(CASE REPORT)

Left Bundle Branch Block Cardiomyopathy in an octogenarian: 4Dimensional XStrain Echocardiography assessment and review of literature

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Abstract

Left bundle branch block (LBBB) is generally associated with a poorer prognosis in comparison to normal intraventricular conduction. LBBB may be the first manifestation of a more diffuse myocardial disease. The typical surface ECG feature of LBBB is a prolongation of QRS above 0.11s in combination with a delay of the intrinsic deflection in leads V5 and V6 of more than 60 ms and no septal q waves in leads I, V5, and V6 due to the abnormal septal activation from right to left. LBBB may induce abnormalities in left ventricular performance due to abnormal asynchronous contraction patterns. Asynchronous electrical activation of the ventricles causes regional differences in workload which may lead to asymmetric hypertrophy and left ventricular dilatation, especially due to increased wall mass in late-activated regions, which may aggravate preexisting left ventricular pumping performance or even induce it.

In left bundle branch block (LBBB), the ventricles are activated in a sequential manner with alterations in left ventricular mechanics, perfusion, and workload resulting in cardiac remodeling. Underlying molecular, cellular, and interstitial changes manifest clinically as changes in size, mass, geometry, and function of the heart. Cardiac remodeling is associated with progressive ventricular dysfunction, arrhythmias, and impaired prognosis. Clinical and diagnostic notions about LBBB have evolved from a simple electrocardiographic alteration to a critically important finding affecting diagnostic and clinical management of many patients. Advances in cardiac magnetic resonance imaging have significantly improved the assessment of patients with LBBB and provided additional insights into pathophysiological mechanisms of left ventricular remodeling. We are presenting an interesting case report of LBBB cardiomyopathy in an octogenarian adult who was referred to us for detailed color echocardiographic assessment.

Keywords: LBBB; Left bundle branch block cardiomyopathy; Systolic dysfunction; Dyssynchrony cardiomyopathy

1. Introduction

1.1. LBBB-ECG criteria

The American Heart Association (AHA), American College of Cardiology Foundation (ACCF), and Heart Rhythm Society (HRS) recommended an updated set of definitions for cardiac conduction disturbances in 2009 and 2018 [1, 2]. Strauss et al [3] then proposed more stringent criteria for LBBB to better predict cardiac resynchronization therapy (CRT) responders. This was motivated by the observation that patients with true LBBB—as opposed to those with conduction delay—were more likely to have more pronounced QRS durations with evidence of slurring and notching. Table 1 compares and contrasts the electrocardiographic criteria defining LBBB.

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Table 1 ECG criteria to define complete LBBB in adults

| Electrocardiographic Criterion	AHA/ACCF/HRS [2]	Strauss et al [3]
QRS duration	>120 ms	>140 ms (men), >130 ms (women)
Left-sided leads (l, aVL, V5, V6)	Broad notched or slurred R waves	Broad notched or slurred R waves*
	Absent Q waves (with possible exception of aVL)	
	Occasional RS pattern in V5 and V6	
Right-sided leads (V1, V2, V3)	Small initial r waves in V1-3	Broad notched or slurred mid-QRS*
		QS or rS in leads V1 and V2
R peak time	>60 ms in V5 and V6 but can be normal in V1-3	Not specifically mentioned
ST and T waves	Usually opposite in direction to QRS	Not specifically mentioned
	Positive concordance (upright T wave with upright QRS) may be observed	

ACCF indicates American College of Cardiology Foundation; AHA, American Heart Association; HRS, Heart Rhythm Society; and LBBB, left bundle branch block.

*$\geq$2 leads (I, aVL, V_1, V_2, V_5, V_6).

Anatomy of the cardiac conduction system, left bundle branch (LBB), LBBB and the ECG criteria are exhibited in Figures 1-5.
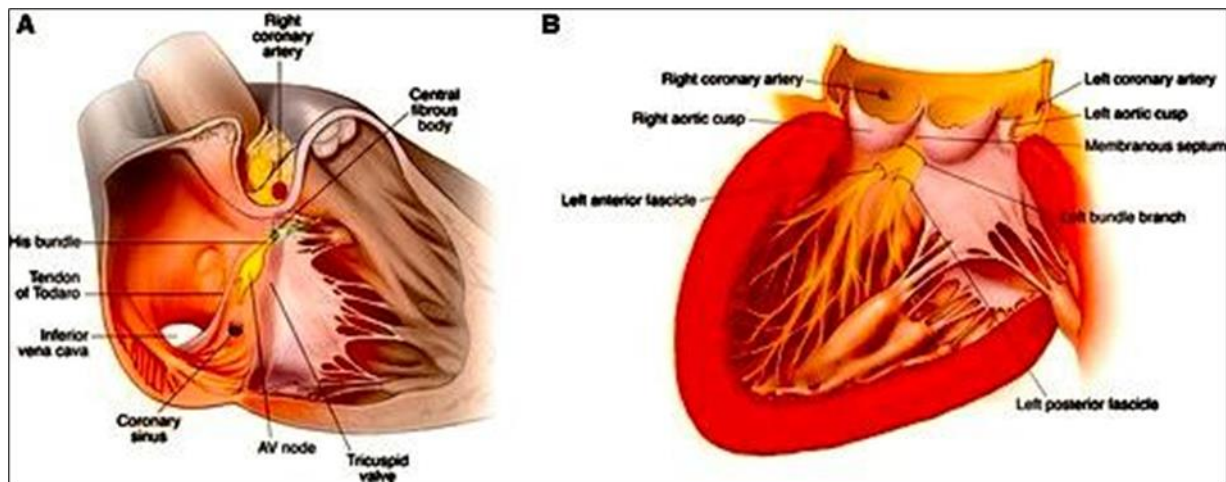
Figure 1 Anatomy of the cardiac conduction system and its relation to surrounding structures
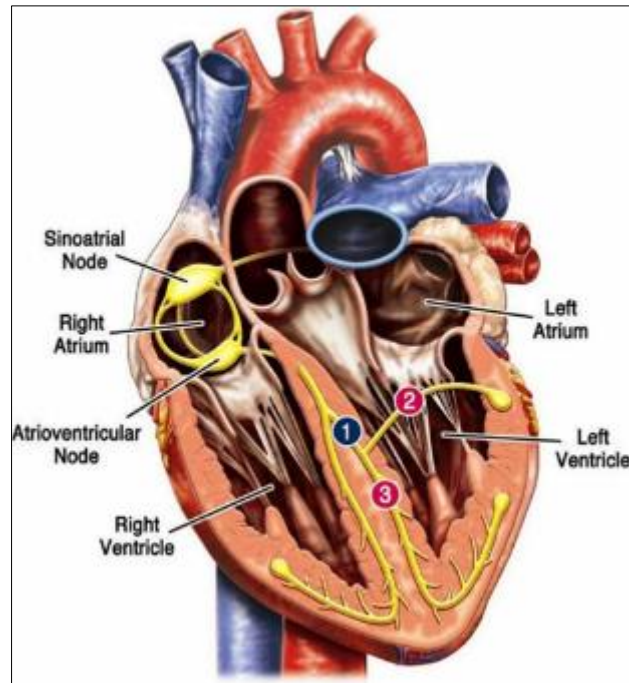
Figure 2 Anatomy of LBB The left bundle branch comprises the main left bundle and distal anterior and posterior fascicles. LBBB from an incident disease requires a lesion just distal to the bundle of His (1) or extensive myocardial damage involving a large portion of the distal conduction system, including both the fascicles (2 and 3)
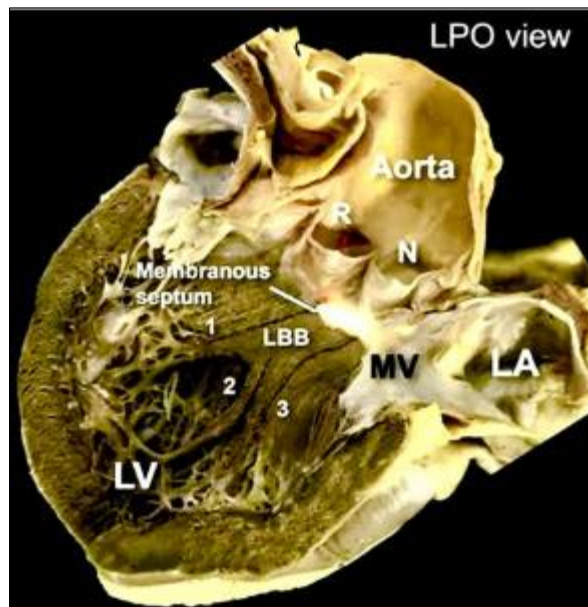
Figure 3 4D tracking of the anatomy of the LBB The Left Posterior Oblique (LPO) view shows the trans illuminated membranous septum located inferior to the interleaflet triangle between the right (R) and noncoronary (N) sinus of the aortic valve. Note that we have highlighted in dark color the limits of the endocardial position of the left bundle branch (LBB) of His and its 3 fascicles, the left anterior fascicle (1), the left septal or middle fascicle (2), and the left posterior fascicle (3). LPO ¼ left posterior oblique
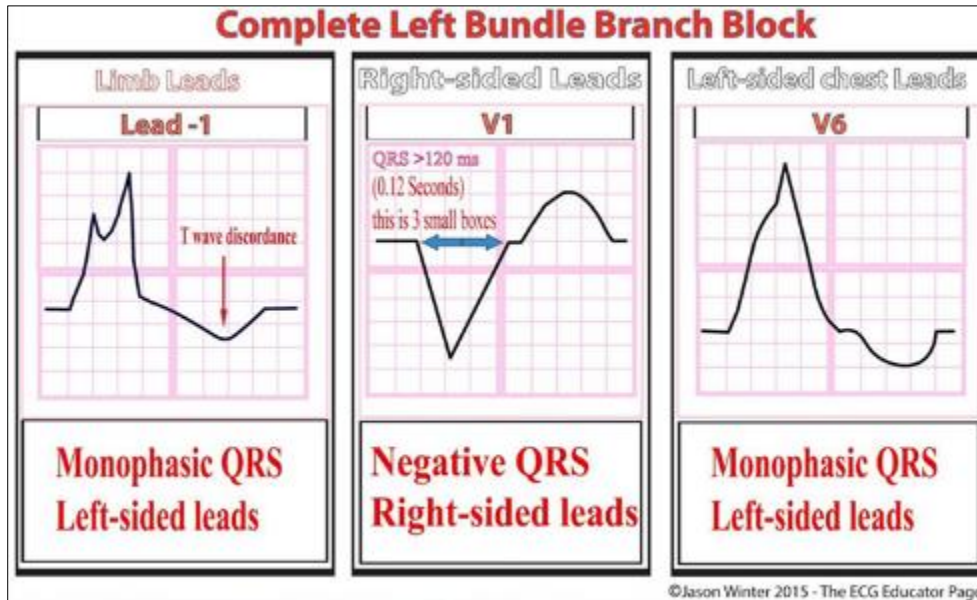
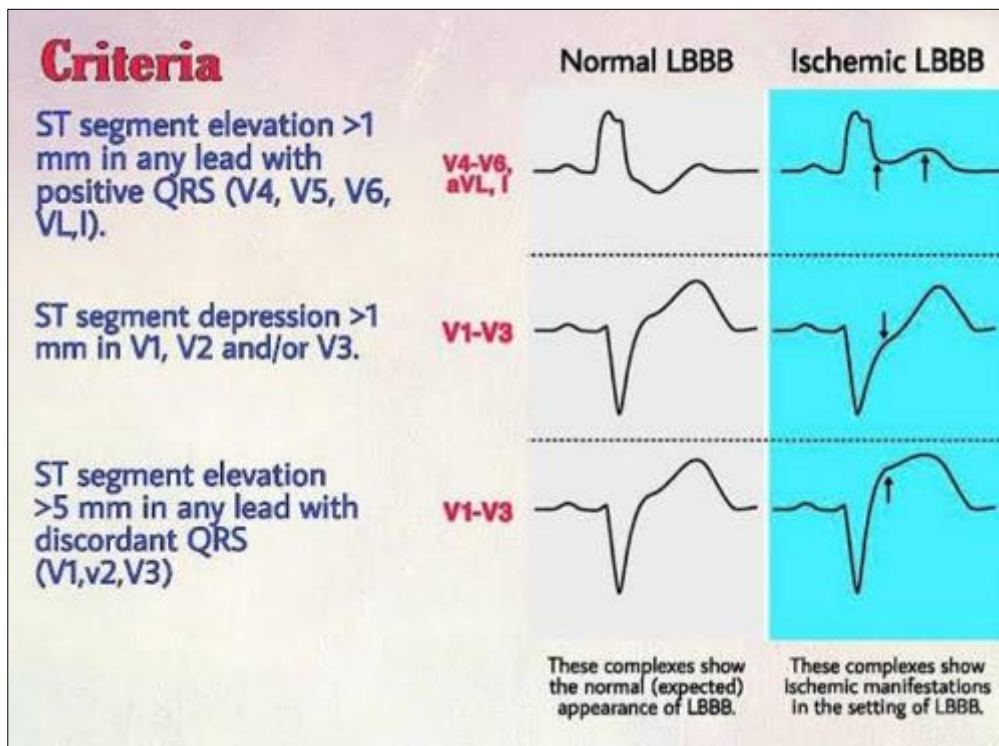**Figure 4** Diagramatic representation of the ECG criteria of LBBB

Figure 5 Diagramatic representation of ECG manifestations of ischemia on LBBB.

The prevalence of left bundle branch block (LBBB) in the general population ranges from approximately 0.1% to 1.0%, the incidence increasing with age [4-6]. LBBB is strongly associated with structural heart and/or coronary artery disease [4, 6-8]. Patients with a newly recognized LBBB are at increased risk of cardiovascular events including heart failure, myocardial infarction, and sudden death [4, 7]. The evaluation of patients with incidental, newly recognized LBBB therefore, necessitates assessments for structural heart disease and coronary artery disease (CAD) in appropriate candidates [2]. Clinical and experimental data support that dyssynchronous left ventricular (LV) contraction (ie, early septal activation with delayed lateral wall contraction) itself may lead to a decline in LV systolic function [9, 10]. In patients with LBBB and a reduced LV ejection fraction (LVEF), cardiac resynchronization therapy (CRT) improves

survival, and reduces heart failure hospitalizations [11]. Among patients treated with CRT, reports describe "super-responders" whereby LVEF normalizes with resolution of heart failure symptoms [12]. These observations have led to the notion that LBBB with resultant dyssynchrony may play a causative role in the development or progression of LV systolic dysfunction. This noteworthy syndrome is now commonly designated "dyssynchrony cardiomyopathy" or "LBBB-associated cardiomyopathy" [13, 14].

The relationship between left bundle branch block (LBBB) and dilated cardiomyopathy is well known. Isolated LBBB can also be seen in individuals with a structurally normal heart. Although LBBB confers increased mortality risk in elderly patients and those with underlying structural heart disease, it has minimal effects on younger healthy individuals [4, 15, 16]. However, chronic LBBB may lead to asynchronous LV contraction and subsequent impairment in LV function. Several studies have suggested a causative link between LBBB and chronic LV dilation, dysfunction, and heart failure [12, 17, 18].

The relationship between LBBB and LV dysfunction is complex and poorly understood. It may appear during the course of the disease indicating the severity and poor prognosis or it may play a causative role in the development of dyssynchronous contraction and worsening of LV function.

2. Case Report

An 82 year old octogenarian gentleman afflicted with LBBB cardiomyopathy was referred to us for a detailed color echocardiography. He was also suffering from multiple comorbidities: (i) coronary artery disease with percutaneous coronary intervention (PCI) and stenting performed to proximal left anterior descending artery and right coronary artery in 2018 (ii) diabetes mellitus type 2 on oral hypoglycemic agents (iii) hypertension (iv) osteoarthritis of both knees.

On clinical examination he was apparently frail and weak. His height was 165 cm weight 50 kg, pulse rate 65/min, BP 120/80 in the right arm, in sitting position, SP02 97% at room air and respiratory rate 15/min. There was no evidence of dyspnea at rest or tachypnea. Cardiovascular and systemic examination were unremarkable.

Resting ECG revealed normal sinus rhythm with a rate of 78/min, regular and a LBBB pattern (QRS width 140 msec, QRS axis-60°) (Figure 6)

Figure 6 Resting ECG consistent with LBBB

2.1. 4Dimensional XStrain Echocardiography

All echocardiographic evaluations were performed by the author, using-My Lab X7 4D XStrain echocardiography machine, Esaote, Italy. The images were acquired using a harmonic variable frequency (1-5 Mhz) electronic single crystal array transducer while the subject was lying in left lateral decubitus position.

Conventional M-mode, two-dimensional and pulse wave doppler (PWD) echocardiography was performed from parasternal long-axis, short axis and apical four chamber views and following parameters were derived: interventricular septum and LV posterior wall thickness in end-diastole and end-systole (IVS d and LVPW d,

respectively), LV internal dimension at end-diastole and end-systole (LVID d and LVID s, respectively), LV end-diastolic and end-systolic volumes (LVEDV and LVESV respectively), ejection fraction (EF%), LV Mass in diastole (LV Mass d), Cardiac Output (CO) and Cardiac Index (CI).

2.2. 4D XStrain speckle tracking echocardiography

From the apical position, 2Dimensional cine loops were acquired from two chamber, three chamber and four chamber views. High quality ECG signal was must for proper gating and a minimum of three cardiac cycles were acquired of each cine loop. The study was performed with a frame rate between 40-75 fps and then stored digitally on a hard disk for offline analysis by software package XStrain™ advanced technology TOMTEC GMGH 3D/4D rendering Beutel™ computation capabilities [19].

The LV bull's eye depiction according to 17 segment model was generated by XStrain 4D software, by integrating the results of each set of cine loops [20, 21]. The unique software provided segmental, regional and global peak systolic values of various LV strains. Moreover, XStrain-4D software created a 3D reconstruction for calculating LV volumes and EF [20], and XStrain 4D-EF by the "Beutel Mode" method (TOMTEC, Germany) [22].

After the extensive echocardiography assessment the following data was obtained, as mentioned below:

Table 2 Transthoracic Echocardiography data

Transthoracic Echocardiography			
M-Mode - at the level of mitral valve			
DE Amp			
DE Amp	0.10 m/s		
EPSS	9.9 mm		
E-F Slope	150 ms		
M-Mode - at the LV level			
Left Ventricle			
IVSd	13.0 mm	IVSS	13.8 mm
LVPWd	8.8 mm	LVPWS	16.1 mm
LVIDS	34.0 mm	%LV FS	20%
EF	41%	LVEDV index	52.7 ml/m2
LVEDV	80.6 ml	LVESV index	31.1 ml/m2
LVESV	47.6 ml	SV	33.0 ml
CI	1.32 l/min/m2	CO	2.02 l/min
%PW	83%	% IVS	6%
LV Mass index	103 g/m2	LV Mass	158 g
LVIDd	42.5 mm	Relative Wall Thickness	0.41
2 Dimensional Echocardiography			
Auto EF - Biplane			
LVAd A4C	33.58 cm2	LVAd index A4C	21.9 cm2/m2
LVAS A4C	26.98 cm2	LVAd A2C	32.76 cm2
LVAd index A2C	15.0 cm2/m2	LVAS A2C	23.01 cm2
LVEDV (MOD A4C)	111.0 ml	LVESV (MOD A4C)	76.9 ml

LVEDV (MOD A2C)	113.3 ml	LVESV (MOD A2C)	69.5 ml
LVEDV (MOD BP)	115.1 ml	LVESV (MOD BP)	77.8 ml
LVEDV index (MOD A4C)	72.5 ml/m2	LVEDV index (MOD BP)	75.2 ml/m2
EF (MOD A4C)	31%	EF (MOD A2C)	39%
EF (MOD BP)	32%		

Table 3 Volumetric data

4Dimensional XStrain Echocardiography	
Volumetric data	
LVEDV	90.01 ml
LVESV	59.90 ml
EF	33.46%
CO	1.92/min
Sph i d	0.48
Sph i s	0.46

Table 4 Regional global strain data

4Dimensional XStrain Speckle Tracking Echocardiography	
Regional GLS	
Bas Ant	-18.54%
BasAntSep	-10.66%
Bas Sep	-7.02%
Bas Inf	-23.51%
Bas Post	-25.61%
Bas lat	-13.46%
Mid Ant	-10.57%
MidAntSep	-2.24%
Mid Sep	-5.54%
Mid Inf	-13.48%
Mid Post	-19.80%
Mid Lat	-9.63%
Apic Ant	-5.87%
Apic Sep	-7.80%
Apic Inf	-3.91%
Apic lat	-10.56%
Apex	-5.51%

Global GLS	
Global Strain (A2C)	-12.04%
Global Strain (A4C)	-9.95%
Global Strain (ALAX)	-12.79%
Global Strain	-11.59%

2.3. Highlighting features

The illuminating features of 4Dimensional XStrain echocardiography are outlined (Figures 7-12) :

- Jerky motion of ventricular septum with severe dyssynchronised oscillatory movement of the LV.
- Small LV with 4D EDV and 4D ESV being 90.01 ml and 59.90 ml respectively
- Severely reduced LVEF:
  - M-mode = 41%
  - 2Dimensional Biplane Simpson's method=32%
  - 4D = 33.46%
- Severely impaired global longitudinal strain of LV.

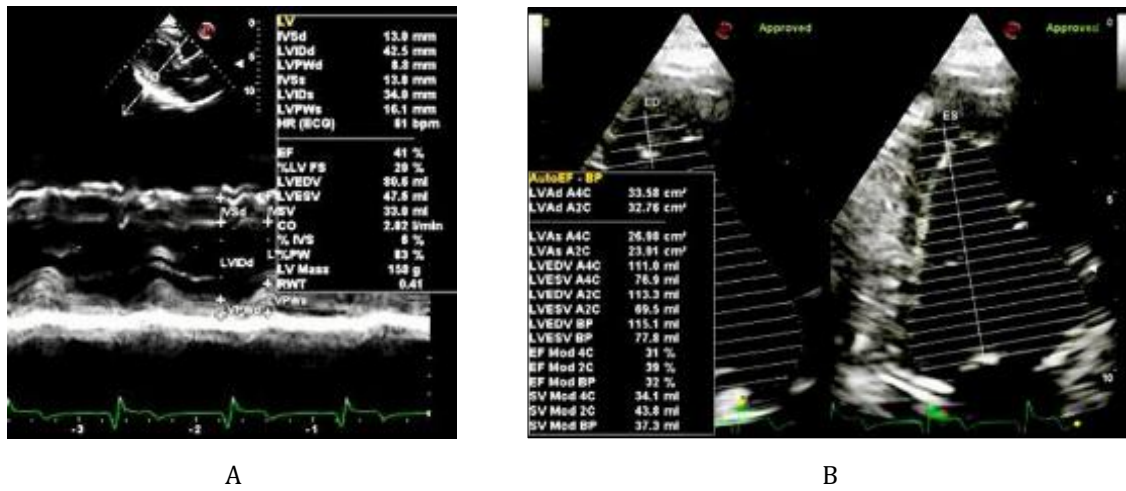|	
Global Strain (A2C)	-12.04%
Global Strain (A4C)	-9.95%
Global Strain (ALAX)	-12.79%
Global Strain	-11.59%

A   B

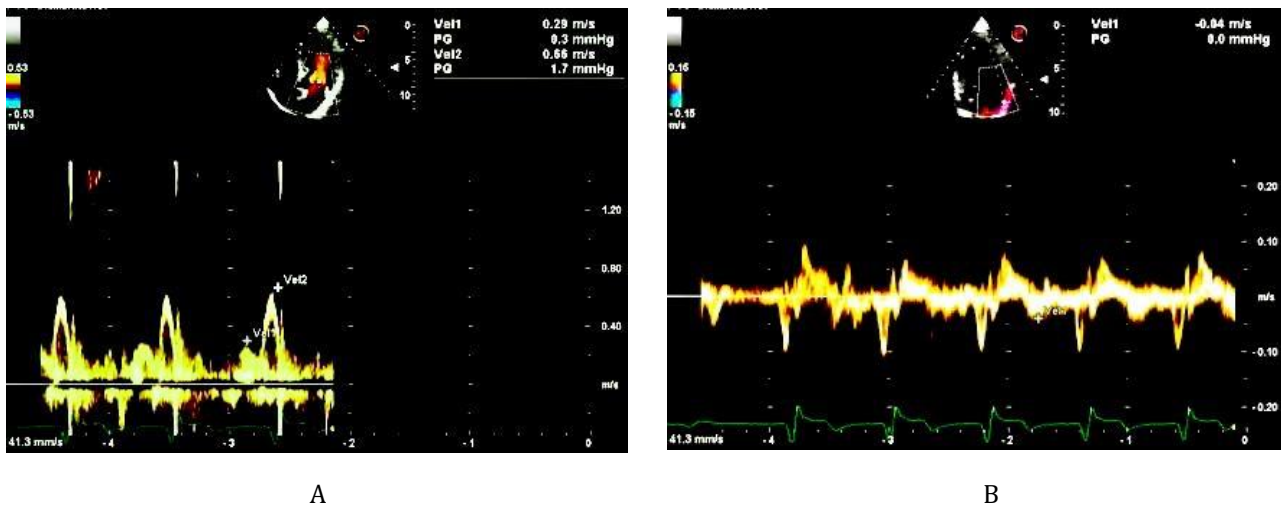**Figure 7** Transthoracic Echocardiography (A) Lax view, (B) 4ch view

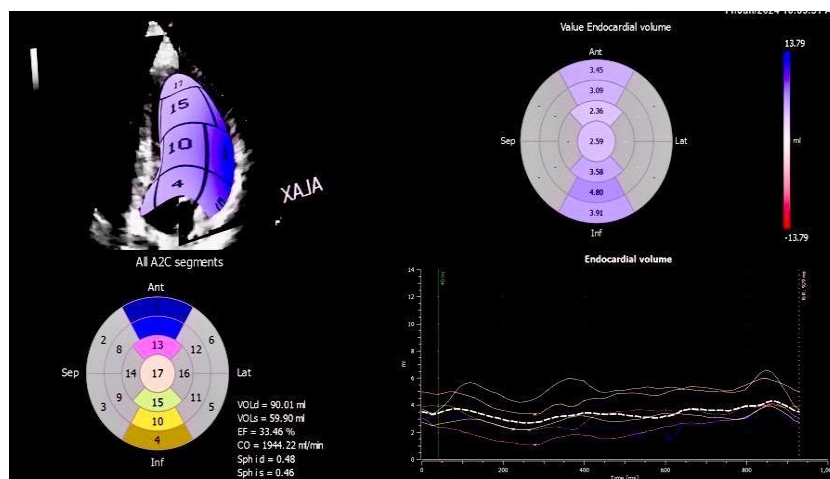A   B

Figure 8 Conventional M-mode and 2-Dimensional Transthoracic Echocardiography : (A) M-mode LV volumes and ejection fraction, (B) Biplane (Simpsons method) method for determining 2-Dimensional LV volumes and ejection fraction

A   B

Figure 9 (A) Pulse wave doppler across MV and (B) Tissue doppler imaging of lateral wall of LV

Figure 10 LV endocardial volumes, 4D-EF%, cardiac output, and sphericity index
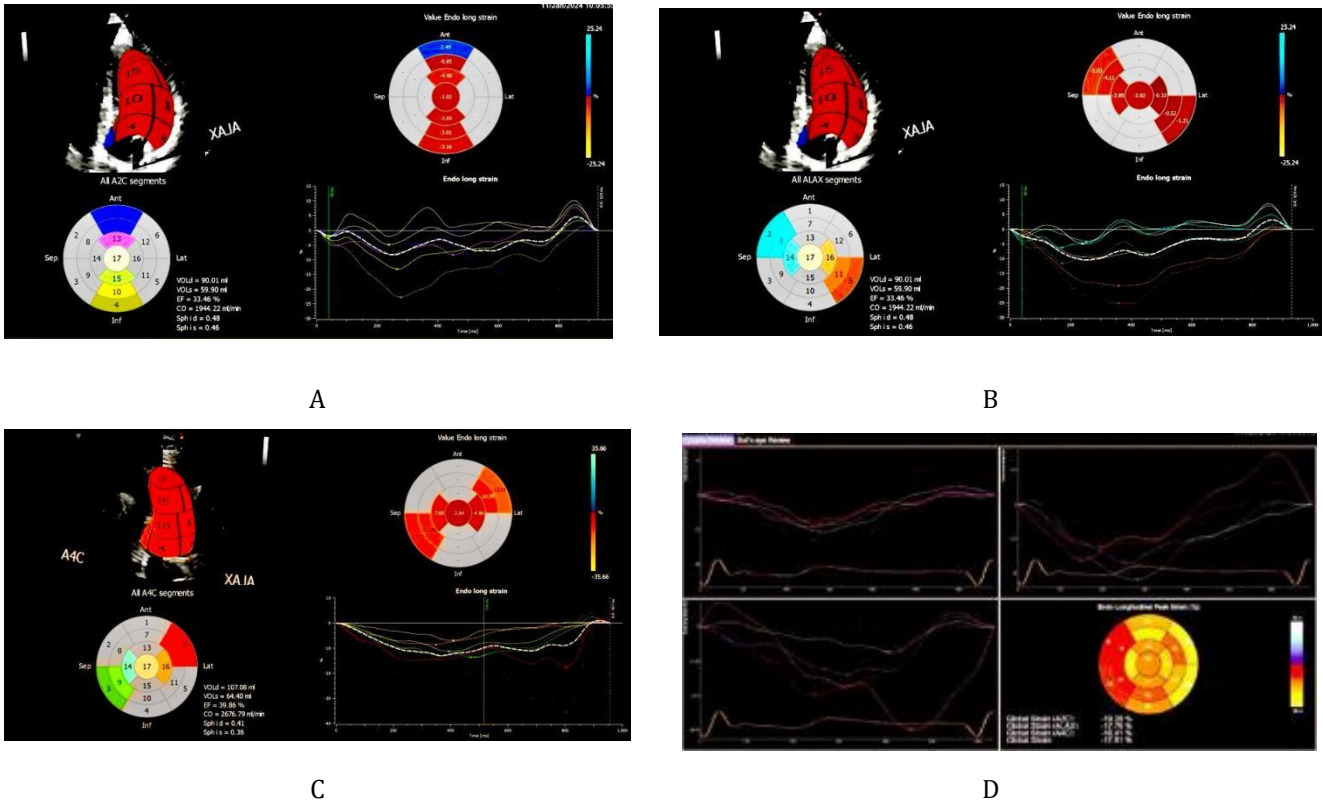
Figure 11 Apical 2CH,apical LAX, apical 4CH regional strain plots and curves (A) Apical 2CH regional strain (B) Apical LAX regional strain (C) Apical 4CH regional strain (D) Combined graphs and bull's eye mapping of global strain values

**Figure 12** Global Longitudinal peak strain (%) of LV

3. Review of literature

3.1. Anatomy of conduction system and left bundle branch [23]

The first portion of the left-sided His system is the penetrating bundle, which is characterized by longitudinal systematization and a length of 75 mm. The second portion is the branching bundle of His that bifurcates at the crest of the muscular septum into the right and left bundle branch (RBB and LBB). The LBB runs to the left as an increasingly broad sheet of cells made up of multiple fine fascicles. Reaching the wall of the LV, the sheet heads toward the apex in the subendocardial layer of the muscular septum.

- *LBB trunk*: Length of 10 mm, the diameter is 5 mm in its onset, and 9 mm at the end (reverse trapezoid shape), the cells are formed by Purkinje fibers.

After a few centimeters, the LBB divides into three groups of fibers (Figure 13).
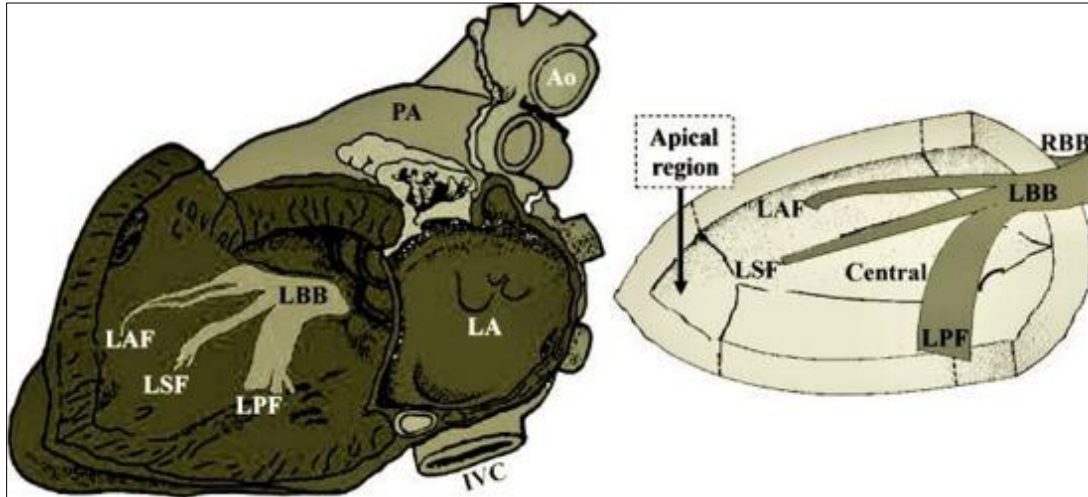

Figure 13 The three fascicles of the left His system in the left sagittal view. Ao: Aorta; IVC: Inferior Vena Cava; LA: Left Atrium; LBB: Left Bundle Branch; LAF: Left Anterior Fascicle; LSF: Left Septal Fascicle; LPF: Left Posterior Fascicle; PA: Pulmonary Artery; RBB: Right Bundle Branch

- Left anterior fascicle (LAF):*is distributed in the base of the anterolateral papillary muscle (ALPM). The LAF has an extension of 35 mm, diameter of 3 mm. The cells are formed by Purkinje fibers.*
- Left posterior fascicle (LPF): *is distributed in the base of the posteromedial papillary muscle (PMPM), basal inferior region of the septum and inferobasal and lateral wall of the LV. Isolated left posterior fascicular block (LPFB) is very rare.*
- Left septal fascicle (LSF): *has a very variable origin and morphologies and is distributed in the apical and centroseptal region and low interventricular septum (IVS). The LSF originates the first 10–20 ms electrical vector.*

3.2. Histology of Left bundle branch

Normal histology of left bundle branch (LBB) is depicted in figures 14, 15 [24, 25].
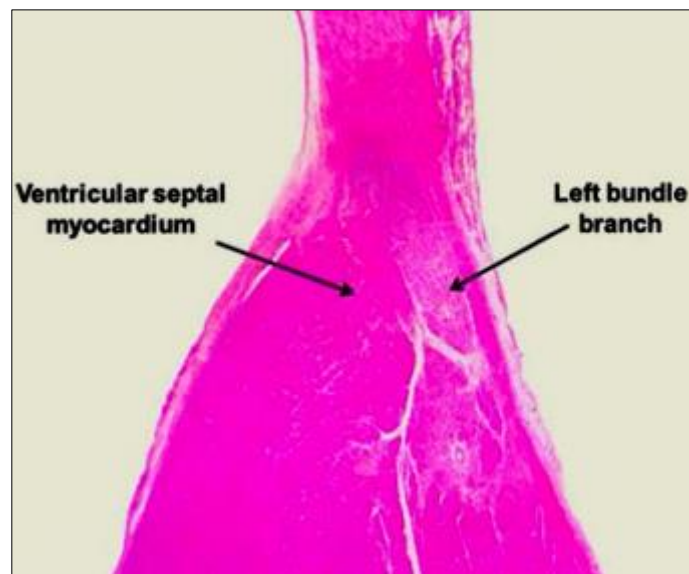
Figure 14 Histology and pathology of left bundle branch (LBB). Normal appearance of LBB which appears lighter in color than the surrounding myocardium
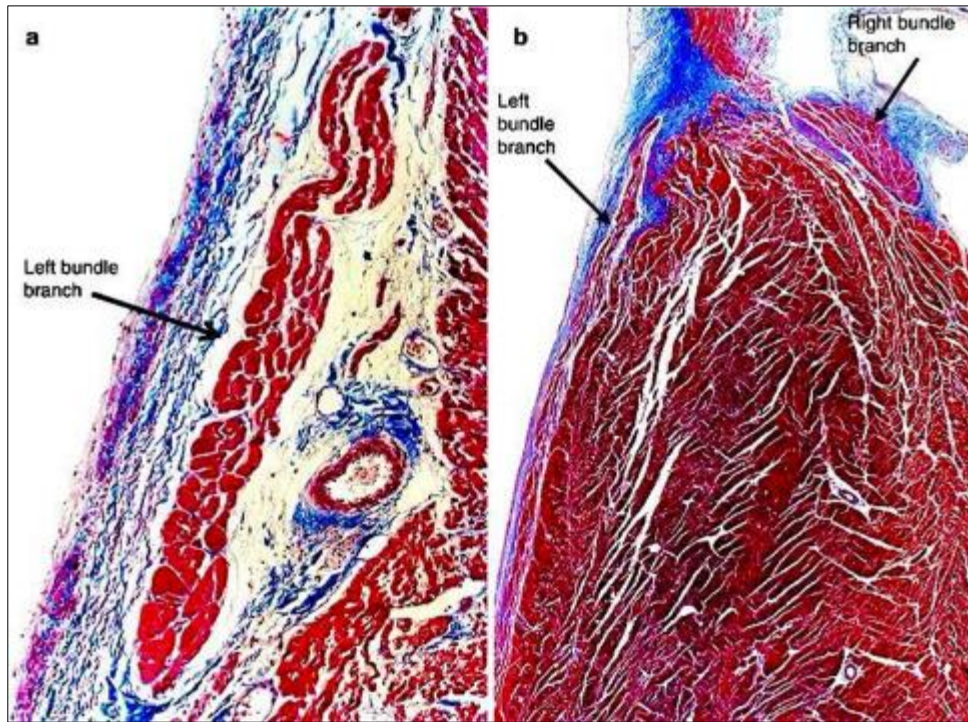
Figure 15 Histology of LBBB. (a) Detail of the left bundle branch under the endocardium. (b) Image showing the emergence of the last of the left bundle branches and the initial portion of the right bundle branch (Masson's trichrome)

3.2.1. LBBB etiologies [23]

- *Hypertension:* Hypertensive patients have an increased risk for LVH. LBBB identifies individuals with worse global and regional LV systolic function and impaired LV relaxation independently of the degree of LVH by echocardiography.
- *Acute coronary syndrome (ACS):* Detection of ACS in the presence of LBBB continues to be a challenge. Serial ECGs and comprehensive ECG analysis may aid in the diagnostic workup.
- *Chronic myocardial infarction (MI).*
- *Dilated cardiomyopathy*
- *Takotsubo cardiomyopathy (TCM)*
- *Transcatheter aortic valve implantation (TAVI):* 30%–50% of patients develop new LBBB. TAVI-induced LBBB is an independent predictor of mortality.
- *Lenègre disease:* hereditary Lenègre disease is caused by a haplo insufficiency mechanism, with a splicing mutation in the SCN5A gene, leading to a progressive cardiac conduction defect, which in combination with aging leads to this dromotropic disturbance.
- *Sclerosis of the left side of the cardiac skeleton*.
- *Cardiac interventions:* Complete LBBB (CLBBB) is the rule after septal myectomy/myotomy in HCM.
- *Left ventricular non-compaction*: The most common dromotropic disturbance is LBBB (40%).
- *Neuromuscular disease* - myotonic dystrophy type 1.
- *Myocarditis.*
- *Aortic valve disease.*
- *Mitral valve disease.*
- *Perinatal exposure to HIV type 1.*
- *Acute pulmonary embolism* (rare).
- *Congenital aortic stenosis.*
- *Primary amyloidosis.*

3.2.2. ECG classification for LBBB [23]

- Criteria (currently more used in the literature):
 - Incomplete LBBB (ILBBB) (QRSd from 90 to 119 ms)

- o Complete LBBB (CLBBB) (QRSd ≥120 ms in adults).
- o Strauss' strict criteria: QRSd ≥140 ms for men and ≥130 ms for women, along with mid-QRS notching or slurring in ≥2 contiguous leads. These new criteria are currently used for CRT.
- Mexican School criteria :
- o First-degree LBBB;
- o Second-degree LBBB (first degree and second degree correspond to ILBBB);
- o Third-degree LBBB or CLBBB.
- Spanish School criteria. Global left ventricular blocks :
- o Advanced or third-degree LBBB (≥120 ms),
- o Non-advanced global left ventricular blocks:
- o First-degree LBBB (partial) corresponds to types I and II of the Mexican school: isolated R in V6 with more or less slurring but QRSd <120 ms.
- o Intermittent or second degree LBBB (ventricular aberrancy).

3.2.3. Natural History of LBBB

The prognosis of LBBB in asymptomatic individuals remains controversial. Although a study among US Airforce personnel did not reveal an association between LBBB and cardiovascular disease [26], data from the Framingham study showed a significantly elevated risk of cardiovascular deaths (50% within 10 years of onset) among individuals with LBBB [1]. More recent studies have highlighted LBBB as an independent predictor for adverse events, including sudden cardiac death (10 fold incidence increase) [8] as well as mortality from HF (3.08x increased risk) and myocardial infraction (2.90x increased risk) [6], particularly among individuals aged 50 years and above [8]. Furthermore, in a Swedish prospective study of middle-aged men spanning 28 years, LBBB at baseline was associated with a markedly increased risk of his grade atrioventricular block compared with men without bundle branch block [27]. Hence, although the prognosis of LBBB in younger patients may be relatively benign, its presence in older subjects may serve as an important marker for cardiovascular disease or death.

3.2.4. Pathophysiology of LBBB

- A: Contractile inefficiency (Figure 16 A): Upper panels display pressure-strain loops from the septum and LV lateral wall in a patient with LBBB and non-ischemic cardiomyopathy. Loop area reflects segmental work. The lateral wall shows normal counter-clockwise rotation of the pressure-strain coordinates with shortening in systole. The septal pressurestrain loop, however, rotates clockwise, which means lengthening in systole and the result is negative (wasted) work as indicated by the blue-colored (dark) loop area. The lower panel displays segmental work distribution in the entire ventricle. Values are given as percentages of the segment with the highest work value. Modified from Russell et al. [28].
- B: Septal hypo-metabolism (Figure 16 B): Fluorodeoxyglucose-positron emission tomographic (FDG-PET) LV short-and long-axis images from a representative patient with LBBB and non-ischemic cardiomyopathy. The point with the highest FDG uptake was used as reference (100%), and segmental values are reported in percent of this value. Green (low intensity) color in septum indicates low metabolism relative to the lateral wall. The reduced septal work illustrated in panel A, explains reduced septal metabolism. Red (high intensity) color in the LV lateral wall indicates high rate of glucose metabolism. Modified from Russell et al. [28].
- C: Abnormal septal motion (Figure 16 C): Left panel: Septal and LV lateral wall strain traces from a representative LBBB patient with non-ischemic cardiomyopathy. There is septal pre-ejection shortening with corresponding LV lateral wall stretch. As the LV lateral wall starts to shorten, there is rebound stretch of the septum and septal shortening at end-systole is reduced. Right panel: Parasternal M-mode image from the same patient. Please note how pre-ejection shortening and rebound stretch are visualized as septal flash.
- D: Apical rocking (Figure 16 D): During isovolumetric contraction the apex is pulled rightwards by early septal and RV free wall contraction (middle panel), whereas later in systole it is pulled back by the forceful contraction in the late-activated LV lateral wall. Modified from Stankovic et al. [29] .
- Mitral regurgitation (Figure 16 E): Echocardiographic recordings from a patient with congestive heart failure and LBBB. The left panel shows severe mitral regurgitation as indicated by large color Doppler jet area. The right panel shows marked reduction of mitral regurgitation with CRT. Modified from Kanzaki et al. [30].
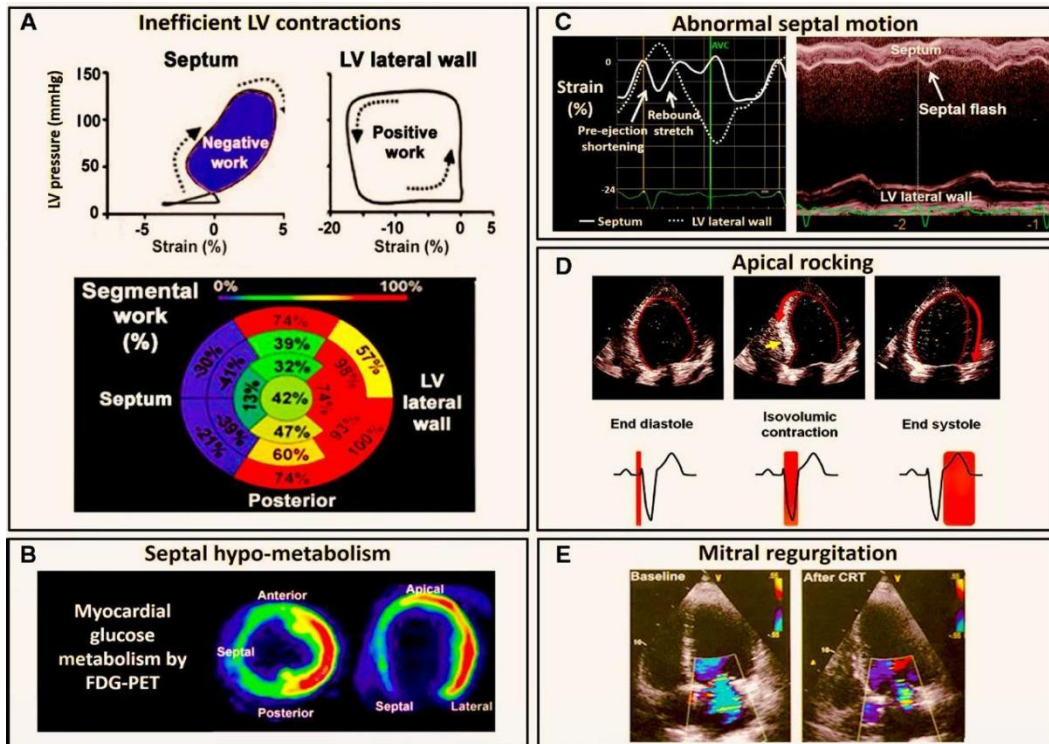
Figure 16 LV mechanical and metabolic features of LBB (A) Inefficient LV contraction (B) Septal hypo-metabolism (C) Abnormal septal motion (D) Apical rocking (E) Mitral Regurgitation

3.2.5. LVEF drop with LBBB

Patients who had a drop in LVEF were more likely to be males and more likely to be hyperlipidemic. The majority of patients who developed LV dysfunction had clearly identifiable causes of worsening LVEF (Figure 17) [31]. It is important to note that patients with other potential causes of cardiomyopathy may, in fact, have developed LV dysfunction due the LBBB. Ischemic heart disease was the most common condition associated with LVEF drop (10%). The cause of cardiomyopathy in the remaining (5.3% patients) was potentially related to the LBBB itself.
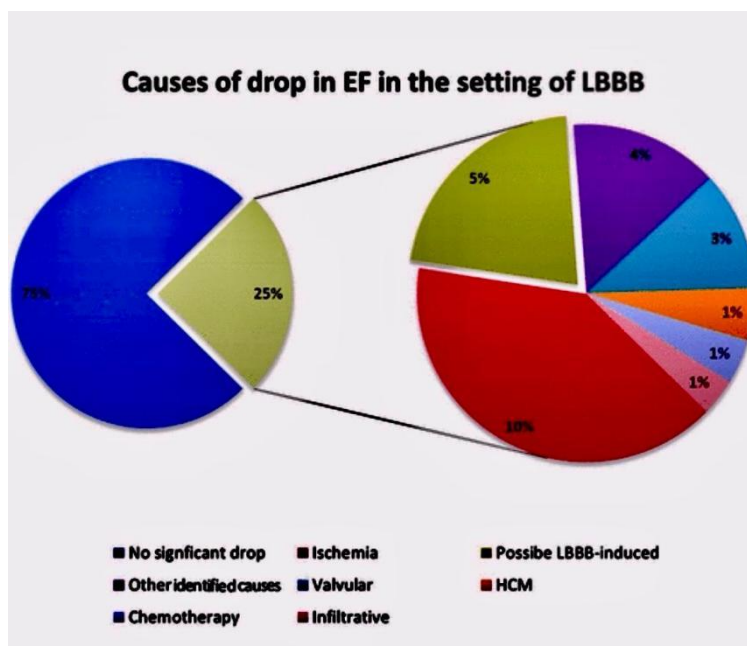
Figure 17 Causes of left ventricular ejection fraction (LVEF) drop in patients with left bundle branch block (LBBB). HCM indicates hypertrophic cardiomyopathy

3.2.6. LBBB in Dilated Cardiomyopathy

Conduction abnormalities may develop in ischemic/non-ischemic cardiomyopathy due to degeneration/fibrosis of the conduction system, adverse ventricular remodeling, or ischemia. In patients with HF with reduced ejection fraction, the presence of LBBB is associated with increased mortality [32, 33].

3.2.7. LBBB prognosis

Several studies have shown that LBBB i s associated with increased mortality among patients with heart disease, particularly those with myocardial infraction [34, 35].

In the Framingham study [36], an increased risk of subsequent development of coronary heart disease or congestive heart failure was shown in men who developed left bundle branch block. The high prevalence rate of antecedent hypertension suggests that it may often play a central role in the pathogenesis of LBBB. Hypertension predisposes to the development of LBBB, primarily by potentiating the development of generalized myocardial fibrosis, sclerosis of the left side of the cardiac skeleton or primary sclerodegenerative changes of the bundle branches themselves, by predisposing to the development of coronary atherosclerosis with resultant ischemic damage to the bundle branches or by another as yet undefined process.

The marked increase in mortality in patients with LBBB is seen only in combination with ischemic heart disease. In LBBB, the depolarization phase is, by definition, prolonged. Furthermore, the prolongation of the vulnerable repolarization phase in combination with an increased number of premature ventricular beats (secondary to ischemic heart disease) would expose the patient to an increased risk of sudden ventricular tachyarrhythmias [29].

4. Conclusion

Advancing age and cardiac disease were associated with an increased risk of LBBB. These findings support the theory that bundle branch block is a marker of slowly progressive degenerative diseases. Because patients with LBBB have an increased risk of developing overt cardiac disease, hence they warrant consideration for more extensive investigation and follow-up.

LBBB is associated with an increased risk of cardiovascular morbidity and mortality. It may affect not only the conduction system but also the myocardium.

The sequence LBBB-intra-ventricular asynchrony-reduced pump function-neurohormonal activation-asymmetric hypertrophy-dilatation, followed by emerging heart failure seems established. CRT can interrupt this sequence in moderate to severe heart failure patients but it is unknown whether the effects of LBBB-related dyssynchrony could be prevented before deterioration of function and cardiac remodelling.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The case report was approved by the research ethics committee of our institution (approval no. IEC/PDC/PHSD/2021:01, 02).

Statement of Informed consent

Informed consent was obtained from the respected octogenarian patient included in the study.

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