RISK FACTORS OF DEVELOPMENT AND PROGRESSION OF CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction and Aims

Risk factors influencing the natural course of chronic kidney disease (CKD) are complex and heterogenous, seldom systematic reviews or meta-analyses have focused on this issue. In this study, we thus aim to identify the currently known risk factors for disease development and progression in various stages of CKD.

Material and Methods

We systematically searched PubMed, MEDLINE, Scopus, and the Cochrane Library for English publications from the earliest available date of indexing through 15 Oct 2012, for observational studies evaluating the risk factors of renal function decline. Eligible studies should collect repeated information for evaluating the decline in renal function. Studies in patients with any stage of CKD, as well as studies among the general population, were included. The stages of CKD were defined by the K/DOQI Clinical Practice Guidelines according to glomerular filtration rate and evidence of kidney damage. Hazard ratios of a specific risk factor from studies with the same baseline and follow-up stages of CKD, as well as the same outcome endpoints, were pooled by meta-analysis. The pooled estimates of hazard ratio and 95% confidence interval (CI) of risk factors for development or progression of CKD were calculated using the method of DerSimonian and Laird random-effects model.

Table 1. Studies adopted endpoints that could be classified into a specific range of CKD stages.

Author	Year	Country	Follow-up (months)	Participant number	Age (years)	Sex, female (%)	Baseline CKD stage	Follow-up CKD stage	Risk factors for CKD development and progression
O'Seaghdha	2011	USA		200	63.9	60.0	0	3	Urinary connective tissue growth factor
Iseki	2011	Japan	24	8926	49.6	41.6	0	1-5	C-reactive protein
Ryu	2009	Korea	45.6	10685	37.0	0.0	0	3-5	Metabolic syndrome, triglyceride, HDL
Shastri	2011	USA	56.4	5422	61.0	51.5	0-2	3	Microalbuminuria, cystatin C
Shankar	2006	USA	60	4898	62.3	56.0	0-2	3-5	Current smoking, heavy drinking
Bash	2009	USA	174	14854	54.4	54.8	0-2	3-5	WBC, fibrinogen, von Willebrand factor, factor VIIIc, albumin
Chien	2010	Taiwan	26.4	5168	51.2	36.7	0-2	3-5	Age, BMI, diastolic BP, diabetes, stroke, postprandial glucose, HbA1c, proteinuria, uric acid
Shankar	2011	USA	180	4926	58.4	55.3	0-2	3-5	Tumor necrosis factor-α receptor 2, leukocyte count, interleukin-6
Obi	2010	Japan	38.4	461	67.0	38.0	3-5	5D	Age, proteinuria
Hoefield	2010	UK	26	1325	65.1	36.3	3-5	5D	Age, diastolic BP, hemoglobin, phosphate, proteinuria, stage of CKD
De Nicola	2011	Italy	60	1248	67.0	42.6	3-5	5D	Age, proteinuria, stage of CKD, phosphate, BMI, cardiovascular event, hemoglobin
Pereira	2012	Brazil	56.6	211	65.4	51.2	3-5	5D	Diabetic nephropathy
Evans	2005	Sweden	24	920		35.3	4-5	5D	Age, male, diabetes, GFR
Levin	2008	Canada	31	4231	66.8	42.5	4-5	5D	Age, male, GFR, systolic BP, diastolic BP, hemoglobin, phospahte, PTH, proteinuria, ACEI/ARB
Hallan	2009	Norway	123.6	65589	50.1	53.2	0-4	5D	Age, male, low physical activity, diabetes, systolic BP, antihypertensive drugs, HDL, GFR, albuminuria
Bash	2010	USA	192	15324	54.0	55.0	0-5	5D	GFR, black, age, male, diabetes, systolic BP, CAD, BMI, smoking, triglyceride
Agarwal	2009	USA	84	218	68.4	4.1	1-5	5D	Systolic BP
Kuo	2010	Taiwan		19163	51.6	50.1	1-5	5D	Acetaminophen, aspirin, NSAID, rofecoxib
Baek	2012	Korea	141.6	347	64.0	44.1	3	4-5	Albuminuria, microscopic haematuria, GFR

Results

We identified 40 studies, including 29 prospective cohort studies, 9 retrospective cohort studies, and 2 case-control studies. The follow-up time of the included studies ranged from 1.5 to 12 years. The baseline CKD stages of the included studies were various, ranged from normal to late stages. Only three risk factors from studies of the same baseline and follow-up CKD stages were eligible for meta-analysis, including proteinuria, male gender, and diabetes (Table 1). The hazard ratios of progression from CKD stage 3-5 to CKD stage 5D were 1.64 (95% CI 1.01-2.66, I2 = 89.5%), 1.37 (95% CI 1.17-1.62, I2 = 56.8%), and 1.16 (95% CI 0.98-1.38, I2 = 28.2%) for proteinuria > 1 g/day, male gender, and diabetes, respectively (Figure 1).

Conclusion

To the best of our knowledge, this study is the first systematic review of the various risk factors determining the natural course of CKD. Due to high heterogeneity, most of the studies and risk factors cannot be pooled by meta-analysis. Our findings show that heavy proteinuria and male gender are strong predictors of the progression from late stage CKD to end stage renal disease. Diabetes might play a minor role in late stage CKD.

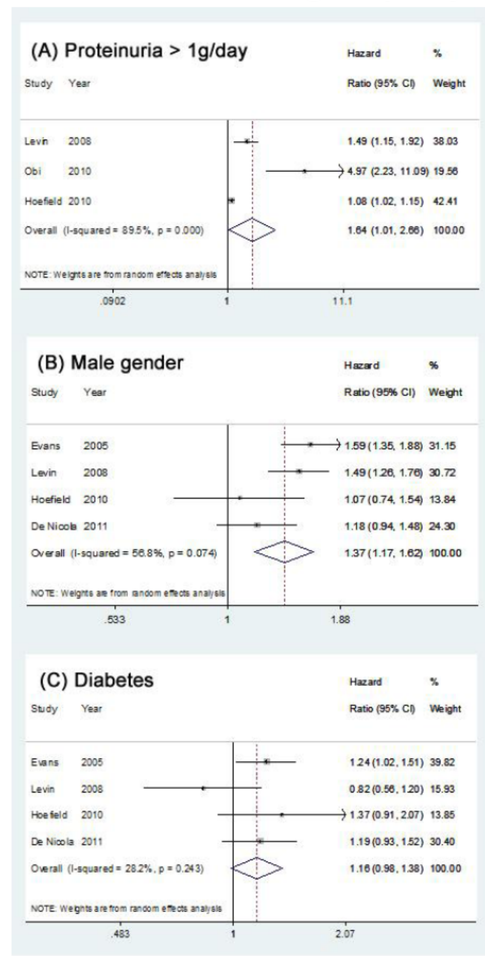

Figure 1. The hazard ratios of progression from CKD stage 3-5 to CKD stage 5D for (A) proteinuria > 1 g/day, (B) male gender, and (C) diabetes.

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