Blood type B antigen is associated with worse New York Heart Association classification in male patients with hypertrophic cardiomyopathy

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Abstract

Objective: ABO blood type is associated with cardiovascular diseases. Several studies have suggested sex-related differences in both hypertrophic cardiomyopathy (HCM) clinical features and ABO blood type. However, few data are available regarding the relationship between ABO blood type and HCM clinical features. We aimed to analyze the relationship between ABO blood type and HCM clinical features, and the potential effects of sex on these relationship.

Methods: A total of 549 patients with HCM were enrolled consecutively. Left ventricular outflow tract gradients at rest (LOVTG-R) were measured by echocardiography. Left ventricular end-diastolic dimension, interventricular septum, left ventricular ejection fraction (LVEF), left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), and left ventricular mass (LVM) were assessed using cardiovascular magnetic resonance imaging.

Results: Compared with the non-B antigen group, patients with B antigen had significantly higher LOVTG-R and LVEF values, worse New York Heart Association (NYHA) classification, lower left ventricular volume index values, as well as no difference in LVM index values. After adjustments for sex, male patients with B antigen still had higher LOVTG-R values and frequency of NYHA classification III/IV as well as lower LVEDV and LVESV index values. These differences were not present in female patients. Additionally, patients with NYHA classification III/IV had lower LVEDV index values.

Conclusion: In males, not females, patients with HCM with blood type B antigens exhibited worse cardiac functional capacity, higher LOVTG-R values, and lower left ventricular volume index values. These relationships are a potential indicator for clinical prevention. We speculate that rehydration is more efficient in relieving symptoms in male patients with HCM with B antigens. *(Anatol J Cardiol 2018; 20: 258-65)*

Keywords: hypertrophic cardiomyopathy, ABO blood type, sex

Introduction

Hypertrophic cardiomyopathy (HCM) is an autosomal dominant inherited myocardial disorder characterized by asymmetrical left ventricular hypertrophy, with a prevalence of 1:500 in the general population (1). The disease affects all age groups, with symptom heterogeneity, ranging from a normal lifespan to poor outcomes, such as heart failure, stroke, atrial fibrillation, and sudden cardiac death (1, 2). Sex-related differences have been recognized in HCM, with women patients exhibiting more severe symptoms of heart failure and more frequent association with LOVT obstruction and men patients exhibiting greater left ventricular mass (LVM) index values and disease penetrance (3).

The ABO blood type system was discovered by Karl Landsteiner and colleagues in 1901 (4). The ABO blood system antigens (A and B antigens), regarded as red cell antigens, comprise complex carbohydrate molecules and expressed on a variety of human tissues, such as the epithelium, sensory neurons, cardiac cells, platelets, and vascular endothelium (5). Is there a relationship between ABO blood type and HCM clinical features?

The responsible gene of ABO blood type on chromosome 9q34 encodes glycotransferases that catalyze the transfer of nucleotide donor sugars to the H antigen to form the ABO blood

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type antigens (6). In addition, NOTCH1, which plays important roles in the development of cardiac hypertrophy and the cardiac outflow tract, is also located on chromosome 9q34 near the ABO locus (7, 8). A study of a large family (31 members; 18 male, 13 female; with a high incidence of HCM) found no linkage between ABO blood type and disease-responsible genes (9), but the author's conclusion was based on a relatively small sample size. Considering the genetic heterogeneity of HCM, it is necessary to analyze the relationship between ABO blood type and HCM clinical features based on a larger sample size. Additionally, sex-related differences in ABO blood type have also been recognized in heart diseases of cardiac carcinoma (10), congenital heart disease (11), and coronary artery disease (12, 13).

To the best of our knowledge, there are no reports regarding an association between ABO blood type and HCM clinical features. Hence, we explored the relationship between ABO blood type and HCM clinical features with a large cohort of patients with HCM. In consideration of the aforementioned sex-related differences in both HCM clinical features and ABO blood type, the aim of this study was to determine the relationship between ABO blood type and HCM clinical features and to evaluate whether sex had an impact on this relationship.

Methods

Study design and study population

This was a retrospective study. We analyzed consecutive patients with HCM who were evaluated at Fuwai Hospital (Beijing, China) between November 2009 and April 2016. Patients who had a complete medical history record and those who had undergone physical examination, 12-lead electrocardiography, echo, blood type examination, and cardiovascular magnetic resonance imaging (CMRI) were enrolled in our study. The cardiac function of all patients with HCM was graded according to the New York Heart Association (NYHA) classification on admission (14). The diagnosis of HCM was based on a maximum LV wall thickness ≥15 mm (or ≥13 mm with an unequivocal family history of HCM), as measured by echocardiography or CMR, and excluded other cardiac or systemic diseases capable of producing such a magnitude of hypertrophy (15). Diabetes mellitus was defined as a fasting plasma glucose level of ≥7.0 mmol/L or self-reported current treatment with anti-diabetic medication (insulin or oral hypoglycemia agents). Hypertension was defined as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg or self-reported current treatment with anti-hypertension medication. Exclusion criteria included patients with fever, infection, valvular heart disease, renal dysfunction (defined as an estimated glomerular filtration rate of <60 mL/min/1.73 m^2), concomitant neoplasm, connective tissue disease, pregnancy, or a medical history of alcohol septal ablation or Morrow Septal Myectomy. Finally, 549 patients were recruited. This study was approved by the Ethics Committee of Fuwai Hospital and performed in accordance with the Declaration of Helsinki as part of routine clinical practice. All participants provided their written informed consent to agree with using their clinical information.

Echocardiography

All transthoracic echocardiography was performed within 1 or 2 days after admission according to the American Society of Echocardiography's recommendation (16), using an iE 33 color doppler ultrasound system (Philips Healthcare, Andover, MA), by medical technologists who were unaware of any clinical information about the studied patients. The peak velocity across left ventricular outflow tract gradients at rest (LOVTG-R) was measured, and the peak pressure gradient was estimated using a simplified Bernoulli equation.

Cardiovascular magnetic resonance imaging

CMRI was performed using a 1.5-T speed clinical scanner (Magnetom Avanto; Siemens Medical Solutions, Erlangen, Germany) within 1 week after admission. Briefly, cine images were obtained in left ventricular two-chamber and four-chamber long-axis, LVOT, and LV short-axis views using true fast imaging by a steady-state precession (TrueFisp) sequence (17). All CMRI analysis was performed using commercial software (Medis Medical Imaging Systems, Netherlands) by a single experienced observer who was blinded to the patients' clinical and procedural data. Endocardial contours of the LV myocardium were manually traced at end-diastole and end-systole on each LV short-axis cine image. LV myocardium (including papillary muscles) was automatically selected with a mask mode. LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), left ventricular ejection fraction (LVEF), stroke volume, and cardiac output were then calculated in a standard fashion. LV mass (including papillary muscles) was derived by multiplying LV myocardial volume measured at end-diastole with the specific gravity of the myocardium (1.05 g/mL). All these variables were indexed to body surface area, except LVEF. The LVED diameter and interventricular septal thickness were traced and measured from the short-axis views at end-diastole. Of note, a total of 73 patients with HCM had AF in our study, and CMR provided adequate images for evaluation in these 73 patients with AF through a well-controlled heart rate (≤80 bpm, with β-blockers).

Blood sample

The ABO blood type was detected with a commercially available hemagglutination technique (Erytype S ABO Microplates, Biotest, Germany).

Statistical analysis

Continuous variables are expressed as mean±SD or median [interquartile range (IQR)], according to their normality. Categorical variables are shown as frequencies (percentages). Comparisons of continuous variables between two groups were assessed using independent Student's t test or Mann-Whitney

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Table 1. Clinical characteristics of 549 patients with HCM stratified by A antigens or B antigens and sex

Variable	A antigens#			B antigens*			Sex		
	With A antigens (n=189)	Without A antigens (n=360)	*P* value	With B antigens (n=220)	Without B antigens (n=329)	*P* value	Female (n=221)	Male (n=328)	*P* value
Age (years)	47.8±13.0	48.5±12.3	0.535	49.4±12.0	47.5±12.8	0.093	51.2±13.3	46.3±11.6	<0.001
Male, n (%)	113 (59.8)	215 (59.7)	0.988	124 (56.4)	204 (62.0)	0.186	-	-	-
Body mass index (kg/m²)	25.1±3.4	25.3±3.4	0.518	25.2±3.2	25.2±3.5	0.840	24.4±3.3	25.7±3.3	<0.001
Heart rate (bpm)	70.0 (65.0-78.5)	70.0 (65.0-78.8)	0.938	70.0 (65.0-77.8)	70.0 (65.0-80.0)	0.420	70.0 (64.0-77.0)	70.0 (65.0-80.0)	0.217
SBP (mm Hg)	120.0±17.6	117.9±16.6	0.223	118.0±17.4	118.9±16.7	0.521	116.4±17.8	120.0±16.3	0.016
DBP (mm Hg)	72.8±10.6	72.2±10.6	0.533	72.2±10.6	72.6±10.7	0.672	70.5±10.6	73.7±10.5	0.000
Hypertension, n (%)	64 (33.9)	126 (35.0)	0.790	75 (34.1)	115 (35.0)	0.835	84 (38.0%)	106 (32.3%)	0.169
Diabetes mellitus, n (%)	15 (7.9)	26 (7.2)	0.760	14 (6.4)	27 (8.2)	0.421	17 (7.7%)	24 (7.5%)	0.870
Hypercholesterolemia, n (%)	64 (33.9)	111 (30.8)	0.469	76 (34.5)	99 (30.1)	0.272	67 (30.3%)	108 (32.9%)	0.520
Current smokers, n (%)	67 (35.4)	135 (37.5)	0.636	76 (34.5)	126 (38.3)	0.372	7 (3.2%)	195 (59.5%)	<0.001
NYHA classification III/IV, n (%)	67 (35.4)	160 (44.4)	0.042	107 (48.6)	120 (36.5)	0.005	97 (43.9%)	130 (39.6%)	0.321
Family history of HCM, n (%)	26 (13.8)	52 (14.4)	0.826	32 (14.5)	46 (14.0)	0.853	31 (14.0%)	47 (14.3%)	0.921
Family history of SCD, n (%)	10 (5.3)	20 (5.6)	0.897	14 (6.4)	16 (4.9)	0.448	12 (5.4%)	18 (5.5%)	0.977
Syncope, n (%)	53 (28.0)	96 (26.7)	0.731	61 (27.7)	88 (26.7)	0.800	64 (29.0%)	85 (25.9%)	0.431
Atrial fibrillation, n (%)	28 (14.8)	45 (12.5)	0.448	25 (11.4)	48 (14.6)	0.275	31 (14.0%)	42 (12.8%)	0.679
Non-sustained VT*, n (%)	18 (9.5)	33 (9.2)	0.891	17 (7.7)	34 (10.3)	0.302	25 (11.3%)	26 (9.3%)	0.180
Medications									
β-Blockers, n (%)	132 (69.8)	270 (75.0)	0.195	166 (75.5)	236 (71.7)	0.334	150 (67.9%)	252 (76.8%)	0.020
CCB, n (%)	31 (16.4)	62 (17.2)	0.808	46 (20.9)	47 (14.3)	0.043	41 (18.6%)	52 (15.9%)	0.408
Diuretic	10 (5.3)	18 (5.0)	0.883	11 (5.0)	17 (5.2)	0.930	19 (8.6%)	9 (2.7%)	0.002
Echocardiographic parameters									
LVOT gradients at rest (mm Hg)	74.2±37.3	70.9±34.1	0.303	77.4±36.7	68.4±33.9	0.003	77.1±35.3	68.6±34.9	0.005
Cardiovascular magnetic resonance									
LAAP diameter (mm)	41.9±8.5	42.0±8.0	0.925	42.1±7.7	41.9±8.4	0.833	42.3±8.2	41.8±8.1	0.476
LVEDD (mm)	46.0 (43.0-50.0)	46.0 (43.0-49.0)	0.882	45.0 (43.0-48.8)	46.0 (43.0-50.0)	0.195	45.0 (42.0-48.0)	47.0 (44.0-50.0)	<0.001
Septal thickness (mm)	23.0 (20.0-26.0)	24.0 (20.3-28.0)	0.116	23.0 (20.0-26.0)	24.0 (20.0-28.)	0.298	22.0 (20.0-26.0)	24.0 (21.0-28.0)	<0.001
LVEF (%)	68.1±8.9	69.8±8.2	0.285	69.7±7.6	68.0±8.9	0.014	69.3±8.4	68.2±8.4	0.120
Cardiac output (l/min)	5.4 (4.7-6.4)	5.6 (4.8-6.9)	0.175	5.4 (4.6-6.3)	5.7 (4.8-7.0)	0.031	5.0 (4.2-6.0)	5.9 (5.0-7.0)	<0.001
Left ventricular mass (g)	147.5 (112.1-196.3)	149.6 (112.7-192.3)	0.856	141.0 (111.4-185.7)	152.9 (113.0-198.4)	0.081	120.0 (94.9-161.0)	166.2 (133.4-213.6)	<0.001
EDV index (mL/m²)	70.5±16.3	70.2±16.6	0.869	68.0±15.4	71.9±17.0	0.005	68.9±15.7	71.3±17.0	0.100
ESV index mL/m²)	21.0(16.0-27.9)	20.6 (15.8-26.3)	0.483	19.0 (15.1-25.0)	21.9 (16.7-28.1)	0.003	19.4 (15.2-26.0)	21.5 (16.5-27.3)	0.059
SV index (mL/m²)	47.6±11.2	48.0±11.2	0.634	20.9±8.3	23.5±10.0	0.178	47.3±10.3	48.2±11.8	0.346
Cardiac index (l/min/m²)	3.0 (2.7-3.7)	3.1 (2.8-4.0)	0.167	3.0 (2.7-3.6)	3.1 (2.8-4.0)	0.124	3.0 (2.8-3.8)	3.0 (2.7-3.9)	0.891
Left ventricular mass index (g/m²)	83.4 (64.6-108.7)	84.0 (64.1-106.0)	0.948	80.7 (65.0-100.1)	85.7 (64.1-112.0)	0.118	73.9 (58.0-97.0)	89.4 (71.9-113.6)	<0.001

Data are expressed as median (interquartile range), mean±SD, or number (percentage).
SBP - systolic blood pressure; DBP - diastolic blood pressure; NYHA - New York Heart Association; HCM - hypertrophic cardiomyopathy; SCD - sudden cardiac death; VT - ventricular tachycardia; CCB - calcium channel blocker; LVOT - left ventricular outflow tract; LAAPD - left atrial anteroposterior diameter; LVEDD - left ventricular end-diastolic dimension; IVS - interventricular septum; LVEF - left ventricular ejection fraction; LVEDD - left ventricular end-diastolic diameter; LVESD - left ventricular end-systolic diameter
#Subgroup with A antigen includes patients with blood type A and AB, and subgroup without A antigen includes patients with blood type B and O.
*Subgroup with B antigen includes patients with blood type B and AB, and subgroup without B antigen includes patients with blood type A and O.

U test depending on the distribution of variables. The chi-square test and binary logistic test were used for comparisons between categorical variables, and Fisher's exact test was used when the expected presence was <5. One-way analysis of variance (ANOVA) test was used to evaluate the difference of constantly measured variables in four groups (A/B/O/AB). A two-tailed p value of <0.05 was considered statistically significant. Statistical analysis was performed using the statistical package SPSS 20.0 (SPSS Inc, Chicago, Illinois, USA).

Results

Clinical features of patients with HCM were stratified by blood type and sex

A total of 549 patients with HCM were enrolled in the study (328 males and 221 females; Table 1). Men were younger (43.3±11.6 vs. 51.2±13.3 years old, p<0.001) than women. Compared with the non-B antigen (blood type A/O) group, patients with B antigen (blood type B/AB) had significantly higher LOVTG-R values (77.4±36.7 vs. 68.4±33.9 mm Hg, p=0.003), frequency of NYHA classification III/IV (48.6% vs. 36.5%, p=0.005), and LVEF values (69.7±7.6% vs. 68.0±8.9%, p=0.014) as well as lower LVEDV (68.0±15.4 vs. 71.9±17.0 l/min/m^2, p=0.005) and LVESV index values [19.0 (IQR 15.1-25.0) vs. 21.9 (IQR 16.7–28.1) l/min/m^2, p=0.003]; there was no significant difference in the LVM index values (p=0.118). None of these variables were different between groups with or without A antigen (blood type A/AB or blood type B/O), except in the presence of NYHA classification III/IV (p=0.042). Compared with female patients, male patients had a significantly higher LVM index (p<0.001), body mass index (p<0.001), systolic blood pressure (p=0.016), and diastolic blood pressure (p<0.001) and lower LOVTG-R values (p=0.005). The values of LVEF, LVEDV index, and LVESV index as well as the presence of NYHA classification III/IV and distribution of the ABO groups were similar between male and female patients.

One-way ANOVA was used to detect the differences in LVEDV index (Fig. 1a), LVESV index (Fig. 1b), LVEF (Fig. 1c), and LOVTG-R (Fig. 1d) values in the four blood type groups (A/B/O/AB). Among male multiple subgroups, those variables were significantly different in the four blood type groups (all p<0.050; Fig. 1), and these differences were not present in female multiple subgroups (all p>0.050; Fig. 1).

Male patients with B antigen had significantly worse cardiac functional capacity

After adjustments for sex, the values of continuous variables are presented in Table 2 with respect to B antigen. In male subgroups, compared with patients with non-B antigen, patients with B antigen had greater presence of NYHA classification III/IV (p=0.0.003) and LOVTG-R (p=0.009) and LVEF (p=0.004) levels as

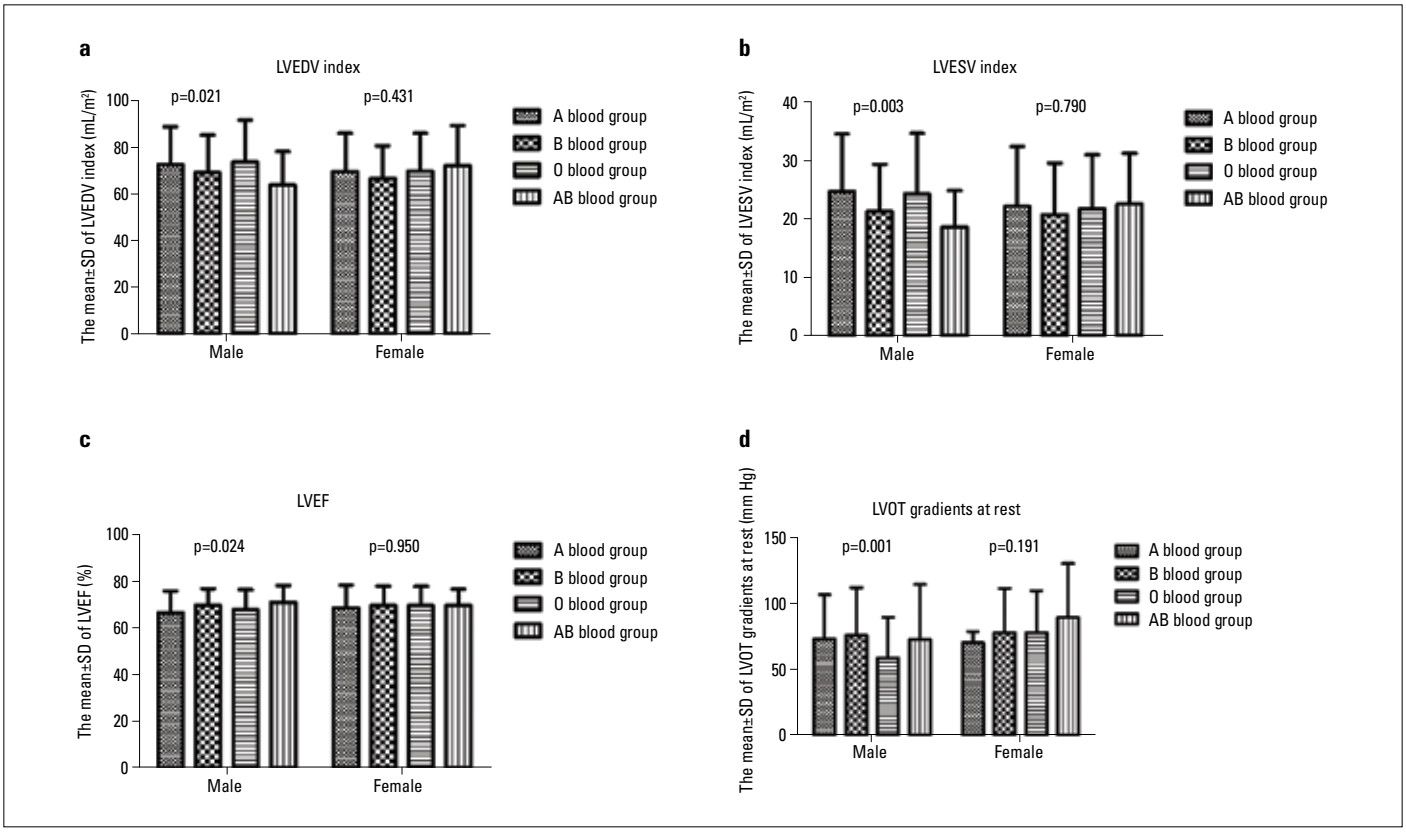

Figure 1. One-way ANOVA test for evaluating differences in the mean±SD of LVEDV index (Fig. 1a), LVESV index (Fig. 1b), LVEF (Fig. 1c), and LOVTG-R (Fig. 1d) values in subgroups of blood type A, blood type B, blood type O, and blood type AB. There were significant differences in male patients (all p<0.050; Fig. 1), and no differences in female patients (all p>0.050; Fig. 1)

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Table 2. B antigen with respect to cardiovascular magnetic resonance imaging parameters in female subgroup or in male subgroup

Variable	Female (n=221)			Male (n=328)		
	B antigen (n=96)	Non-B antigen (n=125)	*P* value	B antigen (n=124)	Non-B antigen (n=204)	*P* value
LVEF (%)	70.3 (65.2-74.7)	70.5 (64.4-75.1)	0.927	69.9±7.3	67.2±8.9	0.004
LVEDV index (mL/m^2)	67.9±14.9	69.7±16.2	0.420	68.0±15.8	73.3±17.3	0.006
LVESV index (mL/m^2)	19.6 (15.1-25.5)	19.4 (15.4-26.8)	0.786	19.0 (15.2-24.7)	22.7 (17.1-28.7)	0.001
LVOT gradients at rest (mm Hg)	80.5±35.7	74.5±35.0	0.210	75.0±37.4	64.7±32.7	0.009

Data are expressed as median (interquartile range) or mean±SD.
LVEF - left ventricular ejection fraction; LVEDV - left ventricular end-diastolic volume; LVESV - left ventricular end-systolic volume; LVOT - left ventricular outflow tract

Table 3. Binary logistic test for the association between B antigen and NYHA classification III/IV with sex-specific difference in all HCM patients or in patients without diuretic therapy

	All patients with HCM (n=549)			Patients without diuretic (n=521)		
NYHA classification III/IV	OR	95% CI	*P* value	OR	95% CI	*P* value
B antigen	1.649	1.166-2.333	0.005	1.717	1.202-2.454	0.003
Gender	0.839	0.594-1.186	0.321	0.813	0.568-1.163	0.257
Gender*B antigen	1.584	1.081-2.322	0.018	1.725	1.161-2.562	0.007
Male*B antigen	2.000	1.267-3.158	0.003	2.058	1.294-3.275	0.002
Female*B antigen	1.239	0.725-2.117	0.433	1.290	0.735-2.261	0.375

NYHA - New York Heart Association; HCM - hypertrophic cardiomyopathy; CI – confidence interval; OR – odds ratio

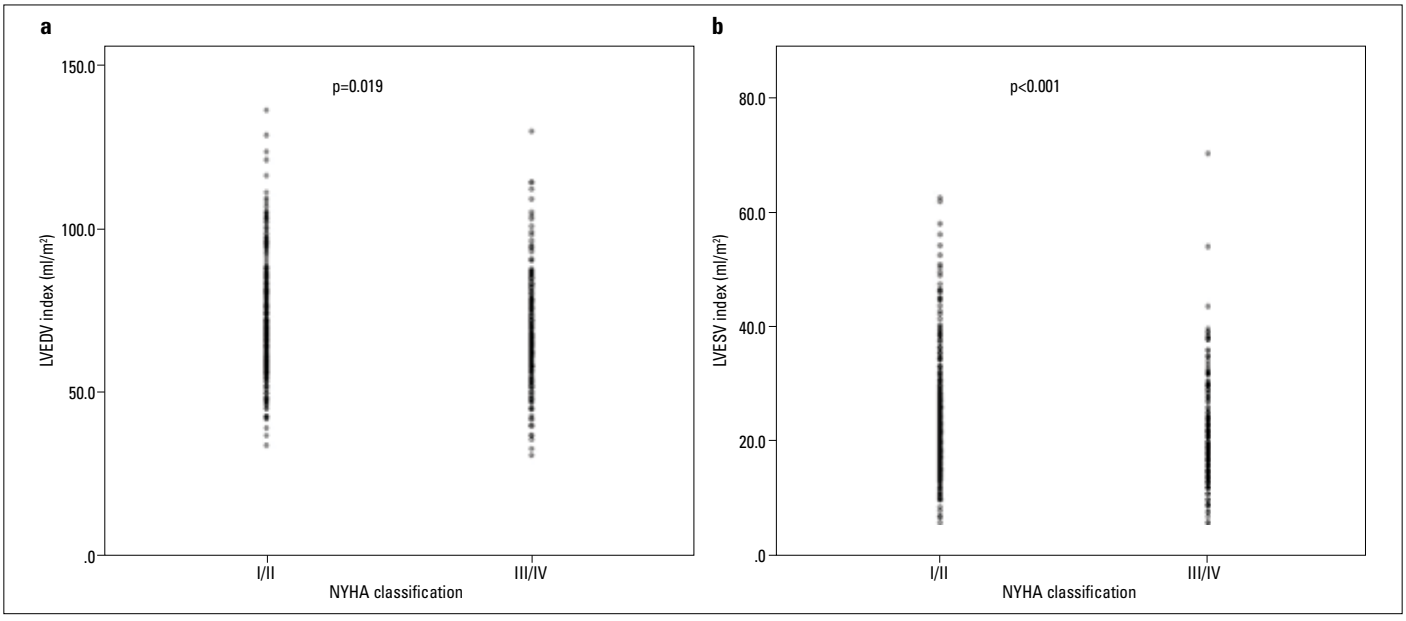

Figure 2. Compared with patients with NYHA classification I/II, those with NYHA classification III/IV had significantly lower LVEDV index (Fig. 2a) and LVESV index (Fig. 2b) values

well as lower LVEDV (p=0.006) and LVESV index levels (p=0.001). In female subgroups, compared with patients with non-B antigen, patients with B antigen had no significant difference in these variables (p>0.050).

In Table 3, the association between B antigen and NYHA classification III/VI with sex-specific difference is presented in all patients with HCM or those without diuretic therapy through using binary logistic test analysis (Forward: LR). B antigen was

positively and significantly associated with NYHA classification III/IV in all patients with HCM (OR 1.649, 95% CI 1.166-2.333, p=0.005), in gender*B antigen (OR 1.584, 95% CI 1.081–2.322, p=0.018), and in male subgroups (OR 2.000, 95% CI 1.267–3.158, p=0.003) but not in female subgroups (p=0.433). The same result was found in patients with HCM even after patients with diuretic therapy were excluded.

Figure 2 shows the LVEDV and LVESV index values with respect to NYHA classification in all patients with HCM. Compared with patients with NYHA classification I/II, patients with NYHA classification III/IV had significantly lower LVEDV [69.3 (IQR 59.6–81.3) vs. 66.7 (IQR 58.1–78.0) l/min/m^2, p=0.019] and LVESV index values [22.1 (IQR 17.3–27.6) vs. 19.0 (IQR 14.6–24.0) l/min/m^2, p<0.001].

Discussion

The present study revealed that the presence of NYHA classification III/IV and LOVTG-R, left ventricular volume index, and LVEF values are influenced by blood type B antigens in male patients with HCM. In contrast, none of these variables were significantly different in female patients, suggesting that in male patients with HCM, patients with blood type B antigens had worse cardiac functional capacity, higher LOVTG-R values and lower left ventricular volume index values. These relationships are a potential marker for clinical prevention. We speculate that rehydration is more efficient in relieving symptoms in male patients with HCM with B antigens through increasing ventricular volume.

In our study, B antigens (blood types AB and B), not A antigens (blood types AB and A), were associated with a significantly higher presence of NYHA classification III/IV and higher LOVTG-R values and smaller ventricular volume index in patients with HCM, but not with higher or lower LVM index. HCM is a heterogeneous, monogenic heart disease. Genetic inheritance may help to explain these relationships. The ABO gene on chromosome 9q34 encodes glycotransferases that catalyze the transfer of nucleotide donor sugars to the H antigen to form the ABO blood type antigens (6). NOTCH1, which is also located on chromosome 9q34 near the ABO locus, plays important roles in the development of cardiac hypertrophy and the cardiac outflow tract (7, 8). It is possible that the near locus of these two responsible genes partly explains this relationship. According to our study, the presence of B antigen was associated with a significantly higher presence of NYHA classification III/IV and higher LOVTG-R values as well as lower ventricular volume index values in patients with HCM, even after adjusting for sex. We did not observe obvious confounding of left ventricular volume index or LOVTG-R which were presented in our analysis when striated by blood type B antigens in male patients. Therefore, our findings are likely to be positive. However, a study of a large family (31 members; 18 males, 13 females; with a high incidence of HCM) found no linkage between ABO blood type and disease-responsible genes (9). Additionally, we did not find an association between ABO blood type and LVM index. Therefore, we speculated that the reason why male patients with HCM with B antigens had a higher presence of NYHA classification III/IV and higher LOVTG-R values and lower ventricular volume index values is not cardiac hypertrophy but abnormal cardiac contractility. The difference between A and B antigens is determined by the terminal sugars of the oligosaccharide chain (D-galactose for B antigen and N-acetyl-D-galactosamine for A antigen). The activity of galactosidase is closely associated with the process of Fabry's disease (18) and accumulated glycosphingolipid substrates leading to LVH (19), indicating that the smaller ventricular volume and higher LOVTG-R values in patients with B antigen may be the result of the influence of D-galactose on the myocardium. The precise mechanism underlying these relationships requires more precise research.

The most meaningful finding in our study was the sex-specific difference in the effect of the ABO blood type on the ventricular volume index in patients with HCM. A significant association between B antigens and the lower ventricular volume index in the entire subject population. In the subgroup analysis by sex, the association was only found in males. Sex has been shown to be a modifying factor in HCM phenotypes (20, 21). As shown in our study, variables such as age, body mass index, blood pressure, smoking, β-blocker therapy, and diuretic therapy may be confounders according to the analyses striated by sex. However, our data revealed that these confounders show no differences between groups stratified by blood type B antigens in male or female patients. Patients with HCM are predisposed to have greater LVM index value with sex difference (22), as seen in our study, but had no differences in the left ventricular volume index values between female and male patients. The presence of B antigens in male patients resulted in smaller left ventricular volume index values, but there were no differences in the LVM index values. We postulated that the effect of B antigens on left ventricular volume index values was relatively stronger in male patients with HCM than in female patients with HCM. The reason for this male-specific difference in ABO blood type in patients with HCM remains unknown. Sex-related differences in the ABO blood type have been found in heart diseases of cardiac carcinoma (10) and congenital heart disease (11). The differences in the gene expression regulation of the sex hormone or B antigen androgens or both could be a reasonable explanation for this sex-specific difference.

As our study indicated, compared with patients with no B antigens, male patients with B antigens had lower left ventricular volume index (LVEDV and LVESV indices) values and higher EF and LOVTG-R values. Past reports have demonstrated that patients with higher LOVTG-R values have worse cardiac functional capacity. In terms of structure and function, we suppose that male patients with B antigens have higher EF, which could contribute to higher LOVTG-R. Patients with higher LOVTG-R values could be partly mechanism of worse cardiac function in patients with B antigens.

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Previous studies have shown that the LVEDV index is regarded as an independent predictor of low exercise capacity in patients with HCM (23), and chamber stiffness is in part determined by mass/volume ratio; diastolic function has been shown to be better in patients with a large ventricular volume (eccentric hypertrophy) than in those with smaller left ventricular volumes (concentric hypertrophy) (24). In our study, patients with NYHA classification III/IV had significantly lower left ventricular volume index values (Fig. 2). We also demonstrated relationships among B antigens, left ventricular volume index, and the presence of NYHA classification III/IV. Male patients with B antigens were significantly associated with a higher presence of NYHA classification III/IV and higher LOVTG-R values and lower left ventricular volume index values. The simple intervention of increasing fluid intake may avoid the physiologic and hemodynamic changes that otherwise produce symptoms in patients with HCM (25), through increasing ventricular volume index and decreasing LOVTG-R values. Consistent with our data, we speculate that male patients with HCM with B antigens have smaller left ventricular volume index values and worse cardiac function, and rehydration may be more efficient in relieving symptoms in male patients with HCM with B antigens through increasing fluid intake. These relationships are a potential marker for clinical prevention. Further studies are required to clarify the mechanism for these sex-related differences regarding the relationship between B antigens and left ventricular volume index.

Study limitations

There were several limitations of the present study. This is a cross-sectional study, which renders conclusions about causality of demonstrated relations impossible, and residual confounding cannot be excluded. However, using a large enough population and CMRI, which has good reproducibility, our study findings can be verified. HCM is a genetic cardiac disease, but no genetic testing was performed in the present study, and further investigation with follow-ups and genetic testing in this population would elucidate the mechanism of ABO blood type antigens in the clinical features of patients with HCM. EF and LVOPG may not be clinically significant with small differences.

Conclusion

In male patients with HCM, not females, patients with blood type B antigens had worse cardiac functional capacity, higher LOVTG-R values, and lower left ventricular volume index values. These relationships are a potential indicator for clinical prevention. We speculate that rehydration is more efficient in relieving symptoms in male patients with HCM with B antigens.

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