

# Major single nucleotide polymorphisms in polypoidal choroidal vasculopathy: a comparative analysis between Thai and other Asian populations

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**Purpose:** To investigate the association in a Thai population between the major age-related macular degeneration (AMD) susceptibility loci, *Y402H* and *I62V* in the complement factor H (*CFH*) and *A69S* in the age-related maculopathy susceptibility 2 (*ARMS2*) genes, and polypoidal choroidal vasculopathy (PCV).

**Methods:** A case-control study included 97 PCV cases and 102 age- and gender-matched controls without any retinopathy. The genotypic profiles of the three polymorphisms were obtained using a real-time polymerase chain reaction assay. The allelic and genotypic association between the polymorphisms and PCV were compared with those from the compiled data of other Asian populations reported previously.

**Results:** Strong associations between the *Y402H*, *I62V*, and *A69S* polymorphisms and PCV were observed in the present study ( $P = 0.002$ ,  $0.003$ , and  $0.0008$  respectively) and in the compiled data ( $P < 0.0001$  for all three polymorphisms). The risk allele frequencies of the polymorphisms in PCVs and in controls from the present study (15.0% and 5.4% for *Y402H*, 71.7% and 57.4% for *I62V*, and 54.1% and 37.3% for *A69S* respectively) were also comparable with the frequencies from the compiled data (10.3% and 6.4% for *Y402H*, 75.2% and 58.3% for *I62V*, and 56.8% and 36.8% for *A69S* respectively). The genotype distribution for each polymorphism was also comparable in both datasets.

**Conclusion:** The findings of this study support a significant genetic association between the major AMD susceptibility genes and PCV across Asian populations. This suggests that AMD and PCV, despite different phenotypic manifestation, may share common genetic risk factors.

**Keywords:** genetic, association, PCV, age-related macular degeneration, *CFH* gene, *ARMS2* gene

## Introduction

A significant association between single nucleotide polymorphisms (SNP) and age-related macular degeneration (AMD) has been reported in diverse populations worldwide.<sup>1</sup> The two most common AMD-associated SNPs, the *Y402H* polymorphism in the complement factor H (*CFH*) gene on chromosome 1q31 and the *A69S* polymorphism in the age-related maculopathy susceptibility 2 (*ARMS2*) gene on chromosome 10q26, have been found in Caucasian and Asian populations.<sup>2,3</sup> The phenotypic manifestation of AMD in a large number of Asian patients, however, are different from those in Caucasian patients.<sup>4</sup> A variant of the neovascular form of AMD in Asians, known as polypoidal choroidal vasculopathy (PCV), has typical characteristics of an abnormal branching vascular network with terminal polypoidal bulbs in inner choroids, which are not commonly found in Caucasians.<sup>5</sup> This has raised a question of whether genotypic manifestations of PCV are different from those of AMD.

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Initial studies on the association between these two genes and PCV among Asians have shown contradictory results. Although the *A69S* SNP has been widely found to exhibit a strong association with PCV in many Asian populations, studies in Japanese, Chinese and Korean populations could not find a significant link between *Y402H* and AMD.<sup>6-8</sup> Interestingly, few studies revealed an association between PCV and the *I62V* polymorphism of another locus in the same *CFH* gene. Recent studies in a Japanese population and a cohort of subjects of European-American descent in the United States, however, have shown a strong association between *Y402H* and PCV.<sup>9,10</sup>

The majority of these data have been obtained from East Asian populations, whereas data from other Asian countries are scarce. This study was conducted to validate the associations between the three SNPs, *Y402H* and *I62V* in *CFH* and *A69S* in the *ARMS2* genes, and PCV in a Thai population. Since the Asian population comprises various ethnic groups that may differ in physical appearance, lifestyle, culture, religion, socioeconomic status, and genetic background,<sup>11</sup> the results were compared with the compiled data of studies from other Asian populations. The results obtained in this study should provide an insight into the genotypic manifestations of PCV with additional data from a Southeast Asian population.

## Methods

### Participants

This study was conducted under approval of the Ethical Committee on Research Involving Human Subjects of Rajavithi Hospital, Bangkok, Thailand. All participants gave written informed consent. A total of 119 patients with PCV and 173 controls were enrolled at the Eye Clinic of the same institute.

The inclusion criteria for PCV were: (1) Thai native; (2) having clinical manifestations of PCV, such as the presence of orange-red subretinal nodules, hemorrhagic retinal pigment epithelial detachment, subretinal hemorrhage, or intraretinal or subretinal fluid with exudates; and (3) having a branching vascular network with terminal polypoidal dilation of choroidal vessels identified by indocyanine green angiography (ICGA). The polyps identified in ICGA should correspond with the orange nodules found in clinical examination. The inclusion criteria for controls were: (1) Thai native; (2) age  $\geq 50$  years; (3) absence of serious systemic or known genetic-influenced diseases such as cancer, diabetes mellitus, and glaucoma; and (4) clinical absence of diseases of the vitreous, retina, retinal pigment epithelium

and choroid, especially drusen, or retinal pigment epithelial abnormality.

The exclusion criteria for both groups were: (1) relatives of any enrolled patients with PCV or controls, (2) any ethnicity other than Thai, (3) any participants whose parents were not born in Thailand, and (4) any participants who did not sign the consent form.

Each participant underwent a comprehensive ophthalmic evaluation using a slit lamp biomicroscope including dilated fundus examination and color fundus photography. All participants with PCV further underwent optical coherent tomography and simultaneous fluorescein and ICGA using a scanning laser ophthalmoscope (Heidelberg Retinal Angiography II®, Heidelberg, Germany) to confirm the diagnosis.

### Genotyping

The genomic DNA was extracted from buffy coat using Compact Nucleic Acid Isolation Kit (MagNA Pure® Compact System, Roche Diagnostics, Mannheim, Germany). DNA concentration was measured and diluted to the final concentration of 50 ng/ $\mu$ L using a spectrophotometer.

The genotyping of the rs1061170 (*Y402H*), the rs800292 (*I62V*), and the rs10490924 (*A69S*) polymorphism were performed in a 480 LightCycler® instrument (Roche Diagnostics) using a commercial real-time assay (LightMix®, Roche Diagnostics). A 10  $\mu$ L reaction mixture was prepared in a 96-well polymerase chain reaction (PCR) plate containing 50 ng genomic DNA, 0.5  $\mu$ L for probe-primers mix (LightMix for the detection of human SNPs, TIB MOLBIOL GmbH, Berlin, Germany), 1  $\mu$ L 2X LightCycler® FastStart DNA Master HybProbe (Roche Diagnostics), 2.7  $\mu$ L deoxyribonuclease (DNase)-free water (PCR-grade), and processed according to the manufacturer's instructions (Roche Diagnostics). Real-time PCR of each SNP was performed by an initial denaturation at 95°C for 10 minutes, followed by 45 cycles of 95°C for 10 seconds, 60°C for 10 seconds, and 72°C for 15 seconds. In order to determine the melting points after the amplification phase, a melting curve analysis was performed at 95°C for 30 seconds and at 40°C for 20 minutes, followed by a slow heating at the rate of 0.2°C per second until reaching 75°C. The polymorphism was determined to have a specific melting point of 55°C for the risk and 62.5°C for the nonrisk allele.

In addition, nine blood samples were randomly selected for DNA sequencing analysis (Macrogen®, Seoul, Korea) to confirm the genotyping results.

## Statistical analysis

The sample size was estimated using Quanto software<sup>12</sup> with type 1 error set at 0.05 and power set at 80%. The minor allele frequency applied for this estimation was based on the lowest frequency of the three investigated SNPs in Asians reported in the literature, which was the frequency of *Y402H* of 0.05.<sup>13</sup> The prevalence of PCV was based on that of neovascular AMD in Thailand, 0.2%.<sup>14</sup> PCV was estimated to be 23% of this prevalence<sup>15</sup> or 0.05%. At least 85 participants were required in each study group using this estimation. The chi-square test was used for testing deviation of genotypic frequency from Hardy–Weinberg equilibrium. The Fisher's exact test was used to test the allelic and genotypic associations of each SNP with PCV. Statistical significance was considered at  $P < 0.05$ .

Logistic regression analysis was used to estimate the odds ratio of having PCV for participants with the homozygous risk genotype compared with those who had the heterozygous, and homozygous nonrisk genotypes. Bonferroni correction was used for assessing the  $P$ -values obtained from these analyses.

For comparison with other Asian populations, data were compiled of association studies between the three SNPs and PCV in Asians published in the literature<sup>9,13,16–22</sup> and calculated the association, allele frequency, and genotype distribution for each SNP using the same protocol. These compiled data gave sample sizes of 1291 PCVs and 2455 controls for *Y402H*, 713 PCVs and 1604 controls for *I62V*, and 747 PCVs and 1331 controls for *A69S*.

## Results

A total of 97 patients with PCV and 102 normal controls were included for genetic analysis. No significant difference between these two groups was found for the demographic characteristics (Table 1). No significant deviation from the Hardy–Weinberg equilibrium was found for each SNP in either study group. The DNA sequencing results of all nine random blood samples confirmed the genotyping results of this study.

## Risk allele frequency

In the cohorts used in this study, the frequency of the risk allele for each SNP, C, G, and T for *Y402H*, *I62V*, and *A69S*

respectively, were found to be similar to that in the compiled data. In addition, the frequency of the risk allele of each SNP was significantly higher in participants with PCV than in controls in both datasets (Table 2).

## Risk genotype

Data in Table 3 show that the genotype distribution in this study's Thai population was similar to that in the compiled Asian population. The only exception was found for the frequency of the homozygous risk genotype (CC) of *Y402H* in the PCV group, which was higher in the present study's population (3.1%) than in the compiled Asian population (0.7%). These frequencies, however, were very low in both populations.

Compared with having the homozygous nonrisk genotype (TT), having the heterozygous genotype *Y402H* (CT) significantly increased the chance (by approximately three times) of having PCV. Individuals with the homozygous risk allele of *I62V* (GG) and *A69S* (TT) were approximately 4–5 times as likely to have PCV as those with the homozygous nonrisk allele (Table 4).

## Discussion

This study showed that both *Y402H* and *I62V* polymorphisms in the *CFH* and the *A69S* in the *ARMS2* genes were strongly associated with PCV in the Thai population. The confirmed genotyping results by DNA sequencing of all nine random blood samples suggested that the dataset was homogenous and unbiased. The strong association of the three SNPs was also observed in the compiled data of previously published studies in other Asian populations.

The *I62V* of *CFH* gene, rather than the *Y402H*, was initially believed to be the SNP associated with PCV in the Asian population.<sup>13,20</sup> The results of this present study, in a Thai population, as well as those in the compiled data indicated that both *I62V* and *Y402H* SNPs were associated with PCV in Asians. This discordance might be due to the low frequency of *Y402H* in Asians compared with the higher frequency of *I62V*. There is no report on the association between *I62V* and PCV or AMD in Caucasians.

Interestingly, the frequency of the risk alleles of the *Y402H* and *A69S* in Asian patients with PCV may be different from that in Caucasian patients with PCV. The frequencies of the risk allele C of the *Y402H* in PCVs, 15.0% in the present study and 10.3% in the compiled data, were much lower than that in a cohort of subjects with PCV of European descent in the United States, which was 49.1%.<sup>10</sup> This is also true for the risk allele T of the *A69S*. These allele frequencies in

**Table 1** Demographic characteristic of the study population

	PCV (n = 97)	Controls (n = 102)	P-value
Gender (male/female)	48/49	50/52	0.948 <sup>a</sup>
Mean age $\pm$ SD (years)	62.9 $\pm$ 8.9	62.2 $\pm$ 7.6	0.595 <sup>b</sup>
Age range (years)	42–87	50–86	

**Notes:** <sup>a</sup>By z-test; <sup>b</sup>by independent t-test.

**Abbreviations:** PCV, polypoidal choroidal vasculopathy; SD, standard deviation.

**Table 2** The allele frequency for each single nucleotide polymorphism in this study and other studies in Asians

	PCV			Controls			P-value	Odds ratio (95% CI)
	N	C <sup>a</sup>	T	N	C <sup>a</sup>	T		
<b>Rs1061170 (Y402H)</b>								
Current study	97	29 (15.0%)	165 (85.1%)	102	11 (5.4%)	193 (94.6%)	0.0023	3.081 (1.493–6.360)
Compiled studies	1291	266 (10.3%)	2316 (89.7%)	2455	314 (6.4%)	4596 (93.6%)	<0.0001	2.467 (2.046–2.973)
Gotoh et al <sup>19</sup>	204	47 (11.5%)	361 (88.5%)	N/A	N/A	N/A	N/A	N/A
Lee et al <sup>20</sup>	72	10 (6.9%)	134 (93.1%)	93	10 (5.4%)	176 (94.6%)	0.6438	1.31 (0.47–3.62)
Kondo et al <sup>13</sup>	130	23 (8.8%)	237 (91.2%)	173	18 (5.2%)	328 (94.8%)	0.0770	1.77 (0.93–3.35)
Hayashi et al <sup>9,b</sup>	510	106 (10.4%)	914 (89.6%)	1342	176 (6.6%)	2508 (93.4%)	9.73 × 10 <sup>-5</sup>	N/A
Nakanishi et al <sup>17</sup>	375	80 (10.7%)	670 (89.3%)	847	110 (6.5%)	1584 (93.5%)	N/A	N/A
	<b>N</b>	<b>G<sup>a</sup></b>	<b>A</b>	<b>N</b>	<b>G<sup>a</sup></b>	<b>A</b>		
<b>Rs800292 (162V)</b>								
Current study	97	139 (71.7%)	55 (28.4%)	102	117 (57.4%)	87 (42.7%)	0.0034	1.879 (1.238–2.854)
Compiled studies	713	1072 (75.2%)	354 (24.8%)	1604	1871 (58.3%)	1337 (41.7%)	<0.0001	2.164 (1.883–2.487)
Lee et al <sup>20</sup>	72	109 (75.7%)	35 (24.3%)	93	113 (60.8%)	73 (39.2%)	0.0045	2.01 (1.21–3.36)
Kondo et al <sup>13</sup>	130	201 (77.3%)	59 (22.7%)	173	197 (56.9%)	149 (43.1%)	1.7 × 10 <sup>-7</sup>	2.58 (1.80–3.69)
Hayashi et al <sup>9,b</sup>	511	762 (74.6%)	260 (25.4%)	1338	1561 (58.3%)	1115 (41.7%)	N/A	N/A
	<b>N</b>	<b>T<sup>a</sup></b>	<b>G</b>	<b>N</b>	<b>T<sup>a</sup></b>	<b>G</b>		
<b>Rs10490924 (A69S)</b>								
Current study	97	105 (54.1%)	89 (45.9%)	102	76 (37.3%)	128 (62.8%)	0.0008	1.987 (1.331–2.960)
Compiled studies	747	849 (56.8%)	645 (43.2%)	1331	980 (36.8%)	1682 (63.2%)	<0.0001	2.259 (1.985–2.571)
Kondo et al <sup>13</sup>	76	95 (62.5%)	57 (37.5%)	94	71 (37.8%)	117 (62.2%)	5.7 × 10 <sup>-6</sup>	N/A
Lee et al <sup>20</sup>	72	80 (55.6%)	64 (44.4%)	93	72 (38.7%)	114 (61.3%)	0.0027	1.98 (1.24–3.15)
Sakurada et al <sup>21</sup>	109	139 (63.8%)	79 (36.2%)	85	60 (35.3%)	110 (64.7%)	<0.0001	3.2 (2.1–4.9)
Gotoh et al <sup>22</sup>	55	61 (55.5%)	49 (44.5%)	74	60 (40.5%)	88 (59.5%)	0.0058	2.0 (1.21–3.29)
Nakanishi et al <sup>17</sup>	375	418 (55.7%)	332 (44.3%)	847	627 (37.0%)	1067 (63.0%)	N/A	N/A
Fuse et al <sup>16</sup>	60	56 (46.7%)	64 (53.3%)	138	90 (32.6%)	186 (67.4%)	0.0077	1.80 (1.17–2.80)

**Notes:** P-values by Fisher's exact test; <sup>a</sup>indicates the risk alleles; <sup>b</sup>the allele frequency was calculated from the reported genotype frequency.

**Abbreviations:** PCV, polypoidal choroidal vasculopathy; CI, confidence interval.

Asians with PCV (54.1% in the present study and 56.8% in the compiled data) were higher than those in Caucasians with PCV (31.8%).<sup>10</sup>

In addition, the minor allele frequency (the risk allele frequency in controls) in Asians may also be different from that in Caucasians. The data from this present study and the compiled data indicated that the frequency of the allele C of the *Y402H* in controls was approximately 6%.<sup>9,13,17,20</sup> This is comparable to the frequency of the allele C in controls, 5.1%, from a meta-analysis of association between this SNP and AMD in Asians.<sup>23</sup> A meta-analysis of association between this SNP and AMD in Caucasian populations,<sup>2</sup> however, indicates a much higher frequency of this allele in controls, 34.9%. For *A69S*, a meta-analysis of association between this SNP and AMD<sup>3</sup> points out that the minor allele frequency is 38.7% in Asians but 21.6% in Caucasians.

These data suggest that although the frequency of *Y402H* or *A69S* is not uniform in diverse populations, its attributed

risk for AMD or PCV exists across them. This supports the notion that the genetic effects of disease-associated variants are usually similar across racial boundaries regardless of their diverse allelic frequency among different populations.<sup>24</sup>

Although PCV is different from neovascular AMD in many aspects, such as the affected age group and response to photodynamic therapy, both diseases share some similarities. Both are diseases of abnormal choroidal vessels, and both respond to anti-vascular endothelial growth factor (anti-VEGF) agent by absorption of exudates and extravascular fluid.<sup>25,26</sup> This response to anti-VEGF, along with evidence that elevated C-reactive protein (CRP) levels is strongly associated with both PCV and AMD,<sup>27</sup> suggests that inflammation plays a role in both diseases.

*CFH* is a critical negative regulator of complement activation and inflammation. The *Y402H* variant is located within complement control protein 7, one of the complement

**Table 3** The genotype distribution for each single nucleotide polymorphism in this study and other studies in Asians

	PCV			Controls			P-value
	CC	CT	TT	CC	CT	TT	
<b>Rs1061170 (Y402H)</b>							
Current study	3 (3.1%)	23 (23.7%)	71 (73.2%)	0 (0%)	11 (10.8%)	91 (89.2%)	0.002
Compiled studies	8 (0.7%)	227 (19.5%)	926 (79.8%)	14 (0.6%)	268 (11.7%)	2000 (87.6%)	<0.001
Gotoh et al <sup>19</sup>	2 (1.0%)	43 (21.1%)	159 (77.9%)	N/A	N/A	N/A	N/A
Lee et al <sup>20</sup>	0 (0%)	10 (13.9%)	62 (86.1%)	1 (1.1%)	8 (8.6%)	84 (90.3%)	N/A
Hayashi et al <sup>9</sup>	5 (1.0%)	96 (18.8%)	409 (80.2%)	8 (0.6%)	160 (11.9%)	1174 (87.5%)	N/A
Nakanishi et al <sup>17</sup>	1 (0.2%)	78 (20.8%)	296 (79.0%)	5 (0.6%)	100 (11.8%)	742 (87.6%)	3.4 × 10 <sup>-4</sup>
<b>Rs800292 (I62V)</b>							
Current study	46 (47.4%)	47 (48.5%)	4 (4.1%)	29 (28.5%)	59 (57.8%)	14 (13.7%)	0.005
Compiled studies	331 (56.8%)	209 (35.8%)	43 (7.4%)	492 (34.4%)	690 (48.2%)	249 (17.4%)	<0.001
Lee et al <sup>20</sup>	41 (56.9%)	27 (37.5%)	4 (5.6%)	36 (38.7%)	41 (44.1%)	16 (17.2%)	0.0175
Hayashi et al <sup>9</sup>	290 (56.8%)	182 (35.6%)	39 (7.6%)	456 (34.1%)	649 (48.5%)	233 (17.4%)	N/A
<b>Rs10490924 (A69S)</b>							
Current study	2 (33.0%)	1 (42.3%)	24 (24.7%)	13 (12.8%)	50 (49%)	39 (38.2%)	0.002
Compiled studies	270 (36.1%)	309 (41.4%)	168 (22.4%)	182 (13.7%)	616 (46.3%)	533 (40.0%)	<0.001
Kondo et al <sup>18</sup>	31 (40.8%)	33 (43.4%)	12 (15.8%)	15 (16.0%)	41 (43.6%)	38 (40.4%)	N/A
Lee et al <sup>20</sup>	25 (34.7%)	30 (41.7%)	17 (23.6%)	12 (12.9%)	48 (51.6%)	33 (35.5%)	0.0034
Sakurada et al <sup>21</sup>	45 (41.3%)	49 (44.9%)	15 (13.8%)	14 (16.5%)	32 (37.6%)	39 (45.9%)	<0.0001
Gotoh et al <sup>22</sup>	18 (32.7%)	25 (45.5%)	12 (21.8%)	12 (16.2%)	36 (48.6%)	26 (35.1%)	N/A
Nakanishi et al <sup>17</sup>	133 (35.5%)	152 (40.5%)	90 (24.0%)	113 (13.3%)	401 (47.3%)	333 (39.3%)	1.6 × 10 <sup>-14</sup>
Fuse et al <sup>16</sup>	18 (30.0%)	20 (33.3%)	22 (36.7%)	16 (11.6%)	58 (42.0%)	64 (46.4%)	0.0069

**Note:** P-value by Fisher's exact test.

**Abbreviation:** PCV, polypoidal choroidal vasculopathy.

control protein modules that contain binding sites for CRP.<sup>28</sup> Previous biological studies have shown that the risk allele variants of *Y402H* have reduced affinity on the binding to CRP.<sup>29</sup> This may indicate that both AMD and PCV share the same genetic risks manifested by dysregulation of the complement system.

The relationship between *A69S* and AMD or PCV is not well understood. Earlier studies propose that the altered function of the putative mitochondrial protein LOC387715/*ARMS2* by *A69S* substitution increases the susceptibility to the aging-associated degeneration of macular photoreceptors.<sup>30</sup> Another study, however, suggests that *ARMS2* might not confer

**Table 4** The likelihood of homozygous or heterozygous risk genotype having PCV in this study and in the compiled data from other studies in Asians

Paired genotype	Current study		Compiled studies		
	P-value	Odds ratio	P-value	Odds ratio	
<b>Rs1061170 (Y402H)</b>	CC vs TT	0.839	8.96 (0.46–176.24)	0.649	1.234 (0.516–2.952)
	CT vs TT	0.006	2.974 (1.364–6.488)	<0.001	1.829 (1.508–2.219)
	CC vs CT	0.869	3.43 (0.16–72.04)	0.513	0.675 (0.278–1.637)
<b>Rs800292 (I62V)</b>	GG vs AA	0.005	5.5514 (1.665–18.513)	<0.001	3.896 (2.739–5.542)
	GA vs AA	0.087	2.7829 (0.861–9.031)	0.002	1.754 (1.225–2.511)
	GG vs GA	0.025	1.991 (1.090–3.636)	<0.001	2.221 (1.804–2.735)
<b>Rs10490924 (A69S)</b>	TT vs GG	0.001	4.0 (1.760–9.091)	<0.001	4.707 (3.645–6.078)
	TG vs GG	0.390	1.333 (0.692–2.565)	<0.001	1.591 (1.276–1.985)
	TT vs TG	0.005	3.002 (1.396–6.454)	<0.001	2.957 (2.344–3.731)

**Notes:** Logistic regression analysis was used to test the likelihood of homozygous or heterozygous risk genotype having PCV when paired with homozygous nonrisk genotype; odds ratios indicate significance at  $P < 0.0167$  (0.05/3, Bonferroni correction); the homozygous risk genotypes are in bold; the studies included in the compiled data are listed in Table 3.

**Abbreviations:** PCV, polypoidal choroidal vasculopathy; vs, versus.

risk to AMD through the mitochondrial pathway.<sup>31</sup> Additional analysis of the LOC387715/*ARMS2* protein with Ala or Ser codon 69 and its function in vivo are needed to better understand its contribution to PCV or AMD pathogenesis.

Limitations in this study include the assessments of only three major SNPs associated with AMD. Other SNPs may also be associated with PCV. To the authors' knowledge there has been no genome-wide study to document other PCV-associated SNPs that may not be associated with AMD. The compiled data from previously published studies were set up only for comparison with the results of this study. The aim was not to conduct a meta-analysis of association between the three SNPs and PCV; therefore, there were no strong criteria for inclusion and exclusion of the studies into the compiled data. Although the results of this study suggest a trend toward association between the three SNPs and PCV, more data from other Asian populations and other ethnic groups are necessary.

Cigarette smoking has been found to be associated with PCV, and there was possible interaction between the *Y402H* and cigarette smoking on PCV.<sup>17</sup> However, some studies on interaction between cigarette smoking and SNPs in AMD showed contradictory results.<sup>32–35</sup> Smoking history was surveyed in the present study's participants, but the data were so varied and unreliable that they were not used for analysis. This is another limitation of this study.

In conclusion, the major AMD-susceptibility genes, *CFH* with *Y402H* and *I62V* and *ARMS2* with *A69S*, are associated with PCV in a Thai population. The results are in concordance with those from the compiled data obtained from previous association studies in other Asian populations. This suggests that AMD and PCV may share the same genetic predisposition. A genome-wide association study for PCV will improve the identification of other possible PCV susceptibility genes. This genetic data will eventually lead to a better understanding of the pathogenesis of PCV.

## Disclosure

The authors report no conflicts of interest in this work.

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