Reverse Redistribution Phenomenon in Thallium-201 Stress Tests: Angiographic Correlation and Clinical Significance

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The reverse redistribution phenomenon (RR) with the apparent worsening of a stress-induced defect or appearance of a new area of relative hypoperfusion does not always indicate coronary artery disease as previously suggested. RR does not correlate closely with the degree of coronary artery disease, nor with the location of the stenosis. Multiple mechanisms are hypothesized wherein the "defect" may be located in the best or worst perfused area.

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Perfusion defects which appear on thallium-201 (^{201}Tl) exercise stress tests and disappear following several hours of rest have long been accepted as strong evidence for reversible ischemic heart disease commonly related to coronary artery atherosclerosis (*1*). However, the observation has been made in several laboratories of ^{201}Tl studies where the delayed ("rest") study shows defects not apparent just after exercise, or where perfusion defects seen with exercise worsened (*2–5*). This phenomenon has been called reverse redistribution (RR) and has been correlated with significant coronary artery disease (Fig. 1A and 1B). We re-examined this phenomenon because of inconsistancies between authors in the localization of coronary artery disease by RR and our discovery of patients with RR and normal coronary angiography.

MATERIALS AND METHODS

Seven hundred and eighty-five consecutive ^{201}Tl exercise studies were reviewed for RR and 35 (5%) were found to demonstrate this phenomenon by consensus reading of both authors. Twenty of these 35 had correlative coronary angiography with the Judkins technique within a month of the ^{201}Tl study and form the basis of this report.

These patients all received 2 mCi of ^{201}Tl intravenously after achieving at least 85% of maximum target heart rate, exercising to exhaustion, severe angina, or dangerous electrocardiographic abnormalities as determined by the attending cardiologist. Four views were obtained beginning within 1-min postexercise: anterior, 45° left anterior oblique and 70° left anterior oblique (all supine) and a left lateral view in the right lateral decubitus position. Four hundred thousand counts were obtained per view. Four hours later the images were repeated in the identical position for the same time per view. No computer analysis was performed during the time of collection of these data. A breast binder was employed for all female patients. We read a study as RR only if both authors independently agreed on the presence of the phenomenon.

RESULTS

Of the 20 patients with RR who had coronary angiography, 11 individuals had stenoses equal to or greater than 50% of the luminal diameter of one or more vessels and were diagnosed (independently of the thallium studies) as having significant coronary artery disease. Five of the eleven with significant stenoses had a new defect or worsening of a pre-existing defect on the

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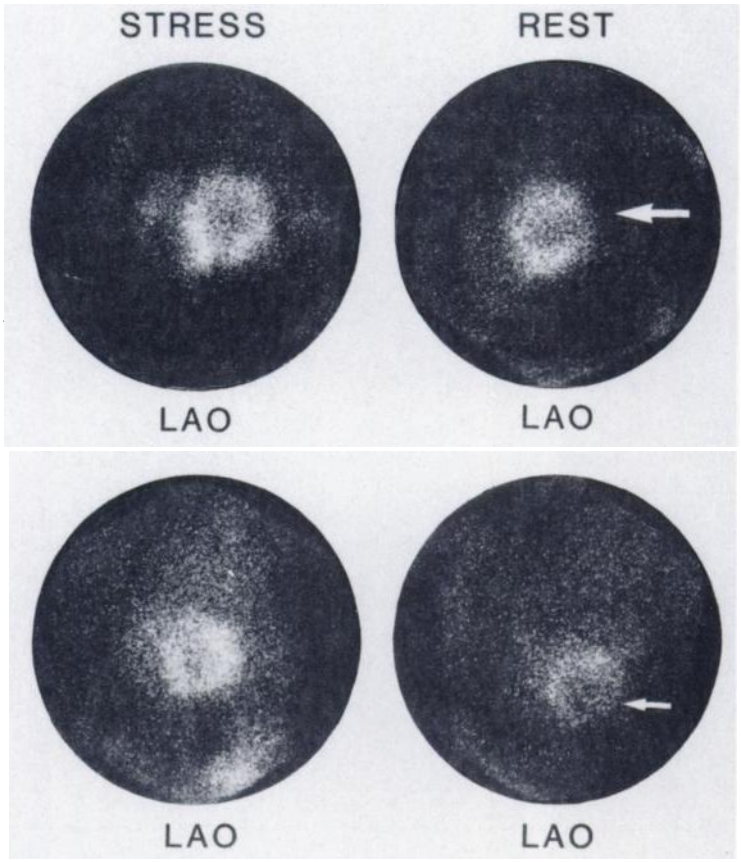

FIGURE 1
Two patients, one with (A) and one without (B) coronary artery disease, both with RR (arrows). Patient in Fig. 1A had 70% occlusion at right coronary artery and 80% occlusion at left anterior descending coronary artery with 30% involvement of circumflex artery

resting view (RR) in the distribution of the most stenosed coronary artery while another five had RR in the distribution of the vessel with the least severe stenosis. Finally, one of these 11 with abnormal angiograms had similar stenosis of all three vessels. Nine patients were judged to have no significant coronary artery stenosis.

Twelve of the 20 patients with RR who had angiography had no co-existent or second defects immediately poststress; six of these had significant coronary artery disease. Of the remaining six without poststress defects who had no coronary artery disease, one had an idiopathic cardiomyopathy. The other eight of the total of 20 RR patients with angiographic correlation had an additional immediate poststress defect. Five of these latter eight had significant coronary artery disease, one had idiopathic cardiomyopathy and two had normal coronary arteries. Thus, the predictive power of a positive test (post-test probability of disease) in our series was 65% (13 of 20) for all heart disease but only 55% (11 of 20) for significant coronary artery disease. Furthermore, the location of RR was not predictive of the site of the most stenosed coronary artery.

DISCUSSION

The RR phenomenon is not extraordinarily unusual, having been seen in 5% of the series we reviewed and in 7% of the cases of Hecht et al. (*4*). However, RR noted on the qualitative interpretation of stress ^{201}Tl studies was found to be an unsatisfactory predictor of heart disease with an unacceptably low positive predictive value.

A comparison of our series with the two other reports providing correlative coronary angiographic data provides some striking contrasts. The data of Hecht et al. (*3*) and of Tanasescu et al. (*4*) yield positive predictive values (PPV) for significant coronary artery disease of 100 and 80%, respectively, while we found a PPV of 55%. Nor does the site of RR predict that the vessel supplying that area will be most severely diseased angiographically. This was true in only 45% of the cases in our series and also in that of Hecht et al. In contrast, none of five RR cases of Tanasescu et al. involved the area supplied by the most severely stenosed vessel.

Multiple mechanisms may be postulated to explain RR, all of which have been documented in one or more of our cases. Figure 2 proposes mechanisms for RR indicating that the phenomenon can occur in both the best and worst perfused regions. In Fig. 2A (LAO view) one notes normal posterolateral myocardium with an ischemic collateralized septum bearing a subendocardial infarct. With exercise the count density of normal and abnormal segments might be the same because of adequate collateral circulation, but 4 hr

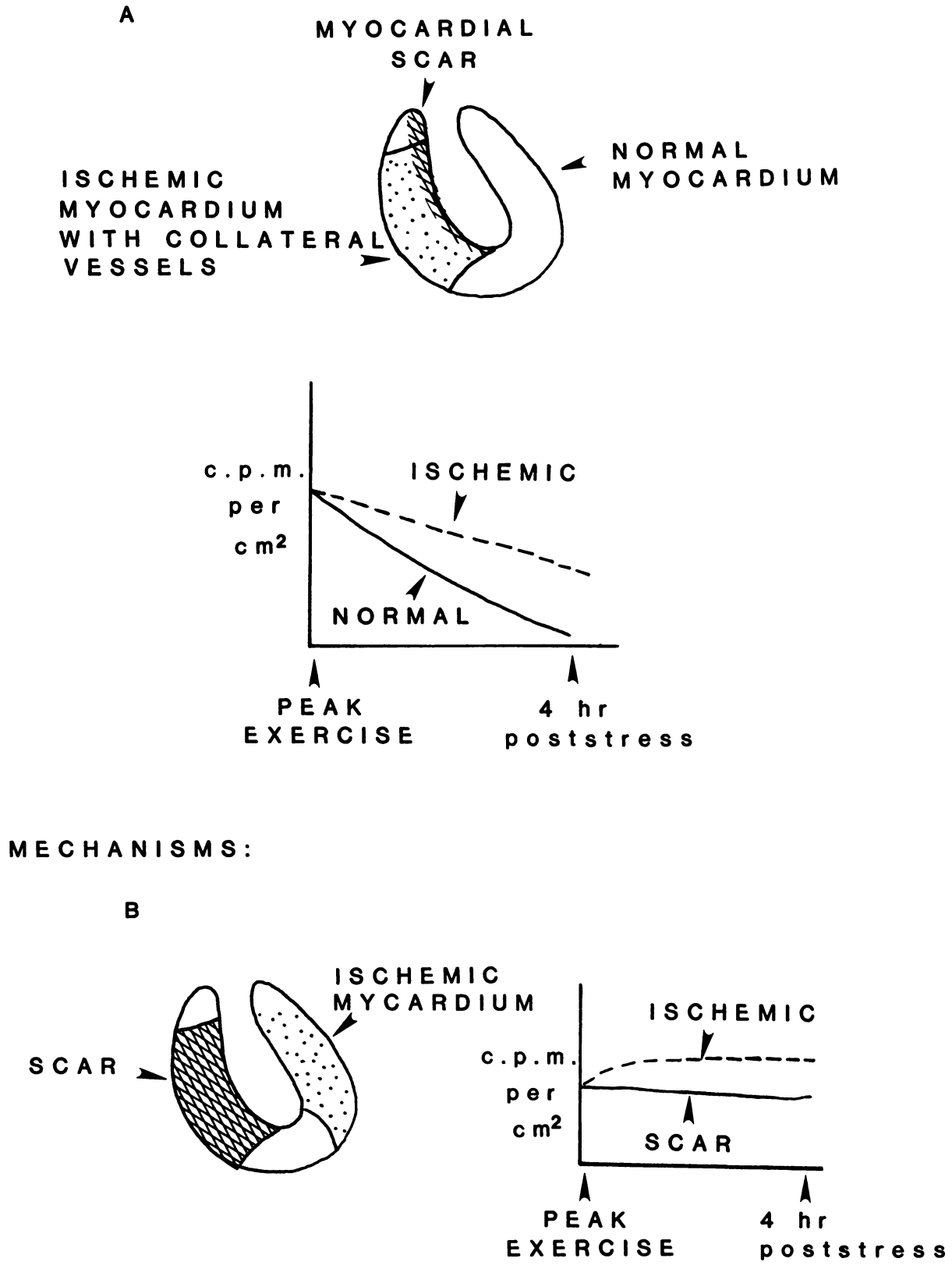

FIGURE 2
A, B: Proposed mechanisms to explain RR (See text)

later washout would be slower from the diseased myocardium than the normal segment so that the healthy heart muscle appears as the "defect", i.e., the area with the lower count density. In contrast with a second mechanism (Fig. 2B) the "defect" is located in the more diseased segment. Here low counts (information density) in both myocardial scar and ischemic myocardium at peak exercise (due to a fixed lesion or to spasm) are followed 4 hr later by reperfusion in the ischemic area. However, the more diseased area of the heart has the lower count density when RR is observed. Such mechanisms could explain why RR may be observed in the area of the angiographically most or least stenosed vessel. Variable background changing with time in unprocessed images may also play a role in producing RR. Subsequent to the collection of these data, routine computer processing, with interpolative background subtraction, has been initiated but this does not eliminate the RR phenomenon. We have initiated a series wherein 13 cases of RR have been noted to date when employing a widely accepted background processing algorithm (*6*).

The prognosis of RR patients, with or without angiographic abnormalities, is difficult to assess in our series, which has a mean follow-up of only 27 mo (range 26–32 mo). However, no deaths have occurred in these 20 patients.

In conclusion, the RR phenomenon does not predict coronary artery disease with high probability and may also be observed in myocardopathies. Where coronary artery disease does exist RR does not correlate well with the degree or location of stenosis. Multiple mechanisms appear to be involved.

Other physiologic variables which we have seen or postulated to explain RR include the combination of spasm and structural blockage; transmural compared with subendocardial infarct; perfusion status of contiguous and/or overlying and underlying segments; recanalization of atherosclerotic plaques in regions of previous infarct; incomplete infarction with intermingled viable and scarred myocardium; variability of the severity and duration of spasm; variability of the postischemic hyperemic response; variability of the exercise effort and physiologic response of the heart to that effort.

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