



## Original article

## Risk factors for the presentation of supraventricular arrhythmias in patients residing at high altitudes

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## Conflicts of interest

None.

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## ABSTRACT

**Objective.** To determine the risk factors associated with the occurrence of supraventricular arrhythmias (SVA) among residents at high altitude. **Material and methods.** We conducted an analytical observational case-control study, including 24-hour electrocardiographic monitoring and transthoracic echocardiography in 192 individuals. Logistic regression analysis was used for statistical evaluation. **Results.** The study included 96 cases and 96 controls. Mean age was higher among cases than controls ( $65.9 \pm 13.6$  vs.  $47.5 \pm 19.5$  years;  $p < 0.001$ ). Progressive increases in age, systolic blood pressure, and pulse pressure were significantly associated with a higher incidence of SVA. In multivariable analysis, hypertension (Odds Ratio [OR] = 3.43, 95% confidence interval [CI]: 1.64-7.16;  $p < 0.001$ ) and pulse pressure greater than 50 mmHg (OR = 3.27, 95% CI: 1.61-6.65;  $p = 0.001$ ) were independently associated with the presence of SVA. Hypertensive patients had more than a threefold increased likelihood of developing SVA compared with normotensive individuals. Episodes of supraventricular tachycardia were significantly more frequent among hypertensive participants than among non-hypertensive participants (60.6% vs. 39.4%;  $p < 0.001$ ). **Conclusion:** Hypertension and elevated pulse pressure are significant risk factors for the development of SVA among residents at high altitude. Further studies are warranted to clarify the clinical implications for prevention and management of SVA in hypertensive patients.

**Keywords:** Arrhythmia; Blood Pressure; Hypertension; Altitude (Source: NLM-MeSH).

## RESUMEN

## Factores de riesgo para la presentación de arritmias supraventriculares en pacientes residentes en gran altitud

**Objetivo.** Determinar los factores de riesgo para la presentación de arritmias supraventriculares (ASV) en pacientes residentes en gran altitud. **Materiales y métodos.** Se realizó un estudio observacional analítico de diseño caso-control, mediante la evaluación electrocardiográfica de 24 h y ecocardiografía transtorácica en 192 personas. Para el análisis estadístico se empleó la regresión logística. **Resultados.** Se consideraron 96 casos y 96 controles, cuyo promedio de edad fue mayor para los casos en comparación con los controles ( $65,9 \pm 13,6$  vs.  $47,5 \pm 19,5$ ;  $p < 0,001$ ). El incremento progresivo de la edad, de los niveles de presión arterial sistólica y de la presión de pulso aumenta la incidencia de ASV de forma significativa. En el análisis multivariado, se identificó que la hipertensión arterial (OR= 3,43; IC95%: 1,64-7,16;  $p < 0,001$ ) y la presión de pulso mayor a 50 mmHg (OR= 3,27; IC95%: 1,61-6,65;  $p = 0,001$ ) se asociaron significativamente con la presencia de ASV. Los pacientes hipertensos tienen más de tres veces la probabilidad de presentar ASV en comparación con los no hipertensos. Los episodios de taquicardia supraventricular fueron significativamente más frecuentes en los sujetos hipertensos en comparación con los sujetos no hipertensos (60,6% vs. 39,4%;  $p < 0,001$ ). **Conclusión.** Los factores de riesgo significativos para el desarrollo de ASV son la hipertensión arterial y el nivel de presión de pulso incrementado en residentes de gran altitud. Se requieren estudios adicionales para profundizar en el impacto clínico en la prevención y el manejo de las ASV en pacientes hipertensos.

**Palabras clave:** Arritmia; Presión Arterial; Hipertensión; Altitud (Fuente: DeCS-BIREME).

## Introduction

Cardiac arrhythmias (CA) are prevalent worldwide <sup>(1)</sup>. Supraventricular arrhythmias (SVA) comprise a group of rhythm disturbances that originate above the His bundle and result from abnormalities in the initiation of cardiac impulses or in their conduction through the heart <sup>(2)</sup>. SVAs can present asymptotically, with mild symptoms (palpitations, dizziness, or chest pain), or with severe clinical manifestations (dyspnoea, hypotension, altered mental status, or shock) when ventricular rates exceed the normal range, thus requiring immediate management <sup>(3,4)</sup>. A previous study reported a prevalence of CA of 19.0% and supraventricular tachycardia of 15.8% based on 24-hour Holter monitoring <sup>(5)</sup>. Atrial fibrillation is the most common CA <sup>(1)</sup>.

Several factors have been associated with SVA, including hypertension, left ventricular diastolic dysfunction, left atrial enlargement, increased sympathetic activity, excessive consumption of caffeine and alcohol, smoking, and electrolyte disturbances <sup>(6)</sup>. Hypertensive heart disease (HHD) can manifest as SVA, with atrial fibrillation contributing to an increased risk of stroke <sup>(7)</sup>.

The complexity of CA may influence morbidity, mortality, and quality of life in hypertensive patients <sup>(8)</sup>. SVAs may occur in hypertensive individuals, particularly in those with left ventricular hypertrophy or heart failure <sup>(9)</sup>. The presence of left ventricular hypertrophy is a strong predictor of the development of atrial fibrillation, ventricular premature beats, and sudden cardiac death <sup>(10)</sup>. Hypoxia, adrenergic stimulation, and alkalosis associated with high altitude predispose individuals to arrhythmias <sup>(11)</sup>. Exposure to altitudes above 4,100 meters above sea level (m.a.s.l.) has been associated with significant bradyarrhythmias and tachyarrhythmias in healthy adult men, supporting the influence of hypobaric hypoxia <sup>(12)</sup>. Moreover, persistent hypoxia over time gradually increases vagal tone, as evidenced by bradycardia during apnoea and an increased incidence of arrhythmias <sup>(13)</sup>.

One study demonstrated an association between acute exposure to high altitude and the occurrence of cardiac tachyarrhythmias, which may be related to electrolyte imbalances resulting from hyperventilation in a hypobaric hypoxic environment <sup>(14)</sup>. Another factor associated with an increased incidence of extrasystoles at altitude may be activation of the beta-adrenergic system, which is also related to elevated blood pressure <sup>(15)</sup>.

In our setting, there are no studies on SVA in patients diagnosed using 24-hour electrocardiography, particularly among populations living at high altitude. In this context, this study was designed to determine the risk factors for the occurrence of SVA in patients residing at high altitude.

## Materials and methods

### Study design and population

An observational, retrospective, analytical case-control study was conducted in the Cardiology Department of the Hospital Regional Docente Clínico Quirúrgico Daniel Alcides Carrión (Huancayo) from March 1, 2023, to June 30, 2024. Individuals were considered residents at high altitude if they had lived continuously for at least 1 year between 2500 and 3500 m.a.s.l. <sup>(16)</sup>.

Sample size was calculated using the formula for comparative analytical studies with two proportions, considering the following parameters: two-sided test, event frequency in the case group (83%) <sup>(8)</sup>, in the control group (64%), a 95% confidence level, 80% statistical power, 5% precision, and an expected loss proportion of 13%, yielding an adjusted sample size of 96 participants in both the case and control groups. The case-to-control ratio was 1:1.

Inclusion criteria were: reporting palpitations, availability of echocardiography and 24-hour electrocardiographic monitoring, with cases defined as those with a diagnosis of SVA and controls as those without any SVA. Exclusion criteria for both groups included age <18 years, acute cardiac disease, acute infectious disease, stroke, or malignant neoplastic disease. Sampling was purposive and directed.

Findings from 24-hour electrocardiographic monitoring were recorded using a SEER Light Connect Holter monitor (General Electric, GE). Echocardiographic studies were performed by a cardiologist specialised in the field, in accordance with the guidelines of the American Society of Echocardiography, using a GE Vivid S7 ultrasound system <sup>(17)</sup>.

### Definition of variables

#### Independent variables

**Hypertension:** defined as blood pressure >140/90 mmHg on three measurements or a prior diagnosis of hypertension with normal blood pressure values under antihypertensive treatment <sup>(18)</sup>. Blood pressure was categorised according to systolic, diastolic, and pulse pressure levels <sup>(19)</sup> to assess the impact of increasing values on the incidence of SVA.

**Diabetes mellitus:** defined as fasting plasma glucose >126 mg/dL on two measurements in the medical record, or a prior diagnosis of diabetes with ongoing pharmacological treatment <sup>(20,21)</sup>.

**Obesity:** defined as a body mass index (BMI) >30 kg/m<sup>2</sup>. BMI was calculated as weight (kg) divided by height squared (m<sup>2</sup>) <sup>(20,21)</sup>.

**Dyslipidaemia:** defined as the presence of at least one abnormal fasting lipid profile value (total cholesterol >200 mg/dL, LDL cholesterol >100 mg/dL, HDL cholesterol >50 mg/dL in women and >40 mg/dL in men, or triglycerides >150 mg/dL) <sup>(20,21)</sup>.

**Left ventricular hypertrophy (LVH):** defined as an increased left ventricular mass  $>115 \text{ g/m}^2$  in men and  $>95 \text{ g/m}^2$  in women. Relative wall thickness (RWT) was calculated as twice the posterior wall thickness divided by the left ventricular diastolic diameter<sup>(17)</sup>. LVH was further categorised as mild ( $116\text{-}131 \text{ g/m}^2$  in men and  $96\text{-}108 \text{ g/m}^2$  in women), moderate ( $132\text{-}148 \text{ g/m}^2$  in men and  $109\text{-}121 \text{ g/m}^2$  in women), and severe ( $>148 \text{ g/m}^2$  in men and  $>121 \text{ g/m}^2$  in women). An increased left atrial volume index (LAVI) was defined as  $>34 \text{ mL/m}^2$  and categorised as mild ( $35\text{-}41 \text{ mL/m}^2$ ), moderate ( $42\text{-}48 \text{ mL/m}^2$ ), and severe ( $>48 \text{ mL/m}^2$ ), respectively<sup>(17)</sup>. Pulse pressure was calculated as the difference between systolic and diastolic blood pressure, and heart rate was measured in beats per minute<sup>(21)</sup>.

#### Dependent variables

- **Supraventricular arrhythmia (SVA):** defined as a cardiac rhythm disturbance caused by a premature supraventricular electrical impulse originating above the His bundle, with QRS complexes similar to the baseline cycle.
- **Supraventricular extrasystole (SVE):** premature contractions independent of the sinus node, characterised by QRS complexes identical to normal baseline beats. Supraventricular tachycardia (SVT): defined as three or more consecutive SVEs.
- **Atrial fibrillation:** characterised by the absence of discernible P waves on the electrocardiogram and irregular ventricular activation<sup>(22)</sup>.

#### Data processing and analysis

Data were entered and stored in an Excel database and analysed using SPSS version 25. Categorical variables are presented as frequencies and percentages, whereas numerical variables are expressed as measures of central tendency and dispersion or as medians and interquartile ranges (IQR), according to their distribution. In the bivariate analysis conducted to identify factors associated with SVA, different statistical tests were applied depending on the nature of the variables. For categorical exposures, the chi-squared test or Fisher's exact test was used, as appropriate. For numerical variables, Student's t test or the Mann-Whitney U test was applied according to data distribution. Logistic regression was used to estimate associations, with 95% confidence intervals (95% CI). Multivariable analysis included adjustment for age and sex, and a p-value  $<0.05$  was considered statistically significant. The strength of association was expressed as odds ratios (OR).

#### Ethical aspects

Authorisation was obtained from the Office of Teaching and Research of the Hospital Regional Docente Clínico Quirúrgico Daniel Alcides Carrión. Throughout the study, a commitment to scientific integrity was maintained, in accordance with the ethical principles set out in the Declaration of Helsinki.

In addition, approval was obtained from the Research Ethics Committee of the Universidad de Huánuco. The collected information was used exclusively by the investigator, ensuring confidentiality and data protection at all times.

## Results

A total of 192 individuals were included in the study; the median age was 63 years (IQR: 18-88); 71 (36.9%) were men and 121 (63.1%) were women. 96 cases and 96 controls were analysed, with a higher median age among cases (65 years, IQR: 40-86) compared with controls (47 years, IQR: 18-88;  $p<0.001$ ). Increasing age, systolic blood pressure, and pulse pressure were significantly associated with a higher frequency of SVA. No significant association was found between progressive increases in BMI, diastolic blood pressure, or heart rate and the frequency of SVA (**Table 1**).

An increased LAVI was observed in 56 (58.3%) cases. Among these, the increase was mild, moderate, and severe in 28 (50.0%), 12 (21.4%), and 18 (28.6%) cases, respectively. A significant difference was found in individuals with severe left atrial enlargement when comparing patients with SVA versus those without SVA (65.0% vs. 42.9%). LVH was not associated with SVA (**Table 2**).

In the bivariate analysis, age greater than 60 years, hypertension, diabetes mellitus, pulse pressure greater than 50 mmHg, increased LAVI, and increased RWT of the left ventricle were significantly associated with the presence of SVA.

Among the 96 (100.0%) cases with SVA, 93 (96.9%) presented isolated SVEs; 76 (80.0%) had supraventricular pairs; 46 (47.9%) had supraventricular tachycardia; and 5 (5.2%) had atrial fibrillation. Episodes of SVT were significantly more frequent in hypertensive individuals compared with non-hypertensive individuals (60.6% vs. 39.4%;  $p<0.001$ ) (**Figure 1**).

In the multivariable analysis, adjusted for age and sex, hypertension (OR = 3.43, 95% CI: 1.64-7.16;  $p<0.001$ ) and pulse pressure (OR = 3.27, 95% CI: 1.61-6.65;  $p = 0.001$ ) were significantly associated with the presence of SVA. Hypertensive patients had more than a threefold higher likelihood of presenting SVA compared with non-hypertensive individuals. In contrast, diabetes mellitus (OR = 7.04, 95% CI: 0.80-61.47;  $p = 0.077$ ), LAVI (OR = 1.57, 95% CI: 0.80-3.11;  $p = 0.186$ ), and RWT (OR = 1.49, 95% CI: 0.74-2.98;  $p = 0.258$ ) were not significantly associated with SVA in this model (**Table 3**).

## Discussion

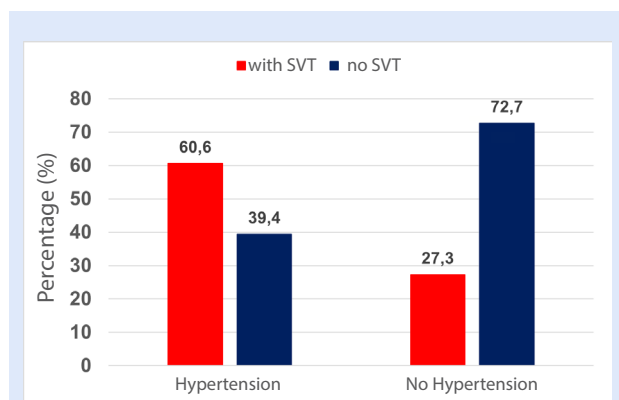
Hypertension and elevated pulse pressure greater than 50 mmHg were the factors significantly associated with SVA among residents at high altitude. Rojas *et al.* reported that SVA are more frequent in women than in men (4.6% vs. 2.7%)<sup>(23)</sup>.

**Table 1.** Clinical characteristics of patients according to the presence of supraventricular arrhythmias.

Characteristic	Supraventricular arrhythmia		p-value
	Yes (n=96) n (%)	No (n=96) n (%)	
Age group (years)			
18 and 40	7 (15.9)	37 (84.1)	<0.001
41 and 60	19 (40.4)	28 (59.6)	
>60	70 (69.3)	31 (30.7)	
Body mass index (kg/m <sup>2</sup> )			
<18.5	0 (0.0)	4 (100.0)	0.101
18.5 and 24.9	42 (48.3)	45 (51.7)	
>24.9	54 (53.5)	47 (46.5)	
Systolic blood pressure (mmHg)			
90 and 110	44 (63.3)	71 (61.7)	<0.001
120 and 139	40 (48.1)	20 (33.3)	
>139	12 (70.6)	5 (29.4)	
Diastolic blood pressure (mmHg)			
60 and 69	50 (47.2)	56 (52.8)	0.266
70-89	44 (55.7)	35 (44.3)	
>89	2 (28.6)	5 (71.4)	
Pulse pressure (mmHg)			
30 and 50	41 (35.0)	76 (65.0)	<0.001
51 and 59	32 (78.0)	9 (22.0)	
≥60	23 (67.6)	11 (32.4)	
23 (67.6)	11 (32.4)		
Heart rate (beats per minute)			
<60	27 (61.4)	17 (38.6)	0.116
60 and 80	57 (49.1)	59 (50.9)	
>80	12(37.5)	20 (62.5)	

**Table 2.** Echocardiographic findings in adult patients with supraventricular arrhythmias.

Echocardiographic findings	Supraventricular arrhythmias		p-value
	Yes n(%)	No n (%)	
Left ventricular hypertrophy (g/m <sup>2</sup> )			
-Normal	49 (46.2)	57 (53.8)	0.475
-Mild increase	14 (53.8)	12 (46.2)	
-Moderate increase	8 (44.4)	10 (55.6)	
-Severe increase	25 (59.5)	17 (40.5)	
Left atrial volume index (mL/m <sup>2</sup> )			
-Normal	40 (39.6)	61 (60.4)	0.004
-Mild increase	28 (64.0)	21 (42.9)	
-Moderate increase	12 (42.9)	2 (14.3)	
-Severe increase	16 (65.0)	12 (42.9)	



**Figure 1.** Percentage of supraventricular tachycardia (SVT) in patients with and without hypertension.

Another report indicates that women have a twofold higher risk of developing SVT compared with men<sup>(4)</sup>. Similar findings were observed in our series. Individuals older than 65 years have more than a fivefold increased risk of developing SVT compared with younger individuals<sup>(4)</sup>. In our study, a higher frequency of SVA was observed among individuals older than 60 years.

Sustained elevation of blood pressure increases cardiac workload, leading to structural and functional changes in the heart, known as HHD<sup>(24)</sup>. Poor blood pressure control may impair diastolic function and promote left atrial remodelling; moreover, the mechanical overload caused by elevated blood pressure may induce abnormal expression of ion channels and/or junctional complexes, thereby triggering focal ectopic activity and re-entry mechanisms<sup>(9)</sup>.

Among hypertensive individuals, a frequency of SVA of 50.7% has been reported<sup>(8)</sup>, whereas in our series the frequency was 28.0%, lower than previously reported. SVEs are the most common arrhythmia associated with hypertension<sup>(25)</sup>. A previous study reported a higher prevalence of SVA in hypertensive patients compared with non-hypertensive individuals (5.2% vs. 2.7%)<sup>(8)</sup>. The

incidence of frequent SVEs and atrial tachycardia was significantly higher in patients with white-coat hypertension and sustained hypertension compared with normotensive individuals<sup>(26)</sup>. In our series, hypertensive patients exhibited a higher proportion of SVEs compared with normotensive subjects.

A common feature of HHD is LVH, which may manifest as CA<sup>(7,21)</sup>. SVAs reported in hypertensive patients include isolated extrasystoles, bigeminy, couplets, atrial fibrillation, atrial flutter, as well as sinus tachycardia and bradycardia<sup>(27)</sup>. In our series, the types of SVAs identified were very similar to those reported in previous studies.

Most SVAs in hypertensive individuals are associated with long-standing uncontrolled hypertension, LVH, left atrial enlargement, increased sympathetic activity, electrolyte disturbances, and excessive consumption of caffeine and alcohol<sup>(27,28)</sup>. These factors may induce electrical remodelling, leading to shorter refractory periods, greater dispersion of atrial repolarisation, and increased susceptibility to arrhythmogenesis, particularly atrial fibrillation<sup>(29,30)</sup>. In our cohort, a high proportion of hypertensive individuals presented pulse pressure values above the normal range, which was associated with a higher frequency of SVAs.

In most cases, individuals with SVAs are asymptomatic. However, those who do develop symptoms commonly experience palpitations or dizziness, which often prompt them to seek medical attention<sup>(31)</sup>. For this reason, timely screening is essential to detect arrhythmias and implement appropriate preventive measures, thereby reducing the risk of cardiovascular events. This is particularly relevant in individuals with hypertension, given its strong association with arrhythmias, and supports the use of 24-hour electrocardiographic monitoring.

Hypertension is the most prevalent comorbidity in patients with atrial fibrillation<sup>(9)</sup>. A characteristic feature of HHD is LVH, which may manifest as CA<sup>(7,24)</sup>, among which atrial fibrillation is one of the most frequent and is associated with

**Table 3.** Crude and adjusted analysis of factors associated with supraventricular arrhythmias in adult subjects.

Associated factors	Crude OR	95% CI	p-value	Adjusted OR	95% CI	p-value
Age >60 years	6.00	3.20-11.23	<0.001			
Male sex	1.14	0.63-2.05	0.654			
Hypertension	5.98	3.08-11.62	<0.001	3.43	1.64-7.04	<0.001
Diabetes mellitus	10.98	1.38-90.90	0.023	7.04	0.80-62.50	0.077
Obesity	1.18	0.52-2.63	0.683			
Dyslipidaemia	1.30	0.63-2.65	0.469			
Pulse pressure >50 mmHg	5.10	2.69-9.61	<0.001	3.27	1.61-6.66	0.001
Left atrial volume index (mL/m <sup>2</sup> )	2.33	1.30-4.16	0.004	1.57	0.80-3.10	0.186
Left ventricular hypertrophy (g/m <sup>2</sup> )	1.66	0.93-2.94	0.082			
Relative wall thickness (>0.42)	2.30	1.27-4.16	0.006	1.49	0.74-2.98	0.278

Crude OR: crude odds ratio. Adjusted OR: adjusted odds ratio. 95% CI: 95% confidence interval.

an increased risk of stroke<sup>(7)</sup>. In our setting, a higher association between atrial fibrillation and cardioembolic cerebrovascular events is also observed.

SVAs may affect quality of life, morbidity, and mortality in affected individuals<sup>(8)</sup>. Hypertension has been identified as an independent risk factor for the incidence or progression of atrial fibrillation, the most common arrhythmia<sup>(9)</sup>. Among individuals with hypertension alone, atrial fibrillation may be asymptomatic in up to 35% of cases<sup>(9)</sup>. Given the high proportion of asymptomatic individuals with SVAs, timely screening is warranted to enable detection and appropriate treatment, with the aim of preventing fatal cardiovascular events.

A strength of this study is that it enables a comprehensive evaluation of strategies to identify factors associated with SVAs in adult patients presenting with palpitations, based on an extensive assessment beyond resting electrocardiography, including 24-hour or prolonged Holter monitoring.

Among the study limitations, residual confounding may be present, as certain variables were not controlled, given the

observational, single-centre, and cross-sectional design. In addition, the sample size was relatively small compared with other studies. These factors limit the ability to establish causal relationships and may introduce selection bias due to the absence of random sampling.

In conclusion, hypertension and elevated pulse pressure are significant risk factors for the development of SVAs in residents living at high altitude. These findings highlight the importance of blood pressure control not only for preventing cardiovascular complications but also for reducing the risk of cardiac rhythm disturbances. Further studies are required to better understand the clinical implications for the prevention and management of SVAs in hypertensive patients.

#### Author contributions

**ADL:** conceptualisation, data collection, methodology, data analysis, writing, and approval of the final version. **JBB:** review and approval of the final version. **RM:** data analysis, review, and approval of the final version.

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