Comparison of thallium deposition with segmental perfusion in pigs with chronic hibernating myocardium

Sunil Baldwa,1,2,3,4 Muzamil Rana,1,4 John M. Canty, Jr.,1,3,4,5 and James A. Fallavollita1,3,4

1Veterans Affairs Western New York Health Care System at Buffalo, 2Canandaigua Veteran Affairs Medical Center, 3Center for Research in Cardiovascular Medicine, and Departments of 4Medicine and 5Physiology & Biophysics at the University at Buffalo, Buffalo, New York

Submitted 21 July 2008; accepted in final form 20 October 2008

Baldwa S, Rana M, Canty JM, Fallavollita JA. Comparison of thallium deposition with segmental perfusion in pigs with chronic hibernating myocardium. Am J Physiol Heart Circ Physiol 295: H2522–H2529, 2008; doi:10.1152/ajpheart.00761.2008.—Via-ble, chronically dysfunctional myocardium with reduced resting flow (or hibernating myocardium) is an important prognostic factor in ischemic heart disease. Although thallium-201 imaging is frequently used to assess myocardial viability in patients with ischemic heart disease (4), there are limited data regarding its deposition in hibernating myocardium, and this data suggest that thallium retention may be supernormal compared with control myocardium. Accordingly, pigs (n = 7) were chronically instrumented with a 1.5 mm Delrin stenosis on the proximal left anterior descending coronary artery (LAD) to produce hibernating myocardium. Four months later, severe an-teroapical hypokinesis was documented with contrast ventriculography (wall motion score, 0.7 ± 0.8; normal = 3), and microsphere measurements confirmed reduced resting flow (LAD subendocardium, 0.78 ± 0.34 vs. 0.96 ± 0.24 ml/min·1·g−1 in remote; P < 0.001). Absolute deposition of thallium-201 and insulin-stimulated 18F-2 fluoro-2-deoxyglucose (FDG) were assessed over 1 h and compared with resting flow (n = 704 samples). Thallium-201 deposition was only weakly correlated with perfusion (r2 = 0.20; P < 0.001) and was more homogeneously distributed (relative dispersion, 0.12 ± 0.03 vs. 0.29 ± 0.10 for microsphere flow; P < 0.01). Thus after 1 h relative thallium-201 (subendocardium LAD/remote, 0.96 ± 0.16) overestimated relative perfusion (0.78 ± 0.32; P < 0.0001) and underestimated the relative reduction in flow. Viability was confirmed by both histology and preserved FDG uptake. We conclude that under resting flow conditions, thallium-201 redistribution in hibernating myocardium is nearly complete within 1 h, with similar deposition to remote myocardium despite regional differences in flow. These data suggest that in this time frame thallium-201 deposition may not discriminate hibernating myocardium from dysfunctional myocardium with normal resting flow. Since hibernating myocardium has been associated with a worse prognosis, this limitation could have significant clinical implications.

Thallium-201; 18F-fluorodeoxyglucose; myocardial viability; coronary artery disease

The initial deposition and subsequent redistribution of thallium in acutely ischemic and acutely stunned myocardium is well characterized (9, 18, 20, 22). Nevertheless, there is a paucity of information regarding thallium deposition in viable, chronically dysfunctional myocardium [chronically stunned and hibernating myocardium (5)]. This limitation is especially conspicuous in view of the important influence of hibernating myocardium on morbidity and mortality in patients with ische-mic heart disease (1). The only data are from a small clinical trial in patients with end-stage ischemic heart disease undergoing cardiac transplantation (19). This study suggested that thallium deposition was supernormal in a number of samples with reduced perfusion, which could not be explained by redistribution (9, 22), prolonged accumulation, or a delayed peak of maximum thallium uptake (19). Since these patients had end-stage heart disease requiring cardiac transplantation, most segments had increased fibrosis, and we hypothesized their findings could have been confounded by their assessment of thallium uptake. Segmental thallium uptake in their study was normalized to the retention in the most normal region of each patient. Thus relatively reduced thallium uptake in the normal segments could have accounted for the supernormal retention in samples with hibernating myocardium.

We hypothesized that initial thallium uptake in hibernating myocardium should be proportional to resting perfusion, and even with subsequent redistribution thallium retention should not be higher than the remote, normally perfused myocardium. To clarify thallium uptake in hibernating myocardium, the present study was performed in a very well-characterized chronic porcine model (10, 11, 13). This model produces a large volume of viable dysfunctional myocardium, but overall left ventricular systolic function is preserved (13), thereby reducing the likelihood of remote region remodeling, which could affect remote region thallium retention. Furthermore, our methodology assured the direct quantification of thallium depo-sition (regional retention corrected for average arterial concentra-tion), and viability in individual segments would be confirmed with simultaneous quantification of insulin-stimu-lated 18F-2 fluoro-2-deoxyglucose (FDG) deposition (10). Our results confirm the finding of enhanced thallium retention relative to resting flow and therefore support the clinical utility of late thallium imaging to identify myocardial viability. However, after 1 h of accumulation, thallium deposition in hibernating myocardium was nearly identical to that in the normally perfused remote myocardium and thus did not support the previous contention for supernormal thallium deposition in hibernating myocardium (19). Furthermore, these data suggest that within 1 h the assessment of thallium deposition has limited utility in differentiating viable, chronically dysfunctional myocardium with reduced resting flow (hibernating myocardium) from viable segments with normal perfusion (chronically stunned myocardium) (5). This has potential clinical implications for patients undergoing interventional therapy.
(3, 4, 14) and especially those destined to be treated medically (1, 7, 8, 12).

METHODS

Experimental protocol. All experimental procedures and protocols conformed to the Institutional Guidelines for the Care and Use of Animals in Research and were approved by the University of Buffalo Institutional Animal Care and Use Committee. Initial instrumentation to produce hibernating myocardium has been previously published in detail (10, 11, 13). Briefly, the proximal left anterior descending coronary artery (LAD) of juvenile pigs (n = 7; weight, 9.0 ± 1.3 kg) was instrumented with a Delrin occluder with a fixed internal diameter of 1.5 mm. Approximately 4 mo later (130 ± 8 days; weight, 95 ± 13 kg), the pigs were fasted overnight. Anesthesia was induced with a mixture of Telazol (tiletamine, 50 mg/ml; and zolazepam, 50 mg/ml)/xylazine (100 mg/ml) (0.22 ml/kg im) and maintained by isoflurane (1–3%) supplemented with additional Telazol/xylazine (0.011 ml/kg im as needed). Catheters were placed retrograde from the carotid arteries into the left atrium for pressure monitoring and microsphere injection and into the left ventricle for contrast ventriculography. Arterial pressure and reference withdrawal samples for microsphere flow quantification were taken from a femoral artery. Pharmacological agents were administered through a jugular vein. Animals were heparinized (100 units/kg iv), and hemodynamic parameters were allowed to equilibrate for ~30 min.

Myocardial function was assessed with contrast ventriculography, and anteroapical wall motion was quantified by wall motion score (3, normal; 2, mild hypokinesis; 1, severe hypokinesis; and 0, akinesis (13)). Regional perfusion was assessed with fluorescent microspheres (6). The boundaries of the LAD perfusion territory were determined by flow during adenosine vasodilation (0.9 mg·kg⁻¹·min⁻¹ iv) with phenylephrine (11.3 ± 3.3 µg·kg⁻¹·min⁻¹ iv) infused to maintain arterial pressure. While hemodynamic parameters returned to baseline, selective coronary angiography was performed to quantify LAD stenosis severity (13).

Nuclear isotopes were injected after the heart was exposed by a median sternotomy to limit radiation exposure while contending with extensive adhesions from the chronic coronary instrumentation. A continuous dextrose (10%) and insulin (10 U/ml, regular purified pork insulin; Novo Nordisk, Bagsvaerd, Denmark) infusion (573 ± 77 ml/h; glucose, 10 mg·kg⁻¹·min⁻¹; and insulin, 1 µU·kg⁻¹·min⁻¹) was used to maximize myocardial FDG uptake and was continued until the heart was excised (10). After hemodynamics had equilibrated, resting myocardial blood flow was quantified for direct comparison with the deposition of the nuclear tracers. Resting perfusion was assessed 135 ± 13 min (minimum, 119 min) after adenosine and phenylephrine were discontinued.

Quantification thallium and FDG deposition by ex vivo tissue counting. Thallium-201 (mean, 0.19 ± 0.17 mCi; range, 0.10–0.53 mCi; mean, 1.8 ± 1.3 µCi/kg; range, 1.0–4.4 µCi/kg) and FDG (mean, 1.2 ± 0.4 mCi; range, 0.8–1.7 mCi; mean, 12.5 ± 5.4 µCi/kg; range, 7.2–20.1 µCi/kg) were injected as an intravenous bolus, and an arterial sample was continuously withdrawn (1 ml/min) for 60 min to determine the integrated thallium and FDG time-activity curves (10). After isotope accumulation, the heart was arrested with intravenous KCl and rapidly excised. Myocardial samples were placed into tared vials and weighed, and 18F annihilation γ-radiation at 511 keV (window, 400–600 keV) was quantified in a γ-counter (Model 1470; EG&G Wallac, Gaithersburg, MD). Twenty-four hours later, after the 18F activity had decayed to baseline (half-life, 110 min), the samples were assayed for thallium activity at 70 keV (window, 60–90 keV). The activity of each sample was decay corrected to the time the heart was excised. FDG deposition was determined by dividing FDG activity in individual samples by the integrated arterial input curve (10, 24). Thallium deposition was determined in an analogous manner (24). After all radioactivity had decayed to baseline, the same tissue samples were used for microsphere flow determinations (6).

Myocardial sampling and histological evaluation. The heart was sectioned into three concentric rings from apex to base. Each ring was divided into ~12 full-thickness wedges, which were subdivided into subendocardial, midmyocardial, and subepicardial layers. There was a total of 704 samples (101 ± 5 samples/pig) with an average sample weight of 0.91 ± 0.40 g. Flow and isotope deposition in the LAD and normally perfused remote regions represent weighted means for all samples within a given region after the perfusion boundaries were determined from the distribution of vasodilated flow (Fig. 1). Core samples from the LAD and normally perfused regions were trichrome stained, and regional connective tissue staining was quantified by standard point counting techniques (13).

Data analysis. Data are presented as means ± SD. Hemodynamic parameters in the open chest state were compared with those before thoracotomy with paired t-tests. Correlation coefficients were used to compare resting perfusion and isotope deposition in individual tissue samples. To more clearly illustrate the relationships between flow and isotope deposition, values in the LAD region are also shown relative to the average value of the samples from the same transmural layer of the remote normally perfused region of each animal. These were compared by a two-way ANOVA to account for parameter (flow, thallium, FDG) and transmural layer. Relative dispersion (SD/mean) was determined on a regional basis per pig and was also compared with a two-way ANOVA to account for parameter (flow, thallium, FDG) and region (LAD and remote). A P value of <0.05 was considered statistically significant.

RESULTS

All animals were in good health at the time of study. The average LAD stenosis severity was 87 ± 14%, and this was associated with severe anteropapical hypokinesis and an average wall motion score of 0.7 ± 0.8. The quantification of flow during adenosine vasodilation delineated a large LAD perfusion territory in each animal (Fig. 1), with a total of 213 LAD samples (30 ± 7/animal) and 384 remote samples (55 ± 9/animal). Postmortem histological analysis confirmed myocardial viability with no gross evidence of myocardial infarction in any animal. Furthermore, there was a similar amount of connective tissue staining in both the LAD territory and the normally perfused remote myocardium (6.7 ± 3.3% vs. 5.4 ± 0.7%; P = 0.31).

Thallium and FDG deposition in hibernating myocardium. At the time that resting perfusion was quantified and the isotopes were administered, the open chest hemodynamic parameters (heart rate, 83 ± 10 beats/min; systolic pressure, 128 ± 14 mmHg; and left atrial pressure, 13.9 ± 7.1 mmHg) were similar to those in the closed chest state (heart rate, 72 ± 7 beats/min, P = 0.02; systolic pressure, 127 ± 15 mmHg, P = 0.91; and left atrial pressure, 16.8 ± 3.2 mmHg, P = 0.48). There was a significant reduction in resting subendocardial and full-thickness perfusion in the LAD samples compared with the remote region (Table 1). The coefficient of variation in resting perfusion between animals was 0.26 in the LAD region and 0.21 in remote myocardium.

The relationship between thallium deposition and absolute resting perfusion is shown in Fig. 2 (left). The relationship between LAD values normalized to the corresponding remote myocardium is shown at top left of Fig. 3, and values for individual animals are shown at bottom left of Fig. 3. As expected, thallium deposition was correlated to resting flow (y = 7.3 x + 20.2; r² = 0.20; P < 0.001), with similar...
Fig. 1. Perfusion and thallium deposition in a representative myocardial ring. Labels A–L on the x-axis represent the 12 circumferential myocardial samples from an unrolled ring beginning at the posterior descending coronary artery and progressing to the freewall of the left ventricle (samples A–H) and then the septum (samples I–L). Vasodilated perfusion (top, gray squares) within a myocardial ring was used to identify the left anterior descending coronary artery (LAD) perfusion boundaries. The 2 border zone samples with intermediate vasodilated perfusion (gray shading) were excluded from subsequent analyses. The region with reduced flow reserve was considered the LAD distribution (samples H–J in this example), and the remaining samples were considered the normally perfused remote region (Remote; samples L and A–F in this example). The same approach was used to define perfusion territories for each myocardial ring sampled. Bottom: resting perfusion (white squares) and thallium deposition (black diamonds) in these same samples.

Regression slopes for samples from both LAD and remote regions. Relative thallium deposition versus relative flow in the LAD region was even more tightly correlated (y = 0.22X + 0.78; r² = 0.33; P < 0.001). However, the linear regression slope of 0.22 was much shallower than a line of identity (slope = 1). Thus, in hibernating myocardium with reduced resting perfusion, relative thallium deposition after 1 h underestimated the relative difference in flow.

Figure 4 (left) illustrates the transmural variation in mean values for relative thallium deposition and relative resting flow. Relative thallium deposition in hibernating myocardium was uniform in each layer of the left ventricle and was significantly higher than the corresponding relative flow values in the subendocardium and midmyocardium. More homogeneous deposition of thallium relative to resting flow was further supported by the significantly lower relative dispersion of thallium (all samples, 0.12 ± 0.03) than that of resting flow (0.29 ± 0.10, P < 0.01; Fig. 5).

Insulin-stimulated FDG uptake is considered the gold standard assessment of metabolic viability. As expected, there was a very flat relationship between absolute FDG deposition and resting flow (y = −0.30X + 2.15; r² = 0.01; P < 0.01; Fig. 2, right). Although the correlation was statistically significant due to the large number of samples, resting flow only accounted for ~1% of the variability in FDG deposition. A similar flat relationship was present for relative FDG deposition versus relative resting flow (y = 0.09X + 1.11; r² = 0.01; P = 0.18; Fig. 3, top and bottom right). Furthermore, in 210 out of 212 LAD samples (99%), FDG deposition was >75% of the corresponding remote region, confirming viability. The transmural variation in FDG deposition (Fig. 4, right) showed enhanced FDG uptake relative to resting flow in the endocardial two-thirds of hibernating myocardium. This is consistent with the clinical imaging of a flow-metabolism mismatch that is characteristic of hibernating myocardium. Finally, the relative dispersion of FDG deposition (Fig. 5) was similar in both the LAD and remote regions, with intermediate values between those for resting flow and thallium deposition.

**DISCUSSION**

This is the first detailed examination of thallium deposition in relation to myocardial blood flow in an animal model with viable, chronically dysfunctional myocardium. This chronic porcine model recapitulates all of the physiological features of hibernating myocardium (10, 11, 13) and demonstrated that thallium deposition 1 h after injection was significantly more homogeneous than resting perfusion. Thus thallium redistribution was nearly complete after 1 h, and at this point relative thallium deposition exceeded relative flow in hibernating myocardium and underestimated the reduction in flow (Figs. 3 and 4).

**Thallium deposition in acute myocardial ischemia.** Immediately after injection, thallium distribution is proportional to blood flow in normal, stunned, and infarcted myocardium (9, 18, 20). For example, Sochor et al. (24) determined thallium deposition following reperfusion in a myocardial infarction model in dogs. A 3-h mid-LAD occlusion was performed percutaneously, and after 20 h of reperfusion, microspheres and thallium were administered with deposition determined after 15 min of accumulation. Thallium deposition and blood

---

**Table 1. Rest and vasodilated perfusion**

<table>
<thead>
<tr>
<th></th>
<th>LAD Region</th>
<th></th>
<th></th>
<th>Remote Region</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Endo</td>
<td>Mid</td>
<td>Epi</td>
<td>FT</td>
<td>Endo</td>
<td>Mid</td>
</tr>
<tr>
<td>Rest, ml·min⁻¹·g⁻¹</td>
<td>0.78±0.34*</td>
<td>0.82±0.23</td>
<td>0.80±0.31*</td>
<td>0.80±0.29*</td>
<td>0.90±0.24</td>
<td>0.88±0.24</td>
</tr>
<tr>
<td>Adenosine, ml·min⁻¹·g⁻¹</td>
<td>0.96±0.73*†</td>
<td>1.70±1.02*†</td>
<td>2.22±0.98*†</td>
<td>1.63±1.05*†</td>
<td>4.44±1.35*†</td>
<td>5.26±1.47*†</td>
</tr>
</tbody>
</table>

Values are means ± SD. *P < 0.05 vs. remote; †P < 0.05 vs. rest. LAD, left anterior descending coronary artery; Endo, subendocardium; Mid, midmyocardium; Epi, subepicardium; FT, full-thickness.
flow were very closely correlated, with a coefficient of 0.92. Furthermore, the slope was very close to unity (1.08) (24), consistent with a nearly ideal relation.

In contrast with this near perfect association between thallium and blood flow, the relationship in viable myocardium with reduced resting perfusion is more variable. Although the immediate distribution of thallium in acutely ischemic myocardium is proportional to the reduction in flow (17, 20), there is a well-described redistribution of thallium over time with differential washout in normal compared with ischemic myocardium (9, 20, 22). A greater washout rate in normal myocardium results in a progressive reduction in the relative difference in thallium deposition in normal and ischemic myocardium (9, 20, 22). For example, in dogs with a partial coronary stenosis, Pohost et al. (2) compared thallium activity at 10 min, 2 h, and 4 h with microsphere-quantified blood flow measurements. The initial deposition of thallium was linearly proportional to flow (r = 0.91) and close to the identity relationship (slope = 0.80). Although the subsequent time points continued to show linear correlations, there was a progressive decrease in the slope at 2 h (slope = 0.58; r = 0.79) and 4 h (slope = 0.39; r = 0.66) after thallium administration. Thus thallium redistribution progressed but was still incomplete at 4 h. Similarly, Sinusas et al. (23) evaluated thallium accumulation in dogs over the final 20 min of a 1-h partial coronary occlusion. They noted that relative thallium uptake in the subendocardial samples was linearly proportional to relative microsphere flow (correlation coefficient of 0.78). Consistent with redistribution, the relative thallium uptake was systematically and significantly greater than relative perfusion (23). When thallium was allowed to accumulate for 2.5 h, there was a further increase in relative thallium uptake (22).

In contrast with these previous studies of prolonged acute ischemia [or short-term hibernation (15)], redistribution of thallium was nearly complete within 1 h in this porcine model of chronic hibernating myocardium (slope = 0.22). This is most likely explained by the less severe reduction in blood flow in the pigs with hibernating myocardium. Furthermore, the severity of ischemia in these prior acute studies likely exceeded that which could be chronically sustained without infarction (16).

Previous studies of thallium deposition in hibernating myocardium. Before the present study, there was very little data regarding the relationship between thallium and blood flow in viable, chronically dysfunctional myocardium. An excellent study by Parodi et al. (19) examined this relation in six patients with ischemic cardiomyopathy before cardiac transplantation. Myocardial blood flow was quantified with 99mTc-pertechnetate-labeled albumin microspheres and compared with thallium administered 4 h before explantation. Data from these 93 myocardial samples revealed no significant correlation between thallium retention and blood flow (r = 0.05). Matched reductions in thallium and flow were reported in 46 samples (49%), with matched normal levels in 20 samples (22%); however, in the remaining 27 samples (29%), they noted supernormal thallium retention. Despite the fact that these segments had reduced resting flow (0.43 ± 0.29 vs. 0.97 ± 0.28 ml·min⁻¹·g⁻¹ in normal), they had greater thallium retention than the most normal regions (107 ± 16% vs. 81 ± 14% in normal, P < 0.05; relative thallium/relative flow > 1.25) (19).

The present study in pigs extends the results of this earlier study by confirming viability by both normal levels of connective tissue staining and preserved FDG deposition and by quantifying thallium as absolute deposition (Fig. 2) as well as relative to remote myocardium (Fig. 3). Our results confirmed enhanced thallium deposition relative to resting flow in hibernating myocardium. Approximately two-thirds of the samples (137 out of 212, 65%) from the LAD distribution had a relative thallium deposition-to-relative flow ratio of >1, and 23% (49 out of 212 samples) exceeded the ratio of 1.25 (19). Similar to the previous study, samples with a thallium-flow mismatch had...
lower levels of resting perfusion (relative flow, 0.55 ± 0.03 vs. 1.04 ± 0.03 ml·min⁻¹·g⁻¹; *P* < 0.001), but we also found that these samples were more frequently subendocardial and had enhanced FDG deposition (relative FDG deposition, 1.29 ± 0.07 vs. 1.16 ± 0.03; *P* < 0.05).

However, in contrast with the previous clinical study, we did not find evidence for supernormal thallium retention. Absolute thallium deposition in 61% of the LAD samples (130 out of 212) was less than that in the corresponding remote region (relative thallium deposition <1); and as shown in Fig. 5, average values were <1 in each transmural layer. Although the average reduction in resting flow in hibernating myocardium in the present study was less than that found by Parodi et al. (19), there was no suggestion for supernormal thallium deposition even in the selected samples with very low flow (Figs. 2 and 3).

We believe that the most likely explanation for this discrepancy was the fact that the clinical study enrolled patients with end-stage heart disease (19) and the basis for quantifying thallium retention was relative to the most normal region of each patient. However, as would be anticipated in patients with diffuse coronary disease requiring heart transplantation, significant remodeling had occurred and even the segments with
normal levels of matched flow and thallium retention had relatively high fibrosis (17 ± 16%). They found a highly significant negative correlation between thallium retention and segmental fibrosis ($r = -0.62; P < 0.0001$), and interestingly, the samples with hibernating myocardium had relatively limited fibrosis (8 ± 8%) (19). Thus thallium retention in the most normal samples was almost certainly reduced, accounting for the artifactually supernormal thallium retention in hibernating myocardium.

Methodological limitations. The vast majority of patients with chronic coronary artery disease and hibernating myocardium have coexisting myocardial infarction, which does not occur in this porcine model. The absence of infarction in this model is a distinct advantage for the basic investigation of chronic myocardial adaptations to ischemia; however, we were unable to simultaneously determine thallium deposition in nonviable myocardium and its relation to FDG uptake. Nevertheless, this has been the focus of numerous prior investigations, which have consistently shown low thallium deposition in nonviable myocardium (27).

We interpreted the limited relative dispersion of thallium as additional evidence for more homogeneous distribution than regional flow as assessed with microspheres. However, it should be noted that this finding might also be the result of inherent differences between molecular and particulate tracers of perfusion (2). Nevertheless, the average values do support a greater regional difference in flow with microspheres than deposition of thallium.

In various details, the protocol used in the present study was different from that used with routine clinical imaging. The 1-h delay to isotope quantification is intermediate between the 10 –15 min used for thallium stress imaging and the 3 to 4 h imaging of redistribution. Nevertheless, this time frame is consistent with the rest imaging phase of a rest-redistribution protocol, which is specifically recommended when the clinical question is to determine the presence and extent of myocardial viability (9). In this protocol, initial imaging is performed ~30–60 min after thallium injection (rest image). If defects are present on these images, then additional imaging is performed ~4 h after thallium injection (redistribution image). Our data suggest that thallium redistribution is nearly complete by 1 h; thus in rest phase imaging, hibernating myocardium would be correctly identified as viable but would not be differentiated from stunned myocardium (with normal resting perfusion). Despite the fact that thallium and FDG were administered in the open chest state, hemodynamic parameters and quantification of absolute blood flow with fluorescent microspheres confirmed comparable physiology with the closed chest state. Finally, the simultaneous assessment of metabolic viability with insulin-stimulated FDG deposition necessitated a glucose-insulin infusion during the time of thallium deposition. Although this is not routinely performed in clinical practice, previous clinical studies have suggested that a glucose-insulin infusion can improve diagnostic accuracy by increasing thallium uptake in severely ischemic myocardium (21, 25, 26).
Summary/Clinical Implications

These data have shown that within 1 h thallium deposition in chronic hibernating myocardium is enhanced relative to resting perfusion and similar to the deposition in the remote, normally perfused region. However, it should be acknowledged that chronically instrumented pigs with hibernating myocardium had modest reductions in resting flow, and it is possible that more severe flow reductions in patients with viable dysfunctional myocardium would be associated with a more prolonged redistribution phase of thallium. This study did not test a specific mechanism by which thallium is preferentially accumulated in hibernating myocardium. However, our results are consistent with previously proposed mechanisms which include greater redistribution relative to normal myocardium (9, 22), more efficient extraction at lower flow rates (23), and enhanced thallium uptake during glucose-insulin stimulation (21, 25, 26).

The preferential accumulation of thallium in viable, chronically dysfunctional myocardium improves the discrimination from infarcted myocardium and thereby enhances its utility as a marker of myocardial viability for predicting recovery of function following revascularization. However, within 1 h there is relatively homogenous deposition of thallium, which limits the ability to differentiate viable myocardium with reduced resting flow (hibernating myocardium) from dysfunctional segments with normal perfusion (chronically stunned myocardium) (5). Thus clinical imaging at ~1 h might incorrectly characterize hibernating myocardium as chronically stunned myocardium. Clinical implications of this may be significant since hibernating myocardium has been associated with increased mortality in the setting of delayed revascularization (4) and slower recovery of regional function following revascularization (3, 14). Furthermore, hibernating myocardium has been associated with increased cardiac mortality in patients treated with medical therapy (1, 7) and appears to be an important substrate for sudden death in patients with ischae-mic cardiomyopathy (1, 8, 12).

ACKNOWLEDGMENTS

We appreciate the technical assistance of Deana Gretka, Joanne Schlosser, Randall Bassett, and Amy Johnson. Anne Coe was instrumental in the preparation of this manuscript.

GRANTS

This work was supported by grants from the Department of Veterans Affairs, the American Heart Association, the National Heart Lung and Blood Institute (HL-55324), the Albert and Elizabeth Rekate Fund, and the John R. Oishei Foundation.

REFERENCES


