Electrophysiological properties of the South Asian heart

James O'Neill, Muzahir Hassan Tayebjee

Department of Cardiology, Leeds Teaching Hospitals NHS Trust, Leeds General Infirmary, Leeds, UK

Correspondence to
Dr James O'Neill, Department of Cardiology, Leeds Teaching Hospitals NHS Trust, Leeds General Infirmary, Leeds, LS1 3EX, UK; james.o'neill1@nhs.net

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ABSTRACT

Objective The South Asian population has a lower burden of arrhythmia compared with Caucasians despite a higher prevalence of traditional cardiovascular risk factors. We aimed to determine whether this was due to differences in the electrophysiological properties of the South Asian heart.

Methods We performed a retrospective cohort study of South Asian and Caucasian patients who underwent an electrophysiology study for supraventricular tachycardia between 2005 and 2017. Surface ECG, intracardiac ECG and intracardiac conduction intervals were measured and a comparison between the two ethnic cohorts was performed.

Results A total of 5908 patients underwent an electrophysiology study at the Yorkshire Heart Centre, UK, during the study period. Of these 262 were South Asian and 113 met the eligibility criteria. South Asians had a significantly higher resting heart rate (p=0.024), shorter QRS duration (p=0.012) and a shorter atrioventricular (AV; p=0.001)) and ventriculoatrial (VA; p=0.013) effective refractory period (ERP). There was no difference in atrial or ventricular ERP. On linear regression analysis, South Asian ethnicity was independently predictive of a higher resting heart rate, narrower QRS and shorter AV-ERP and VA-ERP.

Conclusions South Asians have significant differences in their resting heart rate, QRS duration and AV nodal function compared with Caucasians. These differences may reflect variations in autonomic function and may also be influenced by genetic factors. Electrophysiological differences such as these may help to explain why South Asians have a lower burden of arrhythmia.

Key messages

What is already known about this subject?

- South Asians have a lower prevalence of atrial fibrillation and bradycardias compared with Caucasians. This is despite South Asians having a higher rate of conventional cardiovascular risk factors such as hypertension, diabetes mellitus and coronary artery disease. The reason for this disparity is currently unclear.

What does this study add?

- South Asians have significant differences in resting heart rate, QRS duration and atrioventricular nodal function compared with Caucasians.
- This may reflect variations in autonomic function and may also be influenced by genetic factors.

How might this impact on clinical practice?

- These findings suggest that cardiac conduction varies between ethnic groups and may help to explain why South Asians have a lower burden of arrhythmia.

INTRODUCTION

The South Asian population is a diverse ethnic group that originates from the Indian subcontinent, a vast geographic area incorporating India, Pakistan, Sri Lanka, Bangladesh and Nepal. They comprise more than a fifth of the world's population, make up the largest minority ethnic group in the UK[1] and represent one of the fastest growing immigrant populations in North America.[2]

It is well established that South Asians have a higher prevalence of hypertension, diabetes mellitus, coronary artery disease and cerebrovascular disease compared with Caucasians,[3 4] conditions which are closely associated with the development of atrial fibrillation (AF). It would be reasonable to expect this ethnic group to have high rates of arrhythmia, but observational studies have consistently shown that South Asians have a low prevalence of AF compared with Caucasians.[3–5] Interestingly, there is also evidence to suggest that South Asians are at less risk of developing bradycardias[6] but at more risk of ventricular arrhythmias.[7]

The aetiology underlying this altered susceptibility to developing arrhythmia remains unclear. The cardiac electrophysiology of South Asian hearts has not previously been investigated and it is possible that South Asians have differences in the physiology of their cardiac conduction system which might help to explain the low prevalence of AF and bradycardia.

The Yorkshire Heart Centre provides cardiac electrophysiology services for a population of over 2 million patients, 11.9% of whom are of South Asian descent.[1] It is therefore an ideal setting to perform a novel comparison of South Asians and Caucasians while minimising potential bias from confounding environmental factors.

Thus, in order to improve our understanding of South Asian cardiac electrophysiology, we aimed to investigate baseline electrocardiographic and intracardiac conduction intervals in a retrospectively selected cohort of South Asian and Caucasian patients undergoing invasive electrophysiology studies. In view of the lower burden of arrhythmia in South Asians, we hypothesised that they would have differences in cardiac conduction compared with Caucasians.

METHODS

Study population

A single-centre retrospective cohort study was performed on patients undergoing electrophysiology studies for supraventricular tachycardia (SVT) at the

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Yorkshire Heart Centre, Leeds Teaching Hospitals NHS Trust, between 1 January 2005 and 31 December 2017. Patients were identified from the local cardiac electrophysiology database and all South Asian patients were considered for enrolment into the study. Patients were excluded if they were under the age of 16 years, underwent ablation for AF, atrial flutter or ventricular tachycardia or had a history of congenital or structural heart disease. Caucasian controls matched for age and sex, who also had a diagnosis of SVT, were identified from the same local cardiac electrophysiology database.

Ethnicity was identified using data from the NHS Patient Administration System. Patients were defined as South Asian if they had self-reported their ethnicity as Indian, Pakistani, Bangladeshi, Sri Lankan or Nepalese. Patients were defined as Caucasian if they had self-reported their ethnicity as White British.

Electrophysiology study

All patients underwent electrophysiology study in a fasted state. Antiarrhythmic or rate-limiting medications were discontinued for at least five half lives prior to the procedure. Procedures were either performed under general anaesthetic or under local anaesthetic with the option of sedation. Three or four diagnostic electrophysiology catheters were introduced into the right and/or left femoral veins. Quadripolar or octapolar catheters were positioned at the His bundle and right ventricular apex. A decapolar catheter was positioned in the coronary sinus. At the operator's discretion, a quadripolar catheter was also positioned in the high right atrium. Surface and intracardiac ECGs were continuously recorded and stored using the CardioLab Electrophysiology recording system (General Electric Medical Systems, Milwaukee, Wisconsin, USA). Programmed right ventricular stimulation was performed with a single extrastimulus at a cycle length of 600 ms until either ventricular or ventriculoatrial (VA) ERP was reached. Programmed atrial stimulation was performed with a single extrastimulus at a cycle length of 600 ms until either atrial ERP or atrioventricular (AV) ERP was reached. Incremental atrial pacing was performed until atrioventricular block occurred in order to record atrioventricular Wenkebach (AVW) cycle length. In patients with atrioventricular nodal re-entrant tachycardia or a concealed accessory pathway, measurements were taken at the start of the study, prior to the administration of isoprenaline. In patients with a manifest accessory pathway, measurements were taken following ablation, after the administration of isoprenaline and once the heart rate had returned to baseline.

Data collection

Electrophysiology studies were analysed for the surface ECG, intracardiac ECG and intracardiac conduction intervals using CardioLab analysis software (General Electric Medical Systems). The intervals were measured using electronic callipers at a sweep speed of 200 mm/s. All surface ECG intervals were measured in lead II. For P-wave duration, the onset and offset points of the P wave were defined as the intersection point of the upward or downward deflection in relation to the isoelectric line.

Electronic patient records were examined and information on patients' comorbidities, medication history, length of cardiology follow-up following the electrophysiology study and evidence of SVT recurrence was recorded. The study was reviewed by the Research and Innovation Department at Leeds Teaching Hospitals NHS Trust and approved as a Service Evaluation Project.

Statistical analysis

Statistical analysis was performed using SPSS V.22.0. Normality of data was tested using a Shapiro-Wilk test. Continuous variables were expressed as mean±SD if normally distributed or median (IQR) if non-normally distributed. Student's t-test or Mann-Whitney U test were used to compare continuous variables depending on normality. Categorical variables were expressed as percentages and compared using Pearson's χ^2 test. P values of less than 0.05 were considered statistically significant.

Linear regression analysis was used to further evaluate the relationship between ethnicity and any statistically significant electrophysiological intervals with adjustment for age, gender, left atrial diameter, hypertension and diabetes mellitus. Univariable linear regression was initially performed and any variable with a statistical significance of <0.1 was included in the multivariable regression model.

RESULTS

Study cohort

During the study period, a total of 5908 electrophysiology studies were performed at the Yorkshire Heart Centre with 5583 procedures performed in Caucasians and 262 procedures performed in South Asians. Our total referral population includes 1 814 206 Caucasians and 264 438 South Asians. Therefore, electrophysiological studies were performed in 0.31% of the Caucasian population and 0.09% of the South Asian population. A summary of the indications for the electrophysiology studies in each cohort is found in table 1.

Table 1 Summary of the indications for electrophysiology studies in all Caucasians and South Asians

	Caucasian (n=5583)	South Asian (n=262)
Atrial fibrillation	1713 (30.7%)	20 (7.6%)
Atrial flutter	1052 (18.8%)	21 (8.1%)
Atrial tachycardia	202 (3.6%)	6 (2.3%)
Supraventricular tachycardia	1413 (25.3%)	135 (51.5%)
Wolff-Parkinson-White syndrome	563 (10.1%)	49 (18.7%)
Ventricular arrhythmia	640 (11.5%)	31 (11.8%)

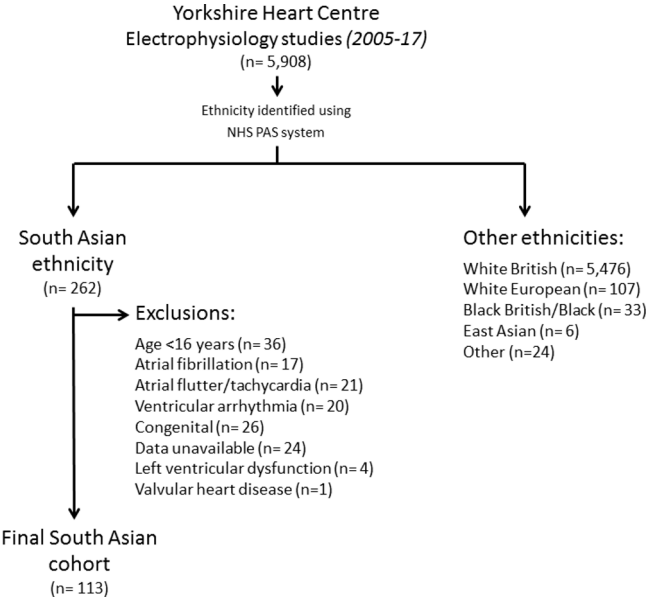

Figure 1 Flow chart of study population.

Table 2 Baseline characteristics

	South Asian	Caucasian	P values
N	113	113	1.000
Age	41.3±13.6	41.3±13.6	0.981
Male gender, n (%)	39 (34.5)	39 (34.5)	1.000
Height, cm	163.8±7.9	169.8±10.4	**0.023**
Weight, kg	76.5±18.1	76.1±20.4	0.592
Left atrial diameter, mm	34.0±5.9	33.7±3.9	0.840
Hypertension, n (%)	13 (11.5)	10 (8.8)	0.509
Diabetes mellitus, n (%)	12 (10.6)	6 (5.3)	0.140
Previous stroke/TIA, n (%)	1 (0.9)	2 (1.8)	0.561
Venous thromboembolism, n (%)	0 (0.0)	1 (0.9)	0.316
Ischaemic heart disease, n (%)	6 (5.3)	2 (1.8)	0.150
Peripheral arterial disease, n (%)	0 (0.0)	0 (0.0)	1.000
CKD stage III–V, n (%)	2 (1.8)	1 (0.9)	0.561
Diagnosis			
AVNRT, n (%)	78 (69.0)	81 (71.6)	0.662
Accessory pathway, n (%)	15 [13.3)	9 (8.0)	0.195
No inducible arrhythmia, n (%)	20 (17.7)	23 (20.4)	0.611
Medication			
ACE-i/ARB, n (%)	15 (13.3)	9 (8.0)	0.195
Beta-blocker, n (%)	52 (46.0)	39 (34.5)	0.078
Calcium-channel blocker, n (%)	17 (15.0)	9 (8.0)	0.095
Diuretic, n (%)	1 (0.9)	2 (1.8)	0.561
Aldosterone antagonist, n (%)	0 (0.0)	0 (0.0)	1.000
Statin, n (%)	10 (8.8)	10 (8.8)	1.000
Antiplatelet, n (%)	8 (7.1)	7 (6.2)	0.789
Anticoagulation, n (%)	0 (0.0)	1 (0.9)	0.316
Antiarrhythmic, n (%)	14 (12.4)	10 (8.8)	0.677
Procedural anaesthesia			
General anaesthetic, n (%)	6 (5.3)	6 (5.3)	1.000
Local anaesthetic+sedation, n (%)	73 (64.6)	71 (62.8)	0.771
Local anaesthetic only, n (%)	34 (30.1)	36 (31.9)	0.771
Follow-up			
Length of follow-up, days	107 (153)	103 (129)	0.929
Recurrence of arrhythmia, n (%)	4 (3.5)	5 (4.4)	0.734

Bold values represent the significant p values i.e. those < 0.05.
ACE-i, ACE inhibitor; ARB, angiotensin II receptor blocker; AVNRT, atrioventricular nodal reentrant tachycardia; CKD, chronic kidney disease; TIA, transient ischaemic attack.

A final South Asian cohort of 113 subjects was identified and matched with Caucasian controls after 149 patients failed to meet the eligibility criteria (figure 1).

Baseline characteristics

The characteristics of the study participants are summarised in table 2. The two cohorts were well matched with no significant difference in comorbidities, medication, length of follow-up or the recurrence of arrhythmia. There was a non-significant trend towards a higher prevalence of diabetes mellitus and ischaemic heart disease among South Asians.

Surface ECG intervals

Resting heart rate was significantly higher (p=0.024) and QRS duration was significantly shorter (p=0.012) in South Asians as shown in table 3. There was no significant difference in the P-wave duration or PR interval between the ethnicities, and once corrected for heart rate, there was no difference in the QT interval.

Table 3 Electrocardiographic and conduction intervals

	South Asian	Caucasian	P values
Surface ECG intervals			
Heart rate, beats per minute	82.5 (18)	78.0 (18)	**0.024**
P-wave duration, ms	107.0 (19)	105.0 (22)	0.221
RR, ms	726.5 (171)	764.0 (177)	**0.025**
PR, ms	155.9±20.7	158.7±22.6	0.351
QRS, ms	92.0 (16)	96.0 (15)	**0.012**
QT, ms	372.5 (43)	387.0 (36)	**0.001**
QTc, ms	433.9 (53)	441.0 (42)	0.182
Intracardiac ECG intervals			
AA, ms	720.0 (180)	763.0 (161)	0.070
PA, ms	44.0 (18)	41.0 (14)	0.169
AH, ms	66.0 (23)	71.0 (26)	0.093
HV, ms	37.0 (12)	37.5 (13)	0.841
Intracardiac conduction intervals			
Atrial ERP, ms	250 (60)	240 (40)	0.332
Total number of measurements*	66	54	
Atrioventricular ERP, ms	280 (50)	300 (60)	**0.001**
Total number of measurements*	47	59	
AVW cycle length, ms	320 (58)	340 (68)	**0.045**
Total number of measurements	113	113	
Ventriculoatrial ERP, ms	300 (60)	320 (93)	**0.013**
Total number of measurements*	51	52	
Ventricular ERP, ms	240 (30)	240 (35)	0.172
Total number of measurements*	62	61	

Bold values represent the significant p values i.e. those < 0.05.
*Measurements recorded at a cycle length of 600 ms.
AVW, atrioventricular wenckebach ; ERP, effetive refractory period;

Intracardiac ECG and conduction intervals

South Asians had significantly shorter AV-ERP (p=0.001) and VA-ERP (p=0.013) intervals (table 3). The AVW cycle length (p=0.045) was correspondingly shorter (table 3). There were no differences in atrial or ventricular ERP between the two groups and no differences were seen in the intracardiac ECG intervals (table 3).

Linear regression analysis

On univariable analysis, South Asian ethnicity was associated with a higher heart rate, narrower QRS and lower AV-ERP and VA-ERP (table 4). Male gender was associated with a lower heart rate and wider QRS while diabetes mellitus was predictive of a higher heart rate (table 4). No variable was found to be associated with AVW cycle length. On multivariable analysis, South Asian ethnicity and male gender remained independently predictive of heart rate, QRS duration and AV-ERP (table 4).

DISCUSSION

To the best of our knowledge, this is the first study to compare the electrophysiological properties of South Asian and Caucasian hearts using invasive techniques. Within a diverse multiethnic population over a 13-year period, we have found that electrophysiology studies were performed three times more often in Caucasians than in South Asians. We have shown a significant difference in heart rate, AV nodal function and QRS duration between South Asians and Caucasians but no difference in atrial ERP or P wave duration.

Table 4 Univariable and multivariable linear regression analysis for predictors of heart rate, QRS, AV-ERP, VA-ERP and AVW

	Univariable model			Multivariable model		
	B	(95% CI)	P values	B	(95% CI)	P values
Heart rate						
Age	0.005	(−0.145 to 0.155)	0.950			
Male gender	−6.800	(−10.985 to −2.615)	**0.002**	−6.687	(−10.815 to −2.559)	**0.002**
SA ethnicity	4.354	(0.321 to 8.387)	**0.034**	4.049	(0.108 to 7.990)	**0.044**
LA diameter	−0.274	(1.353 to 0.805)	0.612			
Hypertension	5.312	(−1.375 to 11.999)	0.119			
Diabetes mellitus	8.254	(0.625 to 15.884)	**0.034**	7.220	(−0.240 to 14.680)	0.058
QRS						
Age	−0.075	(−0.200 to 0.050)	0.238			
Male gender	5.985	(2.498 to 9.472)	**0.001**	5.997	(2.539 to 9.456)	**0.001**
SA ethnicity	−3.597	(−6.967 to −0.227)	**0.037**	−3.616	(−6.908 to −0.324)	**0.032**
LA diameter	0.198	(−0.496 to 0.893)	0.568			
Hypertension	0.065	(−5.552 to 5.681)	0.982			
Diabetes mellitus	−3.033	(−9.459 to 3.393)	0.353			
AV-ERP						
Age	−0.230	(−1.078 to 0.618)	0.591			
Male gender	17.082	(−4.951 to 39.115)	0.127			
SA ethnicity	−36.158	(−56.976 to −15.340)	**0.001**	−96.721	(−169.363 to −24.079)	**0.012**
LA diameter	8.147	(−0.961 to 17.256)	0.076	9.121	(1.379 to 16.864)	**0.024**
Hypertension	0.407	(−35.559 to 36.373)	0.982			
Diabetes mellitus	−19.342	(−58.518 to 19.834)	0.330			
VA-ERP						
Age	−0.475	(−1.751 to 0.800)	0.461			
Male gender	24.841	(−11.196 to 60.878)	0.174			
SA ethnicity	−47.894	(−82.973 to −12.814)	**0.008**			
LA diameter	−0.439	(−8.131 to 7.252)	0.905			
Hypertension	−34.946	(−110.857 to 40.964)	0.363			
Diabetes mellitus	−58.447	(−140.675 to 23.782)	0.162			
AVW cycle length						
Age	−0.132	(−0.722 to 0.458)	0.660			
Male gender	13.971	(−2.845 to 30.787)	0.103			
SA ethnicity	−13.803	(−29.840 to 2.234)	0.091	−12.820	(−28.809 to 3.168)	0.115
LA diameter	2.629	(−1.166 to 6.424)	0.170			
Hypertension	−25.985	(−52.659 to 0.690)	0.056	−24.560	(−51.204 to 2.083)	0.071
Diabetes mellitus	−22.831	(−53.756 to 8.094)	0.147			

Bold values represent the significant p values i.e. those < 0.05.
AV-ERP, atrioventricular effective refractory period; AVW, atrioventricular wenckebach; LA, left atrial; SA, South Asian; VA-ERP, ventriculoatrial effective refractory period.

Heart rate and AV nodal function

Our results indicate that South Asians have a higher resting heart rate, lower AV-ERP and lower VA-ERP compared with Caucasians and that these differences are independently associated with ethnicity. A possible explanation for this is that South Asians have differences in autonomic function.

The autonomic nervous system (ANS) heavily influences cardiac conduction and this effect is most apparent at the AV node and sinoatrial node. There is limited evidence to suggest that South Asians have impaired autonomic function with less vagal contribution and increased sympathetic tone.[8] This would support our findings of an increased heart rate and reduced AV nodal refractoriness in South Asians.

Differences in autonomic function might also influence South Asians susceptibility to developing AF. It is now well recognised that the ANS plays an important role in the genesis of AF. The onset of paroxysmal AF is often preceded by an increase in parasympathetic activity, particularly in those without structural heart disease.[9] This is likely to be due to the fact that vagal stimulation causes heterogeneous shortening of atrial action potential durations and ERPs creating an environment suitable for the development of atrial re-entrant circuits.[10–12] If South Asians do have more sympathetic tone, this may play a role in preventing the development of AF. However, further research is required to confirm these findings.

QRS duration

Our findings show that South Asians have a shorter QRS duration. Despite previous studies having demonstrated ethnic differences in QRS duration between black and white Americans[13] and in a multiethnic Asian population,[14] the aetiology behind these differences has not been established.

QRS duration has been shown to correlate with body size[15] and South Asians are known to be of a smaller stature[16] with smaller hearts[17] compared with Caucasians. Therefore, in our South Asian cohort, it is possible that a shorter QRS duration simply relates to their smaller heart size.

More interestingly, the difference in QRS duration could be related to genetic variation. The QRS complex represents ventricular depolarisation and conduction time, processes which occur due to the fast activation of voltage-dependent sodium channels. Genome-wide association studies have been performed to examine genes, such as SCN10A and SCN5A, which are responsible for the expression of voltage-gated sodium channels within cardiac tissue.[18–20]

They have identified a number of single-nucleotide polymorphisms which can affect the length of the QRS complex. Genetic factors therefore appear to influence QRS duration and could explain the differences seen in our study. However, further research exploring the relationship between the South Asian genome and electrocardiographic parameters is required to clarify this.

Atrial ERP and P wave duration

We observed no difference in atrial ERP or P wave duration between our study cohorts. This would suggest that atrial refractoriness and intra-atrial conduction time are similar among the two ethnicities and that the lower prevalence of AF in South Asians is unrelated to these factors. However, it must be remembered that atrial ERP could only be measured in around half of subjects. It is therefore conceivable that there is a difference between the ethnic groups which we were not able to demonstrate.

Burden of arrhythmia in South Asians

During a study period of 13 years, we found that 0.31% of Caucasians underwent electrophysiology studies compared with only 0.09% of South Asians. Potential reasons for this include ethnic variations in the use of healthcare resources although the evidence for this is mixed. South Asians have been found to have less engagement with cancer screening programmes,[21 22] antenatal services[23] and smoking cessation facilities.[24] However, they have also been shown to be more likely to access specialist chest pain clinics.[25] An alternative theory is that South Asians have biological variations which make them less susceptible to arrhythmia. Recent evidence suggests that South Asians are less likely to develop bradycardia[6] and the same may be true of tachyarrhythmias such as AF. Our results suggest ethnic differences in cardiac conduction which may have a genetic basis. If the mechanisms responsible for the reduced arrhythmia burden in South Asians can be fully determined, they may help in the development of novel treatment approaches in the future.

Limitations

This study should be in interpreted in the context of several limitations. First, this is a retrospective cohort study raising the possibility of selection and recall bias. Selection bias was minimised through the recruitment of consecutive South Asian patients who met the eligibility criteria and through the selection of Caucasian controls based only on age and gender, prior to any screening of their medical records or electrophysiology study. Recall bias was minimised through the comprehensive assessment of the subjects' medical records. Second, our data was taken from a single centre and so it may not be generalisable to the whole South Asian population. However, our centre covers a large geographical area which includes over 260 000 South Asians and so is likely to provide a broad overview of the ethnic group.

CONCLUSION

South Asians have differences in heart rate, QRS duration and AV nodal function compared with Caucasians and these effects are independently associated with South Asian ethnicity. These differences may reflect variations in autonomic function or even genetic variants and may help to explain why South Asians seemingly have a lower burden of arrhythmia.

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REFERENCES

1. 2011 Census. 2011, Office of National Statistics.2011
2. Hoeffel EM, Rastogi S, Kim MO. *The Asian population: 2010*. In:*U.S.C. Bureau*. U.S. Census Bureau, 2012.
3. Conway DS, Lip GY. Ethnicity in relation to atrial fibrillation and stroke (the West Birmingham Stroke Project). *Am J Cardiol* 2003;92:1476–9.
4. Gillott RG, Willan K, Kain K, *et al*. South Asian ethnicity is associated with a lower prevalence of atrial fibrillation despite greater prevalence of established risk factors: a population-based study in Bradford Metropolitan District. *Europace* 2017;19:356–63.
5. Mathur R, Pollara E, Hull S, *et al*. Ethnicity and stroke risk in patients with atrial fibrillation. *Heart* 2013;99:1087–92.
6. Yuyun MF, Squire IB, Ng GA, *et al*. Evidence for reduced susceptibility to cardiac bradycardias in South Asians compared with Caucasians. *Heart* 2018;104:1350–5.
7. Singh N, Gupta M. Clinical characteristics of South Asian patients hospitalized with heart failure. *Ethn Dis* 2005;15:615–9.
8. Bathula R, Hughes AD, Panerai R, *et al*. Indian Asians have poorer cardiovascular autonomic function than Europeans: this is due to greater hyperglycaemia and may contribute to their greater risk of heart disease. *Diabetologia* 2010;53:2120–8.
9. Chen PS, Tan AY. Autonomic nerve activity and atrial fibrillation. *Heart Rhythm* 2007;4(3 Suppl):S61–S64.
10. Chen YJ, Tai CT, Chiou CW, *et al*. Inducibility of atrial fibrillation during atrioventricular pacing with varying intervals: role of atrial electrophysiology and the autonomic nervous system. *J Cardiovasc Electrophysiol* 1999;10:1578–85.
11. Hirose M, Carlson MD, Laurita KR. Cellular mechanisms of vagally mediated atrial tachyarrhythmia in isolated arterially perfused canine right atria. *J Cardiovasc Electrophysiol* 2002;13:918–26.
12. Sharifov OF, Fedorov VV, Beloshapko GG, *et al*. Roles of adrenergic and cholinergic stimulation in spontaneous atrial fibrillation in dogs. *J Am Coll Cardiol* 2004;43:483–90.
13. Randolph TC, Broderick S, Shaw LK, *et al*. Race and sex differences in qrs interval and associated outcome among patients with left ventricular systolic dysfunction. *J Am Heart Assoc* 2017;6:e004381.
14. Tan ES, Yap J, Xu CF, *et al*. Association of age, sex, body size and ethnicity with electrocardiographic values in community-based older asian adults. *Heart Lung Circ* 2016;25:705–11.
15. Gijsberts CM, Benson L, Dahlström U, *et al*. Ethnic differences in the association of QRS duration with ejection fraction and outcome in heart failure. *Heart* 2016;102:1464–71.
16. Lean ME, Han TS, Bush H, *et al*. Ethnic differences in anthropometric and lifestyle measures related to coronary heart disease risk between South Asian, Italian and general-population British women living in the west of Scotland. *Int J Obes Relat Metab Disord* 2001;25:1800–5.
17. , Echocardiographic Normal Ranges Meta-Analysis of the Left Heart Collaboration. Ethnic-Specific Normative Reference Values for Echocardiographic LA and LV Size, LV Mass, and Systolic Function: Study. *JACC Cardiovasc Imaging* 2015;8:656–65.
18. Holm H, Gudbjartsson DF, Arnar DO, *et al*. Several common variants modulate heart rate, PR interval and QRS duration. *Nat Genet* 2010;42:117–22.
19. Sotoodehnia N, Isaacs A, de Bakker PI, *et al*. Common variants in 22 loci are associated with QRS duration and cardiac ventricular conduction. *Nat Genet* 2010;42:1068–76.
20. Jeff JM, Brown-Gentry K, Buxbaum SG, *et al*. SCN5A variation is associated with electrocardiographic traits in the Jackson Heart Study. *Circ Cardiovasc Genet* 2011;4:139–44.
21. Szczepura A. Access to health care for ethnic minority populations. *Postgrad Med J* 2005;81:141–7.
22. Palmer CK, Thomas MC, McGregor LM, *et al*. Understanding low colorectal cancer screening uptake in South Asian faith communities in England – a qualitative study. *BMC Public Health* 2015;15:998.
23. Boerleider AW, Wiegers TA, Manniën J, *et al*. Factors affecting the use of prenatal care by non-western women in industrialized western countries: a systematic review. *BMC Pregnancy Childbirth* 2013;13:81.
24. White M, Bush J, Kai J, *et al*. Quitting smoking and experience of smoking cessation interventions among UK Bangladeshi and Pakistani adults: the views of community members and health professionals. *J Epidemiol Community Health* 2006;60:405–11.
25. Sekhri N, Timmis A, Hemingway H, *et al*. Is access to specialist assessment of chest pain equitable by age, gender, ethnicity and socioeconomic status? An enhanced ecological analysis. *BMJ Open* 2012;2:e001025.