



## Correspondence

## Lower risk of venous thromboembolism in multiple Asian ethnic groups

## A B S T R A C T

Lower risk of venous thromboembolism in Asians compared to Whites has been suggested. Despite the biological and cultural diversity of Asian Americans, data are sparse for specific ethnic groups.

In our prior study of lower Asian American risk, the small number of subjects (337 in all races) precluded accurate study of specific Asian American groups. We present here a new study with 4674 venous thromboembolism subjects diagnosed between 1996 and 2015. Our study population was derived from 61,459 voluntary health examinees in a comprehensive northern California health plan with self-classified ethnicity: 53.0% Whites, 28.4% Blacks, 11.6% ASAMs, 6.8% Others. Of Asian Americans, 44.7% were Chinese, 32.8% Filipinos, 12.9% Japanese, 4.5% South Asians, and 5.0% Other Asians.

Chinese, Japanese, Filipinos, and Other Asians each had lower venous thromboembolism risk than both Whites and South Asians, who had risk similar to each other. These data indirectly support a genetic explanation.

## 1. Background

Lower risk of venous thromboembolism (VTE) in Asians compared to Whites has been suggested (Klatsky et al., 2000; White, 2003; Klatsky and Baer, 2004; Stein and Matta, 2010; Lee et al., 2017; Chen and Liao, 2015). Despite biological and cultural diversity of Asian Americans (ASAM), data are sparse for specific ethnic groups. In our prior study (Klatsky et al., 2000) of lower ASAM risk, the small number of subjects (337 in all races) precluded accurate study of specific ASAM groups. We present here a new study with 4674 VTE subjects.

## 2. Methods

Our study population included 61,459 persons in a comprehensive northern California health plan, who underwent voluntary health examinations 1978–85 and remained plan members in 1996, when outpatient diagnoses were computerized. The questionnaire item “What is your race?” ascertained self-classified ethnicity: 53.0% Whites, 28.4% Blacks, 11.6% ASAMs, and 6.8% Other. Of ASAMs, 44.7% were Chinese, 32.8% Filipinos, 12.9% Japanese, 4.5% South Asians (SAs) and 5.0% Other Asians. SAs, mostly Asian Indians, were identified independently before analyses by two investigators using name, birthplace (subject and/or grandparents), gender, and religion. U.S.-born proportions varied markedly: 8% Filipinos, 10% SAs, 11% Other Asians, 43% Chinese, and 79% Japanese.

Through 2015,  $\geq 1$  VTE diagnoses (ICD-9 codes 451-3 and/or 415.1) were made for 4674 persons during an outpatient visit or hospitalization. With Whites as referent for the entire cohort and SAs as referent for interethnic ASAM comparisons, we studied composite VTE risk by logistic regressions with 5 covariates.

## 3. Results

Chinese, Japanese, Filipinos, and Other Asians each had lower VTE risk than both Whites and SAs, who had risk similar to each other (Table 1). Reduced ASAM risk was similar in men, women and subgroups with primary VTE diagnosis of either pulmonary embolism or

venous thrombosis (data not shown). Gender, education and smoking were unrelated; increasing age and body mass index were related to progressively increasing risk (data not shown).

## 4. Discussion

Concordant lower VTE risk vs. Whites among Chinese, Japanese, Filipinos, and Other Asians suggests presence of acquired or genetic protective traits in East and Southeast Asian ethnic groups (Klatsky and Baer, 2004; Stein and Matta, 2010; Lee et al., 2017; Chen and Liao, 2015). Explanatory acquired traits would need to be present in all groups and persist through many years of acculturation. Known VTE risk traits include factors associated with venous stasis (age, obesity, immobility, trauma, surgery, and travel), and with thrombophilia (estrogen use, pregnancy, cancer, endothelial damage, and certain arteriopathies) (Klatsky and Baer, 2004; Stein and Matta, 2010; Lee et al., 2017; Chen and Liao, 2015). Since we were unable to control most of these or other potential lifestyle factors such as diet or exercise, we cannot rule out a contribution of environmental factors to our findings, which are limited to ASAM in Northern California and may have limited generalizability to other populations.

Possible genetic explanations involve genetic polymorphisms leading to dysfunctional anticoagulant systems or decreased hypercoagulable susceptibility. Most prominently this affects the activated protein C anticoagulant system with decreased factor V Leiden (Klatsky and Baer, 2004; Stein and Matta, 2010). Found in ~5% of Caucasians, but rare in East Asians, it may contribute to the ASAM/White disparity (Klatsky and Baer, 2004; Stein and Matta, 2010). Asians may also have lower mean fibrinogen levels and/or lower prevalence of Factor VIIc, Factor VIIIc and prothrombin gene G20210A (Klatsky and Baer, 2004; Stein and Matta, 2010). Although involved in only a minority of VTE cases, clustering and synergy with other coagulation factors may occur.

How do SAs fit in this picture? The vast Indian subcontinent is neither culturally nor genetically homogeneous. Genetic studies (Reich et al., 2009; Moorjani et al., 2013) indicate that many northern Indians have gene pools “close to Middle Easterners, Central Asians, and Europeans.” These persons may be geographically Asian but genetically

<https://doi.org/10.1016/j.pmedr.2019.01.006>

Received 20 November 2018; Received in revised form 5 January 2019; Accepted 14 January 2019

Available online 15 January 2019

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**Table 1**  
Adjusted risk of venous thromboembolisms.<sup>c</sup>

Group (n subjects)	n VTE	HR (95% CI)	p value
Adjusted <sup>a</sup> risk of venous thromboembolism (VTE) versus Whites			
White (32,557)	2576	Referent	–
Black (17,442)	1554	1.2 (1.1–1.2)	< 0.001
All Asian (7254)	268	0.5 (0.5–0.6)	< 0.001
Chinese (3246)	115	0.5 (0.4–0.6)	< 0.001
Japanese (934)	35	0.5 (0.3–0.6)	< 0.001
Filipino (2381)	92	0.6 (0.5–0.7)	< 0.001
South Asian (328)	17	0.9 (0.5–1.4)	0.59
Other Asian (365) <sup>b</sup>	9	0.4 (0.2–0.8)	0.005
Adjusted <sup>a</sup> risk of VTE vs South Asians			
South Asian (328)	17	Referent	–
Chinese (3246)	115	0.6 (0.3–0.9)	0.02
Japanese (934)	35	0.4 (0.2–0.9)	0.01
Filipino (2381)	92	0.5 (0.2–0.9)	0.10
Other Asian (365) <sup>b</sup>	9	0.4 (0.2–1.0)	0.04

<sup>a</sup> Logistic regressions controlled for baseline age, sex, education, BMI, and smoking.

<sup>b</sup> Mostly Korean and Vietnamese.

<sup>c</sup> Studied 1996–2015 in Northern California at Kaiser Permanente.

closer to Whites, which would suit our data.

## 5. Conclusion

Chinese, Japanese, Filipinos and Other Asian Americans, but not South Asians, had substantially lower VTE risk than Whites. These data indirectly support a genetic explanation.

## Support

This work was supported by a Community Budget Grant from The Kaiser Foundation Research Institute to H. Nicole Tran, MD, PhD, PI, in Oakland, CA. Data collection from 1978 to 1985 was supported by a

grant from the Alcoholic Beverage Medical Research Foundation to Arthur L. Klatsky, MD, PI, in Oakland, CA. Neither of the authors has any relationship with industry to report.

## Acknowledgments

We are grateful to Natalia Udaltsova, PhD and Jeanne Darbinian, MS for help with data analysis and to David Baer, MD for advice.

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