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Review

Non-invasive assessment of coronary artery disease in patients with left bundle branch block

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ABSTRACT

There is a high prevalence of coronary artery disease (CAD) in patients with left bundle branch block (LBBB); however there are many other causes for this electrocardiographic abnormality. Non-invasive assessment of these patients remains difficult, and all commonly used modalities exhibit several drawbacks. This often leads to these patients undergoing invasive coronary angiography which may not have been necessary. In this review, we examine the uses and limitations of commonly performed non-invasive tests for diagnosis of CAD in patients with LBBB.

1. Introduction

While conventional invasive coronary angiography (ICA) remains the gold-standard for identification and treatment of coronary artery disease (CAD), most pathways for diagnosis and management of chronic stable angina caused by obstructive CAD include a non-invasive test to risk stratify patients and identify those in whom invasive management would be beneficial, particularly in those patients at low to intermediate risk of CAD [1]. Either anatomical or functional imaging can be used. Common non-invasive tests include exercise stress testing (treadmill or bicycle), nuclear perfusion imaging, stress echocardiography, multislice CT coronary angiography and stress cardiac magnetic resonance imaging (CMR).

The presence of left bundle branch block (LBBB) on the resting ECG in patients with suspected angina presents a diagnostic challenge. Common causes of LBBB are aortic stenosis, dilated cardiomyopathy, acute myocardial infarction, pre-existent coronary artery disease, older age and hypertension. Of course, the cause cannot often be identified from the ECG. Prevalence in the general population is estimated to be 0.43% in men and 0.28% in women while incidence is 3.2 per 10,000 per year in men and 3.7 per 10,000 per year in women [2]. Despite the numerous causes of LBBB, CAD accounts for the majority of cases. Indeed, the estimated prevalence of CAD in patients with LBBB has been between the range of 30–52% [2,3].

While acute LBBB accompanied by chest pain remains an indication for immediate primary percutaneous coronary intervention, identifying the presence of CAD in patients with chronic LBBB remains challenging. Each non-invasive cardiac imaging modality has its own pitfalls as well as benefits. The aim of this review is to look at techniques for non-invasive investigation of CAD, specifically in patients with LBBB, and to identify their advantages and disadvantages.

2. Clinical and functional impact of LBBB

The presence of LBBB has been reported in approximately 0.5% of the general population [2,4]. It has been associated with adverse prognosis, including sudden death [5]. In the Framingham study, 48% of patients with LBBB developed CAD or heart failure, while after 18 years of follow-up only 11% of patients with LBBB did not develop any cardiovascular disease [6]. Despite this, in patients with LBBB but without any phenotypic cardiovascular disease, mortality is only slightly increased compared to the general population [4]. Given this, the presence of LBBB often prompts referral to the cardiologist for further evaluation. With the most common cause being CAD, investigations will often be directed towards the exclusion of significant CAD.

Abbreviations: CAD, coronary artery disease; CT, computed tomography; CMR, cardiovascular magnetic resonance; ECG, electrocardiogram; LBBB, left bundle branch block; SPECT, single position emission computed tomography; ICA, invasive coronary angiography; MCE, myocardial contrast echocardiography; MSCT, multi-slice computed tomography; CTCA, computed tomography coronary angiography; CMR, cardiovascular magnetic resonance; RMWA, regional wall motion abnormality; LAD, left anterior descending artery

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The presence of LBBB causes a number of changes in myocardial function which have an important impact on non-invasive testing for angina. The most obvious is the delay in electrical activation of the left ventricle, recognized as the wide QRS complex on the ECG (>120 ms) (Fig. 1) [7]. This manifests itself as abnormal contraction of the interventricular septum, leading to dysynchrony in comparison to the posterior wall during systole. These features impact on both assessment of ST segment changes on the ECG during exercise and on assessment of regional wall motion abnormalities (RWMA). The delay in activation of the septum can make it appear as though there is a RWMA, particularly in inexperienced hands.

In an experimental model of LBBB, the induction of LBBB caused impaired septal systolic thickening and an increase in intramyocardial pressure, leading to a relative reduction in myocardial perfusion and glucose uptake within the septum compared to the lateral wall [8]. This phenomenon was actually found to be related to hyperperfusion of the lateral wall, and was also found in patients with permanent pacemakers (who are typically paced from the right ventricle, causing an LBBB equivalent), and was also exacerbated by exercise [9]. In this study, the authors explained the presence of lateral hyperperfusion by the delay in lateral wall contraction, causing a reduction in workload in the septum and reduced oxygen demand compared to the lateral wall. During exercise, this phenomenon would be further increased as the lateral wall does more work, causing a more pronounced hyperemic response. This could potentially cause the misrepresentation of septal perfusion defects as indicative of significant coronary stenoses.

The early septal contraction also means that the septum is thinner at end-systole. As described above, this may cause difficulty with the interpretation of wall motion abnormalities. It also may cause difficulties in the interpretation of perfusion at systole if the spatial resolution of the technique is not high, known as a partial volume effect. In a cohort of LBBB patients without significant CAD examined using positron emission tomography and CMR, the thinned septum had reduced deformation and reduced glucose metabolism in comparison to the lateral wall [10].

The combination of these myocardial features specific to LBBB may cause difficulties in the use of non-invasive imaging to assess for the presence of CAD, as we shall now describe.

3. Exercise ECG stress testing

This refers to the recording of the electrocardiogram with the patient exercising to achieve a predefined target heart rate (adjusted by age). This is achieved either by exercise on a treadmill or on a bicycle. The level is gradually increased in stages, with ECG monitoring carried out continuously. The test can be considered diagnostic if the patient reaches 85% of their maximum predicted heart rate or if typical symptoms are brought on. Commonly, if either of these points is reached at "low workload" (e.g. less than 6 min on exercise treadmill test using full Bruce protocol), patients can then commonly go on to have QCA.

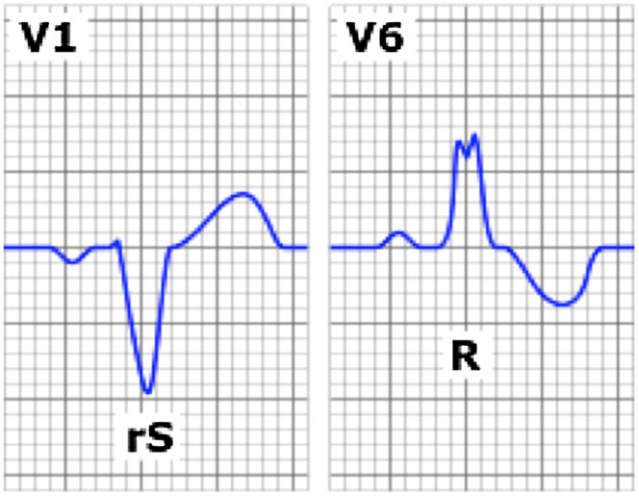

Fig. 1. The typical electrocardiographic pattern of left bundle branch block. Note the wide QRS complex, the QS complex in V_1 and the rSR in V_6.

The principal diagnostic endpoint on the ECG is of horizontal or downsloping ST-segment depression. In LBBB however, due to the resting ECG abnormality, it is very difficult to interpret any changes in the ECG during exercise (Fig. 2). Although the exercise ECG may provide some additional diagnostic and prognostic information regarding exercise tolerance, heart rate and blood pressure response and symptoms, the exercise ECG is not presently recommended as a routine investigation in patients with LBBB [1,11]. Given this, imaging modalities must be used in the evaluation of patients with LBBB.

4. Nuclear imaging

Nuclear imaging, most commonly performed using single positron emission tomography (SPECT) is one of the most validated techniques for assessment of stable angina.

Intravenous technetium-99 is most commonly used, with thallium-201 less favoured due to its increased radiation dose [12]. The myocardium is stressed either by exercise (bicycle or treadmill) or pharmacologically (vasodilator — adenosine, dipyridamole; or inotropic — dobutamine +/— atropine). Current recommendations are that exercise should be used whenever possible in order to provide a physiological response, with pharmacological stress only being used in patients unable to exercise. Vasodilator stress works on the principle of coronary artery "steal". At rest, the stenosed coronary artery is vasodilated in order to maximize blood flow to its supplied territory (i.e. its coronary vasodilator reserve has been utilized). When a vasodilator such as adenosine or dipyridamole is given, the non-diseased arteries dilate, increasing coronary blood flow to 4 to 5 times above normal. The diseased artery however is unable to dilate further, resulting in relative hypoperfusion distal to the coronary stenosis. Conversely, when dobutamine is used as stressor the aims are to mimic exercise by increasing the myocardial contractility and heart rate. The contractility of areas of ischemic myocardium initially improves with low dose dobutamine, however at higher doses the blood supply is unable to match demand and wall motion abnormalities become more obvious.

Whatever means of stress is used, there is relative hypoperfusion — known as the "steal phenomenon" — of myocardial areas subtended by stenosed coronary arteries and therefore there is a relative decrease in radioactive tracer uptake, suggesting significant CAD. The presence of transient left ventricular dilatation and reduced ejection fraction at stress are also suggestive of the presence of significant CAD.

Nuclear medicine has been the most studied imaging modality. In general nuclear medicine has been shown to be relatively robust in the assessment of CAD in the general population. In the general population with suspected obstructive SPECT has a sensitivity of 87% and specificity of 73% [13]. It is recognized that in LBBB however SPECT does suffer some limitations, predominantly explained by the impact of LBBB on the myocardium described earlier in this review; because of these several early studies found a high rate of positive test results in the LAD territory with inducible perfusion defects being seen in patients without CAD on angiography [14,15].

There are technical reasons that cause an apparent decrease in perfusion in the septum. It has been observed that resting septal radionuclide counts are lower compared to the lateral wall — this is accepted as the lateral wall is closer to the gamma camera, while the partial volume effect also causes an apparent decrease in perfusion due to the limitations of spatial resolution [16]. Despite this, there is also evidence that there is a definite reduction in septal perfusion in patients with LBBB that is picked up during SPECT imaging not caused by significant