Isolated left ventricular apical hypoplasia: Review and analysis of the 37 cases reported so far

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Abstract

BACKGROUND
Isolated left ventricular apical hypoplasia (ILVAH), also known as truncated left ventricle (LV), is a very unusual cardiomyopathy which can be easily detected on echocardiography. It is characterised by a truncated, spherical, and non-apex forming LV. The true apex is occupied by the right ventricle. Due to the rarity of the disease, just a few case reports and limited case series have been published in the field. This review aims at analysing the so far 37 reported ILVAH cases worldwide. Age at diagnosis, gender prevalence, clinical presentation, electrocardiographic features, imaging (ultrasounds, and cardiac MRI) appearance, associated cardiac abnormalities, therapy, and outcome are here analysed to help clinicians in the difficult management of this extremely rare congenital heart disease.

AIM
See above

METHODS
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RESULTS
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CONCLUSION
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INTRODUCTION
Isolated LV apical hypoplasia (ILVAH) is an extremely rare and unclassified cardiomyopathy that has been recognized as a distinct entity since 2004 [3]. ILVAH is also known as truncated left ventricle (LV) It is a very unusual cardiomyopathy which can be easily detected on echocardiography. It is characterised by a truncated, spherical, and non-apex forming LV with some degree of systolic dysfunction [3]. The true apex is occupied by the right ventricle, which wraps around the distal LV and whose systolic function is usually normal [2]. ILVAH is usually not accompanied by other abnormalities [3]. Its diagnosis is often refined by means of CT or cardiac MRI [4]. Clinical presentation varies a lot, ranging from the lack of symptoms to fatigue, breathlessness, palpitations, chest pain, syncope [5,6]. The death of an adolescent patient was reported in literature. He suffered from arrhythmia with fulminating cardiac insufficiency and non-responsive to therapy pulmonary hypertension [7].

Due to the rarity of the disease, just a few case reports and limited case series have been published in the field.

The aims of this paper is making a literature review concerning to so far reported cases of ILVAH with related features and outcomes.

MATERIALS AND METHODS
Search strategy
The electronic database PubMed was investigated from its establishment up to December 13th 2022. The MeSH (Medical Subject Headings) search terms were “case report” and/or “case series” and/or “isolated left ventricular
hypoplasia” and/or “truncated left ventricle”. We excluded any animal studies, and papers with language other than English.

**Study Selection.** The authors separately looked into the selected abstracts and evaluated whether they were eligible. Full-texts were checked when all the reviewers of the abstracts felt that the latter might match the inclusion criteria.

**Data Extraction.** Information from the selected single case reports and case series were taken. The reported points were: age at diagnosis, gender, clinical presentation, electrocardiographic features, imaging (ultrasounds and cardiac MRI), associated cardiac abnormalities, therapy, and outcome.

**Data presentation.** Data were presented in the form of mean+/−SD. Chi square test and Mann-Whitney U test were used to check statistical significance when needed. Statistical significance was set to p<0.05.

**RESULTS**

**Results.** Overall, 4,427 potential single case reports of ILVAH/truncated left ventricle were detected on the PubMed. Twenty were duplicates. Other 4,378 papers were excluded after checking the abstract. The remaining 29 manuscripts were used for analysis of the patients’ features and disease outcome (**Table 1**).

The majority of cases reported occurred in males (54%; male-to-female ratio 1.25/1). Mean age at diagnosis was 26.8+/−19.9 years; range 3 mo-66 years). For male patients the mean age at diagnosis was 27.9+/−22.2 years, whereas female patients were slightly younger (26.3+/−17.6 years) at diagnosis. This difference was not statistically significant. More than a third of the patients were asymptomatic (37.8%). The most usual clinical presentation was breathlessness (40.5%). There are no statistically significant differences between genders in terms of symptoms/absence of symptoms. The most commonly detected ECG changes were T wave abnormalities (33.3%) and right axis deviation with poor R wave progression (30.3%). Atrial fibrillation/flutter was detected in 18.9%. Echocardiography was performed in 97.3% of cases and cardiac MRI in 91.9% of cases.
Ejection fraction was reduced in more than a half of patients (55.5%). An associated congenital heart disease was found in 16.2%, most of all in the form of patency of ductus arteriosus with or without pulmonary hypertension. Heart failure therapy was administered in 37.8% of patients. The outcome was favorable in the vast majority of patients, with just one death.

The results of the review are summarised in Table 2.

**DISCUSSION**

From the case series analysis, there is a slight prevalence of ILVAH in males, though the disease is quite equally distributed between genders. The age of diagnosis is extremely variable, ranging from infancy to elderly. ILVAH is easily detected by echocardiography and diagnosis is confirmed by cardiac MRI (**Figures 1 and 2**).

On cardiac MRI the established features of ILVAH are four, namely: (1) a truncated and spherical LV shape with systolic and/or diastolic functions which are often impaired and rightward bulging of the interventricular septum in diastole; (2) defective LV apex with adipose tissue infiltrating it; (3) anomalous origin of the papillary muscles in the flattened LV apex; (4) elongation of the right ventricle wrapping around the deficient LV apex. In this report, we demonstrate these characteristic features with cardiac magnetic resonance imaging and summarize the existing information on Isolated LV apical hypoplasia [5].

Differential diagnosis includes:

a) hypoplastic left heart syndrome, which is characterised by underdevelopment of the aortic valve and artery, and **the whole LV** [30]. Mitral valve is stenotic or atretic in most of the cases [31];

b) LV non-compaction, resulting from interrupted **endomyocardial morphogenesis** leading to LV dysfunction. It is characterised by a diffusely enlarged LV with a
markedly trabeculated endocardium ("spongy" appearance) [32]. Interestingly, in Table 1, a patient with a unique combination on ILVAH and LV non-compaction is reported; c) congenital LV aneurysm, which is an idiopathic anomaly of the endocardial and myocardial layers, and LV diverticulum, belonging to a syndrome with multiple defects. However, LV is elongated rather than truncated with involvement of the papillary muscles and surrounding myocardium (as opposed to isolated apical involvement). These conditions are usually deadly early in life owing to associated intracardiac and extracardiac abnormalities [33,34]; d) congenital LV dysplasia with or without right ventricular dysplasia. On cardiac MRI, at tissue characterisation, diffuse transmural fibrofatty replacement is noted, whereas in ILVAH it is predominantly apical [35,36].

Of note, isolated dysplasia can also involve just the right ventricle, with lack of trabeculated apex [37].

The clinical course of ILVAH is variable. It can be benign, but complications, such as heart failure, supraventricular and ventricular arrhythmias, and pulmonary hypertension, have been described even in young patients [2,7,8]. Only one death has been reported so far [7].

A possible association with patency of ductus arteriosus is suggested by the analysis of the cases reported in this review.

ILVAH embryonic aetiology is purely speculative. However, in an article written not in English, and as such not included in the present analysis, a mutation of the lamin A/C gene (p.Arg644Cys) responsible for dilated cardiomyopathy was found associated to the disease [38].

**CONCLUSION**

On balance, the Authors hope that more cases may be published in the field to increase scientific knowledge on ILVAH. The latter is a multifaceted entity with a so far unpredictable course, ranging from benign until the elderly to sudden death during adolescence.
ARTICLE HIGHLIGHTS

Research background
Isolated left ventricular hypoplasia is an extremely rare form of cardiomyopathy

Research motivation
We aimed at shedding light on the disease outcome

Research objectives
The aims of this paper is making a literature review about to so far reported cases of isolated left ventricular apical hypoplasia with related features and outcomes.

Research methods
A literature review was carried out. The electronic database PubMed was investigated from its establishment up to December 13th 2022.

Research results
From the initial 4,427 papers, 29 manuscripts were selected

Research conclusions
The most usual clinical presentation was breathlessness (40.5%). There are no statistically significant differences between genders in terms of symptoms/absence of symptoms. The most commonly detected ECG changes were T wave abnormalities (33.3%) and right axis deviation with poor R wave progression (30.3%). Atrial fibrillation/flutter was detected in 18.9%. Echocardiography was performed in 97.3% of cases and cardiac MRI in 91.9% of cases. Ejection fraction was reduced in more than a half of patients (55.5%). An associated congenital heart disease was found in 16.2%, most of all in the form of patency of ductus arteriosus with or without pulmonary
hypertension. Heart failure therapy was administered in 37.8% of patients. The outcome was favorable in the vast majority of patients, with just one death.

Research perspectives
The search strategy will be repeated after 10 years
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