

Genetic variants at PITX2, CAV1 and KCNN3, hypertensive target-organ damage and atrial fibrillation in an Uzbek population

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Abstract

Background

Hypertension is the most prevalent modifiable risk factor for atrial fibrillation, yet only a minority of hypertensive patients develop the arrhythmia and the severity of target-organ damage varies widely at similar blood pressure. We examined whether common variants at established atrial fibrillation susceptibility loci relate to hypertensive target-organ damage as well as to the arrhythmia itself.

Methods and Results

In a single-centre case-control study, 372 patients with arterial hypertension of Uzbek ancestry (237 with and 135 without atrial fibrillation) were genotyped for five polymorphisms at PITX2, CAV1 and KCNN3 by real-time polymerase chain reaction. Associations with atrial fibrillation were tested by logistic regression under a log-additive model; associations with left ventricular mass index, carotid intima-media thickness, left atrial volume index and estimated glomerular filtration rate were tested by linear regression adjusted for age and systolic blood pressure. Three variants were associated with atrial fibrillation: rs6817105 (odds ratio 2.98 per C allele, 95% confidence interval 2.12–4.20), rs11264280 (2.38, 1.77–3.21) and rs11773845 (0.41, 0.30–0.57). Each rs11264280 T allele was also associated with a higher left ventricular mass index (5.51 g/m², 1.44–9.58) and a greater carotid intima-media thickness (0.05 mm, 0.02–0.08), and both associations were present in patients without atrial fibrillation. The rs11264280 effect allele was more frequent than in any 1000 Genomes super-population.

Conclusions

Genotype at the 1q21/KCNN3 locus may relate to the severity of hypertensive remodelling before the arrhythmia becomes manifest. These exploratory findings require replication in an independent cohort.

Introduction

Arterial hypertension is the most prevalent modifiable risk factor for atrial fibrillation (AF) [1, 2]. It raises left atrial pressure, promotes left ventricular (LV) hypertrophy and atrial dilatation, and creates the structural and electrical substrate on which the arrhythmia develops [2]. Yet only a minority of hypertensive patients ever develop AF, and the severity of target-organ damage varies widely at similar levels of blood pressure. This variation points to a genetic contribution: a family history of AF is itself an independent risk factor [3].

Genome-wide association studies have identified reproducible susceptibility loci for AF. The strongest and most consistently replicated signal lies at 4q25, near PITX2, a gene that regulates left atrial development and the myocardial sleeves of the pulmonary veins [4]. Variants in KCNN3, which encodes

the small-conductance calcium-activated potassium channel SK3, were later associated with lone AF [5], and CAV1, encoding caveolin-1, was identified among further susceptibility loci [6]. These discoveries were made almost entirely in populations of European ancestry, and even large multi-ethnic analyses have included few Central Asian participants [7]. Allele frequencies and effect sizes cannot be assumed to transfer between ancestries, and Central Asian populations remain largely absent from reference panels such as the 1000 Genomes Project [8].

Work in the Uzbek population has begun to address this gap. Variants in the renin–angiotensin–aldosterone system have been associated with hypertension [9], and genetic determinants of hypertension have been described in the Aral Sea region [10]. In hypertensive patients with AF, our group has previously reported associations for the 4q25/PITX2 variant rs6817105 [11], the CAV1 variant rs11773845 [12], and rs6817105 together with the KCNN3 variant rs13376333 [13]. All of these studies addressed susceptibility to the arrhythmia itself.

What remains unclear is whether these variants also relate to the severity of hypertensive target-organ damage, which precedes and prepares the arrhythmia. If a variant is associated with LV hypertrophy, arterial wall thickening or renal impairment in hypertensive patients who do not yet have AF, then it is linked to an earlier stage of the disease than an association with the arrhythmia alone would suggest.

We therefore examined five polymorphisms in 372 hypertensive patients of Uzbek ancestry, with and without AF, with three aims: to test the association of each variant with AF, which was prespecified; to explore, as a secondary, hypothesis-generating analysis, whether any variant — in particular rs11264280 at the 1q21 locus, which has not previously been examined in this population — is associated with markers of hypertensive target-organ damage; and to describe the first effect-allele frequencies for these loci in an Uzbek population, compared with the 1000 Genomes super-populations.

Materials and Methods

Study design and population

This case–control study included 372 patients with arterial hypertension of Uzbek ethnicity, recruited at the Republican Specialized Scientific and Practical Medical Center of Cardiology, Tashkent, Uzbekistan. Patients with AF formed the case group (n = 237) and patients without AF the control group (n = 135). Hypertension was diagnosed according to the 2023 European Society of Hypertension guidelines [17]; AF was confirmed by 12-lead electrocardiography and/or 24-hour Holter monitoring. Exclusion criteria were secondary hypertension, severe heart failure (New York Heart Association class III–IV), haemodynamically significant valvular disease, prior cardiac surgery, permanent pacemaker, and severe renal or hepatic dysfunction.

Clinical and echocardiographic assessment

Clinical, laboratory and echocardiographic measurements were obtained with standardised, calibrated protocols applied identically to both groups [14]. Transthoracic echocardiography provided LV mass index, left atrial diameter and volume index, ejection fraction and diastolic indices. Carotid intima-media thickness was measured by ultrasound, and the estimated glomerular filtration rate was calculated with the Chronic Kidney Disease Epidemiology Collaboration equation. Serum lipids and uric acid were measured by standard assays. Blood pressure is reported in mm Hg.

Genotyping

Genomic DNA was extracted from peripheral venous blood using the QIAamp DNA Blood Mini Kit (Qiagen, Hilden, Germany); DNA concentration and purity were verified by fluorometry (Thermo Fisher Scientific, Waltham, MA, USA). Five polymorphisms – rs6817105 (PITX2), rs11773845 and rs3807990 (CAV1), and rs13376333 and rs11264280 (1q21/KCNN3 region) – were genotyped by real-time polymerase chain reaction with allele-specific assays, following the manufacturer’s protocol. Laboratory personnel were blinded to case or control status. Cases and controls were processed in separate genotyping batches.

Genotyping quality control

Call rates were calculated separately in cases and controls, and Hardy–Weinberg equilibrium was tested in both groups with an exact test. Variants with a call rate below 95% in either group, or with an exact $P < 0.001$ in controls, were to be excluded. Quality-control metrics for all five variants are given in Table 2.

Table 2
Genotyping call rates and Hardy–Weinberg equilibrium in cases and controls

Gene / variant	Genotyped cases, n (%)	Genotyped controls, n (%)	HWE <i>P</i> , cases	HWE <i>P</i> , controls
PITX2 / rs6817105	237 (100.0)	127 (94.1)	5.8×10^{-4}	0.26
CAV1 / rs11773845	237 (100.0)	131 (97.0)	0.13	0.06
KCNN3 / rs13376333	237 (100.0)	135 (100.0)	0.85	0.02
1q21-KCNN3 / rs11264280	235 (99.2)	135 (100.0)	2.5×10^{-10}	0.007
CAV1 / rs3807990	237 (100.0)	135 (100.0)	0.02	0.95
Call rates are the number (%) of successfully genotyped samples out of 237 cases and 135 controls. Hardy–Weinberg equilibrium (<i>HWE</i>) was tested by exact test in each group separately				

Statistical analysis

Continuous variables are presented as mean (SD) and were compared with Student’s t-test; categorical variables are presented as n (%) and were compared with the χ^2 test. Associations with AF were

analysed by binary logistic regression under a log-additive (allele-dose) model and are reported as crude odds ratios with 95% confidence intervals.

The association of rs11264280 with markers of target-organ damage was evaluated by linear regression of each continuous phenotype on allele dose, adjusted for age and systolic blood pressure, with additional adjustment for AF status in the pooled cohort. These analyses of target-organ damage were exploratory; the analysis of AF was prespecified. Effect-allele frequencies were compared with the 1000 Genomes Project phase 3 super-populations [8] accessed through Ensembl [15]. Findings are reported with confidence intervals rather than relying on hypothesis testing alone; a two-sided $P < 0.05$ was considered significant, and a Bonferroni threshold was applied for the five variants tested. Analyses were performed with the SNPAssoc package in R [16].

Use of large language models

A large language model (Claude, Anthropic, San Francisco, CA, USA) was used for English-language editing of the manuscript text. It was not used for study design, data analysis or interpretation. All authors reviewed the edited text and take full responsibility for its content.

Results

Study population

Of 372 hypertensive patients, 237 had AF and 135 did not. The groups were similar in age (56.9 (6.2) vs 56.1 (11.2) years; $P = 0.46$) and in duration of hypertension. Patients with AF showed markedly greater target-organ damage: a higher LV mass index (110.3 (31.5) vs 100.0 (30.5) g/m²; $P = 0.002$) and a higher prevalence of LV hypertrophy (73.8% vs 48.5%), a larger left atrium (volume index 39.0 (13.0) vs 23.8 (6.3) ml/m²), a thicker carotid intima-media (left 1.0 (0.2) vs 0.9 (0.2) mm; $P = 0.004$), a lower ejection fraction, and a lower estimated glomerular filtration rate (75.9 (19.1) vs 85.6 (19.1) ml/min; all $P < 0.001$). Coronary artery disease, heart failure and prior stroke were more frequent in patients with AF (all $P \leq 0.005$). Office blood pressure was lower in the AF group (systolic 141.2 (23.3) vs 154.6 (17.3) mm Hg; $P < 0.001$), consistent with ongoing antihypertensive treatment (Table 1).

Table 1
Baseline characteristics of hypertensive patients with and without atrial fibrillation

Characteristic	With AF (n = 237)	Without AF (n = 135)	P
Age, years	56.9 (6.2)	56.1 (11.2)	0.456
Duration of hypertension, years	10.5 (7.4)	10.2 (6.5)	0.656
Body mass index, kg/m ²	30.8 (5.5)	30.8 (5.0)	0.925
Waist circumference, cm	104.3 (16.2)	96.4 (16.7)	< 0.001
Office systolic blood pressure, mm Hg	141.2 (23.3)	154.6 (17.3)	< 0.001
Office diastolic blood pressure, mm Hg	87.8 (12.0)	94.9 (9.6)	< 0.001
Left ventricular mass index, g/m ²	110.3 (31.5)	100.0 (30.5)	0.002
Left ventricular hypertrophy, n (%)	175 (73.8)	64 (48.5)	< 0.001
Left atrial diameter, cm	5.3 (0.8)	3.8 (0.4)	< 0.001
Left atrial volume index, ml/m ²	39.0 (13.0)	23.8 (6.3)	< 0.001
E/A ratio	1.0 (0.8)	0.9 (0.3)	0.272
Left ventricular ejection fraction, %	57.4 (7.7)	65.9 (6.3)	< 0.001
Carotid intima-media thickness, left, mm	1.0 (0.2)	0.9 (0.2)	0.004
Carotid intima-media thickness, right, mm	1.0 (0.2)	0.9 (0.6)	0.505
Estimated glomerular filtration rate, ml/min	75.9 (19.1)	85.6 (19.1)	< 0.001
Uric acid, mg/dl	5.6 (1.7)	6.1 (1.9)	0.015
Glucose, mmol/l	5.4 (1.0)	5.5 (0.9)	0.628
Total cholesterol, mg/dl	191.1 (45.2)	205.2 (47.2)	0.006
LDL cholesterol, mg/dl	107.4 (45.4)	116.1 (47.0)	0.086
HDL cholesterol, mg/dl	44.0 (11.1)	46.7 (11.1)	0.027
Triglycerides, mg/dl	146.6 (89.9)	178.2 (140.9)	0.020
Current smoking, n (%)	54 (23.1)	32 (25.0)	0.681
Coronary artery disease, n (%)	203 (86.4)	71 (55.9)	< 0.001
Diabetes mellitus, n (%)	33 (14.1)	20 (15.7)	0.673
Values are mean (SD) or n (%). P values from Student's t-test (continuous variables) or the χ^2 test (categorical variables). AF atrial fibrillation, HDL high-density lipoprotein, LDL low-density lipoprotein			

Characteristic	With AF (n = 237)	Without AF (n = 135)	P
Prior stroke, n (%)	22 (9.4)	2 (1.6)	0.005
Heart failure, n (%)	180 (76.6)	21 (17.5)	< 0.001
Obesity, n (%)	125 (53.0)	61 (58.1)	0.380
Family history of cardiovascular disease, n (%)	170 (72.3)	124 (97.6)	< 0.001
Values are mean (SD) or n (%). <i>P</i> values from Student's t-test (continuous variables) or the χ^2 test (categorical variables). <i>AF</i> atrial fibrillation, <i>HDL</i> high-density lipoprotein, <i>LDL</i> low-density lipoprotein			

Genotyping quality control

Call rates ranged from 235 to 237 of 237 in cases and from 127 to 135 of 135 in controls; the lowest was 94.1% for rs6817105. No variant fell below the prespecified threshold of 95% in both groups. In controls, Hardy–Weinberg equilibrium was preserved for rs6817105 ($P = 0.26$), rs11773845 ($P = 0.06$) and rs3807990 ($P = 0.95$), with nominal deviation for rs13376333 ($P = 0.02$) and rs11264280 ($P = 0.007$); none reached the prespecified exclusion threshold of $P < 0.001$, and no variant was excluded. Exact-test P values in cases were 5.8×10^{-4} for rs6817105, 0.13 for rs11773845, 0.85 for rs13376333, 2.5×10^{-10} for rs11264280 and 0.02 for rs3807990 (Table 2).

Association with atrial fibrillation

Under the log-additive model, three variants were associated with AF (Table 3): rs6817105 near PITX2 (odds ratio 2.98 per C allele, 95% confidence interval 2.12–4.20), rs11264280 at the 1q21/KCNN3 locus (2.38, 1.77–3.21) and rs11773845 in CAV1 (0.41, 0.30–0.57); all $P < 10^{-7}$, well below the Bonferroni threshold. The CAV1 variant rs3807990 was borderline (0.74, 0.55–1.00; $P = 0.050$) and rs13376333 in KCNN3 was not associated (1.21, 0.85–1.71; $P = 0.29$).

Table 3
Genotype associations with atrial fibrillation under a log-additive model

Gene / variant	Effect allele	Frequency, with AF	Frequency, without AF	Odds ratio per allele (95% CI)	<i>P</i>
PITX2 / rs6817105	C	0.49	0.22	2.98 (2.12–4.20)	1.0×10^{-11}
1q21-KCNN3 / rs11264280	T	0.59	0.33	2.38 (1.77–3.21)	1.7×10^{-9}
CAV1 / rs11773845	C	0.39	0.61	0.41 (0.30–0.57)	1.7×10^{-8}
CAV1 / rs3807990	T	0.34	0.41	0.74 (0.55–1.00)	0.050
KCNN3 / rs13376333	T	0.24	0.20	1.21 (0.85–1.71)	0.29
Odds ratios per effect allele from log-additive (allele-dose) logistic regression, unadjusted; <i>P</i> by likelihood-ratio test. The effect allele is the allele associated with atrial fibrillation; frequencies are effect-allele frequencies in each group. <i>AF</i> atrial fibrillation, <i>CI</i> confidence interval					

Allele frequencies across populations

Effect-allele frequencies in the Uzbek cohort differed from those of the 1000 Genomes reference populations (Table 4). The rs11264280 effect (T) allele was more frequent in this cohort (0.33) than in any super-population (European 0.31, South Asian 0.21, African 0.11, East Asian 0.09; global 0.17). Frequencies of the CAV1 variants were likewise higher (rs11773845 C allele 0.61; rs3807990 T allele 0.41), whereas the PITX2 rs6817105 C allele (0.22) was intermediate between European (0.16) and East Asian (0.45) values.

Table 4
Effect-allele frequencies in the Uzbek cohort compared with 1000 Genomes super-populations

Gene / variant	Effect allele	Uzbek (this study)	European	East Asian	South Asian	African	Global
PITX2 / rs6817105	C	0.22	0.16	0.45	0.14	0.25	0.25
CAV1 / rs11773845	C	0.61	0.40	0.27	0.35	0.70	0.44
KCNN3 / rs13376333	T	0.20	0.30	0.03	0.20	0.30	0.21
1q21-KCNN3 / rs11264280	T	0.33	0.31	0.09	0.21	0.11	0.17
CAV1 / rs3807990	T	0.41	0.25	0.20	0.23	0.38	0.27
Values are effect-allele frequencies. The Uzbek frequency is that of the control group (patients without atrial fibrillation), taken as the population baseline; reference frequencies are from the 1000 Genomes Project phase 3, accessed through Ensembl							

rs11264280 and target-organ damage

After adjustment for age and systolic blood pressure, each rs11264280 T allele was associated with a higher LV mass index (5.51 g/m², 95% confidence interval 1.44–9.58) and a greater carotid intima-media thickness (0.05 mm, 0.02–0.08). Both associations were also present in patients without AF (LV mass index 9.25 g/m², 1.26–17.24; carotid intima-media thickness 0.07 mm, 0.01–0.14), that is, in the absence of the arrhythmia (Fig. 1). In the whole cohort, the same allele was associated with a larger left atrial volume index (2.38 ml/m², 0.82–3.95) and a lower estimated glomerular filtration rate (– 3.83 ml/min, – 6.30 to – 1.35), but neither association was present in patients without AF (Table 5).

Table 5
Association of rs11264280 with markers of hypertensive target-organ damage

Parameter	Without AF: β (95% CI); <i>P</i>	With AF: β (95% CI); <i>P</i>	All patients: β (95% CI); <i>P</i>
Left ventricular mass index, g/m ²	9.25 (1.26 to 17.24); 0.023	4.72 (– 0.06 to 9.50); 0.053	5.51 (1.44 to 9.58); 0.008
Left atrial diameter, cm	0.09 (– 0.04 to 0.22); 0.177	0.15 (0.03 to 0.27); 0.013	0.14 (0.05 to 0.23); 0.003
Left atrial volume, ml	–0.25 (– 4.22 to 3.73); 0.902	4.82 (0.93 to 8.71); 0.015	3.85 (0.76 to 6.95); 0.015
Left atrial volume index, ml/m ²	0.05 (– 1.81 to 1.91); 0.961	2.93 (0.95 to 4.91); 0.004	2.38 (0.82 to 3.95); 0.003
Left ventricular ejection fraction, %	0.40 (– 1.51 to 2.31); 0.679	–1.15 (– 2.35 to 0.05); 0.061	–0.83 (– 1.84 to 0.17); 0.103
Carotid intima-media thickness, left, mm	0.07 (0.01 to 0.14); 0.026	0.04 (0.01 to 0.07); 0.006	0.05 (0.02 to 0.08); <0.001
Carotid intima-media thickness, right, mm	–0.04 (– 0.23 to 0.16); 0.704	0.05 (0.02 to 0.09); 0.004	0.03 (– 0.03 to 0.09); 0.321
Estimated glomerular filtration rate, ml/min	–1.99 (– 7.02 to 3.04); 0.437	–4.36 (– 7.25 to – 1.47); 0.003	–3.83 (– 6.30 to – 1.35); 0.002
β is the regression coefficient per rs11264280 T allele with its 95% confidence interval, from linear regression adjusted for age and systolic blood pressure; the all-patients column is additionally adjusted for atrial fibrillation status. <i>P</i> values are not corrected for multiple comparisons across phenotypes and subgroups; these analyses are exploratory. AF atrial fibrillation, CI confidence interval			

Discussion

In this case–control study of hypertensive patients of Uzbek ancestry, three of five polymorphisms were associated with AF: rs6817105 near PITX2, rs11773845 in CAV1 and rs11264280 at the 1q21 locus, which harbours KCNN3. Of these, rs11264280 was the only variant associated with a consistent, multi-organ pattern of hypertensive injury. Carriers had a higher LV mass and a greater carotid intima-media thickness, and these associations were also seen in hypertensive patients without AF. The variant is therefore associated with hypertensive remodelling itself and not only with the arrhythmia – susceptibility to a disease and the severity of its course being distinct questions.

These associations are biologically plausible. KCNN3 encodes the small-conductance calcium-activated potassium channel SK3, which is expressed in atrial myocardium, contributes to repolarisation, and has been implicated in the electrical and structural remodelling that underlies AF [5]. PITX2 at 4q25 is the most reproducible AF locus identified to date and regulates left atrial development and the myocardial sleeves of the pulmonary veins [4]; our data extend this association to a Central Asian population in

which it had not previously been tested. CAV1 encodes caveolin-1, a regulator of endothelial nitric oxide signalling and of fibrosis [6], and thus offers a mechanistic link between vascular and atrial remodelling.

Patients with AF had greater target-organ damage despite a lower office blood pressure. This may partly reflect differences in antihypertensive treatment, which was not recorded. The lower ejection fraction in this group (57.4% vs 65.9%) offers an alternative, purely haemodynamic explanation, since reduced cardiac output can lower measured pressure independently of treatment intensity. Either way, remodelling was more advanced at a lower measured pressure, which argues against the genetic association being a simple proxy for higher blood pressure.

Effect-allele frequencies differed by ancestry. The rs11264280 effect allele was more frequent in this cohort than in any 1000 Genomes super-population, and the PITX2 allele frequency was intermediate between European and East Asian values, consistent with an admixed Central Asian background. To our knowledge these are the first such data for an Uzbek population. Because published allele frequencies and effect estimates derive largely from European populations and may not transfer directly, population-specific data matter for the interpretation of genetic risk.

A further caveat concerns the left atrium: because AF itself enlarges the atrium, an association between genotype and atrial size in a cross-sectional design cannot be read as causal. For this reason the observation that the genotype is associated with damage in the absence of AF rests on LV mass and carotid intima-media thickness, both of which were already increased in patients without the arrhythmia.

Limitations

The design is cross-sectional and case–control; although genotype precedes phenotype, the sequence of clinical events cannot be established and causality cannot be inferred. Cases and controls were genotyped in separate batches and call rates differed between groups; rs11264280 also departed from Hardy–Weinberg equilibrium in cases, so confirmation of these genotypes by an independent method would strengthen the findings. The effect estimates are larger than those reported at these loci in European populations, which may reflect the clinically selected cohort. There was no replication cohort, the study was single-centre, and the control group was small ($n = 135$), so the findings require confirmation in an independent sample. The analyses of target-organ damage were exploratory: several phenotypes were screened, and the reported P values are not corrected for multiple comparisons across phenotypes and subgroups. Ancestry was not verified with genetic markers, so residual population stratification is possible, although all participants were of Uzbek ethnicity. Sex was not available in the dataset and could not be included as a covariate, and antihypertensive treatment was not recorded, so office blood pressure reflects treated values and adjustment for achieved pressure only partly accounts for therapy. Finally, this was a candidate-gene study limited to five loci and cannot exclude effects at other variants.

Conclusion

In hypertensive patients of Uzbek ancestry, rs11264280 at the 1q21/KCNN3 locus was associated with greater cardiac and vascular target-organ damage irrespective of AF status, suggesting that genetic susceptibility may relate to the severity of hypertensive organ damage before the arrhythmia develops, and not only to the risk of the arrhythmia itself. The priority for future work is replication in an independent Central Asian cohort with recorded sex and antihypertensive treatment and with confirmation of genotypes by a second method, followed, if the association holds, by prospective assessment of whether genotype adds to conventional predictors of hypertensive remodelling.

Abbreviations

AF, atrial fibrillation; CI, confidence interval; LV, left ventricular; OR, odds ratio; SD, standard deviation

Declarations

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Author contributions All authors contributed to the study conception and design. Patient recruitment and clinical characterisation were performed by Mashkurova Zaringiz Tolkunovna, Abdullaeva Guzal Jaloliddinovna, Radjabova Guliruh Muhamadrizovna, Yusupova Khafiza Furkatovna, Pulatova Muazzam Turgunova, Shukurova Dilafruz Yusufovna, Ibrokhimov Nodirbek Normatovich and Doniyorov Shukhratjon Nimatullaevich. Genotyping and statistical analysis were performed by Zakirova Darya Vladimirovna and Sakhulova Nargiza Borisovna. The clinical part of the study was supervised by Khamidullaeva Gulnoz Abdusattarovna and Fozilov Khurshid Gayratovich; the laboratory part was supervised by Turdikulova Shahlo Utkurovna and Abdullaev Alisher Abdumavlyanovich. The first draft of the manuscript was written by Zakirova Darya Vladimirovna and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the Republican Specialized Scientific and Practical Medical Center of Cardiology, Ministry of Health of the Republic of Uzbekistan (27 January 2025, protocol no. 2).

Consent to participate Written informed consent was obtained from all individual participants included in the study.

Consent to publish The manuscript contains no individual person's data in any form, and no identifying information is included.

Data availability The genotype and phenotype data analysed during this study are openly available in figshare at <https://doi.org/10.6084/m9.figshare.33028601>

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Figures

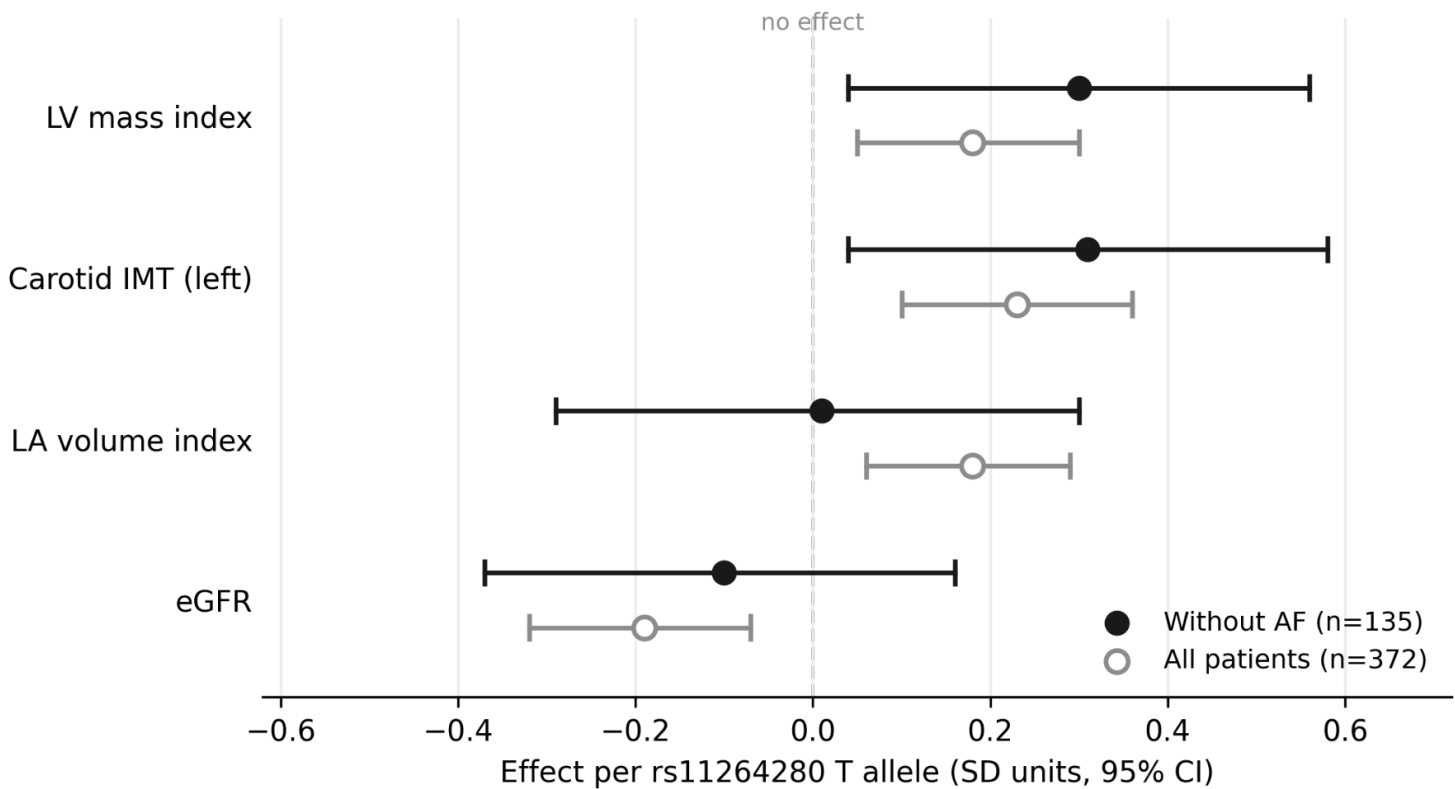


Figure 1

Association of rs11264280 with markers of hypertensive target-organ damage. Effect sizes are standardised regression coefficients (change in SD units per rs11264280 T allele) with 95% confidence intervals, adjusted for age and systolic blood pressure; the analysis of all patients is additionally adjusted for atrial fibrillation status. Filled circles, patients without atrial fibrillation (n = 135); open circles, all patients (n = 372). The dashed line marks no effect