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MYOCARDIAL PERFUSION SCINTIGRAPHY

MUHAMMAD SHEHZAD AFZAL
Punjab Institute of Nuclear Medicine Faisalabad

MUHAMMAD ALEEM KHAN
Punjab Institute of Nuclear Medicine Faisalabad

MUHAMMAD BABAR IMRAN
Punjab Institute of Nuclear Medicine Faisalabad

Javaid Irfanullah
Punjab Institute of Nuclear Medicine Faisalabad

Muhammad Saeed Akhtar
Punjab Institute of Nuclear Medicine Faisalabad

Kahn Muhammad
Punjab Institute of Nuclear Medicine Faisalabad

Naeem Aslam
Cardiology department , Allied Hospital Faisalabad.

Chaudhry Abdul Hafeez
Medica Unit III, Allied Hospital Faisalabad

ABSTRACT

Background: Reduced septal uptake of myocardial perfusion agents is frequently observed in patients having left bundle branch block (LBBB) without any significant coronary artery disease. **Objective:** To evaluate the incremental value of gated SPECT myocardial perfusion scintigraphy (MRS) on apparent regional perfusion and wall thickening, in order to standardize the protocol for reporting myocardial perfusion scintigraphy in LBBB patients with the aim of avoiding false positive reports. **Material & Methods:** Resting gated SPECT MPS was performed in 8 frames mode with intravenous injection of 740 MBq 99mTc-MIBI in 10 normal controls and 19 LBBB patients having low probability of coronary artery disease (CAD). Visual analyses and quantitative analyses on non gated (NG), end diastolic (ED), end systolic (ES), peak septal and peak lateral wall count frame images was carried out which include calculation of septal to lateral wall ratio (SLR), end systolic myocardial thickening index (MTI) and peak MTI. **Results:** Septal hypo perfusion was noted in 15 patients in NG and 19 in ES images, whereas only 1 patient showed abnormalities on ED images. Fourteen patients demonstrated worsening of apparent perfusion on ES images than that of NG. In NG study of LBBB group SLR (0.69 ± 0.08) was lower than that of control (0.89 ± 0.07) group. Further worsening was observed in ES (0.61 ± 0.06), which markedly improved in ED (0.87 ± 0.07) to reach near that of control (0.89 ± 0.08). End systolic MTI for septum was markedly lower in LBBB group (22.821 ± 11.78) than that of control (65.02 ± 21.45). Lateral wall in LBBB group demonstrated values (68.14 ± 15.8) similar to those of control (71.61 ± 22.06). Within the LBBB group septum demonstrated much lower values than that of lateral wall. In all control subjects, frames showing peak lateral and peak

septal wall counts were the same as their respective ES frame. Similar trend was noted for lateral wall of LBBB patients. However time bin showing peak septal wall counts were different from ES frame in all LBBB subjects. In controls, same value of SLR (0.86 ± 0.04) was found for ES frame and at peak myocardial thickening. In LBBB patients, peak SLR ratio (0.73 ± 0.09) is significantly higher than that observed in ES frame (0.61 ± 0.06), relatively higher than that in NG study, but still lower than that observed in controls. Comparison of end systolic MTI with peak MTI shows same value for lateral wall (71.61 ± 22.06) and IVS (65.02 + 21.45) of control group and lateral wall (68.14 ± 15.8) of LBB group respectively. However significantly higher value of septal peak MTI than end systolic MTI (42.6 ± 26 vs. 22.82 ± 11.78) are observed due to out of phase contraction of septum. **Conclusion:** Smaller count increase in the septal region during systole is basically responsible for apparent septal perfusion artefacts in NG images in LBBB patients having low probability of CAD. Out of phase contraction of septum is responsible for apparent worsening of septal perfusion from NG to ES. Septal hypoperfusion artefacts can be eliminated by conducting gated myocardial perfusion scintigraphy in LBBB patients instead of nongated studies, and reporting perfusion status on end diastolic images.

Key Words: Left bundle branch block, LBBB, Myocardial perfusion scintigraphy, gated myocardial perfusion scintigraphy, GMPS, MIBI, Myocardial thickening index, MTI, Septal to lateral wall ratio, SLR

INTRODUCTION

Left bundle branch block is a conduction abnormality, which upsets the normal polarization pattern & contraction sequence of left ventricular myocardium, and also affects the extent of septal wall thickening during systole[1]. This altered sequence of polarization of myocardium results in ECG changes which render it non interpretable for the diagnosis of reversible ischemia and myocardial infarction, hence exercise tolerance test is also of little diagnostic value[2-3].

Although tissue markers like creatine kinase MB (CKMB) and troponin can be helpful for diagnosis of acute myocardial infarction, but have no role in detection of reversible ischemia[4]. Although coronary angiography is considered as gold standard, it cannot be conducted in every LBBB patient because of its invasive nature, high cost and associated morbidity and mortality[5]. This situation demands the need of some alienate diagnostic modality, which can be used as accurate prbcedure to identify the existence of coronary artery disease (CAD), and is yet cost effective, non invasive and have low mortality and morbidity. Myocardial perfusion scintigraphy (MRS) was introduced to take this challenge. However it has been noted that in resting nongated studies, most of the patients having complete LBBB demonstrate interventricular septum (IVS) perfusion artefact with tracers like 201 Tl[6],99mTc MIBI[7-8], as well as 99mTc tetrofosmin[9] etc. Further augmentation of these septai artefacts has been noted on stress perfusion scintigraphy if chronotropic stresses are used[10-11], which may result in reporting of reversible perfusion defect. Thus pharmacological stress with adenosine[12] and dipyridamole[13,14] are preferred over physical and dobutamine stress. With the advent of gated SPECT MRS studies, it is possible to judge both the appearance of regional perfusion in ED and E3 phases, as well as regional wall motion and myocardial,thickening[15-17]. In the present study, we evaluated perfusion on gated SPECT MRS in patients with complete LBBB, having low probability of CAD. Aim was to evaluate the incremental value of gating in SPECT myocardial

perfusion scintigraphy to aprehence wall thickening, in order to standardize the protocol for reporting myocardial perfusion scintigraphy in LBBB patients with the aim of avoiding false positive reports.

MATERIALS & METHODS

Resting gated MRS was performed on 10 normal controls, and 19 LBBB patients having constant block along with low probability of IHD. Control group consisted of 3 female and 7 males with mean age of 45.2 ± 19.42 years (range 27 - 72 years). Female to male ratio in LBBB group was 1:1.4 having mean age of 52.60 ± 17.13 years (range 20-75 years). LBBB patients having incomplete and pacemaker-related LBBB, previous history of myocardial infarction, cardiomyopathy, valvular heart diseases, congenital heart disease and pregnancy were excluded from the study. Informed written consent was taken from all subjects. In resting state, 740 MBq of 99mTc-MIBI was injected intravenously. Fifteen minutes later fatty meal was given, and 30 minutes after fatty meal gated SPECT cardiac imaging was performed by dividing cardiac cycle into 8 frames. Patient was positioned supine on the imaging table of a single headed Siemen's E-CAM Gamma camera equipped with high resolution parallel hole collimator. Energy window was set at 140 KeV 20%, with R-to-R window set at 15 % of the mean R-R interval. Thirty two projections (each for 20 seconds) were acquired in 128 x 128 word matrix with step & shoot mode, from the right anterior oblique to left posterior oblique in 180^{Q} noncircular arc.

After acquiring the gated SPECT study, preprocessing application was used to get information regarding the quality of acquired data and patient motion. With autoperfusion software, tomographic reconstruction was performed by filtered back projection with a butterworth filter having a cutoff frequency of 0.48 and an order of 5. Upper and lower limits of heart were defined followed by creation of transaxial images, and then drawing the long axis of the heart. Short axis, vertical long axis and horizontal long axis slices were displayed. On the comparative page, suitable time bin having the smallest cavity size, representing the end systole was found (tfme bin 4 in most cases), and first time bin was used as end diastolic frame. ROI was drawn over the septum of suitable short axis slice and time activity curve (counts vs. time bins) for the cardiac cycle was generated. From this curve, the frame showing peak septal wall counts, representing the maximal thickening of septal myocardium was recorded. Similar process was repeated for lateral wall to determine the frame showing its maximal thickening. Nongated images were reconstructed from the projection data summed with the data of 8 frames. On these reconstructed tomographic slices, visual analysis along with further processing was done.

Perfusion of walls of left ventricular cavity was visually analyzed in non gated and gated (end-diastolic and end-systolic images) data by interpretation of short axis, vertical and horizontal long axis slices. Perfusion status was scored into three grades (normal, mild hypoperfusion and severe hypoperfusion) by the consensus of two independent observers. For the quantitative assessment of the perfusion and wall thickening, oblong regions of interest (ROI) were drawn on the septum and lateral walls of the horizontal long axis slices This exercise was done on nongated study, end diastolic and end systolic frames, and time bins showing maximal septal and lateral wall thickening of each patient.

Normalized counts (counts per pixel) were calculated from septal and lateral wall ROIs by using inbuilt statistics of the icon software. Then average normalized counts (average of values recorded by two observers) were found and recorded. Septal to lateral wall count ratio (SLR) was calculated for nongated study, end diastolic and end

systolic frames, and time bins showing maximum septal and lateral wall thickening. Then myocardial thickening index (MTI) was calculated as % count increase from end-diastolic to end-systolic frame by analyzing gated data with the following equation.

$MTI = (^{(Ces - Ced)} /Ced) * 100$

Where MTI = myocardial thickening index

Ces = end systolic counts in myocardium

Ced = end diastolic counts in myocardium

In the same way MTI for peak myocardial thickening (peak MTI) was calculated for septum and lateral wall by using similar equation. Septum to lateral wall count ratio represent perfusion parameter for the septum and MTI was taken as a parameter of wall thickening. Values in LBBB group were compared with those of control by applying unpaired student's t-test. A p value of <0.05 was considered significant.

RESULTS

Fig 1 & 2 show apparent perfusion status of IVS in NG, ED & ES images in control & LBBB group respectively. In LBBB group, 3 patients (15.79%) having normal perfusion of IVS in NG study, demonstrated mild hypoperfusion in ES images, which turn normal in ED frames. In 11 LBBB patients (57.89%), IVS was having mild hypoperfusion defects in NG study. This septal hypoperfusion in this subgroup of patient turn severe in ES, and normal in ED images. Three patients (15.8%) who were having severe hypoperfusion defects in both NG and ES images, turn normal in ED frames.

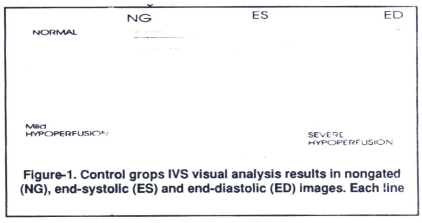

Figure-1. Control grops IVS visual analysis results in nongated (NG), end-systolic (ES) and end-diastolic (ED) images. Each line

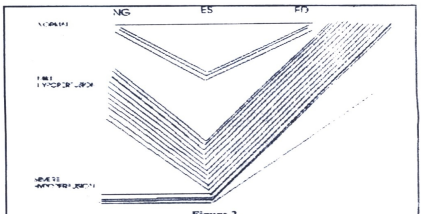

Figure 2.

Figure-2. LBBB groups visual analysis results of IVS in nongated (NG), end-systolic (ES) and end-diastolic (ED) images. Each line presents one LBBB patient.

One person (5.26%) who was having severe hypoperfusion defect of IVS in NG and ES images, showed partial improvement to mild hypoperfusion defect in ED. Only one patient (5.26%) demonstrated absence of any perfusion defect in NG, ES & ED images.

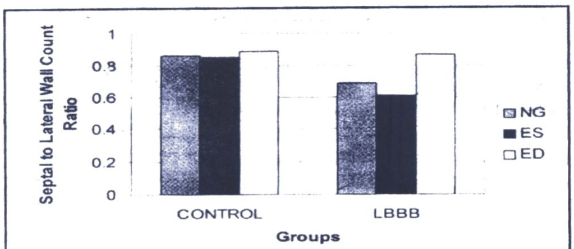

Figure-3. Septal to lateral wall counts ratio in non gated (NG), end systolic (ES) and end diastolic (ED) images of control and LBBB groups

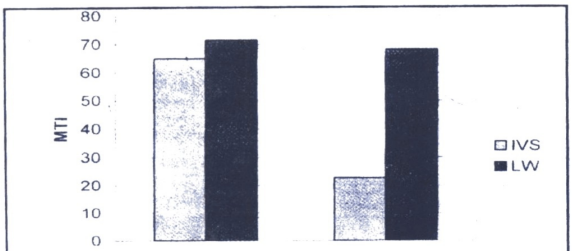

Figure-4. Comparison of end systolic myocardial thickening index (MTI) of septum (IVS) and lateral wall (LW) in control & LBBB groups

Comparison of LBBB group with control shows that in contrast to normal septal perfusion observed in all control subjects (100%) in KG study, septal perfusion was normal in nongated images of only 21.05% LBBB patients, and remainder (88.95%) demonstrated septal perfusion abnormalities. In ES images, only 10% control subjects were having septal perfusion defects (all mild), while most of LBBB patients (94.74%) demonstrated IVS hypoperfusion in ES frames. In ED images, normal septal perfusion was seen in 100% control subjects, and 94.74% LBBB patients. Thus ED images of LBBB patients showed results similar to those of control.

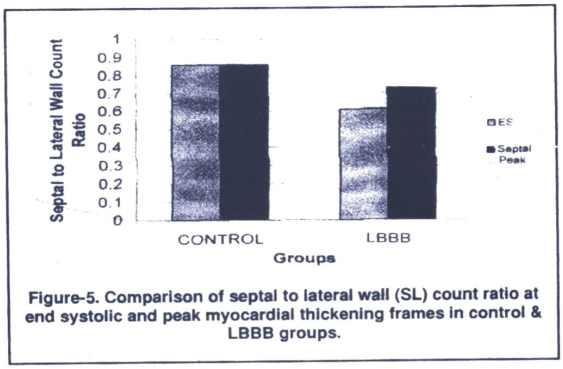

Figure-5. Comparison of septal to lateral wall (SL) count ratio at end systolic and peak myocardial thickening frames in control & LBBB groups.

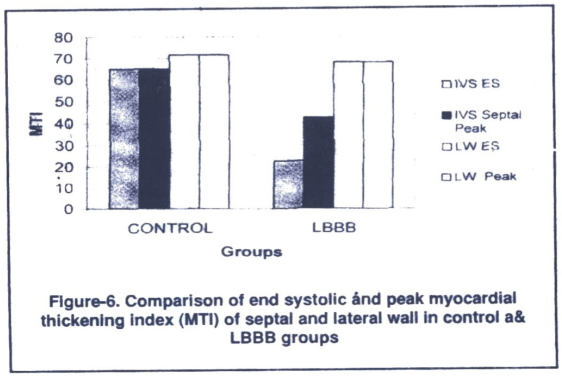

Figure-6. Comparison of end systolic ánd peak myocardial thickening index (MTI) of septal and lateral wall in control a& LBBB groups

Table-1. Septal to lateral wall count ratio in nongated, endsystolic, and diastolic phase in control & LBBB groups.

Group	Control	LBBB
Non Gated	0.86±0.04	0.69±0.08
End Gated	0.85±0.06	0.61±0.06
End Dias ystole	0.89±0.08	0.87±0.07

Numerical values of SLR (mean ± SD) for control and LBBB group are given in table-l and graphically presented in fig 3. Absence of any significant difference between these values obtained from NG study, ES and ED images of control group is evident. In LBBB group, SLR is markedly low in nongated images, and further reduces in end systolic images. Marked improvement is seen in end diastolic images indicating improvement in septum perfusion. Comparison of SLR in control and LBBB groups in NG study demonstrated lower value in LBBB than that of control, which gives an impression that septal perfusion is impaired in LBBB group. In ES images, SLR showed similar trends to that of nongated data; however difference between control and LBBB group for SLR is higher than that in nongated study. It signifies further worsening of septal perfusion from NG to ES phase in LBBB patients. As compared to NG and ES phases, marked improvement in value of this ratio is seen in ED phase of LBBB group, almost approaching to that of control group.

Table-1I. End systolic Myocardial thickening index (MTI) in control & LBBB groups

Group	Control	LBBB
Septum	65.02±21.45	22.82±11.78
Lateral wall	71.61±22.06	68.14±15.8

Table-III. Septal to lateral wall ratio of control and LBBB groups at end sysole and time showing peak septal and lateral wall

Group	Control	LBBB

End systole	0.86±0.04	0.61±0.06
Septal Peak	0.86±0.04	0.73±0.09

Table-1V. End systolic Peak myocardial thickening index (MTI) in control & LBBB groups

Group	Control		LBBB	
	E. Systole	Peak	E. Systole	Peak
Non Gated	0.86±0.04		0.69±0.08	
End Systolic	0.85±0.06		0.61±0.06	
End Diastole	0.89±0.08		0.87±0.07	

Numerical values related with end systolic MTI in control and LBBB group are given in table-ll and graphically presented in fig 4. As end systolic MTI of the septum and lateral wall in control subjects ranges from 65% to 71% only, hence no significant difference exists in terms of myocardial thickening, and more or less, myocardium of both walls behave similarly.

In LBBB group, IVS demonstrated markedly reduced end systolic MTI as compared to lateral wall, signifying reduced thickening during systole. Graphical comparison of end systolic MTI of septum and lateral wall [fig 4] between control and LBBB group shows almost similar increase in counts by lateral wall, representing normal thickening. Septum shows lower value of end systolic MTI in LBBB group showing markedly reduced thickening of IVS during systole in this group of patients. All this gives an impression that in LBBB patients markedly reduced septal thickening during systole is responsible for induction of septal perfusion artifacts.

In all control subjects, frames showing peak lateral and septal wall counts were the same as their respective ES frame. Similar trend was noted for lateral wall of LBBB patients. However time bin showing peak septal wall counts were different than ES frame in all LBBB subjects and represent out of phase contraction of septum. Numerical data of peak SLR (mean ± SD) for comparison at peak septal and peak lateral wall thickening with that at ES frame is given in table-Ill and graphically presented in fig 5. In controls, values of SLR for ES frame and peak thickening are the same. In LBBB patients, peak septal to peak lateral wall ratio is significantly higher than that observed in ES frame, relatively higher than that in NG study, but still lower than that observed in controls. Comparison of end systolic MTI with peak MTI (table-IV & fig 6) shows same value for lateral wall and IVS of control group and lateral wall of LBBB group respectively. However significantly higher value of septal peak MTI than end systolic MTI is observed due to out of phase contraction of septum.

DISCUSSION

In this study we investigated the nature of septal perfusion artifacts in LBBB group having low probability of CAD, in NG, and different phases of gated study. Visual analyses demonstrated existence of septal perfusion artifact on NG images of the most LBBB patients, which further worsens in ES, and in most cases disappear in ED phase. In LBBB patients, SLR was having values lower than control in nongated study, which further decreased in ES images, and improved in ED images to approach the values observed in control group. In contrast to almost equal myocardial thickening of septum and lateral wall of left ventricular cavity in control group, IVS demonstrated less than half increase in end systolic MTI in LBBB group. This gives an impression that reduced thickening of IVS during systole is responsible for induction of apparent perfusion artifacts in ES & NG images.

In LBBB patients out of phase contraction of septum, higher peak SLR than that of endsystolic and NG study, along with peak MTI of septum having values in between ES and control signifies

that reduced thickening of septum during systole is not the only factor responsible for induction of septal perfusion artefacts on NG study. Other factors may also contribute. It also shows that worsening of apparent perfusion status of septum from NG study to ES frame is not due to impaired thickening, but as a result of its out of phase contraction.

In short our results demonstrated presence of septal hypoperfusion on nongated images in the majority of LBBB patients, their ED images were almost the same as those of normal subjects (qualitative as well as quantitative assessment). With respect to NG studies, our data is concordat with the previous studies[718] suggesting diminished uptake of 99mTc MIBI in septal segment of left ventricle as a common phenomenon. In contrast to demonstration of septal perfusion artefact in 50% LBBB patients by Altehoefer et. al.[19], our study showed 81.25%, which is quite higher. Although use of both qualitative and quantitative data makes our study more reliable, however this difference may be due to differnce in type of population studied, and the fact that LBBB is not a manifestation of single etiology.

Evolution of ECG gated myocardial perfusion scintigraphy has revolutionized the field of nuclear cardiology, making simultaneous assessment of myocardial perfusion status, regional wall motion, thickness and pumping function of heart possible[15-16]. In our study, use of this gating technique has provided useful information regarding the septal perfusion status of I BBB patients having low probability of CAD in different phases of cardiac cycle indicating homogenous & normal perfusion in end diastolic images. Our results are similar to those of Inanir et. al.[20] who found best correlation of angiographic data of LBBB patients with that of end diastolic images and concluded that resolution of an LBBB pattern on end-diastolic data would significantly improve the diagnostic role of myocardial perfusion scintigraphy in these patients.

Recent studies have reported that regional wall thickening can be quantitatively judged by measuring the count increase from ED to ES phase[21-22]. Count based evaluation of myocardial thickening has been justified on the principle of partial volume effect by *Marcassa et. al,[22] and Cooke et. al[23]* which states that recovery counts by the instrumentation is a function of the object size. Systo-diastolic changes in the detected radioactivity would therefore reflect changes in myocardial wall thickness. Our study shows septal hypoperfusion artefacts in ES and nongated images as a result of reduced septal thickening during systole. Almost similar results have been quoted by Hasegawa et. al[24]. Eisner et. al[25] also reported that abnormal segmental contraction can create abnormalities on SPECT myocardial perfusion scintigraphy images in a canine experimental study. The pathophysiological mechanism of reduced wall thickening in the septal region with relatively preserved perfusion remains unknown. However abnormal conduction has been proposed as the cause. There is critical need for more precise investigation of regional contraction and potential mechanism using echo and MR metabolic imaging. Positron emission studies have showed normal septal perfusion with 13N-NH3. Divergent metabolic effects of conduction abnormality in LBBB with consecutive reduced septal exogenous glucose utilization but unaffected septal beta oxidation of fatty acids like 18F-FTHA has also been observed. To avoid possible overestimation of necrosis in LBBB patients, especially in LAD territory of LBBB, this phenomenon must be considered in evaluation of myocardial viability using 18F-FDG images[26-27]. SPECT MPS has been an important prognostic tool for predicting future cardiac events in patients with pre-existing LBBB and aids in their risk stratification for coronary artery disease[28]. The size of perfusion abnormality and lung thallium uptake stratified patients into

high and low risk groups with a three fold difference in hard events and total cardiac events[29]. Normal myocardial perfusion scintigraphy in patients with suspected CAD and LBBB has been found to have a very good prognosis, a low rate of clinical events occurring only 2 years after the myocardial scintigraphy, and no hard events[30].

Our results showed that abnormal wall thickening may mimic hypoperfusion on nongated images. Thus in patients with disproportionate decrease in regional myocardial contraction as seen in patients with LBBB, actual perfuoion should be carefully assessed at ED images to avoid reporting of septal perfusion artefacts as true CAD related perfusion abnormalities. Every et. al.[31] has also concluded that end diastolic frames enhance the diagnostic efficacy in CAD and should be routinely used for commenting septal perfusion status in LBBB patients. Similarly the effects of wall thickening should be considered to evaluate regional distribution of tracers in any other myocardial perfusion radionuclide studies.

This study showed that lateral and septal cardiac walls of normal subjects show synergy in wall motion, with maximal thickening during end systolic frame. Lateral wall of LBBB patients also behave similarly. However septal movements are out of phase in LBBB patients. Thus, extent of worsening of septal perfusion observed in ES frames from NG is mainly due to out of phase contraction of septum. Thus in addition to impaired nyocardial thickening, other factors are probably also involved in induction of perfusion artefacts on nongated study, which need to be further investigated. One of these factor might be reduce flow demands to the septum as a result of abnormal wall motion, resulting in reduction of coronary blood flow with little ischemia.

However this study had several limitations. Although the number of LBBB patients included in our study is less, but even then significant differences were obtained. Another limitation is that coronary angiography was not performed in them. However all patients were having low pretest likelihood of CAD, and we evaluated myocardial perfusion at rest but not during stress.

There is critical need for performance of further studies to assess regional function and perfusion with EGG gated tomograph; in LBBB patients with different subgroups based on etiology of disease.

CONCLUSION

In LBBB patients without coronary artery disease, septal perfusion artefact is quite common on nongated images. These nongated images being the sum of gated frames represent the effects of both regional perfusion as well as wall thickening. In LBBB patients reduced septal thickening resulting in less increase in septal counts during systole is basically responsible for septal perfusion artefacts on rest nongated images. Out of phase contraction of septum is responsible for apparent worsening of septal perfusion from NG to ES. In presence of myocardial contraction abnormalities as observed in LBBB patients, end diastolic images are better for evaluation of true perfusion status of walls of left ventricular cavity than nongated images. Septal hypoperfusion artefacts can be eliminated by conducting gated myocardial perfusion scintigraphy in LBBB patients instead of nongated studies, and reporting perfusion status on end diastolic images.

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