

Detection of Coronary Collaterals Using Dipyridamole PET Myocardial Perfusion Imaging with Rubidium-82

Dahlia Garza, Andrew Van Tosh, Roberto Roberti, Prateek Dalal, Carl Reimers, Fukiat Ongseng, Barbara Ventura, Jennifer Pompliano and Steven F. Horowitz

Division of Cardiology, Department of Medicine, Beth Israel Medical Center, New York, New York

This study evaluated the ability of dipyridamole PET myocardial perfusion imaging to detect coronary collaterals. A previous study showed an association between dipyridamole-induced coronary steal on PET imaging and the presence of coronary collaterals on angiography. **Methods:** Dipyridamole PET myocardial perfusion imaging using ^{82}Rb was performed in 45 patients who had recent coronary angiography. The stress/rest count ratio (rubidium activity with stress divided by activity at rest) was used to express the change in regional tracer uptake with dipyridamole and was calculated manually and automatically. The accuracy of the stress/rest count ratio for detecting coronary collaterals was determined. **Results:** A manual stress/rest count ratio ≤ 0.80 identified coronary collaterals with 81% sensitivity, 92% specificity and 90% accuracy ($p < 0.0001$). An automated ratio ≤ 0.80 had 90% sensitivity, 88% specificity and 90% accuracy ($p < 0.0001$). Vascular beds incorrectly identified by PET as having collaterals had an increased frequency of severe stenoses and abnormal wall motion. **Conclusion:** PET perfusion imaging using the stress/rest count ratio can serve as a unique imaging method to identify coronary collaterals noninvasively.

Key Words: myocardial perfusion; rubidium-82; PET; coronary collaterals

J Nucl Med 1997; 38:39-43

The presence of coronary collateral circulation has a significant influence on the long-term prognosis of patients with ischemic heart disease and is thus an important factor in clinical decision making (1,2). Previously, identification of collaterals has required coronary angiography and has not been achieved with noninvasive scintigraphic methods (3-7).

A recent study suggested that PET, using dipyridamole stress and ^{82}Rb as a perfusion tracer, can determine the presence or absence of coronary collaterals (8). In that study, regional tracer activity was used as an index of myocardial blood flow. Change in regional tracer uptake with dipyridamole was expressed as a stress/rest count ratio: activity with stress divided by the activity at rest was expressed in a manually outlined region of interest (ROI). Absolute perfusion was not quantified (8-10). Myocardial regions supplied on angiography by collaterals showed a decrease in tracer uptake in response to dipyridamole (analogous to coronary steal) and had stress/rest count ratios < 1.0 (8,9). Regions supplied by coronaries with moderate or severe stenoses showed an increase or no change in tracer uptake in

response to dipyridamole, respectively; stress/rest count ratios were ≥ 1.0 (8,9).

A computerized algorithm for comparing cardiac PET studies is now available which calculates stress/rest count ratios automatically. This offers a simple means of assessing the relative change in regional tracer activity in response to dipyridamole and noninvasively identifying coronary collaterals.

In the current study, we analyzed a group of patients who had undergone dipyridamole ^{82}Rb PET and coronary angiography. We calculated regional myocardial stress/rest count ratios using both the manual and automated methods and compared the accuracy of each method for identifying coronary vascular beds supplied by collaterals. This analysis provides another assessment of whether a dipyridamole-induced decrease in regional myocardial tracer uptake (as assessed by the stress/rest count ratio) is a specific marker of collateral circulation and coronary steal.

MATERIALS AND METHODS

Study Population

The study population consisted of 45 patients (25 men, 20 women; mean age 64 yr) who had dipyridamole ^{82}Rb -PET and coronary angiography separated by an interval of 3 mo or less. Only 4 of 45 patients had PET imaging performed before angiography. Neither the presence of collaterals on angiography nor the findings on PET imaging were factors in selecting patients for the study. No patient had a cardiac event in the time between the two tests.

Cardiac Catheterization

Coronary angiography was performed using the Sones' or Judkins' technique. Left ventriculography in the right anterior oblique projection was performed in 41 of 45 patients.

Two experienced angiographers (blinded to the PET results) visually graded the severity of coronary obstructions and the presence or absence of collateral circulation in each coronary vascular bed. Coronary stenoses of severity $\geq 50\%$ were deemed hemodynamically significant. Stenoses $> 70\%$ were deemed severe. Collaterals were considered present when there was any angiographic filling of a major coronary artery (or branch vessel), distal to a significant stenosis or occlusion, by flow originating from another coronary artery.

Left ventriculograms were graded visually for regional asynergy. Wall motion abnormalities in the anterior/apical regions were ascribed to the left anterior descending artery. Abnormalities in the inferior wall were ascribed to the right or circumflex coronary artery.

Received Jul. 27, 1995; revision accepted May 10, 1996

For correspondence or reprints contact: Dahlia Garza, MD, Division of Cardiology, Beth Israel Medical Center, 10 Nathan D. Perlman Place, New York, NY 10003.

TABLE 1
Stress/Rest Count Ratio for Detection of Vascular Distributions Supplied by Coronary Collaterals

| Vascular distributions having a perfusion defect with: | Angiographic coronary collaterals | | p value | Sens. | Spec. | (+) Pred. value (%) | (-) Pred. value (%) | Diag. accur. (%) |
|--|-----------------------------------|--------|-----------|-------|-------|----------------------|----------------------|------------------|
| | Present | Absent | | | | | | |
| Man. S/R ≤ 0.75 | 13 | 8 | <0.000001 | 62 | 92 | 62 | 92 | 87 |
| Man. S/R > 0.75 | 8 | 90 | | | | | | |
| Auto. S/R ≤ 0.75 | 15 | 12 | <0.000001 | 71 | 88 | 56 | 93 | 85 |
| Auto. S/R > 0.75 | 6 | 86 | | | | | | |
| Man. S/R ≤ 0.80 | 17 | 8 | <0.000001 | 81 | 92 | 68 | 96 | 90 |
| Man. S/R > 0.80 | 4 | 90 | | | | | | |
| Auto. S/R ≤ 0.80 | 14 | 2 | <0.000001 | 90 | 88 | 61 | 98 | 88 |
| Auto. S/R > 0.80 | 13 | 86 | | | | | | |
| Man. S/R ≤ 0.85 | 18 | 13 | <0.000001 | 86 | 87 | 58 | 97 | 87 |
| Man. S/R > 0.85 | 3 | 85 | | | | | | |
| Auto. S/R ≤ 0.85 | 20 | 1 | <0.000001 | 95 | 86 | 59 | 99 | 87 |
| Auto. S/R > 0.85 | 14 | 84 | | | | | | |
| Man. S/R ≤ 0.90 | 19 | 15 | <0.000001 | 90 | 85 | 56 | 98 | 86 |
| Man. S/R > 0.90 | 2 | 83 | | | | | | |
| Auto. S/R ≤ 0.90 | 20 | 1 | <0.000001 | 95 | 84 | 56 | 98 | 86 |
| Auto. S/R > 0.90 | 16 | 82 | | | | | | |
| Man. S/R ≤ 0.95 | 19 | 16 | <0.000001 | 90 | 84 | 54 | 68 | 85 |
| Man. S/R > 0.95 | 2 | 82 | | | | | | |
| Auto. S/R ≤ 0.95 | 21 | 22 | <0.000001 | 100 | 78 | 49 | 100 | 82 |
| Auto. S/R > 0.95 | 0 | 76 | | | | | | |

Man. = manual; auto. = automatic; S/R = stress/rest count ratio; Sens. = sensitivity; Spec. = specificity; +Pred. value = positive predictive value; -Pred. value = negative predictive value; Diag. accur. = diagnostic accuracy.

Dipyridamole PET Myocardial Perfusion Imaging

PET imaging was performed on the positron positron, a 21-slice bismuth germanate oxide system with an 11.5-cm field of view, 5.0-mm inplane intrinsic resolution. A transmission scan for attenuation corection was performed with a ⁶⁸Ge line source and fanbeam rejection method for minimizing random counts (12).

PET myocardial perfusion imaging was performed at rest and after dipyridamole stress (0.56 mg/kg; with handgrip to minimize vasodilator effects) as previously described (13). Identical doses of 40–50 mCi (1420–1650 MBq) ⁸²Rb were administered from a strontium/rubidium generator. A 6-min static acquisition was started 70 sec after completion of the infusion to allow for clearance of activity from the blood pool.

Image data were reconstructed into 21 transaxial tomograms using reconstruction algorithms providing 10–12-mm resolution for the heart (Butterworth filter, cutoff 0.4, order 5.0, z-axis smoothing). Transaxial images were rotated into long-axis and short-axis tomograms. Polar coordinate maps were constructed from the short-axis data, with counts normalized to peak myocardial values, and data were displayed in an isocount color format (15).

Two physicians, experienced in PET imaging (and blinded to the angiographic results) qualitatively reviewed the rest and stress tomograms and polar maps of each patient and recorded the presence of perfusion defects.

Calculation of the Stress/Rest Count Ratio with User-Defined ROIs

Five to six transaxial tomograms encompassing the superior-to-inferior regions of the heart, including all perfusion defects were analyzed. The rest slices were matched to the corresponding stress transaxial tomograms and divided into septal, apical and lateral wall segments.

ROIs of ≥20 pixels were manually drawn in each segment of each pair of matched transaxial slices. To allow for errors due to partial volume losses or spillover (15), the ROI included peak

myocardial activity in normal segments and minimal activity in segments with a perfusion defect. Mean counts per pixel within each ROI were determined. A stress/rest count ratio was calculated for each segment of each matched pair of tomograms (Fig. 1).

By using the transaxial tomograms, a manual stress/rest count ratio was assigned to each coronary vascular bed. The distribution of the left anterior descending artery included the anterior, septal and apical regions, right coronary artery, inferior and posterior/posteroseptal regions and the circumflex artery of the lateral wall region. Since coronary vascular beds usually extended through adjacent transaxial tomograms, the lowest stress/rest count ratio found within a coronary artery territory was the value used for analysis.

Patients' perfusion defects often overlap more than one coronary artery territory. To analyze whether individual patients had any area of abnormally perfused myocardium supplied by collaterals, the lowest manual stress/rest count ratio found for each patient was determined.

Calculation of Stress/Rest Count Ratio Using the Automated Method

With the use of true-count data from the original polar maps, an automated computerized algorithm calculated the ratio of stress-to-rest rubidium activity, displaying the stress/rest count ratios in polar coordinate form (11). A continuous color spectrum is used in which ratios ≤0.9 are coded purple/blue to ratios of 1.8–2.0, which are coded orange/white. The count ratio map is divided into anterior, septal, apical, lateral and inferior sectors. The algorithm then determines the stress/rest count ratio 2% of pixels with the lowest ratios in each sector, which is the minimum count ratio for that sector (Fig. 2).

By using the count ratio maps, the minimum (automated) count ratio was determined for each coronary vascular territory. The distribution of the left anterior descending artery included the anterior, septal and apical sectors, right coronary artery, inferior, circumflex artery and lateral sector.

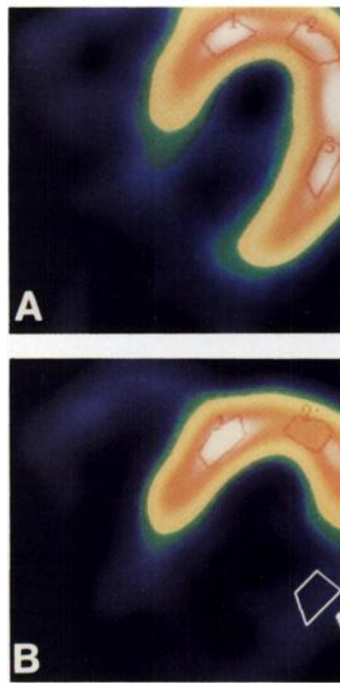


FIGURE 1. Stress/rest count ratio (manual method). (A) Midventricular transaxial rest tomogram showing ROI in the septal, apical and lateral wall segments. (B) Matching tomogram after dipyridamole stress showing a severe lateral wall perfusion defect.

To analyze whether individual patients had any area of abnormally perfused myocardium supplied by collateral circulation, the lowest automated stress/rest count ratio found for each patient was determined.

Data Analysis

The clinical characteristics of patients with and without angiographic collaterals were compared using the t-test for unpaired samples or chi square test. The lowest stress/rest count ratios found in patients with collaterals on angiography were compared to ratios found in patients without collaterals using a t-test for unpaired samples.

The diagnostic accuracy of the manual and automated stress/rest count ratio for identifying individual coronary vascular beds supplied by collaterals was determined. Accuracy was computed at cutoff values for the ratio of 0.75–0.95; the value yielding the highest accuracy for each method was identified. The diagnostic accuracy of the stress/rest count ratio for identifying individual patients having any coronary vascular territory supplied by collaterals was determined in a similar manner. The significance of the relationship between the stress/rest count ratio and the presence of collaterals on angiography was tested using the chi square statistic.

To ascertain whether abnormal wall motion alone, in the absence of collaterals, was associated with stress/rest count ratios <1.0, we analyzed the count ratios in arteries without collaterals in relation to the wall motion of the myocardial segments they supply. Stress/rest count ratios in arteries supplying segments with abnormal wall motion were compared to the ratios in arteries supplying segments with normal wall motion using the Z-test for proportions; p values <0.05 were considered significant.

RESULTS

Angiographic

Forty-four of the 45 patients in the study group had significant coronary disease, 32 of whom had multivessel disease. One patient, with an anterior myocardial infarction and a corresponding ventriculographic wall motion abnormality, had no significant coronary stenoses angiographically. Seventeen of 45 patients had a previous myocardial infarction as determined by history or ECG. Seventeen patients had abnormal wall motion on left ventriculography.

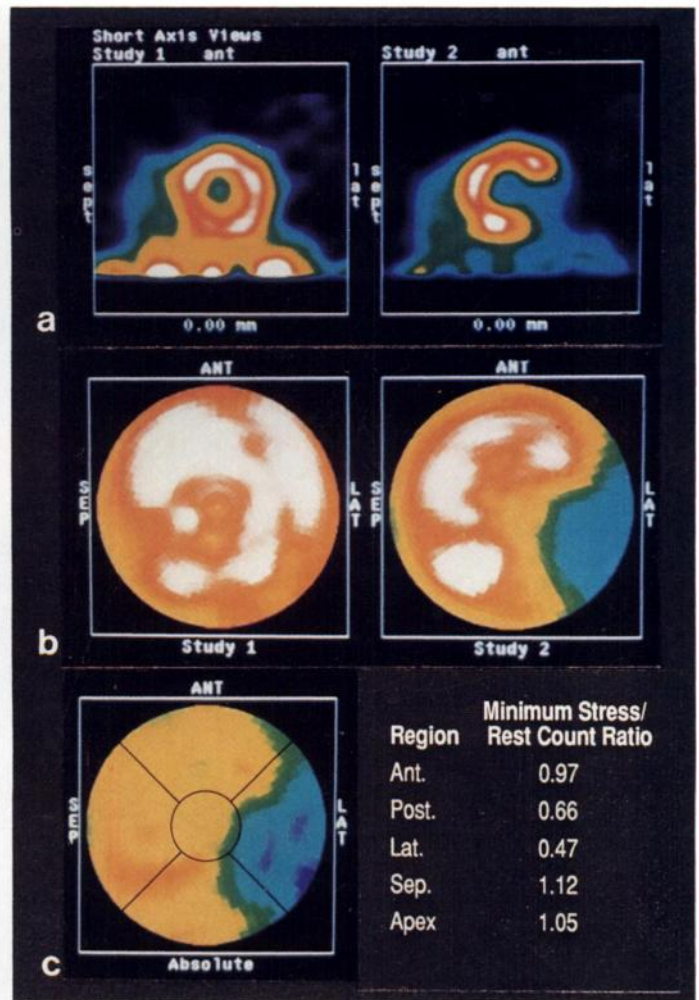


FIGURE 2. Stress/rest count ratio (automated method). (A) Short-axis tomograms, (B) polar maps and (C) count ratio maps in the patient shown in Figure 1 (study 1: rest; study 2: dipyridamole stress). There is a lateral/inferoposterior perfusion defect with count ratio maps suggesting collateral circulation blood supply. Angiography showed a 90% stenosis of the circumflex artery with collaterals from the right coronary.

Collaterals were demonstrated by angiogram in one or more coronary vascular beds in 18 patients, three of whom had two arteries supplied by collaterals. Twenty-one individual coronary vascular beds were collateralized: the left anterior descending artery in 7 patients, circumflex in 5 patients and right coronary artery in 9 patients; 27 patients had no collaterals.

There were no significant differences between patients with and without collaterals in age or frequency of three-vessel coronary disease (15/18 versus 17/27, $p = ns$). Male gender was seen more frequently in patients with collaterals than in patients without collaterals (14/18 versus 11/27, $p < 0.01$). There were no differences between patients with and without collaterals in blood pressure and heart rate at rest or change in blood pressure and heart rate in response to dipyridamole.

Identification of Collaterals

The lowest stress/rest count ratios found in patients with collaterals was significantly less than those found in patients without collaterals (manual method 0.67 ± 0.12 versus 0.93 ± 0.76 , $p < 0.0001$; automated method 0.67 ± 0.14 versus 0.94 ± 0.15 , $p < 0.001$).

The diagnostic accuracy of the stress/rest count ratio for identifying individual coronary vascular beds supplied by collateral circulation is shown in Table 1 (16 vascular beds which had no significant coronary stenoses were excluded from

TABLE 2
Stress/Rest Count Ratio for Detection of Patients Having Coronary Collaterals

| Patients having a perfusion defect with | Angiographic coronary collaterals | | p Value | Sens. | Spec. | (+) Pred. value (%) | (-) Pred. value (%) | Diag. accur. (%) |
|---|-----------------------------------|--------|----------|-------|-------|------------------------------|------------------------------|------------------------|
| | Present | Absent | | | | | | |
| Man. S/R ≤ 0.75 | 12 | 6 | <0.004 | 67 | 78 | 67 | 78 | 73 |
| Man. S/R > 0.75 | 6 | 21 | | | | | | |
| Auto. S/R ≤ 0.75 | 12 | 8 | <0.02 | 67 | 70 | 60 | 76 | 69 |
| Auto. S/R > 0.75 | 6 | 19 | | | | | | |
| Man. S/R ≤ 0.80 | 15 | 6 | <0.0001 | 83 | 78 | 63 | 88 | 80 |
| Man. S/R > 0.80 | 3 | 21 | | | | | | |
| Auto. S/R ≤ 0.80 | 16 | 8 | <0.0001 | 89 | 70 | 70 | 90 | 78 |
| Auto. S/R > 0.80 | 2 | 19 | | | | | | |
| Man. S/R ≤ 0.85 | 16 | 10 | <0.0006 | 89 | 63 | 62 | 89 | 73 |
| Man. S/R > 0.85 | 2 | 17 | | | | | | |
| Auto. S/R ≤ 0.85 | 17 | 8 | <0.00007 | 94 | 70 | 68 | 95 | 80 |
| Auto. S/R > 0.85 | 1 | 19 | | | | | | |
| Man. S/R ≤ 0.90 | 17 | 10 | <0.0001 | 94 | 63 | 63 | 94 | 76 |
| Man. S/R > 0.90 | 1 | 17 | | | | | | |
| Auto. S/R ≤ 0.90 | 17 | 8 | <0.0001 | 94 | 70 | 68 | 95 | 80 |
| Auto. S/R > 0.90 | 1 | 19 | | | | | | |
| Man. S/R ≤ 0.95 | 17 | 10 | <0.0001 | 94 | 63 | 63 | 94 | 76 |
| Man. S/R > 0.95 | 1 | 17 | | | | | | |
| Auto. S/R ≤ 0.95 | 18 | 10 | <0.00001 | 100 | 63 | 64 | 100 | 78 |
| Auto. S/R > 0.95 | 0 | 17 | | | | | | |

Man. = manual; Auto. = automatic; S/R = stress/rest count ratio; Sens. = sensitivity; Spec. = specificity; +Pred. value = positive predictive value; -Pred. value = negative predictive value; Diag. accur. = diagnostic accuracy.

this analysis). For the manual method, maximal diagnostic accuracy (90%) occurs at a ratio of ≤ 0.80 : 17 of 21 coronary vascular beds supplied by collaterals had manual stress/rest count ratios ≤ 0.80 , while 90 of 98 vascular beds without collaterals had ratios of > 0.80 (sensitivity 81%, specificity 92%, $p < 0.00001$). For the automated method, maximal accuracy (87%) occurred at a ratio of ≤ 0.80 : 19 of 21 vascular beds supplied by collaterals, and 85/98 without collaterals were correctly identified (sensitivity 90%, specificity 88%, $p < 0.00001$). There were no differences in accuracy, sensitivity or specificity between the methods.

The diagnostic accuracy of the stress/rest count ratio for identifying individual patients with any vascular bed supplied by collaterals is shown in Table 2. For the manual method, accuracy is maximal (80%) at a ratio of ≤ 0.80 : The perfusion defects of 15/18 patients with collaterals have manual stress/rest count ratios ≤ 0.80 . The ratio is > 0.80 in 21/27 patients without collaterals (sensitivity 83%, specificity 78%, $p < 0.0001$). For the automated method, accuracy is maximal (80%) at a ratio of ≤ 0.90 , correctly identifying 17/18 patients with collaterals and 19/27 patients without collaterals (sensitivity 94%, specificity 70%, $p < 0.0001$). There were no significant differences in sensitivity, specificity or overall accuracy between the two methods.

Two factors were associated with vascular territories being misidentified by PET as being supplied by collaterals: severe coronary stenoses and regional wall motion abnormalities. Severe stenoses ($> 70\%$) were present in 8/8 vascular beds misidentified as having collaterals by the manual method versus 47/85 correctly identified by PET as not having collaterals ($Z = 8.3$, $p < 0.0001$). Of seven myocardial segments with abnormal wall motion supplied by arteries without collaterals, four (57%) had automated stress/rest count ratios ≤ 0.8 . Of 48 segments with normal wall motion supplied arteries without collaterals, only 6 (12%) had ratios < 0.8 ($Z = 5.7$, $p < 0.0001$).

There were no significant differences in the hemodynamic

response to dipyridamole between patients correctly and incorrectly identified by PET as having collaterals.

DISCUSSION

The presence of coronary collateral circulation significantly influences the prognosis and management of coronary disease (1). In patients with a recent myocardial infarction, collateral blood supply to the infarct vessel results in limitation of infarct size, prevents the formation of ventricular aneurysms and is associated with improvement in ventricular function after revascularization (16-20). Consequently, the presence of collaterals has become an important factor influencing the choice of therapy in patients with coronary disease and has led to an interest in their noninvasive identification (21).

Noninvasive Identification of Coronary Collaterals Using PET Imaging

Single-photon perfusion imaging have shown that the presence of coronary collaterals is associated with more extensive perfusion defects but has not defined specific scintigraphic predictors which identify coronary collaterals (4-7).

PET imaging, with coincidence counting of high-energy annihilation photons and the ability to perform attenuation correction (22), may be capable of identifying myocardial regions in which tracer uptake decreases in response to dipyridamole. Such a decrease could serve as a noninvasive marker of coronary steal, a pathophysiologic property unique to collateralized vascular beds (2,9).

The current study confirms that quantification of regional myocardial tracer uptake on dipyridamole ^{82}Rb PET can be used to noninvasively identify collateralized coronary vascular beds. A stress/rest count ratio ≤ 0.8 distinguishes collateralized from noncollateralized beds with a diagnostic accuracy exceeding 80%. Both manual and automated methods of computing the stress/rest count ratio yield comparable results.

Our data corroborate the results of Demer et al. (8) but differ

in that the stress/rest count ratio had a somewhat lower positive predictive value for collaterals than was reported previously (69% versus 84%). In the current study, 13 vascular beds fulfilled the stress/rest count ratio criteria for collaterals but had no collaterals at angiography. There are several possible explanations for this finding.

First, collaterals could exist in these vascular beds but be smaller than 1.0 mm, the limits of resolution for angiography (3). Myocardial contrast echocardiography has demonstrated evidence of collateral circulation in patients with no collaterals seen on coronary angiography (20). Second, regional wall motion abnormalities could produce low stress/rest count ratios in the absence of collaterals. Dipyridamole can induce wall motion abnormalities or worsen wall motion in regions with asynergy at rest (23,24). Because of partial volume effects, this may reduce the recovery of counts from a myocardial segment by the PET camera (15), resulting in a low stress/rest count ratio in the absence of collaterals or coronary steal. In this study, abnormal wall motion was more frequent in regions misidentified by PET as being supplied by collaterals. The lower predictive value of the stress/rest count ratio in this study versus that of Demer et al. (8) might be due to a higher prevalence of resting or dipyridamole-induced wall motion abnormalities in our population.

Study Limitations

Absolute myocardial perfusion was not quantified in this study. In severely stenotic coronary arteries, without collaterals, blood flow does not increase in response to dipyridamole, but peripheral vasodilation may occur thereby reducing arterial rubidium input function (23,24). Regional rubidium uptake may decrease (and the stress/rest count ratio be <1.0) without a true decrease in regional blood flow (9,22). This may have occurred in this study and could be the mechanism for the association noted between severe coronary stenoses and false-positive stress/rest count ratios.

However, quantitation of myocardial perfusion is technically demanding and requires determination of cardiac output, time arterial concentration of tracer and correction for partial volume losses, spillover and isotope extraction fraction (10,22,25). Our data suggest that simple quantitation of tracer uptake using the stress/rest count ratio reflects the direction of change in perfusion in response to dipyridamole and may be a clinically useful marker of collaterals.

Patients in this study were not selected for inclusion because of their coronary angiographic or PET findings, limiting the influence of post-test referral bias on our results (26). However, patients with unstable coronary syndromes were excluded because of our use of dipyridamole stress. Thus, our data applies only to populations with clinically stable ischemic heart disease.

CONCLUSION

The stress/rest count ratio on ⁸²Rb dipyridamole PET perfusion imaging is a significant predictor of coronary collateral circulation. By using count ratio maps, which are constructed automatically by computer algorithm, collateralized vascular beds can be identified as areas in which rubidium uptake decreases in response to dipyridamole.

Our data indicate that the stress/rest count ratio has a higher sensitivity but lower specificity and predictive value for detecting collaterals than was previously reported. Because of partial volume effects or reduced arterial rubidium input function in response to dipyridamole, severe coronary stenoses or wall

motion abnormalities may cause a low stress/rest count ratio in the absence of collaterals. Nevertheless, stress/rest count ratios and automated count ratio maps may serve as unique imaging descriptors that can noninvasively identify coronary collaterals without requiring quantitation of regional myocardial blood flow.

ACKNOWLEDGMENTS

This work was supported by the following organizations: Haim and Lila Luxembourg Cardiac PET Research Fund, Dina and Raphael Recanati Cardiology Research Fund, Charles M. Schnurmacher Research and Education Fund and Pumpkin Foundation.

REFERENCES

1. Hansen JF. Coronary collateral circulation: clinical significance and influence on survival in patients with coronary artery occlusion. *Am Heart J* 1989;117:290-295.
2. Schaper W, Gorge G, Winkler B, Schaper J. The collateral circulation of the heart. *Prog Cardiovasc Dis* 1988;30:57-77.
3. Gensini GG, daCosta B. The coronary collateral circulation in living man. *Am J Cardiol* 1969;24:393-400.
4. Chambers CE, Brown KA. Dipyridamole-induced ST segment depression during thallium-201 imaging in patients with coronary artery disease: angiographic and hemodynamic determinants. *J Am Coll Cardiol* 1988;12:37-41.
5. Inamura T, Araki H, Fukuyama T, et al. Significance of collateral circulation on the peri-infarct zone: assessment with stress thallium-201 scintigraphy. *Clin Cardiol* 1986;9:137-144.
6. Berger BC, Watson DD, Taylor GJ, Burwell LR, Martin RP, Beller GA. Effect of coronary collateral circulation on regional myocardial perfusion assessed with quantitative thallium-201 scintigraphy. *Am J Cardiol* 1980;46:365-370.
7. Rigo P, Becker LC, Griffith LSC. Influence of coronary collateral vessels on the results of thallium-201 myocardial stress imaging. *Am J Cardiol* 1979;44:452-458.
8. Demer LL, Gould KL, Goldstein RA, Kirkeeide RL. Noninvasive assessment of coronary collaterals in man by PET perfusion imaging. *J Nucl Med* 1990;31:259-270.
9. Demer LL, Gould KL, Kirkeeide R. Assessing stenosis severity: coronary flow reserve, collateral function, quantitative coronary angiography, positron imaging and digital subtraction angiography. A review and analysis. *Prog Cardiovasc Dis* 1988; 30:307-322.
10. Schelbert HR, Czernin J. Noninvasive quantification of regional myocardial blood flow: assessment of myocardial perfusion reserve and collateral circulation. *J Nucl Med* 1990;31:271-273.
11. Hicks K, Ganti G, Mullani N, Gould KL. Automated quantitation of three-dimensional cardiac positron emission tomography for routine clinical use. *J Nucl Med* 1989;30: 1787-1797.
12. Carroll LR, Kretz P, Orcutt S. The orbiting rod source: improving performance in PET transmission correction scans. *IEEE Trans Nucl Sci* 1988;35:735-742.
13. Van Tosh A, Garza D, Roberti R, et al. Serial myocardial perfusion imaging with dipyridamole and ⁸²Rb to assess restenosis after angioplasty. *J Nucl Med* 1995;36: 1553-1560.
14. DePasquale EE, Nody AC, DePuey EG, et al. Quantitative rotational thallium-201 tomography for identifying coronary artery disease. *Circulation* 1988;77:316-327.
15. Parodi O, Schelbert HR, Schwaiger M, Hansen H, Selin C, Hoffman E. Cardiac emission computerized tomography: underestimation of regional tracer concentration due to wall motion abnormalities. *J Comput Assist Tomogr* 1984;8:1083-1092.
16. Habib GB, Heibig J, Forman SA, et al. Influence of coronary collateral vessels on myocardial infarct size in humans. Results of phase I thrombolysis in myocardial infarction (TIMI) trial. *Circulation* 1991;83:739-746.
17. Forman MB, Collins HW, Kopelman HA, et al. Determinants of left ventricular aneurysm formation after anterior myocardial infarction. *J Am Coll Cardiol* 1986;8: 1256-1262.
18. Nohara R, Kambara H, Murakami T, Kazunori K, Tamaki S, Kawai C. Collateral function in early acute myocardial infarction. *Am J Cardiol* 1983;52:955-959.
19. Saito Y, Yasuno M, Ishida M, et al. Importance of coronary collaterals for restoration of left ventricular function after intracoronary thrombolysis. *Am J Cardiol* 1985;55: 1259-1263.
20. Sabia PJ, Powers ER, Ragosta M, Sarembock IJ, Burwell R, Kaul S. An association between collateral blood flow and myocardial viability in patients with recent myocardial infarction. *N Engl J Med* 1992;327:1825-1831.
21. Marcus ML. Physiologic basis for myocardial perfusion imaging. In: Marcus ML, Schelbert HR, Skorton DJ, Wolff GL, eds. *Cardiac imaging*. Philadelphia: WB Saunders; 1991:8-23.
22. Gould KL. Quantitation of PET perfusion images. In: *Coronary artery stenosis*. New York: Elsevier Science Publishing Company; 1991:159-168.
23. Klein HO, Niniio R, Elyahu S, et al. Effects of dipyridamole on left ventricular function in coronary artery disease. *Am J Cardiol* 1992;69:482-488.
24. Picano E, Lattanzi F. Dipyridamole echocardiography. A new diagnostic window on coronary artery disease. *Circulation* 1991;78(suppl III):19-26.
25. Budinger TF, Huesman RH. Ten precepts for quantitative data acquisition and analysis. *Circulation* 1985;72:(suppl IV):53-61.
26. Rozanski A. Referral bias and efficacy of radionuclide stress tests: problems and solutions. *J Nucl Med* 1992;33:2074-2079.