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IS THERE A RELATIONSHIP/AN ASSOCIATION BETWEEN ABO BLOOD GROUP SYSTEM AND CARDIAC CONDUCTION DISORDERS?

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Rezumat

Introducere*. Datele din literatură sugerează o creștere ușoară a riscului cardiovascular pentru persoanele care au grupe sangvine non-O. Scopul studiului este de a evalua existența unei asocieri între tulburările de conducere cardiace și grupele sangvine.*

Material și metodă. *În acest studiu retrospectiv au fost incluși pacienți cu tulburări de conducere atrio-ventriculară și boală de nod sinusal, care aveau indicație de cardiostimulare permanentă, și un grup de control format din pacienți la care s-a efectuat coronarografie sau angiografie periferică electivă. Toți pacienții aveau determinate grupele sangvine. S-au folosit metode statistice univariate și multivariate.*

Rezultate. *Populația studiată a inclus 640 de pacienți, cu vârsta medie de 72±11ani, 55,3% bărbați, dintre care 320 pacienți cu tulburări avansate de conducere atrio-ventriculară sau disfuncție de nod sinusal în lotul de studiu și 320 pacienți în lotul de control. Grupul sangvin tip A a avut prevalența cea mai mare (46,8%), urmat de grupele sangvine tip O (28,95%), B (16,74%) și AB (7,51%). În grupul cu tulburări de conducere cardiace, pacienții cu grup sangvin tip A au avut un risc crescut de bloc atrio-ventricular (OR 1,38, p =0,02), nu și de boală de nod sinusal (OR 1,02, p =0,98). Grupul sangvin tip O a avut un rol protector atât pentru blocul atrio-ventricular, cât și pentru disfuncția de nod sinusal (OR 0.65, p =0,01).*

Concluzii. *Grupul sangvin tip A s-a dovedit a fi un predictor independent pentru tulburări de conducere atrio-ventriculară la pacienții cu tulburări severe de ritm cardiac cu indicație de cardiostimulare permanentă.*

Cuvinte cheie*: grup sangvin, bloc atrio-ventricular, boală cardiovasculară, factori de risc.*

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Abstract

Introduction. *Data from the literature suggest a slight increase in cardiovascular risk for people with non-O blood types. The purpose of the study was to evaluate if there is an association between advanced cardiac conduction disorders and blood groups.*

Material and methods. *In this retrospective study, a group of patients with atrio-ventricular conduction disorders or sinus node disease, having an indication for permanent cardiostimulation, was analyzed and compared with a control group consisting of patients who underwent coronary angiography or elective peripheral angiography. The blood group was determined in all patients. Univariate and multivariate statistical methods were used.*

Results. *Six hundred forty patients, mean age 72±11y, 55.3% men, were included: 320 patients with advanced atrio-ventricular conduction disorders or sinus node dysfunction in the study group and 320 patients in the control group. Blood type A had the highest prevalence (46.8%), followed by blood types O (28.95%), B (16.74%) and AB (7.51%). In the group with heart rhythm disorders, patients with blood type A had an increased risk of atrio-ventricular block (OR 1.38, p= 0.02), but not with sinus node disease (OR 1.02, p= 0.98). Blood type O had a protective role both for atrio-ventricular block and for sinus node dysfunction (OR 0.65, p= 0.01).*

Conclusion: *Blood type A proved to be an independent predictor for atrio-ventricular conduction disorders in patients with severe heart rhythm disorders with indication for permanent cardiostimulation.*

Keywords: *blood type**,** atrioventricular block, cardiovascular disease, risk factors.*

Introduction

Atrioventricular conduction disorders are a common pathology in the general population. While the connection between ABO groups and others cardiovascular disease like coronary artery disease (CAD), peripheral arterial disease, venous tromboembolism (VTE), diabetes mellitus type 2 is already established, the study of the link between the ABO groups and cardiac conduction disorders is lacking[1,2,3].

Atrioventricular block (AVB) is a disturbance of impulse conduction that can be permanent or transient, depending on the anatomic or functional impairment. The severity of atrioventricular block (AVB) varies: first, second, advanced and third-degree AV block.

Sinus node dysfunction (SND) comprises a wide spectrum of sinoatrial dysfunctions, ranging from sinus bradycardia, chronotropic incompetence, sinoatrial block, and sinus arrest to bradycardia-tachycardia syndrome.

Pathological bradyarrhythmias can be broadly categorized into intrinsic and extrinsic aetiologies. It is essential to differentiate reversible from non-reversible causes of bradycardia. Potential reversible causes of bradycardia include adverse drug effects, myocardial ischemia, toxic exposure, infections, surgery, and electrolyte disorders[4]. The ABO blood group system is the most well-known human blood typing system. It determines the presence or absence of specific carbohydrate molecules, called antigens, on the surface of red blood cells. In the AB system are two main antigens involved: A and B. People may have either A, B, both (AB), or neither (O) antigens on their red blood cells.

Plasma antibody may also be synthetized against antigens which are not present on the red blood cells surface.

- People with type A blood have anti-B antibodies.
- People with type B blood have anti-A antibodies.
- People with type AB blood have neither anti-A nor anti-B antibodies (universal recipients).
- People with type O blood have both anti-A and anti-B antibodies (universal donors)[5].

In the study we analyzed the link between ABO blood types and cardiac conduction disorders (AVB and SND) in patients with indications for permanent cardiac pacing.

Material and methods

Population

This is a retrospective study performed in the cardiology department between December 2019 and February 2024. The study protocol was approved by the Hospital's Ethical Board, in accordance with the Declaration of Helsinki.

We included patients admitted consecutively to the Cardiology Department with indication for pacemaker implantation according to European Society of Cardiology Guidelines on cardiac pacing and cardiac resynchronization therapy (with second or third degree atrioventricular block or sinus node disease)[4]. Patients with age <18 years, congenital AV block and reversible cause AV block (ischemia, drug-induced, metabolic and electrolyte imbalance, iatrogenic) were excluded.

In the control group were included 320 patients who performed elective angiography, either coronary angiography or peripheral vascular angiography for chronic coronary syndrome or peripheral artery disease, whose ABO blood group was available and had

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	Total N=640	Conduction disorder N=320	Control N=320	p
Gender male, n, %	354 (55.3%)	168 (52.5%)	186 (58.13%)	0.15
Age, years±S.D.	72±11	76±10	68±10	0.03
Blood type				
O, n, %	**185 (28.95%)**	**79 (24.7%)**	**106 (33.23%)**	**0.01**
Non-O, n, %	**454 (71.05%)**	**241 (75.3%)**	**213 (66.77%)**	**0.01**
➢ A, n, %	**299 (46.8%)**	**164 (51.25%)**	**135 (42.32%)**	**0.02**
➢ B, n, %	107 (16.74%)	49 (15.3%)	58 (18.2%)	0.23
➢ AB, n, %	48 (7.51%)	28 (8.75%)	20 (6.3%)	0.24

Table 1. *The distribution of ABO blood type in the study group*

normal atrioventricular conduction and no history of sinus node disease. In all patients an ABO blood type lab test was performed.

Statistical analysis

SPSS 20 and EpiInfo 2007 were used for statistical analysis. Univariate and multivariate statistical methods were used. Descriptive statistics were presented as absolute numbers and percentages for categorical variables, while normally distributed data were depicted as mean with standard deviation. Anova and Mann-Whitney-Wilcoxon tests were used to compare independent continuous data. ROC curve analysis was performed to evaluate the correlations between numerical and categorical variables. Multiple logistical regression was used to test the independent associations between variables. A p value <0.05 was considered significant statistic.

Results

640 patients were included in the study, 320 patients with cardiac conduction abnormality

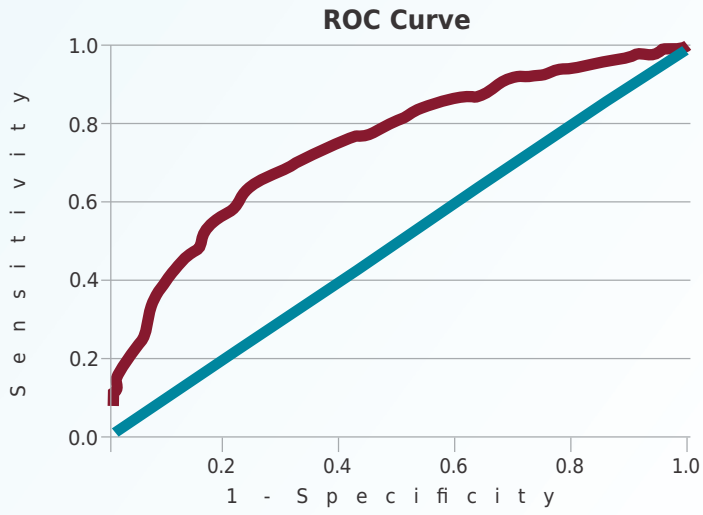

Figure 1. *AUC for age and conduction disorder*

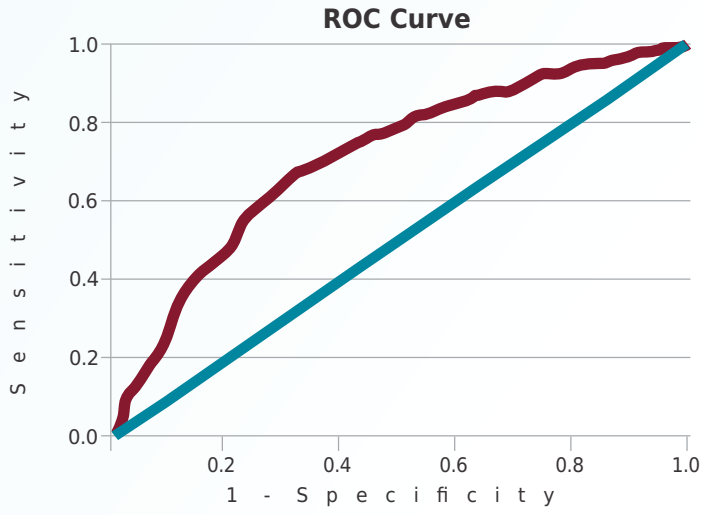

Figure 2. *AUC for age and AV block*

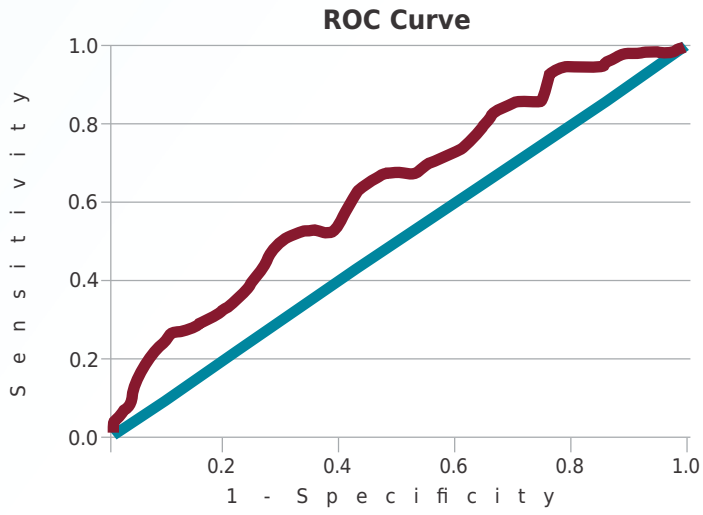

Figure 3. *AUC for age and sinus node disease*

(either AVB or SND), having an indication for pacemaker implantation, and 320 patients in the control group, without cardiac conduction disorders.

The baseline characteristics of the study group are presented in Table No.1. The mean age of the patients was 72±11 years, 55.3% were males. Patients with cardiac conduction disorders were significantly older than patient in the control group (76±10y vs 68±10y, p=0.03). There was no significant difference between the gender in the two groups. In the study group (n=640), type A blood group was the most prevalent (46.8%), followed by O type (28.95%), B type (16.74%) and AB type (7.51%).

Type A blood group was significantly more prevalent in the patients with conduction disorder than in the control subjects (p 0.02), while O type had a higher prevalence in the control group (p 0.01) (Table 1). In patients with cardiac conduction disorders A blood group had a higher prevalence in patients with AV block when compared to SND (51.5% vs 47.3%, p 0.046).

In univariate analysis, type A blood group was associated with a higher risk of AV block (OR 1.38, p 0.02), but not SND (OR 1.02, p 0.98), while O group portends a protective role for both types of disorders (OR 0.65, p 0.01) (Table No.2, 3, 4) .

Not surprisingly, a strong factor associated with cardiac conduction disorders was age (AUC 0.75, p<0.001) (Figure 1, 2, 3). After adjusting for age and sex, in multivariable analysis, type A blood group and age, were independent predictors of AV block.

Discussion

The ABO system goes beyond just blood transfusions. Previous studies suggested the potential associations between ABO blood types and various diseases. In patients with cardiovascular disease**,** the association between thrombosis and ABO blood groups has a long history suggesting that non-O blood groups confer a higher risk of myocardial infarction, angina, peripheral vascular disease and venous thrombo-embolism than group O. In a systematic review and meta-analysis of 17 studies with 225810 participants, type A blood group and non-O group are associated with an increased risk of coronary artery disease CAD[6,7,8,9]. Several genome-wide association studies have shown that carriers of single nucleotide polymorphisms that mark non-O blood group types have higher levels of plasma von Willebrand Factor (VWF) when compared to O individuals[10]. In a recent cohort study blood group O carriers had a 25% average reduction in plasma VWF levels when compared with non-O blood group carriers[11].

It has been demonstrated a relationship between Factor VIII plasma concentrations

Type	OR (95%CI)	P value
Non-O	**1.51 (1.1-2.14)**	**0.01**
A	**1.43 (1.04-1.95)**	**0.02**
B	0.81 (0.53-1.23)	0.33
AB	1.43 (0.78-2.60)	0.23
O	0.65 (0.46-0.92)	0.01

Table 2. *Univariate analysis of blood type and conduction disorder*

Type	95%CI	P value
Non-O	**1.46 (1.02-2.08)**	**0.03**
A	**1.38 (1.1-.1.89)**	**0.01**
B	0.83 0.54 -1.27)	0.40
AB	1.35 (0.75-2.44)	0.31
O	**0.68 (0.47-0.97)**	**0.03**

Table 3. *Univariate analysis of blood type and atrio-ventricular block*

Type	OR (95%CI)	p
Non-O	0.99 (0.54-1.82)	0.98
A	1.02 (0.58-1.77)	0.94
B	0.97 (0.45-2.04)	0.93
AB	0.96 (0.33-2.78)	0.94
O	1.01 (0.54-1.85)	0.98

Table 4. *Univariate analysis of blood type and sinus node disease*

Determinants	HR (95%CI)	P value
Age	1.07 (1.05 -1.09)	<0.001
Type A	1.38 (1.1-1.89)	0.046

Table 5. *Multivariate analysis*

and ABO blood groups. As VWF binds and transports Factor VIII, the correlation between the ABO groups and Factor VIII is most likely mediated via VWF[12]. VWF and Factor VIII are glycoproteins that circulate together in normal plasma and both play important roles in normal hemostasis. These factors participates in the coagulation cascade. Thus, both VWF and Factor VIII are proteins involved in the formation of occlusive thrombi in injured vessels.

Some studies suggested an increase in the risk of myocardial infarction for non-O blood type individuals. It is plausible that ABO modulation of VWF related thrombosis accounts for the ABO association with myocardial infarction. Also, ABO antigens are expressed on platelet proteins, including GPIIb, and may modulate specific platelet functions in arterial thrombosis and myocardial infarction[11].

In cardiac conduction diseases there are emerging evidence indicating a possible link between non-O blood types and high-grade AV block. There was only one study that has evaluated the potential relationship between atrioventricular block and ABO blood groups, suggesting that patients with non-O blood group types have a higher risk for development of atrioventricular block compared with O blood group patients[13].

In our study, the presence of type A blood group was associated with higher risk of AV block, but not with sinus node disease. The presence of O grup portends a protective role for both cardiac conduction disorders. Not surprinsingly, age was associated with a higher risk for conduction disorders, already established from other studies[14].

The previous study mainly focused to the blood group non-O and O, and did not analyze the relationship between blood groups A, B and AB. Compared with the study of Emrah et al, we included in the study patients with advanced AV block and patients with SND with an indication for pacemaker implantation[13].

Moreover, we focus on each non-O blood types. In our study the type A blood group was associated with higher risk for conduction disorders and was an independent predictor for advanced AV block with the indications for permanent pacing.

The clinical implication of the relationship between cardiac conduction disorders and blood group is a targeted follow-up of patients at risk of cardiac conduction abnormalities according to ABO blood type. Much larger epidemiological and genetic studies are required to determine risks of cardiac conduction disorders with particular ABO blood group.

The study limits: The observational, retrospective study with a limited number of patients.

Conclusions

Type A blood group proved to be a predictor for atrio-ventricular conduction disorders in patients with severe cardiac conduction disease with indication for permanent cardiostimulation and could be added to the traditional risk factors for atrio-ventricular block.

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