β2-adrenergic receptor polymorphism and venous thromboembolism

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Dear Sir,

Zee et al. recently reported a nested case-control study of 92 gene polymorphisms in relation to venous thromboembolism (VTE) incidence (1). They discovered a statistically significant association of idiopathic, but not total, VTE with the Q27E β_2-adrenergic receptor (β_2-AR) polymorphism (gln27glu substitution). Odds ratios for genotypes containing the variant allele were modest, ranging from 1.4–1.8 depending on the model (additive, dominant, or recessive). In contrast, Nossent et al. found no association between the Q27E polymorphism and VTE in the Leiden Thrombophilia Study (2), and O'Donnell et al. found no association in a small case-control study (3). Because we had measured this Q27E polymorphism in the large Atherosclerosis Risk in Communities (ARIC) Study cohort (4), we sought to replicate the finding by Zee et al. We also examined another β_2-AR polymorphism (gly16arg) that Zee et al., Nossent et al., and O'Donnell et al. found unassociated with VTE (1–3).

The ARIC cohort was recruited in 1987–1989 from four U.S. communities, underwent epidemiologic examinations, and was followed for cardiovascular events (4). Among 14,210 ARIC participants at risk, 278 VTEs (n = 111 idiopathic) were verified between 1987 and 2002. Like Zee et al., we found no association of the gly16arg polymorphism with VTE. We also found a modest positive but statistically non-significant association between the Q27E polymorphism and both total and idiopathic VTE occurrence in ARIC (Table 1).

Table 1: Hazard ratio (HR) for β_2-AR Q27E (gln27glu) polymorphism and venous thromboembolism (VTE) in ARIC.

	Minor allele (G)			Age-, sex-, and race-adjusted	
Endpoint	**Frequency**	**Model**		**HR**	**95% CI**
All VTE	0.37	Additive	CC	1.00	Ref
			CG	1.01	(0.77, 1.32)
			GG	1.34	(0.94, 1.90)
		Dominant		1.08	(0.84, 1.39)
		Recessive		1.33	(0.97, 1.83)
Idiopathic VTE		Additive	CC	1.00	Ref
			CG	0.93	(0.60, 1.43)
			GG	1.41	(0.81, 2.43)
		Dominant		1.03	(0.69, 1.54)
		Recessive		1.47	(0.90, 2.40)

Further adjustment for body mass index and diabetes, two other risk factors for VTE in ARIC, did not change this finding.

In conclusion, the Q27E β_2-AR polymorphism was not related to VTE in ARIC, unlike the study by Zee at al. (1). It is possible that there is a modest association that we had insufficient power to detect, so a meta-analysis of existing studies could be helpful.

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