143,595 (13.03)	67,911 (13.2)	246,396
70–74	27,332 (9.08)	114,695 (10.41)	52,207 (10.15)	194,234
≥75	14,930 (4.96)	61,593 (5.59)	23,825 (4.63)	100,348
BMI, kg/m^2				
<18.5	16,608 (5.52)	27,234 (2.47)	2,475 (0.48)	46,317
18.5–22.9	162,537 (53.99)	402,599 (36.54)	72,771 (14.14)	637,907
23.0–24.9	82,674 (27.46)	338,373 (30.71)	123,609 (24.02)	544,656
≥25.0	39,211 (13.03)	333,594 (30.28)	315,745 (61.36)	688,550
WC, cm				
<90	301,030 (100)	918,346 (83.34)	206389 (40.11)	1,425,765
≥90	0	183,454 (16.66)	308,211 (59.89)	491,665
Triglycerides, mg/dL				
<150	301,030 (100)	796,209 (72.26)	110,865 (21.54)	1,208,104
≥150	0	305,591 (27.74)	403,735 (78.46)	709,326
HDL cholesterol, mg/dL				
≥40	301,030 (100)	989,384 (89.8)	322,583 (62.69)	1,612,997
<40	0	112,416 (10.2)	192,017 (37.31)	304,433
Hypertension				
No	301,030 (100.00)	521,232 (47.31)	92,554 (17.99)	914,816
Yes	0	580,568 (52.69)	422,046 (82.01)	1,002,614
Diabetes				
Normal	301,030 (100.00)	632,804 (57.43)	109,226 (21.23)	1,043,060
Pre-diabetes	0	361,921 (32.85)	278,724 (54.16)	640,645
Diabetes	0	107,075 (9.72)	126,650 (24.61)	233,725
Smoking status				
Non	106,060 (35.45)	381,514 (34.81)	170,126 (33.25)	657,700
Ex	86,319 (28.85)	339,812 (31.01)	166,163 (32.47)	592,294
Current	106,816 (35.7)	374,522 (34.18)	175,440 (34.28)	656,778

Table 1 (*continued*)

Table 1 (*continued*)

Metabolic disease	Non-component	1 or 2 components	≥3 components	Total
Alcohol consumption status				
Non	132,930 (45.96)	431,701 (41.05)	185,435 (37.99)	750,066
1–2 days/week	102,307 (35.37)	369,920 (35.17)	171,933 (35.22)	644,160
3–4 days/week	37,154 (12.85)	170,296 (16.19)	90,437 (18.53)	297,887
≥5 days/week	16,854 (5.83)	79,802 (7.59)	40,362 (8.27)	137,018
Regular exercise				
0–1 day/week	196,434 (66.35)	717,216 (66.17)	340,579 (67.27)	1,254,229
2–4 days/week	68,394 (23.1)	249,366 (23.01)	115,215 (22.76)	432,975
≥5 days/week	31,241 (10.55)	117,316 (10.82)	50,462 (9.97)	199,019

Data are presented as number (%). BMI, body mass index; WC, waist circumference; Hypertension, systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg; Pre-diabetes, fasting serum glucose level ≥100 mg/dL; Diabetes, fasting serum glucose level ≥126 mg/dL.

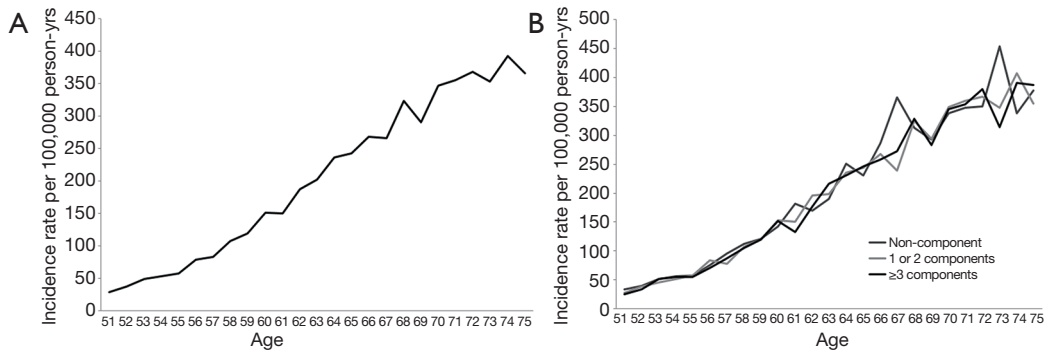

Figure 2 Incidence rate of prostate cancer: (A) total incidence rate of prostate cancer, (B) incidence rate of prostate cancer according to the number of metabolic syndrome-like components.

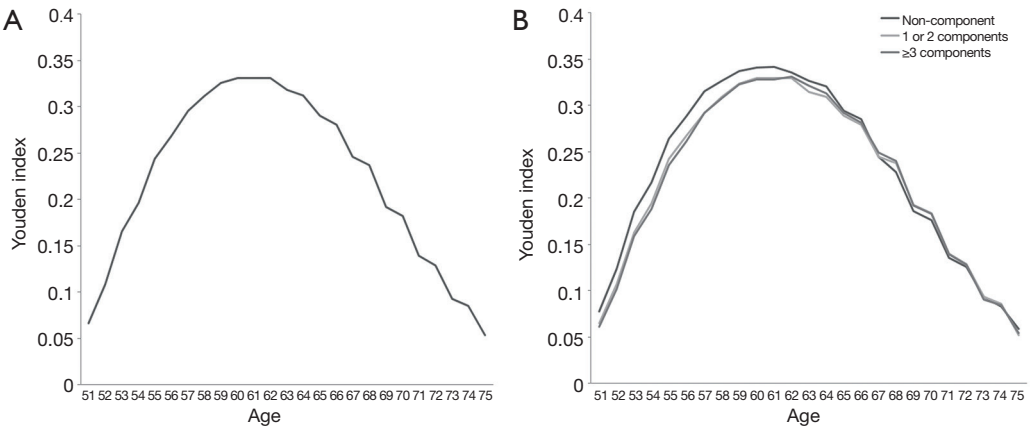

Figure 3 Youden index for predicting the development of prostate cancer with different age cut-off values. (A) All subjects, (B) based on the number of metabolic syndrome-like components.

Table 2 Age- and multivariable-adjusted HRs for prostate cancer according to metabolic syndrome-like components

Metabolic disease	Event	Person-years	Incidence*	HR (95% confidence interval)		HR (95% confidence interval)	
				Model 1†	P value	Model 2‡	P value
Non-component	3,387	2,327,477	145.52	Ref.		Ref.	
1 or 2 components	13,151	8,459,308	155.46	0.997 (0.960–1.035)	0.874	0.992 (0.954–1.031)	0.679
≥3 components	6,046	3,954,513	152.74	0.986 (0.946–1.029)	0.526	0.974 (0.933–1.018)	0.241

*, all rates are expressed as number per 100,000 person-years; †, adjusted for age; ‡, adjusted for age, alcohol consumption, smoking status, and regular exercise. HR, hazard ratio.

component group, the group with 1 or 2 components, and the group with ≥3 components.

Discussion

The main findings of this study are as follows: (I) the risk of prostate cancer increases with age; (II) the age of 62 years (with the maximum value of the Youden index) may be a point of inflection; (III) when stratified by the number of metabolic syndrome-like components, the age with the highest Youden index of each group was 61 or 62 years; and (IV) there was no statistically significant difference in the incidence rate among the non-component group, the group with 1 or 2 components, and the group with ≥3 components.

The prevalence of components of metabolic syndrome including obesity, hypertension, dyslipidemia, and diabetes has sharply increased worldwide (3). Similar to other developing or newly developed countries, this increasing trend is also observed in Korea due to lifestyle changes associated with westernization such as a greater intake of dietary fat and meat. Lee *et al.* recently reported that the prevalence of metabolic syndrome increased significantly from 28% in 2009 to 30% in 2013, and this increase was more pronounced in men than in women using the Korean NHIS data (17). Prevention of metabolic syndrome is important, because numerous data have shown the association between metabolic diseases with development of various cancers (6).

Components of metabolic syndrome could also be risk factors for prostate cancer development. However, conclusions of previous studies about the link between prostate cancer and metabolic syndrome have been inconsistent (7). Beebe-Dimmer *et al.* (8) reported that features of metabolic syndrome are associated with prostate cancer in African-American men. Hypertension and abdominal obesity have been reported to be more common among men with prostate cancer, although diabetes is not associated with the risk of prostate cancer. These authors have also found that the association between metabolic syndrome and prostate cancer risk differs by race. There is a significant association in African-American men, but no association in white men (9). Additionally, Lund Haheim *et al.* (10) reported that metabolic syndrome could predict the incidence of prostate cancer in a cohort of middle-aged Norwegian men.

However, some studies have reported no association or a negative association between metabolic syndrome and prostate cancer. Wallner *et al.* (12) found that metabolic syndrome is only minimally and inversely associated with prostate cancer and that there is no monotonic association between the number of metabolic components and prostate cancer in Caucasian men. Tande *et al.* (13) even reported that metabolic syndrome is associated with a decreased incidence of prostate cancer using data from the Atherosclerosis Risk in Communities (ARIC) Study, a multicenter prospective cohort in the United States. Recently, Xu *et al.* reported that components of metabolic syndrome were not associated with biochemical recurrence through a retrospective analysis of a Chinese cohort (18). Like these studies, in our study, there was no statistically significant association between metabolic syndrome and prostate cancer development. Additionally, the age with the maximum Youden index value for each group was similar when subjects were stratified by the number of metabolic syndrome-like components.

Differences in factors such as the size of the cohort, follow-up period, and the cut-off value of components of metabolic syndrome could provide rational for why previous studies have inconsistent conclusions. Numerous definitions of metabolic syndrome have been proposed by various organizations like the World Health Organization

(WHO), the European Group for Study of Insulin Resistance (EGIR), the American Association of Clinical Endocrinologists (AACE), the National Cholesterol Education Program (NCEP), among others (19). Therefore, definitions of metabolic syndrome components could differ from those used in other previous studies. For example, for the definition of abdominal obesity, the WHO defines central obesity as waist/hip ratio >0.9 in men; however, the EGIR and the NECP use waist circumference. In this study, the waist circumference cut-off value for abdominal obesity was ≥90 cm for men, according to Korean guidelines (20).

In addition, there are several limitations that must be considered. The present study only analyzed the effect of metabolic syndrome-like components on prostate cancer risk in one geographic site, though the use of large-scale nationwide cohort data is obviously a strength of this study which had a high statistical power. Second, detection bias could have occurred. Compared with the non-component group, groups with metabolic syndrome-like components could be more likely to visit a hospital for any health problems. These participants are consequently more likely to have a PSA test. Finally, since metabolic syndrome-like components of an individual can change during the follow-up period, the results of this study should be interpreted with consideration. Our study used single measurements of waist circumference, triglycerides, cholesterol, blood pressure, and fasting serum glucose at baseline. Therefore, future studies should also consider effects of changes in components of metabolic syndrome on prostate cancer risk.

Conclusions

The current study found that there was no statistically significant association between metabolic syndrome and prostate cancer development. The ages with the maximum Youden index value of each group were similar when subjects were stratified by the number of metabolic syndrome-like components. However, results of this study should be interpreted with consideration due to several limitations. Therefore, further study is needed to analyze the association between metabolic syndrome and prostate cancer development.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://dx.doi.org/10.21037/tau-21-249

Conflict of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/tau-21-249). The authors have no conflicts of interest to declare.

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study protocol was approved by the Institutional Review Board of Bucheon St. Mary's Hospital of Korea (HC20ZISI0062). The study was performed in accordance with the ethical principles of the Declaration of Helsinki. Informed consent was waived because anonymous and de-identified information was used for analysis.

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Supplementary

Table S1 Incidence rate of prostate cancer

	Non-component			1 or 2 components			≥3 components			Total		
Age, years	Prostate cancers	Person-years	Incidence rate*	Prostate cancers	Person-years	Incidence rate*	Prostate cancers	Person-years	Incidence rate*	Prostate cancers	Person-years	Incidence rate*
51	47	141,423	33.23	123	442,610	27.79	49	196,022	25.00	219	780,055	28.07
52	78	200,508	38.90	242	640,472	37.78	98	293,683	33.37	418	1,134,663	36.84
53	61	117,515	51.91	179	389,015	46.01	92	180,811	50.88	332	687,341	48.30
54	103	184,222	55.91	322	625,172	51.51	165	298,907	55.20	590	1,108,301	53.23
55	55	95,526	57.58	194	337,702	57.45	89	162,480	54.78	338	595,708	56.74
56	99	131,820	75.10	399	474,926	84.01	165	233,274	70.73	663	840,020	78.93
57	79	82,158	96.16	237	305,829	77.49	131	149,492	87.63	447	537,479	83.17
58	124	110,768	111.95	434	405,111	107.13	205	195,262	104.99	763	711,141	107.29
59	71	58,668	121.02	267	224,330	119.02	129	107,676	119.80	467	390,674	119.54
60	171	120,534	141.87	686	449,860	152.49	333	219,623	151.62	1,190	790,017	150.63
61	98	53,982	181.54	316	209,437	150.88	134	101,348	132.22	548	364,767	150.23
62	204	119,963	170.05	903	460,166	196.23	400	226,286	176.77	1,507	806,415	186.88
63	75	39,406	190.33	320	161,279	198.41	168	77,836	215.84	563	278,521	202.14
64	212	84,409	251.16	787	333,822	235.75	369	159,859	230.83	1,368	578,090	236.64
65	78	33,884	230.20	346	141,678	244.22	165	66,935	246.51	589	242,497	242.89
66	281	98,057	286.57	1,068	398,428	268.05	484	187,655	257.92	1,833	684,140	267.93
67	94	25,717	365.52	250	104,639	238.92	131	48,114	272.27	475	178,470	266.15
68	268	85,569	313.20	1,144	352,059	324.95	544	165,933	327.84	1,956	603,561	324.08
69	67	22,914	292.40	274	93,100	294.31	129	45,529	283.34	470	161,543	290.94
70	244	72,286	337.55	1,038	297,224	349.23	480	138,904	345.56	1,762	508,414	346.57
71	62	17,869	346.97	266	74,089	359.03	118	33,332	354.01	446	125,290	355.97
72	191	54,590	349.88	839	228,494	367.19	398	104,930	379.30	1,428	388,014	368.03
73	54	11,891	454.12	183	52,674	347.42	72	22,949	313.74	309	87,514	353.09
74	148	43,796	337.93	746	183,013	407.62	311	79,627	390.57	1,205	306,436	393.23
75	366	96,859	377.87	1414	398,573	354.77	605	156,198	387.33	2,385	651,630	366.01

*, incidence rate is expressed as the number of prostate cancer cases per 100,000 person-years of the follow-up period.

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Table S2 Sensitivity and specificity for predicting prostate cancer using different age cutoffs

	Non-component			1 or 2 components			≥3 components			Total		
Age, years	Sensitivity	Specificity	Youden's index*	Sensitivity	Specificity	Youden's index*	Sensitivity	Specificity	Youden's index*	Sensitivity	Specificity	Youden's index*
51	0.98317	0.09434	0.07751	0.98677	0.07823	0.06500	0.98644	0.07489	0.06133	0.98614	0.079868	0.066008
52	0.96929	0.15406	0.12335	0.97742	0.12951	0.10693	0.97833	0.12358	0.10191	0.97644	0.13177	0.10821
53	0.94627	0.23881	0.18508	0.95901	0.20378	0.16279	0.96212	0.1966	0.15872	0.95793	0.20735	0.16528
54	0.92826	0.28847	0.21673	0.9454	0.2489	0.1943	0.94691	0.24153	0.18844	0.94323	0.25313	0.19636
55	0.89784	0.36649	0.26433	0.92092	0.32143	0.24235	0.91962	0.3159	0.23552	0.91711	0.32702	0.24413
56	0.88161	0.40693	0.28854	0.90617	0.36067	0.26684	0.9049	0.35638	0.26128	0.90214	0.36679	0.26893
57	0.85238	0.46278	0.31516	0.87583	0.41586	0.29169	0.87761	0.41455	0.29216	0.87279	0.42288	0.29567
58	0.82905	0.4976	0.32665	0.85781	0.45145	0.30926	0.85594	0.45179	0.30773	0.85299	0.45879	0.31178
59	0.79244	0.54456	0.337	0.8248	0.49861	0.32341	0.82203	0.5005	0.32253	0.81921	0.50633	0.32554
60	0.77148	0.56945	0.34093	0.8045	0.52477	0.32927	0.80069	0.52742	0.32811	0.79853	0.5325	0.33103
61	0.72099	0.6206	0.34159	0.75234	0.57715	0.32949	0.74562	0.58223	0.32785	0.74584	0.58534	0.33118
62	0.69206	0.64345	0.33551	0.72831	0.60156	0.32987	0.72345	0.6076	0.33105	0.72157	0.60976	0.33133
63	0.63183	0.69441	0.32624	0.65965	0.6552	0.31485	0.65729	0.66416	0.32145	0.65484	0.66376	0.3186
64	0.60968	0.71119	0.32087	0.63531	0.67406	0.30937	0.62951	0.68357	0.31308	0.62991	0.68244	0.31235
65	0.54709	0.74702	0.29411	0.57547	0.71312	0.28859	0.56848	0.72371	0.29219	0.56934	0.72129	0.29063
66	0.52406	0.76149	0.28555	0.54916	0.72978	0.27894	0.54118	0.74056	0.28174	0.54326	0.73766	0.28092
67	0.4411	0.80355	0.24465	0.46795	0.77674	0.24469	0.46113	0.78809	0.24922	0.4621	0.784	0.2461
68	0.41335	0.81461	0.22796	0.44894	0.78919	0.23813	0.43946	0.80031	0.23977	0.44106	0.79617	0.23723
69	0.33422	0.85157	0.18579	0.36195	0.83097	0.19292	0.34949	0.84266	0.19215	0.35445	0.83734	0.19179
70	0.31444	0.86159	0.17603	0.34111	0.84219	0.1833	0.32815	0.8544	0.18255	0.33364	0.84851	0.18215
71	0.2424	0.8934	0.1358	0.26219	0.87802	0.14021	0.24876	0.89039	0.13915	0.25562	0.88376	0.13938
72	0.22409	0.90129	0.12538	0.24196	0.88708	0.12904	0.22924	0.89912	0.12836	0.23587	0.89255	0.12842
73	0.1677	0.92565	0.09335	0.17816	0.91519	0.09335	0.16341	0.92675	0.09016	0.17264	0.91993	0.09257
74	0.15176	0.93099	0.08275	0.16425	0.92176	0.08601	0.15151	0.93291	0.08442	0.15896	0.92621	0.08517
75	0.10806	0.95107	0.05913	0.10752	0.94472	0.05224	0.10007	0.95434	0.05441	0.10561	0.9483	0.05391

*, Youden's index = Sensitivity + Specificity – 1.

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