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Review

Vascular endothelial growth factor gene polymorphisms and vasculitis susceptibility: A meta-analysis



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ABSTRACT

Objective: The aim of this study was to explore whether vascular endothelial growth factor (VEGF) polymorphisms are associated with susceptibility to vasculitis.

Methods: Meta-analyses were conducted on the associations between the –634 C/G, +936 C/T, –1154 A/G, and –2578 A/C polymorphisms of VEGF and vasculitis.

Results: Eight studies on VEGF polymorphisms and vasculitis involving 2740 subjects (vasculitis 834, controls 1906) were included in this meta-analysis. The meta-analysis showed no association between vasculitis and the VEGF –634 C allele ($OR = 1.161$, 95% CI = 0.921–1.464, $p = 0.207$) among study subjects. Meta-analysis showed no association between vasculitis and the VEGF + 936 T allele ($OR = 1.121$, 95% CI = 0.905–1.390, $p = 0.295$). However, stratification by ethnicity indicated a significant association between the VEGF + 936 T allele and vasculitis in Europeans, but not in Asians ($OR = 1.486$, 95% CI = 1.038–2.128, $p = 0.030$; $OR = 0.958$, 95% CI = 0.773–1.253, $p = 0.755$). Meta-analysis showed no association between vasculitis and the VEGF –1154 A/G and 2578 A/C polymorphisms.

Conclusions: This meta-analysis suggests that the VEGF + 936 T allele is associated with susceptibility to vasculitis in Europeans, but not in Asians.

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1. Introduction

Vasculitis is a heterogeneous group of disorders characterized by inflammation and damage in blood vessels, leading to tissue or organ injury [1]. Although the etiology of vasculitis is not fully understood, it has been suggested to occur given suitable interactions between a susceptible genetic background and environmental factors.

Vascular endothelial growth factor (VEGF) is an angiogenic regulator involved in blood vessel formation, mitogenesis, epithelial cell proliferation, and endothelial cell survival [2]. VEGF is expressed in smooth muscle cells, macrophages, neutrophils, and platelets [3], and induces proinflammatory changes in chronic inflammation such as leucocyte accumulation and blood vessel alterations [4]. VEGF serum level is significantly increased in

Table 1

Characteristics of the individual studies included in the meta-analysis.

Author (ref)	Country	Ethnicity	Disease	Subjects		Polymorphisms studied	Association findings
				Case	Control		
Zeng (2009) [10]	China	Asian	HSP	100	100	VEGF –634 C/G	NS
Huang (2008) [11]	Taiwan	Asian	KD	156	672	VEGF –634 C/G, +936 T/C, –2578 A/C	NS
Rueda (2006) [12]	Spain	European	HSP	57	226	VEGF –1154 A/G	NS
Nam (2005) [13]	Korea	Asian	BD	101	138	VEGF +936 T/C, –1154 A/G, –2578 A/C	NS
Rueda (2005) [14]	Spain	European	GCA	103	226	VEGF –634 C/A, –1154 A/G	NS
Kariyazono (2004) [15]	Japan	Asian	KD	103	144	VEGF –634 C/G	NS
Salvarani (2004) [16]	Italy	European	BD	122	200	VEGF –634 C/G, +936 T/C	–634 C/G ($p = 0.020$), +936 T/C (NS)
Boiardi (2003) [17]	Italy	European	GCA	92	200	VEGF –634 C/G, +936 T/C	–634 C/G ($p = 0.039$), +936 T/C (NS)

Ref, reference; HSP, Henoch-Schonlein Purpura; BD, Behcet's disease; KD, Kawasaki disease; WG, Wegener's granulomatosis; OR, odds ratio; CI, confidence interval; NS, not significant.

Table 2

Meta-analysis of the associations between the VEGF –634 C/G and +936 T/C polymorphisms and vasculitis.

Polymorphism	Population	No. of studies	Test of association			Test of heterogeneity		
			OR	95% CI	p-val	Model	p-val	I^2
A								
–634 C vs. G	Overall	6	1.161	0.921–1.464	0.207	R	0.018	63.2
	European	3	1.259	0.841–1.887	0.263	R	0.015	76.2
	Asian	3	1.037	0.857–1.255	0.706	F	0.220	33.9
	GCA	2	1.125	0.616–2.055	0.701	R	0.015	83.0
	KD	2	0.975	0.793–1.198	0.807	F	0.423	0
CC vs. CG + GG (recessive)	Overall	6	1.044	0.727–1.502	0.814	R	0.087	48.0
	European	3	1.097	0.617–1.953	0.752	R	0.072	62.0
	Asian	3	0.916	0.634–1.32	0.639	F	0.154	46.5
	GCA	2	0.814	0.519–1.275	0.368	F	0.985	0
	KD	2	0.799	0.540–1.183	0.263	F	0.894	0
CC + CG vs. GG (dominant)	Overall	6	0.975	0.643–1.478	0.904	R	0.001	77.2
	European	3	0.791	0.606–1.033	0.085	R	0.000	88.4
	Asian	3	1.134	0.854–1.505	0.385	F	0.479	0
	GCA	2	0.589	0.335–1.036	0.066	R	0.073	68.9
	KD	2	1.086	0.797–1.480	0.601	F	0.314	1.51
CC vs. GG	Overall	6	1.367	0.833–2.244	0.216	R	0.016	64.2
	European	3	1.663	0.742–3.730	0.217	R	0.020	74.4
	Asian	3	1.012	0.672–1.525	0.953	F	0.174	42.8
	GCA	2	1.333	0.418–4.257	0.627	R	0.024	80.5
	KD	2	0.875	0.564–1.358	0.552	F	0.575	0
B								
+936 T vs. C	Overall	4	1.121	0.905–1.390	0.295	F	0.248	27.3
	European	2	1.486	1.038–2.128	0.030	F	0.511	0
	Asian	2	0.958	0.733–1.253	0.755	F	0.950	0
	BD	2	1.271	0.898–1.797	0.176	F	0.116	59.6
TT vs. TC + CC (recessive)	Overall	4	1.022	0.533–1.962	0.948	F	0.803	0
	European	2	1.027	0.275–3.833	0.969	F	0.323	0
	Asian	2	1.021	0.482–2.161	0.957	F	0.899	0
	BD	2	1.295	0.461–3.633	0.624	F	0.704	0
TT + TC vs. CC (dominant)	Overall	4	1.013	0.794–1.293	0.915	F	0.101	51.7
	European	2	1.104	0.436–2.793	0.834	R	0.018	82.2
	Asian	2	0.941	0.689–1.285	0.700	F	0.903	0
	BD	2	1.307	0.883–1.934	0.181	F	0.101	62.7
TT vs. CC	Overall	4	1.086	0.563–2.092	0.806	F	0.905	0
	European	2	1.392	0.371–5.218	0.490	F	0.544	0
	Asian	2	1.001	0.470–2.131	0.998	F	0.911	0
	BD	2	1.340	0.475–3.778	0.580	F	0.605	0

OR, odds ratio; CI, confidence interval; R, Random effects model; F, Fixed effects model; NA, not available.

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