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Background: To investigate the influence of metabolic syndrome and its components on the risk of breast cancer.

Methods: Retrospective nationwide cohort study analyzing data of 13,377,349 women older than 19 years from Korean National Health Insurance Service was performed. Cox proportional hazards model was used to calculate hazard ratio (HR) and 95% confidence interval (CI) of breast cancer risk.

Results: The presence of metabolic syndrome decreased the risk of all breast cancer types in all subjects (HR: 0.954; 95% CI: 0.939-0.970). In women with age ≤ 50 years, metabolic syndrome decreased the risk of all breast cancer types, with similar findings for all subject groups (HR: 0.915; 95% CI: 0.892-0.939). In women with age >50 years, metabolic syndrome increased the risk of all breast cancer types (HR: 1.146; 95% CI: 1.123-1.170), especially in age groups of more than 55 years. In women with age > 50 years, HRs increased as the number of metabolic syndrome components increased, while HRs decreased as the number of metabolic syndrome components increased in women with age \leq 50 years.

Conclusion: The presence of metabolic syndrome increased the risk of breast cancers in postmenopausal women, but decreased the risk in premenopausal women. Every metabolic syndrome component played similar roles on the risk of breast cancer to metabolic syndrome and their effects became stronger when the number of components increased.

Impact: Metabolic syndrome is associated with the risk of breast cancer having different effect according to age groups.

Keywords: Breast Neoplasms, Incidence, Korean National Health Insurance, Metabolic Syndrome

Table 1. Baseline characteristics of study subjects according to metabolic **Table 2.** Adjusted hazard ratios of breast cancer risk according to metabolic syndrome in each age group syndrome

	All		Metabolic syndrome					Age group (year)	Type of breast cancer	Metabolic syndrome	Number	Event	Rate	HR (95% Cl)
Subject characteristics			No Yes					Invasive and <i>in situ</i> breast cancers						
-	Number	%	Number	%	Number	%	р			No	9,798,803	62,394	1.333	Reference
Total	13,377,349	100.0	9,798,803	73.3	3,578,546	26.8		-		Yes	3,578,546	25,353	1.431	0.954(0.939,0.970)
Elevated waist circumference							< 0.001		Invasive breast cancer					
No	8,848,361	66.1	7,969,930	81.3	878,431	24.6		Total		No	9,798,803	56,176	1.199	Reference
Yes	4,528,988	33.9	1,828,873	18.7	2,700,115	75.5			x 1	Yes	3,578,546	23,271	1.313	0.965(0.949,0.982)
Elevated blood pressure							< 0.001		In situ breast cancer	N	0 700 002	C 31 0	0 122	Deferreres
No	8,553,448	63.9	7,814,183	79.8	739,265	20.7				INO Voc	9,198,803	0,218	0.132	Reference
Yes	4,823,901	36.1	1,984,620	20.3	2,839,281	79.3			Investive and in situ breast concers	168	3,378,340	2,082	0.117	0.049(0.003,0.097)
Elevated fasting glucose							< 0.001		mvasive and <i>in situ</i> bleast cancers	No	6 027 3/0	12 655	1 222	Deference
No	9,830,971	73.5	8,427,435	86.0	1,403,536	39.2				NO	8/10 870	42,033	1.322	0.915(0.892.0.939)
Yes	3,546,378	26.5	1,371,368	14.0	2,175,010	60.8			Invasive breast cancer	105	049,029	0,915	1.731	0.915(0.092,0.959)
Elevated triglyceride							< 0.001	Age ≤50	mvasive bleast cancer	No	6 937 349	38 076	1 180	Reference
No	9,809,187	73.3	8,926,112	91.1	883,075	24.7				Yes	849.829	6.300	1.595	0.932(0.907.0.957)
Yes	3,568,162	26.7	872,691	8.9	2,695,471	75.3			In situ breast cancer	100	019,029	0,000	11070	
Reduced high-density lipoprotein							< 0.001			No	6,937,349	4,579	0.141	Reference
No	8,741,957	65.4	8,002,636	81.7	739,321	20.7				Yes	849,829	615	0.155	0.777(0.714,0.847)
Yes	4,635,392	34.7	1,796,167	18.3	2,839,225	79.3			Invasive and <i>in situ</i> breast cancers					
Age (year)							< 0.001			No	2,861,454	19,739	1.356	Reference
≤50	5,590,171	41.8	6,937,349	70.8	849,829	23.8				Yes	2,728,717	18,438	1.340	1.146(1.123,1.170)
>50	7.787.178	58.2	2.861.454	29.2	2.728.717	76.3			Invasive breast cancer					
Body mass index (l_{x}/m^2)	- , ,		y y -		y - y		<0.001	Age >50		No	2,861,454	18,100	1.243	Reference
-25	3 514 121	263	8 231 236	84.0	1 631 002	15.6	<0.001			Yes	2,728,717	16,971	1.233	1.146(1.122,1.171)
<2 <i>3</i> >25	9,863,228	20.3 73 7	0,231,230 1 567 567	0 4 .0 16.0	1,031,992	43.0 54.4			In situ breast cancer					
E 23	9,003,220	13.1	1,507,507	10.0	1,940,334	54.4	<0.001			No	2,861,454	1,639	0.112	Reference
No	12 485 205	02.2	0 112 151	02.0	2 272 154	04.2	<0.001			Yes	2,728,717	1,467	0.106	1.143(1.063,1.229)
NO Former	12,403,503	95.5	9,115,151	95.0	50 199	94.2 1 7		A 1.1		1. IID 1.	1			
Former	290,043	Z.Z A 5	230,637	2.4 1.6	<i>J</i> 9,100	1.7		Abbreviati	ons: CI, confidence in	terval; HR, h	azard r	at10.		
Drinking	393,999	4.3	440,793	4.0	147,204	4.1	<0.001	*Adjusted	hazard ratios obtaine	d by Cox pr	coportic	onal ł	laza	rds model
Diliking	0 779 210	72 1	6 752 272	69.0	2 024 046	015	<0.001	after heing	adjusted with and st	noking alcol	hal driv	nking	ΔV	arcise and
$\frac{1}{100}$	9,778,519	/3.1 25.9	0,735,575	08.9 20.0	5,024,940	04.J		and being	aujusieu wiin age, si	noking, alcoi		iking	, СЛ	cicise, and
Moderate (0-50g/day)	3,430,394	23.8	2,923,291	29.9	323,103 28,407	14.7		income.						
Everaise	140,030	1.1	120,159	1.2	20,497	0.8	<0.001							
Exercise	7 596 255	567	5 272 615	510	2 212 710	61.0	<0.001							
NO Vec	7,300,333	JU.7	<i>J</i> , <i>J</i> , <i>J</i> , <i>0</i> 4 <i>J</i>	J4.0 15 D	2,212,710	01.0								
Its	3,790,994	43.3	4,423,138	43.2	1,505,650	30.2	<0.001							
	1 752 179	21.0	2 176 096	22.4	1 077 042	20.1	<0.001							
QI	4,235,128	51.8 69.2	5,170,080	52.4 67.6	1,077,042	50.1 60.0								
Q2-4 Investive and in site breast concern	9,124,221	08.2	0,022,717	07.0	2,301,304	09.9	<0.001							
mvasive and <i>in situ</i> ofeast cancers	12 220 602	00.2	0726400	00.4	2 552 102	00.2	<0.001							
NO Vec	15,269,002	99.5	9,730,409	99.4	5,555,195	99.5								
	8/,/4/	0.7	02,394	0.0	25,555	0.7	-0.001							
mvasive dreast cancer	12 207 002	00.4	0740 607	00.4	2 666 076	00.4	<0.001							
INO	15,297,902	99.4 0.6	9,142,621	99.4 0.6	3,333,273	99.4 07								
ies	/9,44/	0.0	50,170	0.6	23,271	0.7	.0.001							
<i>In situ</i> breast cancer	12 200 040	00.0	0 702 595	00.0	O ETC ACA	00.0	<0.001							
INO	13,309,049	99.9 0.1	9,192,383	99.9 0 1	3,376,464	99.9 0 1								
res	8,300	0.1	6,218	0.1	2,082	0.1		-						

The influence of metabolic syndrome on the risk of breast cancer : a study analyzing nationwide data from the Korean National Health Insurance Service

Age ≤50

Age >50

75



Table 3. Adjusted hazard ratios of breast cancer risk for groups with metabolic syndrome in each subgroup according to age group and breast cancer type

• ()		Invasive and in s	<i>itu</i> breast cancers	Invasive b	reast cancer	In situ breast cancer			
Age group (year)	Subgroup	HR (95% CI)	<i>P</i> for interaction	HR (95% CI)	P for interaction	HR (95% CI)	P for interaction		
Total	Age (year)								
	≤50	0.915(0.892,0.939)	<.001	0.932(0.907,0.957)	<.001	0.777(0.714,0.847)	0.048		
	>50	1.146(1.123,1.170)		1.146(1.122,1.171)		1.143(1.063,1.229)			
	Body mass index (kg/m2)								
	<25	0.830(0.811,0.849)	<.001	0.837(0.817,0.858)	<.001	0.763(0.707,0.823)	<.001		
	≥25	1.056(1.028,1.084)		1.054(1.026,1.084)		1.071(0.975,1.176)			
	Smoking								
	No	0.961(0.945,0.977)	<.001	0.971(0.954,0.989)	<.001	0.859(0.812,0.909)	0.393		
	Former	0.823(0.727,0.932)		0.833(0.732,0.948)		0.728(0.473,1.121)			
	Current	0.905(0.836,0.981)		0.925(0.852,1.005)		0.657(0.475,0.910)			
	Drinking								
	No	1.000(0.982,1.018)	<.001	1.010(0.991,1.030)	<.001	0.899(0.845,0.956)	<.001		
	Moderate (0-30g/day)	0.837(0.806,0.870)		0.850(0.817,0.885)		0.720(0.632,0.820)			
	Heavy (>30g/day)	0.941(0.790,1.121)		0.933(0.777,1.120)		1.038(0.564,1.910)			
	Exercise								
	No	0.981(0.960,1.003)	<.001	0.992(0.970,1.015)	<.001	0.871(0.807,0.940)	0.031		
	Yes	0.923(0.900,0.946)		0.934(0.910,0.958)		0.828(0.764,0.897)			
	Income								
	Q1	0.954(0.926,0.983)	<.001	0.960(0.931,0.991)	<.001	0.888(0.800,0.986)	0.002		
	Q2-4	0.957(0.938,0.976)		0.970(0.905,0.990)		0.837(0.784,0.893)			
Age ≤50	Body mass index (kg/m2)								
	<25	0.882(0.849,0.918)	0.001	0.898(0.861,0.935)	0.007	0.758(0.668,0.861)	0.004		
	≥25	1.008(0.969,1.049)		1.006(0.965,1.049)		1.027(0.897,1.175)			
	Smoking								
	No	0.923(0.898,0.948)	0.635	0.939(0.913,0.966)	0.646	0.786(0.720,0.859)	0.796		
	Former	0.839(0.707,0.995)		0.863(0.723,1.031)		0.613(0.326,1.152)			
	Current	0.824(0.737,0.921)		0.837(0.746,0.940)		0.677(0.444,1.031)			
	Drinking								
	No	0.928(0.900,0.957)	0.813	0.944(0.915,0.975)	0.832	0.791(0.716,0.875)	0.960		
	Moderate (0-30g/day)	0.889(0.846,0.934)		0.905(0.859,0.954)		0.752(0.637,0.888)			
	Heavy (>30g/day)	0.880(0.706,1.098)		0.903(0.717,1.136)		0.657(0.289,1.494)			
	Exercise								
	No	0.897(0.866,0.929)	0.080	0.910(0.877,0.944)	0.045	0.786(0.699,0.884)	0.744		
	Yes	0.938(0.903,0.974)		0.959(0.921,0.998)		0.767(0.677,0.869)			
	Income								
	Q1	0.945(0.903,0.988)	0.037	0.951(0.907,0.997)	0.145	0.885(0.760,1.030)	0.044		
	Q2-4	0.902(0.874,0.931)		0.923(0.893,0.954)		0.735(0.663,0.815)			
Age>50	Body mass index (kg/m2)								
	<25	1.094(1.064,1.125)	0.006	1.089(1.057,1.122)	0.007	1.149(1.043,1.266)	0.567		
	≥25	1.097(1.059,1.135)		1.095(1.056,1.135)		1.120(0.988,1.271)			
	Smoking								
	No	1.149(1.125,1.173)	0.247	1.149(1.123,1.174)	0.380	1.151(1.069,1.239)	0.186		
	Former	1.091(0.918,1.296)		1.077(0.900,1.289)		1.279(0.682,2.397)			
	Current	1.079(0.965,1.206)		1.098(0.979,1.231)		0.798(0.488,1.303)			
	Drinking								
	No	1.158(1.133,1.184)	0.035	1.159(1.132,1.186)	0.034	1.150(1.064,1.243)	0.344		
	Moderate (0-30g/day)	1.068(1.008,1.131)		1.068(1.006,1.134)		1.063(0.865,1.306)			
	Heavy (>30g/day)	1.103(0.836,1.455)		1.033(0.775,1.378)		2.626(0.891,7.741)			
	Exercise								
	No	1.172(1.140,1.204)	0.116	1.173(1.140,1.207)	0.090	1.156(1.047,1.277)	0.794		
	Yes	1.110(1.075,1.146)		1.108(1.072,1.146)		1.125(1.012,1.251)			
	Income	1 101/1 000 1 100	0.500		0.5.1		0		
	QI	1.134(1.090,1.180)	0.500	1.136(1.091,1.184)	0.561	1.107(0.962,1.274)	0.667		
	Q2-4	1.150(1.123,1.179)	-	1.150(1.121,1.179)		1.157(1.063,1.259)			

Abbreviations: CI. confidence interval: HR. hazard ratio.

*Hazard ratios of breast cancer risk for the groups with metabolic syndrome with reference of the group without metabolic syndrome.

Table 4. Adjusted hazard ratios of breast cancer risk according to metabolic syndrome in each age subgroup and breast cancer type

	Metabolic syndrome	Invasive and in situ breast cancers					ancer	In situ breast cancer					
Age group (year)		Number	Event	Rate	HR (95% Cl)	Number	Event	Rate	HR (95% Cl)	Number	Event	Rate	HR (95% Cl)
$20 \le$ Age <25	No	667,290	193	0.070	Reference	667,290	169	0.062	Reference	667,290	24	0.009	Reference
	Yes	15,557	5	0.081	1.169(0.480,2.845)	15,557	3	0.048	0.803(0.256,2.519)	15,557	2	0.032	3.707(0.869,15.822)
$25 \le$ Age <30	No	1,079,352	1,098	0.217	Reference	1,079,352	977	0.193	Reference	1,079,352	121	0.024	Reference
	Yes	29,112	28	0.210	0.950(0.652,1.383)	29,112	27	0.202	1.031(0.703,1.513)	29,112	1	0.007	0.303(0.042,2.167)
$30 \le \text{Age} < 35$	No	776,829	2,074	0.564	Reference	776,829	1,841	0.500	Reference	776,829	233	0.063	Reference
	Yes	40,769	107	0.585	1.029(0.847,1.250)	40,769	97	0.530	1.047(0.853,1.285)	40,769	10	0.055	0.882(0.468,1.664)
$35 \le Age < 40$	No	703,295	4,047	1.223	Reference	703,295	3,618	1.093	Reference	703,295	429	0.129	Reference
	Yes	56,596	275	1.083	0.898(0.794,1.015)	56,596	253	0.997	0.922(0.812,1.048)	56,596	22	0.086	0.688(0.448,1.057)
$40 \le \text{Age} < 45$	No	2,060,090	17,737	1.919	Reference	2,060,090	15,748	1.703	Reference	2,060,090	1,989	0.214	Reference
	Yes	284,406	2,341	1.862	0.959(0.918,1.001)	284,406	2,117	1.683	0.974(0.931,1.020)	284,406	224	0.177	0.834(0.726,0.957)
$45 \le Age < 50$	No	1,215,106	13,273	2.191	Reference	1,215,106	11,907	1.964	Reference	1,215,106	1,366	0.224	Reference
	Yes	278,894	2,890	2.134	0.978(0.939,1.018)	278,894	2,629	1.940	0.991(0.950,1.034)	278,894	261	0.192	0.864(0.757,0.987)
$50 \le Age < 55$	No	1,364,707	12,415	1.818	Reference	1,364,707	11,308	1.655	Reference	1,364,707	1,107	0.161	Reference
	Yes	568,113	4,986	1.776	0.984(0.952,1.017)	568,113	4,587	1.633	0.993(0.959,1.028)	568,113	399	0.141	0.897(0.800,1.006)
$55 \le Age < 60$	No	645,519	5,014	1.535	Reference	645,519	4,594	1.406	Reference	645,519	420	0.128	Reference
	Yes	467,700	3,919	1.662	1.088(1.043,1.134)	467,700	3,582	1.518	1.084(1.038,1.133)	467,700	337	0.142	1.127(0.976,1.301)
$60 \le Age < 65$	No	528,596	3,601	1.310	Reference	528,596	3,287	1.195	Reference	528,596	314	0.114	Reference
	Yes	583,110	4,559	1.521	1.168(1.118,1.221)	583,110	4,184	1.395	1.173(1.121,1.228)	583,110	375	0.125	1.117(0.961,1.298)
$65 \le Age < 70$	No	294,580	1,529	0.972	Reference	294,580	1,403	0.892	Reference	294,580	126	0.080	Reference
	Yes	440,045	2,924	1.259	1.298(1.220,1.381)	440,045	2,671	1.149	1.291(1.210,1.378)	440,045	253	0.109	1.367(1.104,1.693)
$70 \le \text{Age} < 75$	No	257,092	976	0.721	Reference	257,092	909	0.672	Reference	257,092	67	0.049	Reference
	Yes	456,284	2,285	0.973	1.346(1.249,1.451)	456,284	2,138	0.910	1.352(1.251,1.462)	456,284	147	0.062	1.264(0.947,1.688)
$75 \le Age < \!\!80$	No	113,866	290	0.512	Reference	113,866	272	0.480	Reference	113,866	18	0.032	Reference
	Yes	208,341	714	0.708	1.373(1.197,1.573)	208,341	680	0.674	1.392(1.210,1.603)	208,341	34	0.034	1.071(0.605,1.898)
$80 \le Age$	No	92,481	147	0.383	Reference	92,481	143	0.373	Reference	92,481	4	0.010	Reference
	Yes	149,619	320	0.513	1.298(1.067,1.578)	149,619	303	0.485	1.262(1.034,1.541)	149,619	17	0.027	2.564(0.861,7.633)

Abbreviations: CI, confidence interval; HR, hazard ratio. *Adjusted hazard ratios obtained by Cox proportional hazards model after being adjusted with age, smoking, alcohol drinking, exercise, and income.

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Figure 1. Adjusted hazard ratios of each age group according to the total number of metabolic syndrome components (Å) and body mass index (B) regarding all breast cancer types.

