

Observational Study

Significance of inferior wall ischemia in non-dominant right coronary artery anatomy

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Abstract**AIM**

To investigate the relationship of inferior wall ischemia on myocardial perfusion imaging in patients with non-dominant right coronary artery anatomy.

METHODS

This was a retrospective observational analysis of consecutive patients who presented to the emergency department with primary complaint of chest pain. Only patients who underwent single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) were included. Patients who showed a reversible defect on SPECT MPI and had coronary angiography during the same hospitalization was analyzed. Patients with prior history of coronary artery disease (CAD) including history of percutaneous coronary intervention and coronary artery bypass graft surgeries were excluded. True positive and false positive results were identified on the basis of hemodynamically significant CAD on coronary angiography, in the same territory as identified on SPECT MPI. Coronary artery dominance was determined on coronary angiography. Patients were divided into group 1 and group 2. Group 1 included patients with non-dominant right coronary artery (RCA) (left dominant and codominant). Group 2 included patients with dominant RCA anatomy. Demographics, baseline characteristics and positive predictive value (PPV) were analyzed for the two

groups.

RESULTS

The mean age of the study cohort was 57.6 years. Sixty-one point seven percent of the patients were males. The prevalence of self-reported diabetes mellitus, hypertension and dyslipidemia was 36%, 71.9% and 53.9% respectively. A comparison of baseline characteristics between the two groups showed that patients with a non-dominant RCA were more likely to be men. For inferior wall ischemia on SPECT MPI, patients in study group 2 had a significantly higher PPV, 32/42 (76.1%), compared to patients in group 1, in which only 3 out of the 29 patients (10.3%) had true positive results (P value < 0.001 Z test). The difference remained statistically significant even when only patients with left dominant coronary system (without co-dominant) were compared to patients with right dominant system (32/40, 76.1% in right dominant group, 3/19, 15.8% in left dominant group, P value < 0.001 Z test). There was no significant difference in mean hospital stay, re-hospitalization, and in-hospital mortality between the two groups.

CONCLUSION

The positive predictive value of SPECT MPI for inferior wall ischemia is affected by coronary artery dominance. More studies are needed to explain this phenomenon.

Key words: Myocardial perfusion imaging; Single photon emission computed tomography; False positive results; Coronary artery dominance; Inferior wall ischemia

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Core tip: A positive test for ischemia on single photon emission computed tomography (SPECT), myocardial perfusion imaging (MPI) is often followed up with coronary angiography. The aim of our study was to assess the relationship of inferior wall ischemia on SPECT MPI with non-dominant right coronary artery (RCA) anatomy. We found that positive predictive value of inferior wall ischemia on SPECT MPI was significantly lower in patients with non-dominant RCA anatomy. We postulate that in non-dominant RCA anatomy flow tracer may show relatively decreased uptake in the inferior wall that might not be indicative of flow limiting stenosis.

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INTRODUCTION

Single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) is most often used to assess the likelihood of obstructive coronary artery

disease (CAD), presence of ischemia in a patient with known CAD, and evaluating the extent of ischemia for prognostic value^[1]. In essence SPECT MPI accomplishes this by measuring relative changes in perfusion of myocardial territories before and after augmenting coronary blood flow^[1]. SPECT MPI has enjoyed widespread clinical use because of its well documented diagnostic and prognostic utility in CAD^[2].

Coronary artery dominance is determined by the artery supplying the posterior portion of interventricular (IV) septum^[3]. In a right dominant system, the right coronary artery (RCA) supplies this territory and feeds the posterior descending artery, in contrast to left dominant system in which the left circumflex artery (LCX) accomplishes this role^[3]. In a co-dominant system, the supply of posterior IV septum is shared by both RCA and LCX^[3]. Right dominant system is the more prevalent variant occurring in approximately 70% of people, followed by left dominant and co-dominant system^[4].

The prognostic significance of coronary artery dominance in patients with CAD has been studied. Left dominant system has been shown to be an independent risk factor of morbidity and mortality in patients undergoing both surgical and percutaneous revascularization, especially in patients with ST segment elevated myocardial infarction (STEMI)^[4-7].

The effect of coronary anatomy on diagnostic accuracy of cardiac magnetic resonance imaging (CMR) has been studied^[8]. However, no study to our knowledge has evaluated the effect of coronary artery dominance on diagnostic accuracy of SPECT (MPI studies). We present the first report showing the effect of coronary artery dominance on positive predictive value of SPECT MPI.

MATERIALS AND METHODS

Study design

The study was a single center retrospective analysis conducted at a tertiary care center.

Inclusion and exclusion criteria

All patients who underwent rest and stress SPECT MPI from January 1st 2013 to June 30th 2014, for diagnostic purposes were included in our study. All patients who did not undergo a coronary angiogram during the same hospital stay were excluded. Furthermore, all patients who did not have evidence of reversible ischemia on SPECT MPI were excluded.

These patients presented with chest pain that were deemed to be of intermediate pre-test probability for ischemia. The images were initially read by an experienced radiologist and results verified by the cardiologist.

Institute review board approval

The study was approved by the Institute Review Board at University Medical Center of Southern Nevada. This study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of

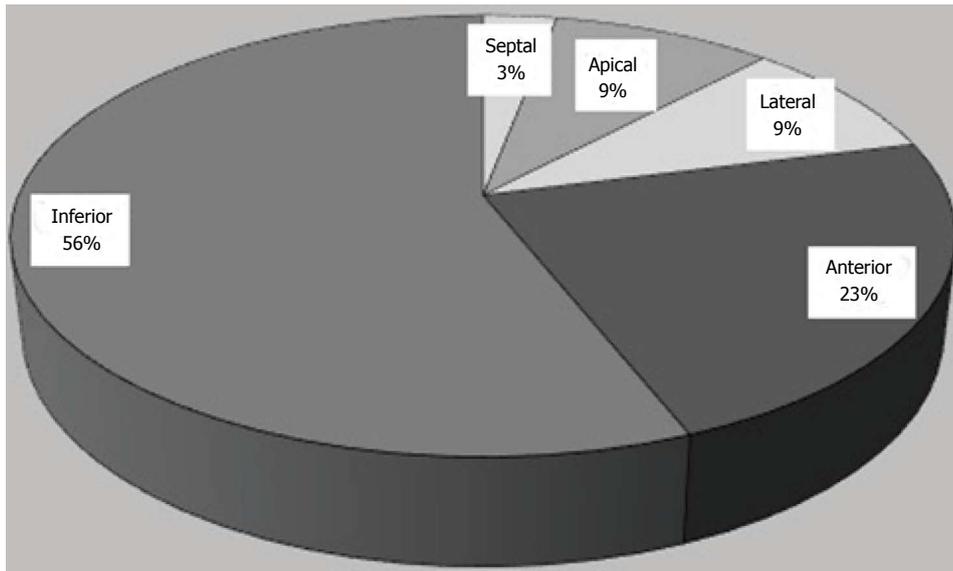


Figure 1 Defect location on single photon emission computed tomography myocardial perfusion imaging.

Helsinki and its later amendments or comparable ethical standards.

Coronary angiography and defining obstructive CAD

All of the patients subsequently underwent a coronary angiogram during the same hospital stay after the SPECT MPI. Patients were divided into two groups on the basis of coronary artery dominance. Group 1 included patients with a non-dominant RCA (left dominant and co-dominant). Group 2 included patients with right dominant coronary artery system.

The coronary angiogram was performed by an experienced interventional cardiologist. It was noted if there was obstructive CAD, in the same distribution as shown by the SPECT MPI the study was deemed to be true positive. Obstructive CAD was defined as maximal coronary artery stenosis of more than 70%.

SPECT MPI and determination of reversible ischemia

SPECT MPI was performed using standard protocols approved by the American Society of Nuclear Cardiology^[9]. An experienced radiologist initially read the images and the presence of any reversible ischemia was verified by the cardiology team. Figure 1 shows representative images of SPECT MPI, showing inferior wall ischemia and normal scan respectively.

Study outcome

The primary study outcome was determining diagnostic accuracy of the SPECT MPI, with the coronary angiogram as gold standard. The positive predictive value of SPECT MPI was compared in both groups.

Statistical analysis

Data for each study variable were summarized initially for the whole cohort and then by dominant coronary artery group, using means for continuous variables

and frequencies/percentages for categorical variables. Means for the non-dominant RCA and dominant RCA groups were compared using independent-samples *t*-tests (or Mann Whitney *U* tests, for variables with non-normally distributed data). Frequencies/percentages were compared using χ^2 tests. Positive predictive values for were compared *via* *Z* tests of proportions. The significance level (alpha) was set at 0.05, and all analyses were completed *via* SPSS, version 22 (IBM).

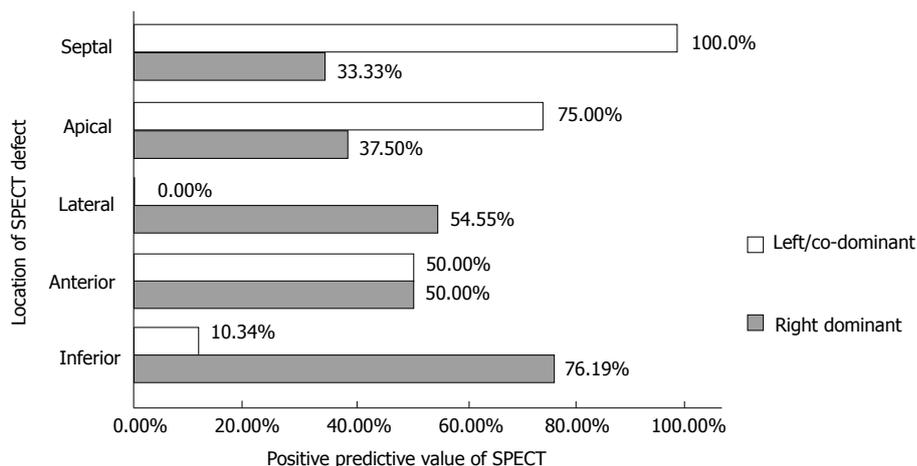
RESULTS

The mean age of the study cohort was 57.6 years. Sixty-one point seven percent of the patients were males. The prevalence of self-reported diabetes mellitus, hypertension and dyslipidemia was 36%, 71.9% and 53.9% respectively. A comparison of baseline characteristics between the two groups showed that patients with a non-dominant RCA were more likely to be men. Table 1 shows comparison of other baseline characteristics.

The most common location for the reversible defect was seen the inferior wall (Figure 2).

The positive predictive value (PPV) was analyzed and compared between the two study groups. Sub-group analysis showed that for inferior wall ischemia on SPECT MPI, patients in study group 2 had a significantly higher PPV, 32/42 (76.1%), compared to patients in group 1, in which PPV was 10.3% (3/29) (*P* value < 0.001 *Z* test) Figure 2 illustrates the results. The difference remained statistically significant even when only patients with left dominant coronary system (without co-dominant) were compared to patients with right dominant system. (32/40, 76.1% in right dominant group, 3/19, 15.8% in left dominant group, *P* value < 0.001 *Z* test).

There was no significant difference in mean hospital stay, re-hospitalization, and in-hospital mortality between the two groups as shown in Table 2.



Significant difference between left/co-dominant and right dominant, $P < 0.001$.

Figure 2 Positive predictive value of single photon emission computed tomography for patients in group 1 and group 2. SPECT: Single photon emission computed tomography.

| | Dominant RCA $n = 87$ | Non-dominant RCA $n = 41$ | P value (test) |
|--------------------|--------------------------|------------------------------|----------------------|
| Age | 56.92 yr | 59.24 yr | 0.252 (t test) |
| Male gender | 48/87 (55.17) | 31/41 (75.61) | 0.026 (χ^2) |
| BMI | 28.29 | 28.87 | 0.459 (Mann-Whitney) |
| PMH of DM | 33/87 (37.93) | 14/41 (34.15) | 0.679 (χ^2) |
| PMH HTN | 64/87 (73.56) | 27/41 (65.85) | 0.369 (χ^2) |
| PMH dyslipidemia | 51/87 (58.62) | 18/41 (43.90) | 0.119 (χ^2) |
| PMH of a fib | 2/87 (2.30) | 1/41 (2.45) | 1.000 (χ^2) |
| PMH of PVD | 17/87 (19.54) | 8/41 (19.51) | 0.997 (χ^2) |
| PMH of COPD | 5/87 (5.75) | 7/41 (17.07) | 0.053 (χ^2) |
| Current smoker | 27/87 (31.03) | 15/41 (36.59) | 0.533 (χ^2) |
| Drug abuse | 10/87 (11.49) | 7/41 (17.07) | 0.386 (χ^2) |
| Alcohol use | 23/87 (26.45) | 11/40 (27.50) | 0.900 (χ^2) |
| PMH of sleep apnea | 3/87 (3.45) | 1/41 (2.44) | 1.000 (χ^2) |
| PMH of CKD | 9/87 (10.34) | 2/41 (4.88) | 0.501 (χ^2) |
| ESRD on HD | 4/87 (4.60) | 2/41 (4.88) | 1.000 (χ^2) |

RCA: Right coronary artery; BMI: Body mass index; PMH: Past medical history; DM: Diabetes mellitus; HTN: Hypertension; a fib: Atrial fibrillation; PVD: Peripheral vascular disease; COPD: Chronic obstructive pulmonary disease; CKD: Chronic kidney disease; ESRD: End stage renal disease; HD: Hemodialysis.

DISCUSSION

Around 15 million patients seek medical attention for symptoms concerning for CAD^[10]. In stable patients, not having acute coronary syndrome non-invasive testing like SPECT MPI, act as gatekeepers to coronary angiography because of risks and costs associated with coronary angiography^[11,12]. Despite the use of conventional non-invasive testing such as SPECT MPI an analysis of almost 400000 coronary angiograms in patients with no prior history of CAD disease revealed no obstructive disease in more than 60% of the cases, resulting in unnecessary risks and costs^[13,14]. Hence, from a public health standpoint, it is imperative that we

study the reasons for false positive diagnoses associated with non-invasive tests such as SPECT MPI.

SPECT MPI is widely used for diagnostic purposes in patients presenting with chest pain when acute coronary syndrome (ACS) has been ruled out^[2]. A recent study showed that SPECT MPI is widely used for diagnostic and risk stratification purposes in the United States and patient's socio-economic status did not significantly affect the use of SPECT MPI by physicians^[15]. In the developing world several studies have shown the widespread use of SPECT MPI by physicians to aid in diagnosis in management^[16,17]. One such report from Iran regarding SPECT MPI referral practices showed that 72.5% (211/291) of the referrals found to be appropriate per ASNC recommendations^[16].

The utilization of SPECT MPI is often on the physician's assessment of pre-test probability. The American College of Physicians pre-test probability assessment and Duke chest pain score are two common objective tools used for this assessment^[18]. In our retrospective analysis, SPECT MPI was done, on the physician's assessment of the patient's pre-test probability.

Our study shows that SPECT MPI in patients with non-dominant RCA has significantly high false positive results for inferior wall ischemia. In a study using positron emission tomography measuring absolute myocardial blood flow (MBF) in low risk normal patients' authors found baseline MBF in the inferior region was significantly ($P < 0.0001$) lower than either the anterior or lateral regions^[19]. However, coronary anatomy was not available in this study population. Nonetheless this finding may contribute to our observation as well. One study using stress CMR also showed a statistically significant difference in false positive rate correlating with dominance^[8]. They also showed a correlation with the vessel size, postulating that the smaller vessel size that usually comes with non-dominant vessels was the factor leading to false positive readings^[8].

Table 2 Comparison of outcomes between study groups

| | Dominant RCA n = 87 | Non-dominant RCA n = 41 | P value (test) |
|--|--------------------------------|--|-----------------------|
| Mean hospital stay (d) | 4.33 | 4.29 | 0.713 (Mann-Whitney) |
| In-hospital mortality | 0/87 | 0/41 | - |
| 30-d re-hospitalization for chest pain | 10/87 (11.49%) | 2/41 (4.88%) | 0.231 (χ^2) |

RCA: Right coronary artery.

Gender differences in vessel caliber and coronary artery dominance could also play a role. As shown in our results patients with non-dominant RCA were more likely to be men. This is consistent with the report by Gebhard *et al*^[5] in which patients with left dominant coronary artery anatomy were more likely to be males. In contrast in a cohort of patients with STEMI, lower percentage of patients with left dominant circulation were men compared to patients with right dominant circulation^[7]. This was not statistically significant. Vessel caliber was not available in either of these studies. Whether gender differences affect coronary artery, dominance is not clear at this time.

Regardless our study finding has important consequences. First, it has been shown that patients with left dominant system are at high risk in terms of cardiovascular events^[6]; hence, it is important that significant CAD is promptly addressed in these patients. If the diagnostic accuracy of SPECT MPI is particularly low in this sub group of patients, then it is important that more studies are done to evaluate the negative predictive value (NPV) in this subset to reach a better understanding about role of SPECT MPI in excluding significant CAD in these patients. In our retrospective analysis patients with negative SPECT MPI imaging did not have a coronary angiogram, hence analysis of NPV was not possible.

Second, if the diagnostic accuracy of inferior wall ischemia on SPECT MPI is affected by coronary artery dominance and it has a significantly lower PPV in patients with non-dominant RCA, it would mean that many patients in this sub-group are exposed to unnecessary invasive procedures. This is in addition to utilizing the resources when it will not help the patient.

In conclusion, based on our findings we hypothesize that the flow tracer in a non-dominant RCA may show relatively decreased uptake in the inferior wall that might not be indicative of flow limiting stenosis. More multi-center studies to explore the relationship of coronary artery dominance on SPECT MPI are needed to reach a better understanding regarding positive or negative results in patients in the context of non-dominant RCA anatomy.

Study limitations

This study was done only at a single center and the

SPECT MPI results were only read by one group of physicians. Prone imaging was not done. Also some patients could have had inferior wall abnormality and coronary computed tomography angiogram was not utilized. Coronary angiograms were not done on patients with normal SPECT MPI results. Hence we could not analyze the effect of coronary dominance on NPV. We did not strictly use objective validated models to quantify SPECT MPI defect so some measurement bias may be present.

COMMENTS

Background

Single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) is most often used to assess the likelihood of obstructive coronary artery disease (CAD), presence of ischemia in a patient with known CAD, and evaluating the ex-tent of ischemia for prognostic value. SPECT MPI has enjoyed widespread clinical use because of its well documented diagnostic and prognostic utility in CAD. The authors' study aims to understand the effect of coronary artery dominance on the positive predictive value (PPV) of SPECT MPI.

Research frontiers

The effect of coronary anatomy on diagnostic accuracy of cardiac magnetic resonance imaging (CMR) has been studied. However, no study to our knowledge has evaluated the effect of coronary artery dominance on diagnostic accuracy of SPECT MPI studies. The authors' present the first report showing the effect of coronary artery dominance on PPV of SPECT MPI.

Innovations and breakthroughs

They studied the effect of coronary artery dominance on the PPV of SPECT MPI. The effect of coronary anatomy on diagnostic accuracy of cardiac magnetic resonance imaging (CMR) has been studied. In a study using positron emission tomography measuring absolute myocardial blood flow (MBF) in low risk normal patients' authors found baseline MBF in the inferior region was significantly lower than either the anterior or lateral regions. However, coronary anatomy was not available in this study population. They studied the effect of coronary artery dominance on the PPV of SPECT MPI.

Applications

In stable patients, not having acute coronary syndrome non-invasive testing like SPECT MPI, act as gatekeepers to coronary angiography because of risks and costs associated with coronary angiography. Despite the use of conventional non-invasive testing such as SPECT MPI an analysis of almost 400000 coronary angiograms in patients with no prior history of CAD disease revealed no obstructive disease in more than 60% of the cases, resulting in unnecessary risks and costs. Hence, from a public health standpoint, it is imperative that the study the reasons for false positive diagnoses associated with non-invasive tests such as SPECT MPI. They show in the study that the PPV of SPECT MPI for inferior wall ischemia in stable patients not having ACS, is affected by coronary artery dominance. Although more studies are needed to explain this phenomenon, maybe this subset of patients should undergo further non-invasive testing before proceeding to invasive coronary angiography.

Terminology

SPECT MPI: SPECT MPI is most often used to assess the likelihood of obstructive CAD, presence of ischemia in a patient with known CAD, and evaluating the ex-tent of ischemia for prognostic value. In essence SPECT MPI accomplishes this by measuring relative changes in perfusion of myocardial territories before and after augmenting coronary blood flow; coronary artery dominance: Coronary artery dominance is determined by the artery supplying the posterior portion of interventricular (IV) septum. In a right dominant system, the right coronary artery (RCA) supplies this territory and feeds the posterior descending artery, in contrast to left dominant system in which the left circumflex artery (LCX) accomplishes this role. In a co-dominant system, the supply of

posterior IV septum is shared by both RCA and LCX.

Peer-review

This is an interesting manuscript about the association of a positive test for inferior wall ischemia on MPI with non-dominant RCA anatomy.

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