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Clinical features of non-compaction cardiomyopathy across age groups: a retrospective study of 415 patients

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ABSTRACT

Background Non-compaction cardiomyopathy (NCM) is a rare inherited cardiac disorder associated with adverse cardiovascular outcomes, including heart failure, arrhythmias and sudden cardiac death. Currently, the clinical manifestations of NCM lack comprehensive characterisation across different age groups in large-scale studies. This investigation aims to systematically analyse the clinical characteristics of patients with NCM across various age demographics.

Methods A retrospective analysis was conducted on 415 patients with NCM treated at the Guangdong Institute of Cardiovascular Disease from January 2013 to January 2023. We comprehensively collected and analysed clinical data, including presenting symptoms, arrhythmia patterns, echocardiographic parameters and cardiac magnetic resonance imaging findings.

Results The study cohort (n=415) was stratified into three age groups: infants (0–1 year, n=169), children/adolescents (1–18 years, n=149) and adults (>18 years, n=97). Heart failure was the predominant clinical manifestation across the entire cohort, affecting 112 patients (27%). Notably, heart failure was most prevalent in adult patients (54.6%, n=53), while cardiac murmur was the primary presenting symptom in both infant and child/adolescent groups (19.5%, n=33 and 17.4%, n=26, respectively). Across all age groups, patients with NCM with concurrent mitral regurgitation (MR) demonstrated significantly reduced left ventricular ejection fraction and fractional shortening compared with those without valvular disease ($p<0.05$). Additionally, left ventricular end-systolic diameter (LVESD) and end-diastolic diameter (LVEDD) were significantly increased in patients with MR ($p<0.05$). A significant correlation was observed between both LVESD and LVEDD measurements and MR area in patients with NCM ($p<0.05$).

Conclusion Patients with NCM with concomitant MR consistently exhibited left ventricular dilatation and systolic dysfunction across all age groups. Significant age-related variations were observed in clinical presentations, arrhythmia patterns and the prevalence of congenital and valvular heart disease. Understanding these age-specific clinical characteristics is crucial for accurate diagnosis, optimal therapeutic management and future research directions in NCM.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Noncompaction cardiomyopathy (NCM) is a rare inherited cardiac disorder characterized by prominent trabeculations and deep intertrabecular recesses.

⇒ NCM is associated with adverse cardiovascular outcomes including heart failure, arrhythmias, and sudden cardiac deathThe clinical spectrum is diverse, but comprehensive characterization across age groups in large-scale studies is lacking.

WHAT THIS STUDY ADDS

⇒ This study of 415 NCM patients provides comprehensive age-stratified analysis of clinical manifestations across infant, pediatric, and adult populations.

⇒ Heart failure was the predominant manifestation overall (27%), but with significant age-dependent variations: most prevalent in adults (54.6%) while cardiac murmur was the primary symptom in younger patients.

⇒ NCM patients with mitral regurgitation consistently exhibited left ventricular dilatation and systolic dysfunction across all age groups.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The findings emphasize the need for age-specific approaches in both clinical management and research of NCM.

⇒ Understanding the association between mitral regurgitation and ventricular dysfunction provides a foundation for targeted therapeutic strategies.

⇒ The distinct age-dependent clinical patterns highlighted can guide more precise diagnostic and monitoring protocols for NCM patients.

INTRODUCTION

Non-compaction cardiomyopathy (NCM) is a primary inherited cardiomyopathy characterised by distinctive pathological features, including prominent trabeculations and deep intertrabecular recesses within the myocardium.[1] The condition manifests in three anatomical variants: left ventricular, right ventricular and biventricular forms, with left ventricular NCM (LVNCM) being the most frequently encountered phenotype.[2] While

the precise population prevalence of NCM remains undetermined, echocardiographic studies suggest that the proportion of LVNCM accounts for approximately 0.014%–1.3% of patients undergoing cardiac imaging.[3] A comprehensive study by Zou *et al*, analysing 11 974 patients who underwent CMR over 5 years, reported a prevalence of 1.5%.[4] Contemporary evidence suggests that NCM results from disrupted myocardial compaction during embryonic cardiac development, with genetic factors playing a fundamental role in its pathogenesis.[5] Genetic studies have demonstrated that pathogenic variants are present in approximately 18%–44% of NCM cases.[6 7] The clinical spectrum of NCM is remarkably diverse, ranging from asymptomatic presentations to severe manifestations including heart failure, arrhythmias and thrombotic events. Furthermore, NCM frequently coexists with other cardiac conditions, such as coronary heart disease (CHD), dilated cardiomyopathy, hypertrophic cardiomyopathy and various arrhythmias.[6] While previous research has largely concentrated on specific age cohorts, there is a notable paucity of comprehensive studies examining the age-dependent variations in NCM's clinical characteristics. Therefore, this investigation aims to systematically analyse the clinical features of NCM across all age groups, addressing this critical knowledge gap in the literature.

METHODS

Study population and clinical data collection

We conducted a systematic electronic medical record review to identify patients diagnosed with NCM at the Guangdong Provincial People's Hospital between January 2013 and January 2023. Potential cases were initially identified through the hospital's electronic health record system using the International Classification of Diseases, Tenth Revision diagnostic codes for NCM. A total of 491 potential cases were identified through this process. Each identified case was then manually reviewed by two independent investigators to confirm the diagnosis based on established Jenni and Chin diagnostic criteria. After excluding patients who did not meet the diagnostic criteria (n=76) and those with incomplete clinical documentation (n=8), a final cohort of 415 patients was established for analysis.

Echocardiography

As part of our retrospective study design, comprehensive echocardiographic examinations were performed using a Philips EPIQ CVx ultrasound system (Philips Healthcare, Best, The Netherlands) with an S8-3 transducer during routine clinical care between January 2013 and January 2023. Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson's biplane method from apical four-chamber and two-chamber views, following the recommendations of the American Society of Echocardiography. All echocardiographic images from each patient were independently analysed by two experienced cardiac imaging specialists. Any discrepancies in measurements or interpretations were resolved through consensus discussion. The diagnosis of NCM was established based on the modified Chin criteria, requiring the presence of all three of the following echocardiographic features: (1) multiple trabeculae on echocardiography; (2) colour Doppler imaging showed multiple deep trabecular recesses communicating with the ventricle, visible in the apex or middle of the ventricle; (3) the endocardium was a two-layer structure, with a non-dense layer/dense layer >2.

Cardiac electrophysiology

All ECG recordings were independently evaluated by two cardiac electrophysiologists. In cases of disagreement, a third expert electrophysiologist was consulted for final adjudication. Cardiac arrhythmias were systematically categorised into four distinct groups: (1) atrial tachycardia (AT), including atrial flutter, atrial fibrillation, pre-excitation syndrome and supraventricular tachycardia, etc; (2) ventricular tachycardia (VT), including VT, ventricular fibrillation, etc; (3) heart block, including second-degree/third-degree atrioventricular (AV) block, bundle branch block, sick sinus syndrome, etc; (4) others, including ST segment change, dextral cardiac rhythm, etc.

Statistics analysis

Continuous variables were presented as mean±SD for normally distributed data, and as median (25th, 95th percentiles) for non-normally distributed data. Statistical comparisons were performed using one-way analysis of variance or independent t-tests for normally distributed variables, and Wilcoxon signed-rank test for non-parametric data. Categorical variables were analysed using either the χ^2 test or the McNemar-Bowker test as appropriate. The relationships between continuous variables were assessed using Pearson's correlation coefficient for normally distributed data or Spearman's rank correlation coefficient for non-parametric data. All statistical tests were two-sided, with statistical significance set at $p<0.05$. Data analyses were conducted using R software (V.4.0) and SPSS (V.24.0, IBM, Armonk, New York, USA).

RESULTS

Patient population and demographics

Based on established diagnostic criteria, we identified a final cohort of 415 patients from an initial screening population of 491 individuals. The cohort comprised three distinct phenotypes of NCM: LVNCM (n=316, 76.1%), right ventricular NCM (n=33, 8.0%) and biventricular NCM (n=66, 15.9%). The study population included 229 females (44.1%) and 232 males (55.9%). Age-stratified analysis revealed three groups: infants (0–1 year; n=169), consisting of 94 males (55.6%) and 75 females (44.4%); children and adolescents (1–18 years; n=149), comprising 68 males (45.6%) and 81 females (54.4%) and adults (>18 years; n=97), including 70 males (72.7%) and 27 females (27.8%). Detailed demographic

characteristics are presented in table 1, with distribution patterns illustrated in figure 1 and online supplemental figure S3.

Clinical presentation

The spectrum of clinical manifestations is detailed in online supplemental table S1. Heart failure symptoms, primarily presenting as dyspnoea and chest tightness, were observed in 112 patients (27.0%). Cardiac murmur was documented in 102 patients (24.6%). Less common presentations included cyanosis, syncope, chest pain and failure to thrive. Notably, 43 patients (10.4%) remained asymptomatic, while 56 patients (13.5%) presented with respiratory symptoms (cough, sputum production and fever) secondary to pulmonary infections. Cardiac arrhythmias, detected either through symptoms of palpitations or ECG abnormalities, were present in 29 patients (7.0%). Age-stratified analysis revealed that heart failure predominated in adults (>18 years), whereas cardiac murmur was more frequently observed in paediatric groups (online supplemental table S1). Advanced heart failure, defined as New York Heart Association functional class III–IV, was present in 164 patients (39.5%), with the highest prevalence in the adult group (51/97, 52.6%). During hospitalisation, eight patients died. The causes of mortality included refractory heart failure (n=4), septic shock (n=1), disseminated intravascular coagulation (n=1) and acute cardiac allograft rejection (n=2) (table 2).

NCM with CHD

In our cohort, 169 patients presented with isolated NCM, while 246 patients (50.3%) had CHD. The most common associated CHD was isolated patent ductus arteriosus or patent foramen ovale (PDA/PFO), occurring in 91 patients (21.9%). Isolated atrial septal defect (ASD) and ventricular septal defect (VSD) were observed in 29 (7.0%) and 37 (8.9%) patients, respectively. Complex CHD, comprising multiple cardiac anomalies, was identified in 76 patients (18.3%). These complex cases included various combinations of ASD, VSD, tetralogy of Fallot, double outlet right ventricle, transposition of the great arteries and functionally univentricular heart, among others (table 1, figure 1 and online supplemental figure S1).

Cardiac electrophysiology

ECG abnormalities were documented in 159 patients (61.7%). The most frequent cardiac conduction disturbance was complex heart block, affecting 69 patients (16.7%). AT was observed in 44 patients (10.7%), while VT occurred in 29 patients (4.1%). Age-stratified analysis revealed that cardiac arrhythmias were most prevalent in adults (>18 years; 67/97, 69.1%), followed by children and adolescents (1–18 years; 72/149, 48.3%), with the lowest frequency observed in infants (0–1 year; 20/169, 11.8%) (table 1).

NCM with valvular regurgitation

Valvular regurgitation was identified in 310 patients (74.7%) with NCM, while 105 patients (25.3%) demonstrated normal valvular function. Multiple valve regurgitation, affecting more than two valves, was the predominant pattern, observed in 162 patients (39.0%). The prevalence of multivalvular involvement was highest in adults (>18 years; 61/97, 62.9%), followed by children and adolescents (1–18 years; 55/149, 36.9%), with the lowest frequency in infants (0–1 year; 46/169, 27.3%) (table 1 and figure 2).

MR was the second most common valvular manifestation, affecting 75 patients (18.1%). Comparative analysis between patients with NCM with isolated MR and those without valvular regurgitation revealed significant differences in cardiac parameters. In infants (0–1 year), patients with isolated MR showed reduced LVEF (70.00 (65.00, 77.00)% vs 63.50 (40.00, 71.00)%, p=0.012) and fractional shortening (FS) (37.00 (33.00, 44.00)% vs 33.00 (18.50, 39.50)%, p=0.018). Additionally, significant chamber dilation was observed in LA diameter (18.60 (15.50, 21.00) vs 22.50 (19.00, 27.00) mm, p<0.001), LVES diameter (16.00 (12.50, 18.50) vs 21.00 (17.00, 27.10) mm, p<0.001) and LVED diameter (24.00 (20.10, 30.00) vs 32.50 (26.00, 36.00) mm, p<0.001) (online supplemental table S1, figure 3).

In the 1–18 years age group with isolated MR, similar patterns of ventricular dysfunction were observed, with decreased LVEF (70.00 (65.00, 77.00)% vs 63.50 (40.00, 71.00)%, p=0.012) and FS (37.00 (33.00, 44.00)% vs 33.00 (18.50, 39.50)%, p=0.018). Significant chamber enlargement was noted in LA diameter (18.60 (15.50, 21.00) vs 22.50 (19.00, 27.00) mm, p<0.001), LVES diameter (16.00 (12.50, 18.50) vs 21.00 (17.00, 27.10) mm, p<0.001) and LVED diameter (24.00 (20.10, 30.00) vs 32.50 (26.00, 36.00) mm, p<0.001) (online supplemental table S2, figure 3).

Adult patients (>18 years) with isolated MR demonstrated marked systolic dysfunction, with reduced LVEF (55.69±16.50% vs 37.59±13.34%, p=0.008) and FS (29.85±10.79% vs 17.82±7.75%, p=0.016). Significant ventricular dilation was evident in LVES diameter (30.00 (27.00, 40.00) vs 50.00 (43.00, 57.00) mm, p=0.003) and LVED diameter (50.00 (45.00, 52.00) vs 61.00 (57.00, 68.00) mm, p=0.002) (online supplemental table S3, figure 3).

Correlation analysis between MR area and cardiac parameters revealed age-specific patterns. In infants, MR area correlated significantly with chamber dimensions (LVED: r=0.434, p=0.008; LVES: r=0.404, p=0.015; LA: r=0.522, p=0.001) but not with systolic function parameters (LVEF: p=0.448; FS: p=0.365). In the paediatric group (1–18 years), strong correlations were observed with both structural (LVED: r=0.691, p<0.001; LVES: r=0.784, p<0.001; LA: r=0.894, p<0.001) and functional parameters (FS: r=0.584, p=0.004; LVEF: r=0.546, p<0.001). Notably, only this age group showed a significant correlation

Table 1 Demographics

	Overall (n=415)	0–1 year old (n=169)	1–18 years old (n=149)	>18 years old (n=97)	P value
Demography					
Male, n (%)	232 (55.9)	94 (55.6)	68 (45.6)	70 (72.2)	<0.001
Height (mean (SD))	87.00 (60.00, 155.50)	58.00 (52.00, 64.00)	101.00 (85.00, 133.00)	165.00 (161.00, 172.00)	<0.001
Weight (kg)	11.50 (5.40, 44.00)	5.00 (3.58, 6.00)	15.00 (11.00, 28.00)	56.50 (53.00, 64.00)	<0.001
Hospital stays (days)	9.00 (5.00, 15.50)	12.00 (7.00, 19.00)	8.00 (5.00, 13.00)	8.00 (5.00, 12.00)	0.001
NYHA, n (%)					<0.001
I	28 (6.7)	6 (3.6)	19 (12.8)	3 (3.1)	
II	223 (53.7)	96 (56.8)	84 (56.4)	43 (44.3)	
III	112 (27.0)	36 (21.3)	35 (23.5)	41 (42.3)	
IV	52 (12.5)	31 (18.3)	11 (7.4)	10 (10.3)	
SaO_2, (%)	97.29 (5.13)	96.99 (4.61)	97.33 (5.76)	97.73 (4.97)	0.525
Combined with valvular regurgitation, n (%)					
No valvular regurgitation	105 (25.3)	47 (27.8)	45 (30.2)	13 (13.4)	<0.001
MR	75 (18.1)	36 (21.3)	22 (14.8)	17 (17.5)	
TR	60 (14.5)	34 (20.1)	22 (14.8)	4 (4.1)	
AR	10 (2.4)	4 (2.4)	4 (2.7)	2 (2.1)	
PR	3 (0.7)	2 (1.2)	1 (0.7)	0 (0.0)	
Multiple valve regurgitation	162 (39.0)	46 (27.2)	55 (36.9)	61 (62.9)	
Combined with CHD, n (%)					<0.001
Isolated NCM	169 (40.7)	26 (15.4)	54 (36.2)	89 (91.8)	
PDA/PFO	91 (21.9)	51 (30.2)	35 (23.5)	5 (5.2)	
ASD	29 (7.0)	7 (4.1)	20 (13.4)	2 (2.1)	
VSD	37 (8.9)	22 (13.0)	15 (10.1)	0 (0.0)	
Multiple CHD	76 (18.3)	58 (34.3)	18 (12.1)	0 (0.0)	
Others	13 (3.1)	5 (3.0)	7 (4.7)	1 (1.0)	
Electrocardiograph					<0.001
Rhythm, n (%)					
SR	256 (61.7)	149 (88.2)	77 (51.7)	30 (30.9)	
AT	44 (10.7)	10 (5.9)	12 (8.2)	22 (22.7)	
VT	29 (7.0)	0 (0.0)	6 (4.1)	23 (23.7)	
Heart block	69 (16.7)	7 (4.1)	20 (27.4)	22 (22.7)	
Others	17 (4.1)	2 (1.8)	14 (9.4)	0 (0.0)	

Continued

Table 1 Continued

	Overall (n=415)	0–1 year old (n=169)	1–18 years old (n=149)	>18 years old (n=97)	P value
QRS duration (ms)	81.00 (65.00, 100.00)	66.00 (60.00, 78.00)	84.00 (70.00, 100.00)	103.00 (94.00, 122.00)	<0.001
PR duration (ms)	128.00 (112.00, 154.00)	120.00 (102.00, 126.00)	130.00 (115.00, 156.00)	160.00 (142.00, 176.00)	<0.001
QT (ms)	314.00 (271.00, 377.00)	276.00 (244.00, 294.00)	336.00 (290.00, 376.00)	400.00 (367.00, 426.00)	<0.001
QRS axis (°)	62.00 (11.00, 89.50)	70.00 (23.00, 98.00)	68.00 (14.00, 92.00)	36.00 (–7.00, 75.00)	0.005
QTc (ms)	431.00 (400.50, 461.50)	418.00 (396.00, 453.00)	431.00 (402.00, 463.00)	448.00 (422.00, 471.00)	0.009
Laboratory examination					
TnT (pg/mL)	44.60 (9.80, 114.00)	57.30 (10.80, 105.70)	61.80 (9.80, 565.00)	19.40 (9.10, 52.10)	0.002
NT-proBNP (pg/mL)	1746.00 (116.10, 5034.50)	3584.00 (1200.00, 15 466.00)	344.00 (33.50, 3485.00)	1062.00 (117.80, 3581.00)	<0.001
CK (U/L)	100.00 (68.50, 168.50)	123.00 (79.00, 241.00)	103.00 (71.00, 147.00)	77.00 (54.00, 103.00)	0.041
CKMB (U/L)	18.60 (11.05, 27.75)	24.10 (18.10, 33.90)	18.20 (11.40, 26.10)	10.50 (8.90, 12.40)	0.001
LDH (U/L)	276.00 (206.50, 347.00)	320.00 (275.00, 396.00)	267.00 (216.00, 345.00)	180.00 (153.00, 229.00)	0.003
INR	1.10 (1.02, 1.22)	1.11 (1.04, 1.26)	1.10 (1.02, 1.19)	1.07 (1.01, 1.18)	0.255
NCM location (%)					<0.001
LVNCM	316 (76.1)	120 (71.0)	102 (68.5)	94 (96.9)	
RVNCM	33 (8.0)	19 (11.2)	12 (8.1)	2 (2.1)	
BVNCM	66 (15.9)	30 (17.8)	35 (23.5)	1 (1.0)	
Echocardiograph					
LA diameter (mm)	26.00 (20.00, 35.00)	20.00 (16.00, 24.00)	29.00 (23.70, 34.00)	40.00 (32.00, 46.00)	<0.001
RA diameter (mm)	23.00 (17.00, 39.50)	17.00 (15.00, 20.00)	25.00 (22.00, 33.00)	48.00 (42.00, 55.00)	<0.001
MR area (cm^2)	0.79 (0.00, 2.55)	0.20 (0.00, 1.00)	0.70 (0.00, 2.70)	3.00 (1.00, 9.60)	<0.001
TR area (cm^2)	0.60 (0.00, 1.70)	0.20 (0.00, 0.90)	0.80 (0.00, 2.00)	1.50 (0.00, 4.00)	<0.001
AR area (cm^2)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 1.30)	<0.001
LVEF (%)	64.00 (38.00, 71.00)	69.00 (50.00, 77.00)	66.00 (52.00, 71.00)	37.00 (29.00, 51.00)	<0.001
FS (%)	33.00 (19.00, 39.00)	37.00 (25.00, 43.00)	36.00 (27.00, 39.00)	19.00 (13.00, 25.00)	<0.001
LVED diameter (mm)	36.00 (27.00, 50.00)	27.00 (21.00, 32.00)	37.00 (32.00, 45.00)	61.00 (53.00, 69.00)	<0.001
LVES diameter (mm)	23.90 (17.00, 36.00)	17.00 (13.00, 22.00)	24.00 (20.00, 32.00)	50.00 (39.00, 57.00)	<0.001
RV diameter (mm)	23.00 (17.00, 44.00)	16.00 (14.00, 19.00)	25.00 (21.00, 33.00)	57.00 (49.00, 62.00)	<0.001

Data are count (%), mean (SD), or median [25th–75th percentiles]
AR, aortic regurgitation; ASD, atrial septal defect; AT, atrial tachycardia; BVNCM, biventricular noncompaction cardiomyopathy; CHD, congenital heart disease; CK, creatine kinase; CKMB, creatine kinase isoenzyme; FS, left ventricular fractional shortening; INR, international normalized ratio; LA, left atrial; LDH, lactic dehydrogenase; LVED, left ventricular end-diastolic; LVEF, left ventricular ejection fraction; LVES, left ventricular end-systolic; LVNCM, left ventricular noncompaction cardiomyopathy; MR, mitral regurgitation; N-BNP, N-terminal pro-B-type natriuretic peptide; NCM, noncompaction cardiomyopathy; NYHA, New York Heart Association functional classification; PDA, patent ductus arteriosus; PFO, patent foramen oval; PR, Pulmonary regurgitation; RA, right atrium; RV, right ventricular; RVNCM, right ventricular noncompaction cardiomyopathy; SaO2, arterial oxygen saturation; SR, sinus rhythm; TnT, troponin T; TR, tricuspid regurgitation; VSD, ventricular septal defect; VT, ventricular tachycardia.

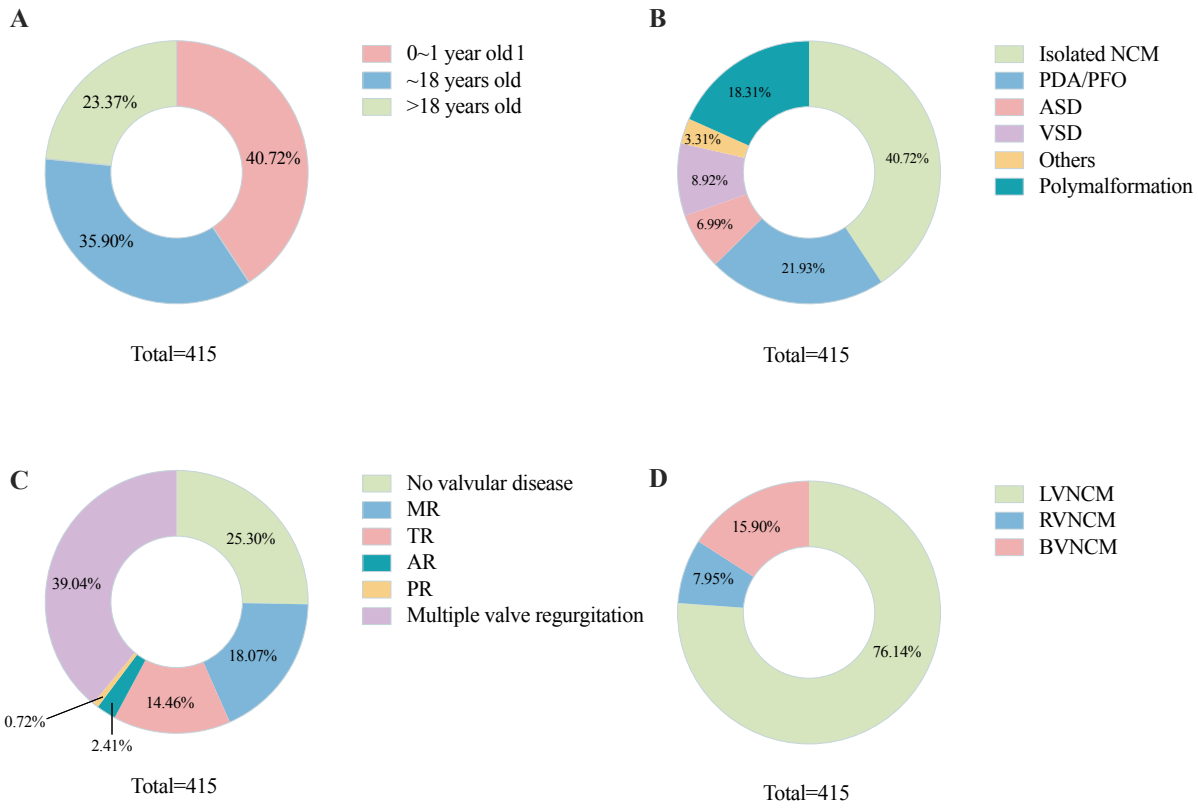

Figure 1 Patient population and demographics. (A) The proportion of patients' age. (B) The proportion of patients with NCM with congenital heart disease. ASD, atrial septal defect; PDA/PFO, patent ductus arteriosus/patent foramen ovale; VSD, ventricular septal defect. (C) The proportion of patients with NCM with valvular heart disease. AR, aortic regurgitation; MR, mitral regurgitation; PR, pulmonary regurgitation; TR, tricuspid regurgitation. (D) The proportion of NCM location. BVNCM, biventricular non-compaction cardiomyopathy; LVNCM, left ventricular non-compaction cardiomyopathy; RVNCM, right ventricular non-compaction cardiomyopathy.

Table 2 The main clinical presentation of patients with NCM

Clinical presentation, n (%)	Overall (n=415)	0–1 year old (n=169)	1–18 years old (n=149)	>18 years old (n=97)
Asymptomatic	43 (10.4)	22 (13.0)	17 (11.4)	4 (4.1)
Newborn with severe malformation	21 (5.1)	21 (12.4)	0 (0.0)	0 (0.0)
Heart failure	112 (27.0)	33 (19.5)	26 (17.4)	53 (54.6)
Palpitation/Abnormal ECG	29 (7.0)	2 (1.2)	14 (9.4)	13 (13.4)
Murmur	102 (24.6)	42 (24.9)	57 (38.3)	3 (3.1)
Cardiomegaly on chest radiograph	10 (2.4)	3 (1.8)	7 (4.7)	0 (0.0)
Dizziness/Syncope	18 (4.3)	0 (0.0)	10 (6.7)	8 (8.2)
Pulmonary infection	56 (13.5)	38 (22.5)	13 (8.7)	5 (5.2)
Chest pain	11 (2.7)	0 (0.0)	2 (1.3)	9 (9.3)
Failure to thrive	5 (1.2)	5 (3.0)	0 (0.0)	0 (0.0)
Others	8 (1.9)	3 (1.8)	3 (2.0)	2 (2.1)

NCM, non-compaction cardiomyopathy.

between MR area and NC ratio (r=−0.441, p<0.04). In adults, MR area correlated with chamber dimensions (LVED: r=0.512, p=0.035; LVES: r=0.508, p=0.037; LA: r=0.748, p<0.001) but not with LVEF (p=0.448) (table 3).

Isolated tricuspid regurgitation (TR) was observed in 60 patients (14.5%). Among patients with isolated TR, significant right heart enlargement was documented only in infants, with increased RV diameter (16.00 (13.00,

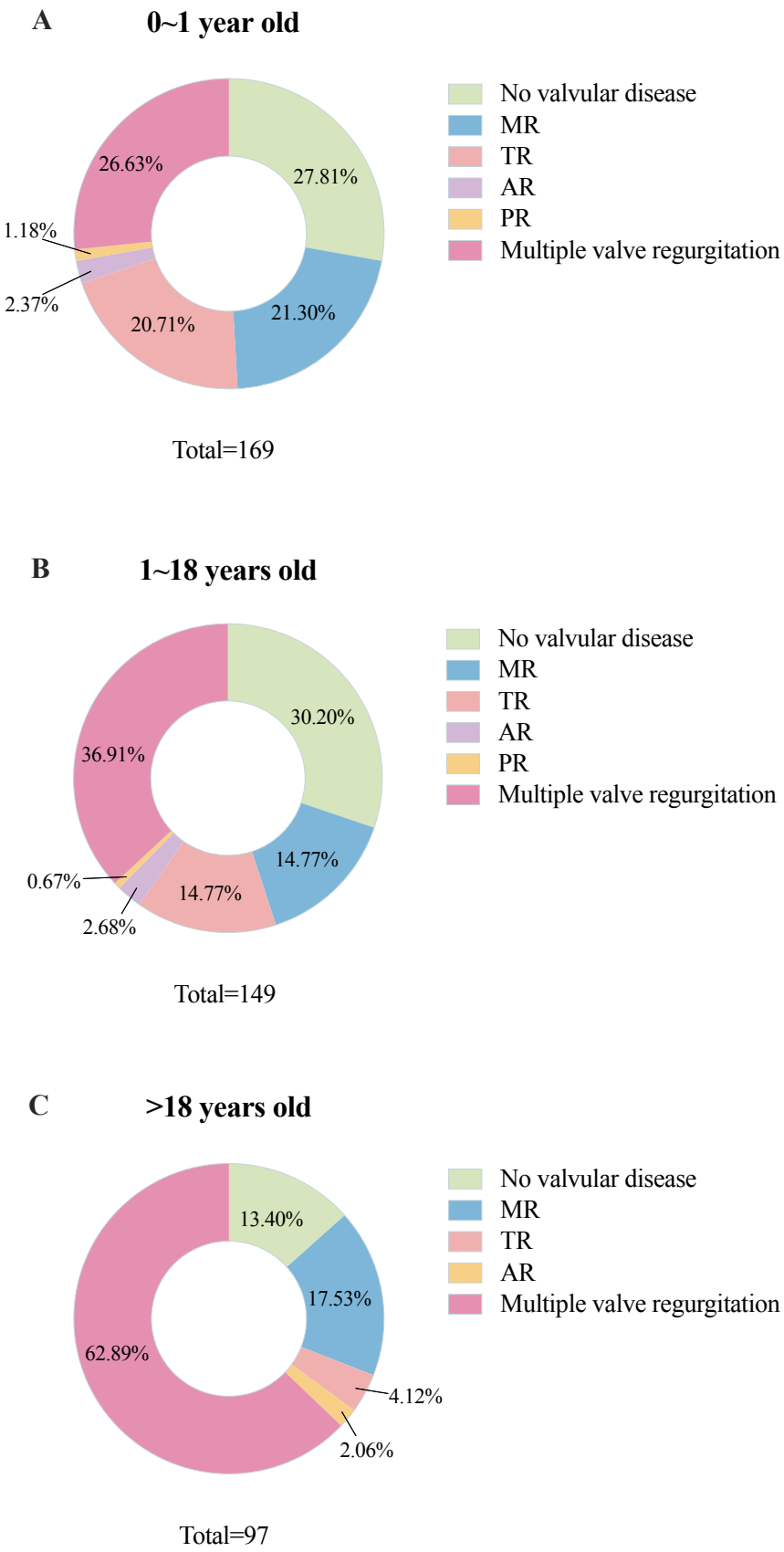

Figure 2 The proportion of patients with non-compaction cardiomyopathy with valvular heart disease in different age groups. AR, aortic regurgitation; MR, mitral regurgitation; PR, pulmonary regurgitation; TR, tricuspid regurgitation.

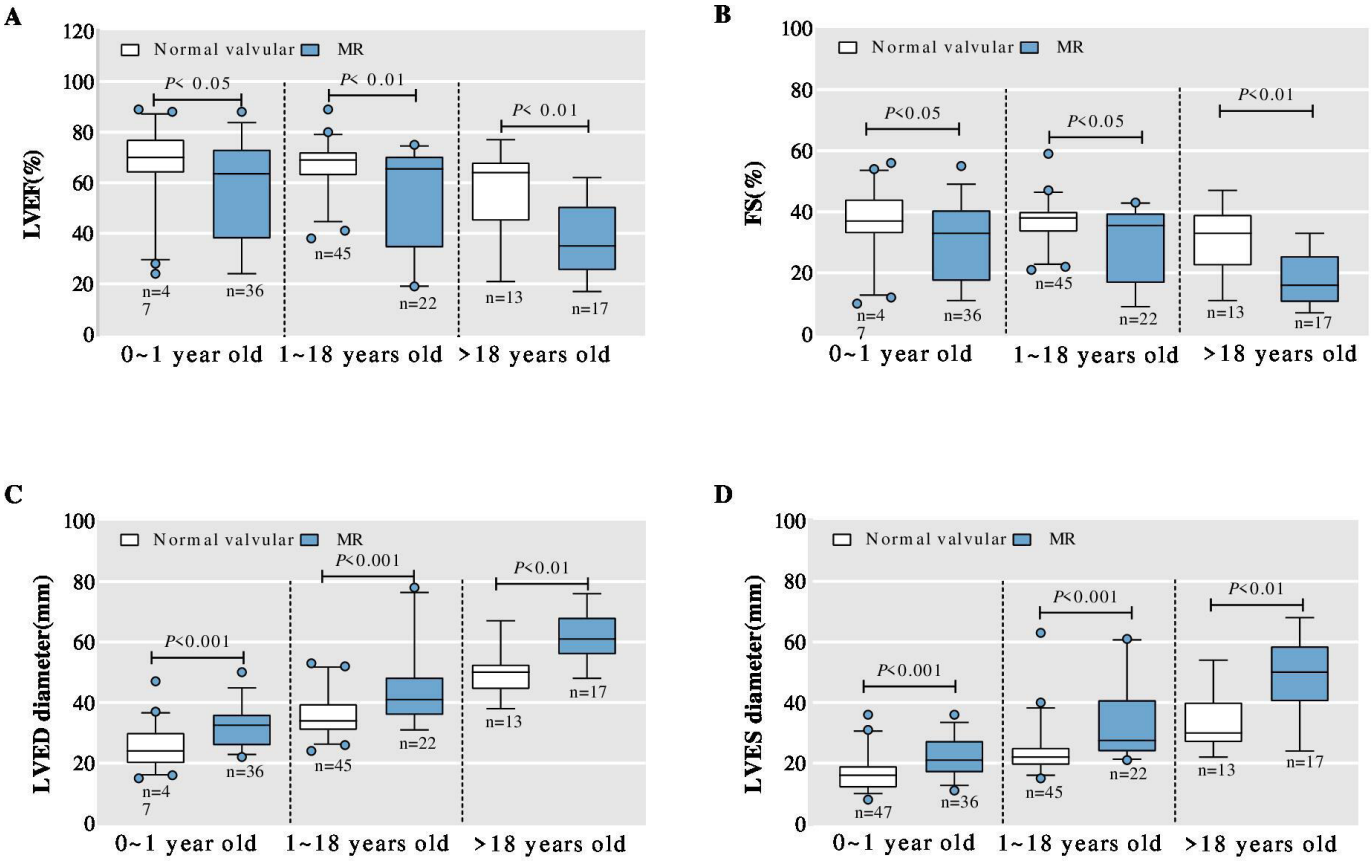

Figure 3 Comparison of left heart function and size between patients with mitral regurgitation and patients without valvular disease across different age groups. (A) Left ventricular ejection fraction (LVEF) comparison. (B) Fractional shortening (FS) comparison. (C) Left ventricular end-diastolic (LVED) diameter comparison. (D) Left ventricular end-systolic (LVES) diameter comparison. MR, mitral regurgitation. White boxes represent patients without valvular disease; blue boxes represent patients with MR. P values indicate statistical significance between groups.

18.00) vs 18.00 (16.00, 21.75) mm, p=0.005) and right atrium diameter (16.00 (14.00, 19.00) vs 19.00 (16.00, 22.00) mm, p=0.005). No significant differences were observed in other age groups (online supplemental table S1 and figure S2).

DISCUSSIONS

We conducted a single-centre, retrospective, observational study encompassing 419 patients to characterise the clinical manifestations of NCM across different age groups. The fundamental nature of NCM—whether

Table 3 Correlation analysis of left ventricular echocardiography parameters and MR area in patients with NCM with MR alone

	MR area (cm^2)					
	0–1 year old (n=36)		1–18 years old (n=22)		>18 years old (n=17)	
	r	P value	r	P value	r	P value
LVEF (%)	−0.130	0.448	−0.546	**0.009**	−0.479	0.052
FS (%)	−0.156	0.365	−0.584	**0.004**	−0.498	**0.042**
LVED diameter (mm)	0.434	**0.008**	0.691	**<0.001**	0.512	**0.035**
LVES diameter (mm)	0.404	**0.013**	0.784	**<0.001**	0.508	**0.037**
LA diameter (mm)	0.522	**0.001**	0.894	**<0.001**	0.748	**<0.001**
NC/C	−0.004	0.980	−0.441	**0.040**	−0.047	0.856

p values less than 0.05 are shown in bold
FS, fractional shortening; LA, left atrial; LVED, left ventricular end-diastolic; LVEF, left ventricular ejection fraction; LVES, left ventricular end-systolic; MR, mitral regurgitation; NC/C, non-compaction myocardium thickness/compaction myocardium thickness.

it represents a congenital or acquired condition—remains controversial in contemporary cardiovascular medicine. Several paediatric studies have provided compelling evidence supporting the congenital origin of NCM.[8 9] However, contrasting with these paediatric findings, a significant proportion of adult cases in various investigations have demonstrated the emergence of NCM later in life.[5] This temporal heterogeneity in presentation has sparked considerable debate, leading some researchers to propose that NCM may manifest through both congenital and acquired pathways.[1 10] Specifically, congenital NCM typically presents during childhood, whereas acquired NCM predominantly affects the adult population.[10] The age-dependent variations in clinical complications and manifestations underscore the critical role of age in shaping the disease phenotype. Therefore, our investigation employed systematic age-based stratification to elucidate distinct patterns of clinical features across different age groups.

Clinical symptom

Heart failure consistently emerges as the predominant clinical manifestation in patients with NCM across various studies, aligning with our findings.[1 6 11] The extensive paediatric cohort study by Waning *et al* reported heart failure as the most prevalent manifestation (27%).[11] Interestingly, our study revealed that among patients under 18 years, heart murmur was the most common presentation (31.1%), with heart failure being least common (18.6%). This divergence likely reflects our centre's high proportion of patients with NCM with left-to-right shunt CHD, which typically presents with heart murmurs. In adults, while Waning *et al* identified arrhythmia as the predominant symptom (26%), our study found heart failure most prevalent (54.6%).[11] Thromboembolism is traditionally considered to be one of the three major clinical symptoms in patients with NCM,[1 10] but in our study, thromboembolism occurred in very few patients, and only in adult patients. In other relevant studies, the proportion of thromboembolism in patients with NCM was also low.[7 11]

Congenital heart disease

The European Society of Cardiology classifies NCM as an unclassified hereditary cardiomyopathy, distinguishing between isolated NCM and NCM with concomitant congenital heart disease.[12] NCM manifests as left ventricular, right ventricular or biventricular involvement, with left ventricular type predominating and isolated right ventricular involvement being rare.[12 13] Our study revealed frequent NCM occurrence with left-to-right shunt congenital heart disease, consistent with previous findings.[14–16] In this study, most patients with left-to-right shunt congenital heart disease combined with left heart volume overload were found, which was similar to the results of previous studies.[16 17] Isolated NCM showed higher prevalence in patients aged >1 year, with PDA/PFO being the most common concurrent congenital heart disease. Notably, 34.3% of infants exhibited multiple congenital heart defects, possibly reflecting earlier hospital presentation due to more severe clinical manifestations.

Arrhythmia

The characteristic deep recessions in NCM may facilitate Purkinje fibre infiltration into the myocardium, potentially causing irregular depolarisation and delayed repolarisation, leading to arrhythmias.[18] Previous studies indicate arrhythmias in over 50% of patients with NCM.[18–20] Our findings showed similar prevalence in patients >1 year of age, while infants demonstrated a notably lower occurrence (11.8%), possibly reflecting their immature cardiac conduction system. Patients with NCM exhibit various arrhythmias, including ventricular premature beats, AV block, bundle branch block and atrial fibrillation, often with multiple types coexisting.[21 22] While previous studies emphasised ventricular arrhythmias,[18 22] we found atrial arrhythmias predominant in children and adolescents, with ventricular arrhythmias slightly more common in adults.

Valvular regurgitation

Recent attention has focused on valvular regurgitation in NCM. While valvular disease generally increases with age,[23] our study showed comparable prevalence between infant and paediatric groups, suggesting age may not strongly correlate with valvular disease in younger patients with NCM. MR emerged as the most prevalent valvular condition, consistent with previous reports.[4 11 20] Zou *et al* demonstrated strong associations between MR and impaired left ventricular function with geometric remodelling,[4] while Gao *et al* identified increased adverse events in patients with NCM with left ventricular dilation.[13] Our analysis confirmed that patients with NCM with MR across all age groups showed significantly impaired left heart function and increased chamber size. This may reflect ventricular remodelling affecting mitral valve mechanics[24] and increased left heart volume load.[25] Regarding TR, right heart enlargement was observed only in infants, primarily attributed to tricuspid valve deformity.

Limitation

This study has several important limitations that merit consideration. First, its retrospective design inherently introduces potential biases and necessitates cautious interpretation of the findings. Second, our investigation did not address therapeutic interventions in patients with NCM, primarily due to the current absence of standardised treatment protocols for this condition. The lack of consensus regarding optimal management strategies for patients with NCM limited our ability to evaluate treatment outcomes systematically.

CONCLUSION

Our analysis of 415 NCM cases demonstrated distinct age-dependent clinical patterns, highlighting the importance

of age-specific approaches in both clinical management and research. Notably, patients with mitral regurgitation consistently exhibited left ventricular dilation and systolic dysfunction across all age groups. These findings enhance our understanding of NCM's clinical spectrum and provide a foundation for age-specific therapeutic strategies in NCM management.

Contributors JC, ZZ and MQ conceived and designed the study. ZZ, MQ and SW established the study protocol. YL, LH and ZZ were responsible for data collection. MT, XL and JT performed the literature search. ZZ, MQ and RZ conducted data analysis and statistical interpretation. ZZ and SZ wrote the initial draft of the manuscript. RZ made substantial contributions to data verification and manuscript revision. All authors reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work. All authors had full access to all the data in the study and shared final responsibility for the decision to submit for publication. ZZ, MQ and RZ contributed equally to this work as co-first authors. ZZ is the guarantor of this work, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study was approved by the Medical Ethics Committee of Guangdong Provincial People's Hospital (No. GDREC2019338H(R2)). This is a retrospective study. The requirement for informed consent was waived due to the retrospective nature of the study. All patient data were anonymised and de-identified prior to analysis. This waiver was approved by the institutional ethics committee.

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