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Research progress of left bundle branch block

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Abstract: Left bundle branch block (LBBB) is an important cause of heart failure. When LBBB occurs, the excitation sequence of the left ventricle changes, leading to the change of cardiac systolic pattern, resulting in cardiac electromechanical asynchronism, and eventually heart failure. At present, there is no unified standard for the diagnosis of true LBBB, and the epidemiological characteristics are not clear. In this paper, we will focus on a comprehensive discussion of LBBB's anatomy, electrocardiogram manifestations, epidemiology, etiology, clinical significance and treatment.
Keywords: Left bundle branch block; Electrical conduction dyssynchrony; Mechanical conduction dyssynchrony; Cardiac synchronization therapy

Left bundle branch block (LBBB) refers to the delay or blockage of left bundle branch conduction caused by various reasons. The excitation is transmitted from the right ventricle to the left ventricle through the ventricular septum, resulting in significant delay of left ventricular excitation, including the blockage of the main trunk of the left bundle branch and the double blockage of the left anterior branch or left posterior branch. The incidence rate is related to age, with a higher rate for older ages.

1 Anatomic features of left bundle branch

The His bundle is a continuation of the distal atrioventricular node, with a length of up to 20 mm and a diameter of up to 4 mm [1]. The left bundle branch (LBB) originates from the lower part of the His bundle branch, and histopathological studies have found that its trunk extends 10 to 15 mm towards the apex of the heart and divides into three bundles: the left anterior branch, the left posterior branch, and the septal branch [2]. Each branch continues to extend downward to form a complex Purkinje fiber network. The LBB is large and runs under the endocardium, located deeply and not easily damaged. Once injured, it is mostly pathological [3]. There are three subtypes of conduction patterns in patients with LBBB: proximal left intrahisian block (46%), LBBB (18%), and intact Purkinje activation without discrete conduction block (36%) [2].

2 Electrocardiogram (ECG) Manifestations of LBBB

In 1909, Eppinger et al. first described the ECG features of LBBB in a study on dogs [4]. However, they misinterpreted this phenomenon as right bundle branch block (RBBB). In 1930, Barker et al. discovered that the ECG that had been considered as RBBB was actually the result of LBBB [5]. The diagnostic criteria for LBBB on ECG mainly include three standards, namely the de Luna standard, the Strauss standard, and the American College of Cardiology (ACC) / American Heart Association (AHA) / Heart Rhythm Society (HRS) standard.

2.1 de Luna Standard

The LBBB in de Luna standard is characterized by: (1) Prolonged QRS duration ≥ 120 ms; (2) QS or rS pattern

in V1 lead; (3) Uniphasic R wave in V6 and I; (4) Intraventricular delay time > 60 ms in the same lead; (5) QS pattern and oppositely directed ST and T waves in the aVR lead [4]. This standard was introduced from dog models to humans in 1941. However, Treger et al. [5] found that among patients with LBBB patterns on surface ECG, 36% still showed activation of Purkinje fibers during intracavitary mapping, and their QRS duration and morphological changes could not be corrected through His-Purkinje system pacing. This suggests that only 64% of LBBB diagnosed according to this standard may be true LBBB.

2.2 ACC/AHA/HRS Standard

In 2009, ACC/AHA/HRS established the diagnostic criteria for LBBB as follows: (1) QRS duration ≥ 120 ms; (2) Wide R waves with notching in I, AVL, V5, and V6 leads (occasionally RS pattern in V5 and V6 leads); (3) Absence of Q waves in I, V5, and V6 leads (narrow Q waves may be present in AVL lead); (4) R peak duration > 60 ms in V5 and V6 leads; (5) ST changes, and T waves usually opposite in direction to QRS [2, 6]. Compared with the de Luna standard, the ACC/AHA/HRS standard pays more attention to the notching of QRS waves in precordial leads, but it still lacks high specificity for the diagnosis of true LBBB.

2.3 Strauss Standard

In 2011, Strauss et al. proposed stricter ECG criteria for LBBB to better predict the response to cardiac resynchronization therapy (CRT) [9]. These criteria include: (1) QRS duration ≥ 140 ms (for males) or 130 ms (for females); (2) QS or rS pattern in V1 and V2 leads; (3) Presence of notching in QRS waves in two or more of the following leads: V1, V2, V5, V6, I, and aVL [9]. They observed that patients with true LBBB may have more pronounced prolongation of QRS duration accompanied by notching in the corresponding leads. However, the value of the Strauss standard in predicting the response to CRT in patients with LBBB and heart failure has not been confirmed.

intracardiac electrophysiologic study is the gold standard for diagnosing true LBBB, which is characterized by the absence of LBB potential. As an ECG phenomenon, LBBB patterns under various standards do not necessarily indicate a complete blockage of LBB conduction. Therefore, the current ECG criteria cannot fully confirm true LBBB, and further improvements are still needed.

3 Epidemiology of LBBB

In 2006, Imanishi et al. [10] followed up the population in Hiroshima and Nagasaki in Japan and found that the age of male patients with LBBB was (70±10) years old, while the age of female patients was (68±11) years old. Eriksson et al. [11] followed up 50-year-old males in Gothenburg in 1998 and found that age was an independent risk factor for LBBB. The prevalence of LBBB in people under 50 years old was less than 1%, while the prevalence in people over 80 years old was 6%. Surkova et al. [12] followed up asymptomatic adults in 2017 and found that the prevalence of LBBB ranged from 0.1% to 0.8%. Hardarson et al. [13] conducted a 10-year follow-up study on the Icelandic population in 1987, and found that the incidence of LBBB was 3.2 cases per 10,000 people per year for males and 3.7 cases per 10,000 people per year for females. Previous studies pointed out that LBBB was an independent predictor of mortality in all age groups [14]. Compared with patients with coronary artery disease (CAD) without LBBB, patients with CAD accompanied by LBBB have a 10-fold increased risk in sudden cardiac death, a 3.08-fold increased risk in heart failure mortality, a 2.90-fold increased risk in myocardial infarction, and a 1.4-fold increased risk in all-cause death risk [15].

Currently, there are no epidemiological studies on LBBB in Asian populations, especially in East Asian populations. There is also a lack of epidemiological studies on LBBB in China and Shaanxi Province. In our work, we conducted an epidemiological survey on people with LBBB electrocardiogram manifestations in Shaanxi Provincial People's Hospital, and established case-control studies and retrospective cohort studies. We hope that our work can contribute to exploring the current situation and disease burden of LBBB patients in China.

4 Causes of LBBB

Multiple risk factors can lead to the occurrence of LBBB, among which advanced age has been proved to be an independent risk factor for LBBB [15]. The occurrence of most LBBB often involves myocardial ischemia, ventricular remodeling, drug poisoning, surgical treatment, and genetic factors, etc. [2].

4.1 Genetic predisposition to LBBB

Although LBBB is not generally considered as a genetic disease, studies have shown that some genetic mutations are related to LBBB. These mutations may involve channel genes, gap junction proteins, desmosomal genes, and cardiac transcription factors [16].

4.2 Common diseases that cause LBBB

LBBB is most commonly seen in organic diseases,

including hypertension, acute coronary syndrome, chronic myocardial ischemia, dilated cardiomyopathy, myocarditis, takotsubo syndrome, transcatheter aortic valve implantation, cardiac interventional therapy (after hypertrophic cardiomyopathy resection), congenital aortic stenosis, aortic valvular disease, mitral valve disease, left ventricular noncompaction, primary amyloidosis, neuromuscular diseases, etc. [6].

4.2.1 LBBB caused by reduced blood supply

The most common cause of LBBB is myocardial ischemia [15]. The main trunk of LBB is mainly supplied by the atrioventricular nodal artery originating from the right coronary artery and the septal branch artery originating from the anterior descending branch of the left coronary artery. The left anterior branch and septal branch are supplied by the anterior descending branch, while the left posterior branch is doubly supplied by the left coronary artery and the right coronary artery [6]. Whether there is a lesion in the left or right coronary artery, it may affect the LBB. Therefore, when encountering a patient with newly developed LBBB, myocardial ischemia should be the first consideration.

4.2.2 Effects of Aging and Mechanical Impact on LBBB

In elderly patients, LBBB is caused by calcification, degradation, and fibrosis in the fibrous triangle region of the conduction system. Since the conduction system is superficially located and fragile on the surface of the endocardium, compression of the LBB due to hypertension and heart failure can lead to LBBB when the left ventricular pressure load is high. Due to the anatomic proximity of the aortic valve to the penetrating His bundle and the proximal cardiac conduction system, LBBB can also be an acquired mechanical complication of surgical intervention, such as aortic valve replacement or transcatheter aortic valve replacement (TAVR). It is also common in severe hypertrophic obstructive cardiomyopathy resection due to resection of the proximal and distal basal septum of the left bundle branch. Right ventricular pacing has physiological similarities with LBBB because the pacing stimulus of the right ventricle leads to late activation of the left ventricular free wall and subsequent electromechanical dyssynchrony, which is believed to have similar effects on hemodynamics and the resulting heart failure.

4.3 Special Types of LBBB

"Painful LBBB syndrome" is a rare clinical phenomenon characterized by chest pain without ischemia. Its occurrence mechanism may be related to left ventricular asynchronous contraction, degenerative fibrosis of the conduction system, slow coronary blood flow, and microvascular dysfunction. Studies have shown that left bundle branch pacing (LBBP) is expected to correct LBBB and relieve symptoms.

Rate-dependent LBBB is associated with acute decline in cardiac contractile function. Depending on the heart rate, it is classified as "fast rate-dependent and slow rate-dependent LBBB". Tachycardia LBBB is believed to be caused by accelerated conduction velocity during phase 3 of repolarization, which occurs when pulses fall into the refractory period of the action potential, resulting in delayed or complete blockage of pulses. LBBB associated with bradycardia may be related to the automatic depolarization of left bundle branch during slower heart rates (phase 4), leading to difficulty in conducting subsequent electrical activity [15]. Therefore, rate-dependent LBBB may not necessarily be due to abnormalities in left bundle branch, but may be related to electrophysiological parameters.

5 Clinical significance of LBBB

5.1 Normal Cardiac Conduction

In the normal cardiac conduction system, excitation reaches the left bundle branch, right bundle branch and Purkinje fibers through the His bundle at a speed of about 1.5 m/s. The earliest depolarization activity of the ventricle starts from the middle of the basal septum, reaches the apical septum, then to the apical anterior wall of the right ventricle and the apical anterior lateral wall of the left ventricle, and finally reaches the entire anterior wall of the right ventricle and the anterior lateral wall and basal area of the left ventricle. In normal patients, the duration from the depolarization of His bundle to the ventricular myocardium is about 35-55 ms, and then continues to propagate through the Purkinje fibers, resulting in an average QRS wave width of 60-100 ms.

5.2 LBBB-induced Cardiac Desynchronization

In LBBB, the right ventricle is activated first, and then propagates to the left ventricle through the slowly activated septum, resulting in a wide and notched QRS in the left ventricle. The remaining parts of the left ventricle are activated in a delayed manner, and the final activation occurs in the lateral basal area, causing electrical desynchronization. In LBBB, the excitation of the right ventricle takes 40-50 ms to cross the septum, and another 90-100 ms for the excitation to reach the endocardium of the left ventricle and then excite the entire left ventricular myocardium. The total QRS duration is 130-150 ms, and this sequential ventricular activation prolongs the QRS duration to ≥120 ms. Moreover, in LBBB, the septum is activated during isometric contraction, stretching the posterior and lateral walls. Subsequently, the posterior and lateral walls are activated during the late phase of contraction, causing passive stretching of the septal wall and

resulting in mechanical desynchronization [15], which further leads to heart failure.

5.3 Special Diseases Associated with LBBB

The impact of electromechanical desynchronization involves the entire cardiac cycle, ultimately manifesting as overall incoordination of the cardiac contraction and relaxation processes, inability to complete effective ejection, decreased left ventricular ejection fraction (LVEF), and increased left ventricular volume, leading to LBBB-related cardiomyopathy [2]. Cardiomyopathy can be reversed after correction of LBBB. Bundle branch reentrant ventricular tachycardia (BBRVT) caused by LBBB is a rare arrhythmia, and the bundle branch is an important component of the reentrant circuit maintaining tachycardia. Most BBRVT patients have LBBB on surface electrocardiogram during sinus rhythm [15], emphasizing the potential role of LBBB in promoting BBRVT and explaining the reason why complete atrioventricular block is a rare complication of RBB ablation.

6 Treatment of LBBB with Heart Failure

LBBB indicates the desynchronization of cardiac electrical and mechanical activities, leading to left ventricular remodeling, which can be treated through cardiac CRT or physiological pacing [7]. In 2021, ESC proposed in its recommendations on cardiac pacing and resynchronization therapy that CRT is recommended for patients with LBBB, sinus rhythm, QRS duration ≥150 ms, LVEF≤35%, and symptomatic heart failure after drug optimization, which is classified as Class I indication; while for patients with LBBB, sinus rhythm, QRS duration between 130 and 149 ms, LVEF≤35%, and symptomatic heart failure after drug optimization, CRT should be considered, which is classified as Class IIa indication [19]. Common pacing methods include bi-ventricular pacing, His bundle pacing (HBP), and LBBP.

6.1 BVP

BVP can be used as the standard treatment for LBBB. BiV-CRT, which involves pacing the right ventricular endocardium and left ventricular epicardium, can alleviate symptoms, inhibit myocardial remodeling, improve exercise tolerance, reduce hospitalization and mortality rates in patients with heart failure, and normalize the electrical activation of the left ventricle, thus correcting cardiac desynchronization more physiologically.

The mechanism of BVP involves placing electrodes in the coronary sinus branches to activate the lateral wall of the left ventricle early, thus improving the electrical synchrony of the left ventricle. Although the treatment effect is significant, the non-response rate is still as high as 30%. Moreover, it cannot correct LBBB and does not fundamentally restore the electrical synchrony of the conduction system. Even though the QRS duration may decrease compared to preoperative levels, it remains prolonged [20]. Additionally, due to the anatomy of the cardiac venous system, which is close to the phrenic nerve and has poor threshold values, placement of the left ventricular lead can be challenging. Even for experienced operators, the proportion of ideal lead placement in the lateral, posterolateral, or posterior veins is less than 90% [19]. Therefore, it is necessary to seek alternative solutions to BVP.

6.2 HBP

HBP involves fixing the pacing electrode to the His bundle or its adjacent areas, allowing the pacing pulse to propagate along the His-Purkinje system, resulting in a QRS wave that closely resembles the morphology under physiological conduction, making it the most physiologically similar pacing mode. Studies have shown that HBP significantly improves QRS width, echocardiographic parameters, and symptomatic physical function. Compared to the BVP group, the HBP group had significantly higher LVEF and lower left ventricular end-systolic volume (LVESV) at 6 months [21], indicating better reverse remodeling with HBP.

While HBP is the most physiologically similar pacing method, many patients with infra-Hisian atrioventricular block have poor improvement in their condition, exceeding the physical contact range of existing tools, and may even lead to progression of conduction disease [22]. Issues such as high pacing thresholds, low R-wave amplitudes, early battery depletion, and the occurrence of distal conduction block limit the clinical application of HBP [23].

6.3 LBBP

LBBP is a new concept proposed during the development of HBP research and has been proven to be an effective means of achieving physiological pacing for bradycardia and heart failure patients undergoing cardiac resynchronization. Due to the larger distribution area of the left bundle branch within the left ventricle, it is easier to locate and capture by fixing the lead to the deep endocardial septum of the left ventricle [23]. Studies have shown that the success rate of LBBP in non-ischemic cardiomyopathy patients with LBBB requiring CRT is 97% [24]. In patients requiring pacing after TAVR, the success rate of LBBP is 93%, while the success rate of HBP is only 63% [25].

The potential mechanism of LBBP for improving

cardiac function may be through the left ventricular conduction system leading to faster and earlier left ventricular contraction, maximizing the correction of electromechanical desynchrony between the left and right ventricles associated with LBBB. In heart failure patients with LBBB, LBBP has a higher super-response rate compared to BVP-CRT [26]. LBBP has a wide target area, stable lead placement, low and stable pacing thresholds, longer battery life, high implantation success rates, and fewer long-term follow-up complications. LBBP produces a narrow QRS wave, and many clinical studies have confirmed the feasibility and safety of LBBP [27-28]. However, LBBP may carry the risks of ventricular septal perforation, right bundle branch injury, electrode detachment and arterial injury in the ventricular septum, so it is necessary to improve the operator's skill level.

7 Future Prospects

This article analyzes the disease characteristics and treatment methods of LBBB. Currently, there is no relevant epidemiological study on LBBB in China, and the diagnostic criteria for LBBB on the surface electrocardiogram vary. Instrumental therapy for LBBB with heart failure has made great progress in technology and methods, bringing good news to patients with LBBB. With the development of electrophysiological technology, the electrocardiogram diagnosis and epidemiological characteristics of true LBBB will become clearer, providing new ideas for the intervention of LBBB etiology. In the future, newer technologies will be applied to LBBB patients, bringing safer and better services to patients with LBBB.

Conflicts of Interest: None

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·学术前沿·

左束支传导阻滞的研究进展

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摘要：左束支传导阻滞（LBBB）是心力衰竭发生的重要病因，LBBB 发生时左心室激动顺序发生改变，引起心脏收缩模式改变，导致心脏电机械不同步，最终导致心力衰竭。目前关于真性 LBBB 的诊断无统一标准，流行病学特点尚不清晰，本文将着重对 LBBB 解剖特征、心电图表现、流行病学、病因、临床意义及治疗方式进行论述。

关键词：左束支传导阻滞；电传导不同步；机械传导不同步；心脏再同步化治疗

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Research progress of left bundle branch block

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Abstract: Left bundle branch block (LBBB) is an important cause of heart failure. When LBBB occurs, the excitation sequence of the left ventricle changes, leading to the change of cardiac systolic pattern, resulting in cardiac electromechanical asynchronism, and eventually heart failure. At present, there is no unified standard for the diagnosis of true LBBB, and the epidemiological characteristics are unclear. This paper will focus on a comprehensive discussion of LBBB's anatomic features, electrocardiographic manifestations, epidemiology, etiology, clinical significance and treatment.

Keywords: Left bundle branch block; Electrical conduction dyssynchrony; Mechanical conduction dyssynchrony; Cardiac resynchronization therapy

左束支传导阻滞（left bundle branch block，LBBB）是指各种原因致左束支传导发生延迟或阻滞，激动由右心室经室间隔传入左心室，导致左心室激动明显延迟，包括左束支主干部阻滞及左前分支或左后分支双阻滞。其发病率与年龄有关，年龄越大，发病率越高。

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QR code for English version

1　左束支的解剖特点

希氏束是房室结远端的延续,长度达 20 mm,直径达 4 mm[1]。左束支起源于希氏束分支部的下方,组织病理学研究发现其主干向心尖方向延伸 10~15 mm,分成三束,分别是左前分支、左后分支、间隔支[2],各分支继续向下延伸形成复杂的浦肯野纤维网;左束支粗大、走行于心内膜下,位置深,不易受损伤,一旦发生损伤后多为病理性[3]。LBBB 患者有三种亚型的传导模式,分别是:左侧希氏束内部传导阻滞(18%)、LBBB(46%)和更远端非特异性室内传导阻滞(36%)[2]。

2　LBBB 的心电图表现

1909 年,Eppinger 等[4]在对狗的研究中首次描述了 LBBB 的心电图(electrocardiograph, ECG)特点,然而,他们将这种现象解释为右束支传导阻滞(right bundle branch block, RBBB)。1930 年,Barker 等[5]发现一直被认为是 RBBB 的 ECG 其实是 LBBB 的结果。LBBB 的 ECG 诊断标准主要包括以下三种,分别是 de Luna 标准、Strauss 标准和美国心脏病学会(ACC)/美国心脏协会(AHA)/心脏节律学会(HRS)标准。

2.1　de Luna 标准　de Luna 标准中 LBBB 的表现为:(1) QRS 波持续时间延长≥120 ms;(2) V1 导联呈 QS 或 rS 型;(3) V_6 和Ⅰ导联的单相 R 波;(4) 相同导联室内延迟时间>60 ms;(5) aVR 导联中的 QS 模式和方向相反的 ST 段和 T 波[6]。此标准是 1941 年从狗模型引入到人类身上,然而 Treger 等[7]的研究显示,在体表心电图呈 LBBB 图形的患者中,有 36%的患者心腔内标测结果仍显示出有浦肯野纤维的激动,且无法通过希浦系统起搏纠正其 QRS 波时限及形态的变化。意味着按此标准诊断的 LBBB 可能只有 64%为真性 LBBB。

2.2　ACC/AHA/HRS 标准　2009 年 ACC/AHA/HRS 确定 LBBB 的诊断标准为:(1) QRS 持续时间≥120 ms;(2) Ⅰ、aVL、V_5 和 V_6 导联宽 R 波伴切迹(V_5 和 V_6 导联偶尔出现 RS 模式);(3) Ⅰ、V_5 和 V_6 导联无 Q 波(AVL 导联可能存在窄 Q 波);(4) V_5 和 V_6 导联 R 峰持续时间>60 ms;(5) ST 段改变, T 波通常与 QRS 方向相反[8]。ACC/AHA/HRS 标准相较于 de Luna 标准更多的关注了胸前导联 QRS 波的切迹,但对于真性 LBBB 的诊断仍缺乏较高的特异性。

2.3　Strauss 标准　2011 年,Strauss 等[9]为了更好地预测心脏再同步化治疗(cardiac resynchronization therapy, CRT)的反应性提出了更严格的 LBBB 的 ECG 标准,包括:(1) QRS 持续时间≥140 ms(男性)或 130 ms(女性);(2) V_1 和 V_2 导联呈 QS 或 rS;(3) V_1、V_2、V_5、V_6、Ⅰ和 aVL 导联中有 2 个以上导联 QRS 中间切迹[9],他们观察到真性 LBBB 患者可能有更明显的 QRS 持续时间延长伴相应导联的切迹,但是 Strauss 标准对于预测 LBBB 合并心衰患者行 CRT 治疗反应性的价值还未得到证实。

心腔内电生理电位标测是诊断真性 LBBB 的金标准,表现为左束支电位消失。LBBB 作为一种 ECG 现象,各种标准下的 LBBB 图形并不完全意味着左束支传导功能的必然阻断。由此可见,目前的心电图标准尚不能完全确诊真性 LBBB,仍需进一步完善。

3　LBBB 的流行病学

2006 年 Imanishi 等[10]对日本广岛和长崎人群随访发现 LBBB 患者的男性年龄为(70±10)岁,女性年龄为(68±11)岁;1998 年 Eriksson 等[11]对哥德堡的 50 岁男性随访发现年龄是 LBBB 的独立危险因素,50 岁以下人群中 LBBB 的患病率小于 1%,80 岁以上人群中 LBBB 患病率为 6%;2017 年 Surkova 等[12]对无症状的成年人随访发现 LBBB 的患病率在 0.1%~0.8%;1987 年 Hardarson 等[13]对冰岛人群进行 10 年的随访发现 LBBB 男性发病率为每年 3.2 例/万人,女性发病率为每年 3.7 例/万人。既往研究指出,LBBB 是所有年龄段死亡率的独立预测因子[14]。与没有 LBBB 的冠状动脉疾病(coronary artery disease, CAD)患者相比,LBBB 伴随 CAD 患者的心源性猝死增加 10 倍、心力衰竭死亡率增加 3.08 倍、心肌梗死增加 2.9 倍、全因死亡风险增加 1.4 倍[15]。

目前尚未有对亚洲人群,特别是东亚人群的 LBBB 的流行病学研究报告,国内包括陕西省也缺乏关于 LBBB 的流行病学研究。本团队对陕西省人民医院存在 LBBB 心电图表现的人群进行了流行病学调查,同时建立了病例对照研究和回归性队列研究。希望能够为中国 LBBB 患者的现况及疾病负担作出探究贡献。

4　LBBB 的病因

多种危险因素可导致 LBBB 的发生,其中高龄已被证实是 LBBB 的独立危险因素[15]。多数 LBBB 的发生往往涉及到心肌缺血、心室重构、药物中毒、手术治疗以及遗传因素等[2]。

4.1　LBBB 的遗传易感性　虽然 LBBB 通常不被认为是一种遗传性疾病,但研究表明一些基因突变与 LBBB 有关。这些突变可能涉及通道基因、间隙连接蛋白、桥粒基因和心脏转录因子[16]。

4.2　引起 LBBB 的常见疾病　LBBB 多见于器质性疾病,包括高血压、急性冠脉综合征、慢性心肌缺血、扩张型心肌病、心肌炎、心碎综合征、经导管主动脉瓣置入术、心脏介入治疗(肥厚型心肌病切除术后)、先天性主动脉瓣狭窄、主动脉瓣膜病、二尖瓣病变、左室致密化不全、原发性淀粉样变性、神经肌肉疾病等[6]。

4.2.1　血供减少造成的 LBBB　LBBB 最常见的病因是心肌缺血[15]。左束支主干主要由右冠状动脉发出的房室结动脉和左冠状动脉前降支发出的间隔支动脉供血,左前分支和间隔支由前降支供血;左后分支由左冠状动脉和右冠状动脉双重供血[6]。无论左冠或右冠有病变时,都可能对左束支造成影响,因此,当遇到新发的 LBBB 患者时,首先需要考虑是否有心肌缺血。

4.2.2　衰老与机械影响对 LBBB 的作用　高龄患者中,LBBB 常由于传导系统纤维三角区域出现的钙化、退化、纤维化引起。由于传导系统走形于心内膜表面,位置表浅且脆弱,所以在高血压及心衰导致左室压力负荷较大时压迫左束支会出现 LBBB。由于主动脉瓣与穿透性希氏束和近端心脏传导系统的解剖接近,LBBB 也可能是手术干预的获得性机械并发症,如主动脉瓣膜置换术或经导管主动脉瓣膜置换术(transcatheter aortic valve replacement, TAVR)。在严重的肥厚性梗阻型心肌病切除术中,由于切除了左束支近端和远端的基底隔,LBBB 的发生也很常见。右心室起搏与 LBBB 具有生理上的相似性,因为右心室的起搏刺激导致左心室游离壁的晚期激活和随之而来的机电不同步,会对血流动力学和由此导致的心力衰竭产生类似的影响。

4.3　特殊类型的 LBBB　“疼痛性 LBBB 综合征”是一种罕见的临床现象,在没有缺血的情况下具有胸部疼痛的临床特点,其发生机制可能与左室非同步收缩、传导系统的退行性纤维化、冠状动脉血流缓慢及微血管功能障碍有关,研究显示左束支起搏(left bundle branch pacing, LBBP)有望纠正 LBBB 并缓解症状[17]。

速率依赖性 LBBB 与心脏收缩功能急性下降有关,根据心率快慢,分为“快频率依赖性和慢频率依赖性 LBBB”。心动过速相关的 LBBB 被认为是由于复极化 3 期传导速度加快引起,即当脉冲落入动作电位的不应期时,脉冲被延迟或完全阻塞;心动过缓相关的 LBBB 可能与左束支在较慢心率下的 4 期自动去极化有关,导致随后的电活动难以传导[15]。所以,频率依赖性 LBBB 可能并非由于左束支出现异常,而是与电生理参数有关。

5　LBBB 的临床意义

5.1　正常心脏传导　在正常的心脏传导系统中,激动通过希氏束以约 1.5 m/s 的速度到达左、右束支和浦肯野纤维,最早心室的除极活动从室间隔基底中部开始,到达室间隔心尖,再到右心室前壁心尖及左心室前侧壁心尖,再到达右心室前壁全部,最后到达左心室前侧壁、基底部。正常患者中,希氏束去极化开始到心室心肌持续时间约为 35~55 ms,再通过浦肯野纤维继续传导,最终 QRS 波的平均宽度为 60~100 ms。

5.2　LBBB 诱发心脏非同步化　发生 LBBB 时,右心室首先被激活,通过缓慢激活间隔传播到左心室,左心室产生宽且有切迹的 QRS,左心室的其余部分以延迟的方式激活,最后的激活部位发生在外侧基底区,引起电传导不同步,LBBB 时右室激动穿过室间隔耗时 40~50 ms;激动抵达左心室心内膜再激动整个左心室心肌耗时 90~100 ms,QRS 波时限共计 130~150 ms,这种顺序的心室激动将 QRS 时间延长到≥120 ms[18]。而且出现 LBBB 时,室间隔在等容收缩期间被激活,拉伸后壁和侧壁,接着后壁和侧壁在收缩期后期被激活,引起室间隔壁的被动拉伸,导致机械不同步[15]。心脏的电机械不同步进一步导致心力衰竭。

5.3　LBBB 相关的特殊疾病　电机械不同步的影响涉及整个心脏周期,最终表现为心脏收缩、舒张过程的整体不协调,无法完成有效射血,引起左室射血分数(left ventricular ejection fraction, LVEF)降低和左室容积增加,导致 LBBB 相关性心肌病,纠正 LBBB 后心肌病可逆转[2]。LBBB 引起的束支折返性室性心动过速(bundle branch reentrant ventricular tachycardia, BBRVT)是一种罕见的心律失常,束支是维持心动过速的折返回路的重要组成部分。大部分的 BBRVT 患者在窦性心律时体表心电图有 LBBB[15]。这些发现强调了 LBBB 在促进 BBRVT 中的潜在作用,同时解释了完全性房室传导阻滞是左束支消融的罕见并发症的原因。

6　LBBB 合并心力衰竭的治疗

LBBB 意味着心脏电和机械不同步导致左心室重构,可以通过心脏 CRT 或生理起搏来治疗[7]。2021 年 ESC 关于心脏起搏和 CRT 中提出:对于 LBBB、窦性心律、QRS 持续时间≥150 ms、LVEF≤35%、药物优化后的症状性心衰患者,推荐使用 CRT,Ⅰ类指征;对于 LBBB、窦性心律、QRS 持续时间在 130~149 ms、LVEF≤35%、药物优化后的症状性心衰患者,应考虑使用 CRT,Ⅱa 类指征[19]。常见的起搏方式有双室起搏(biventricular pacing, BVP)、希氏束起搏(His bundle pacing, HBP)、LBBP。

6.1　BVP　BVP 可作为 LBBB 的标准治疗。使用右心室心内膜和左心室心外膜起搏可以缓解症状,抑制心肌重构,提高运动耐量,降低心力衰竭患者的住院率和死亡率,使正常的电激活左心室,从而更“生理”纠正心脏不同步。

BVP 的作用机制是通过将电极置于冠状静脉窦分支,使左室外侧壁早期激活,从而改善左室电同步性,尽管治疗效果显著,但无反应率仍高达 30%,而且它不能纠正 LBBB,没有从根本上恢复传导系统的电同步性,即使 QRS 时间与术前相比有所下降,但仍然延长[20]。同时,由于心脏静脉系统的解剖,靠近膈神经且阈值不佳,放置左心室导联可能具有挑战性,即使是经验丰富的操作者,左心室导线植入理想分支(外侧,后外侧或后静脉)的比例也低于 90%[19]。因此,寻找 BVP 的替代方案是必要的。

6.2　HBP　HBP 是将起搏电极固定在希氏束或其邻近部位,使起搏脉冲激动沿着希浦系统下传,产生的 QRS 波接近生理传导下的形态,是最接近生理的起搏模式。有研究表明,HBP 显著改善 QRS 宽度、超声心动图参数以及症状体能,与采用 BVP 的患者相比,HBP 组在 6 个月时 LVEF 显著升高、左室收缩末容积(left ventricular end systolic volume, LVESV)显著降低[21],这表明 HBP 有更好的反向重构。

虽然 HBP 是最接近生理的起搏方式,但是许多希氏束下房室传导阻滞病情改善较差,超出了现有工具的物理接触范围,同时可能导致传导疾病的进展[22]。较高的起搏阈值、较低的 R 波幅度、早期电池耗尽以及发生远端传导阻滞等问题限制了 HBP 在临床中的应用[23]。

6.3　LBBP　LBBP 是在 HBP 研究发展过程中提出的新理念,LBBP 已被证明是实现心动过缓和心力衰竭患者心脏再同步化生理起搏的有效手段。由于左束支在左心室内的分布面积较大,因此更易定位,通过将导线固定到足够深的左心室间隔的心内膜很容易被捕获[23]。研究表明,LBBP 在合并 LBBB 需要 CRT 的非缺血性心肌病患者中的成功率为 97%[24]。在 TAVR 后需要起搏的患者中,LBBP 成功率为 93%,而 HBP 成功率只有 63%[25]。

LBBP 改善心功能的潜在机制可能是通过左心室传导系统导致更快和更早的左心室收缩,并最大化纠正了与 LBBB 相关左心室和右心室之间的电机械不同步,在 LBBB 的心衰患者中 LBBP 比 BVP-CRT 具有更高的超反应率[26]。LBBP 由于靶点宽、导线稳定、起搏阈值低且稳定,电池寿命更长,有较高的种植成功率,长期随访并发症少,并产生窄 QRS 波,许多临床研究已经证实了 LBBP 的可行性和安全性[27-28]。但 LBBP 存在室间隔穿孔、右束支损伤、电极脱落以及室间隔内的动脉损伤的可能风险,需要提高术者的操作水平。

7　未来展望

本文分析了 LBBB 的疾病特点及治疗手段。目前无相关 LBBB 在我国的流行性病学研究,且关于 LBBB 在体表心电图上的诊断标准各有特点,对于 LBBB 合并心力衰竭的器械治疗已经在技术和方法上取得了巨大进展,为 LBBB 患者带来了福音。随着电生理技术的开展,关于真性 LBBB 的心电图诊断及流行病学特点将会越来越清晰,为 LBBB 的病因干预提供新思路,未来也将会有更新的技术应用于 LBBB 患者,为 LBBB 的患者带来更安全更优质的服务。

利益冲突　无

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