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Promoting Sustainable Kidney Health: The Asia-Pacific and Beyond

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Acquired metabolic risk factors, genetic risk score and risk of incident chronic kidney disease

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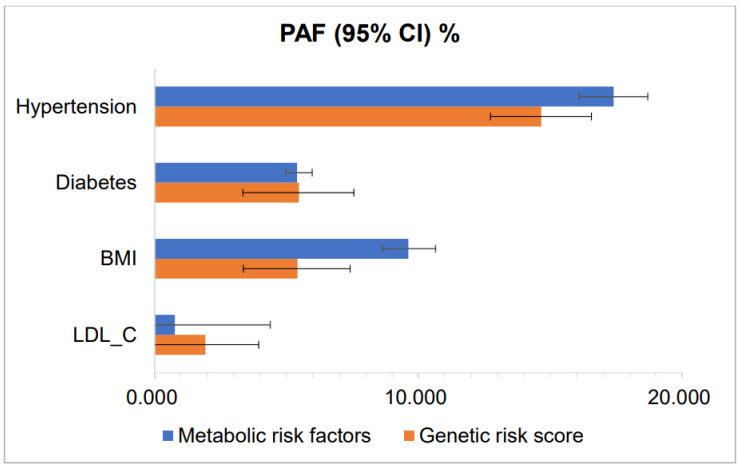
Objectives : Chronic kidney disease (CKD) is associated with various modifiable risk factors, including metabolic factors and genetic predispositions. We aimed to investigate the individual and combined contribution of acquired metabolic risk factors and genetic risk with incident CKD.
Methods : Using UK Biobank study, we selected four acquired metabolic risk factors including hypertension, diabetes obesity, and hyperlipidemia (high low-density lipoprotein cholesterol [LDL-C] level). Polygenic risk scores (PRS) for these factors were also derived from PRS data by Genomics PLC as part of UK Biobank project. The primary outcome was incident CKD. The risk of CKD was determined using Cox proportional hazards model. The population attribution fraction (PAF) of metabolic factors and PRSs were calculated to estimate the relative contribution of each factor to CKD.
Results : This study included 171,955 participants, with a mean age 55.7 years and 86,153 (50.1%) being men. During the 12.8-year follow-up period, 8,641 events of CKD occurred. Hypertension exhibited the highest PAF for CKD at 17.4% (95% CI, 16.1-18.7), followed by diabetes (5.4 [5.0-6.0]) and obesity (9.6% [8.7-10.7]), respectively. However, high LDL-C (>100mg/dL) did not show a significant attribution to CKD risk. Similar to metabolic factors, PRSs for hypertension, diabetes, and BMI, but not LDL-C, significantly contributed to CKD risk, with the corresponding PAFs (95% CIs) of 14.7 (12.7-16.6), 5.5 (3.3-7.6), and 5.4 (3.4-7.4), respectively. The attribution of hypertension to CKD risk was more pronounced in high genetic risk groups of hypertension and diabetes, whereas hypertension did not contribute to CKD risk in high genetic risk groups of obesity and LDL-C.
Conclusions : In this prospective cohort study, there was a complex interplay between acquired metabolic risk factors and genetic predisposition in the development of CKD. This finding may provide an informative insight to the management of modifiable risk factors of CKD, considering their dynamic relationship with genetic risk factors.

figure 1.png

Figure 1. Population attribution fraction of metabolic risk factors and genetic risk score for chronic kidney disease



Abbreviation PAF, population attribution fraction; BMI, body mass index; LDL-C, low-density lipoprotein cholesterol

figure 1.png

Table 1. Population attribution fraction of metabolic risk factors for chronic kidney disease according to the polygenic risk score subgroup

Subgroup		Hypertension		Diabetes		BMI ≥30 Kg/m²		LDL_C >100 mg/dL	
		PAF (95% CI) %	p for interaction	PAF (95% CI) %	p for interaction	PAF (95% CI) %	p for interaction	PAF (95% CI) %	p for interaction
PRS_hypertension	Lowest quintile	9.90 (8.81-10.97)	<0.001	1.44 (1.35-1.53)	0.040	7.28 (6.65-7.90)	0.042	1.06 (-4.52-2.41)	0.471
	Highest quintile	12.45 (11.08-13.80)		9.98 (9.34-10.60)		10.79 (9.86-11.71)		0.96 (-2.22-4.05)	
PRS_diabetes	Lowest quintile	8.20 (7.30-9.10)	<0.001	4.08 (3.83-4.34)	0.067	8.38 (7.65-9.09)	0.125	1.03 (-2.38-4.34)	0.520
	Highest quintile	13.48 (12.00-14.93)		5.69 (5.33-6.05)		9.92 (9.07-10.78)		0.99 (-2.28-4.15)	
PRS_BMI	Lowest quintile	10.22 (9.10-11.32)	0.470	3.59 (3.36-3.81)	0.417	5.47 (5.00-5.95)	<0.001	1.03 (-2.39-4.34)	0.501
	Highest quintile	12.22 (10.88-13.56)		6.46 (6.05-6.86)		13.66 (12.48-14.83)		0.98 (-2.27-4.13)	
PRS_LDL_C	Lowest quintile	11.09 (9.87-12.29)	0.295	5.27 (4.94-5.60)	0.984	9.44 (8.62-10.25)	0.749	0.92(-2.14-3.90)	0.959
	Highest quintile	11.65 (10.37-12.20)		5.18 (4.85-5.50)		9.63 (8.80-10.46)		1.06 (-2.45-4.45)	

Abbreviation PAF, population attribution fraction; PRS, polygenic risk scores; BMI, body mass index; LDL-C, low-density lipoprotein cholesterol