Thallium Washout Analysis: Fact or Fiction?

This issue of the *Journal* includes a paper by Brown and co-workers (*1*) which reports on regional myocardial washout analysis in patients having a prior myocardial infarction. The authors report that a pattern of rapid thallium washout was noted in infarct segments having less initial tracer uptake and more severe wall motion abnormalities than infarct segments showing a more normal washout rate. When quantitative analysis was repeated without any background subtraction, no segments with rapid washout were noted. A phantom model was constructed which demonstrated that tracer (technetium-99m) washout rate was accelerated in initial defect segments when they were ≤1/6 of the count density compared with "normal" adjacent segments. When the quantitative analysis is repeated without interpolative background subtraction, no defects show accelerated thallium washout. This investigation implies that rapid thallium washout is an artifact of background subtraction in these postinfarction patients.

Many questions are raised by this study.

1. Is quantitative analysis of thallium washout ever reliable?
2. If there is a significant artifact introduced by background substraction, how can it be avoided?
3. What is reverse redistribution on thallium scans and does this study help clarify the issue?
4. What is the "gold standard" concerning thallium washout analysis?

The answers to these questions are complex and somewhat controversial, but clearly depend on a firm understanding of myocardial thallium kinetics. Cellular uptake of thallium depends on arterial tracer concentration, nutrient flow and transcapillary extraction. Thallium washout results from a net clearance of isotope from the cellular pool which is greater than the rate of tracer uptake. This dynamic process is reflected in the time activity curve for each myocardial segment. In a series of experimental studies, myocardial thallium kinetics have been evaluated in normal (*2*), ischemic (*3*) and hyperemic (*4*) zones of blood flow utilizing miniature implanted radiation detectors. This technique can measure regional thallium clearance corrected for both background and blood levels. These experiments showed that thallium washout is faster in myocardial zones having higher flow and that final decay rates for normal myocardium and blood were not significantly different. It is interesting to note that ischemic zones reached their peak thallium activity at relatively long times (40–90 min) and consequently, net thallium washout over 2 to 3 hr was relatively slow. When initial flow was severely reduced to levels that are typically associated with myocardial necrosis, the rate of thallium washout was similar to normal zones. Other investigators (*5,6*) have independently demonstrated that thallium washout is directly related to coronary perfusion.

Given these experimental findings, it is not surprising that clinical studies have noted a correlation between the severity of coronary stenoses and thallium washout rates (*7,8*). Slow regional thallium washout would be expected in regions of low flow, but faster washout occurs in necrotic areas. It is also interesting to note that myocardial thallium clearance has also been directly related to peak exercise heart rate (*9*). Specifically, slower tracer washout was associated with lower (≤140 b/min) peak heart rate, which again suggests a strong relationship between coronary flow and thallium redistribution. The problem is not that thallium kinetics are unreliable, but rather that external quantitation of myocardial time-activity curves is not precise. Despite careful attention to repositioning camera angles and computer image reconstructions, background correction can never be completely accurate and the collection of regional thallium activity has poor temporary resolution (6 to 8 min/view).

It is clear that the rate of thallium washout in clinical studies is very much dependent on background subtraction as suggested by Brown et al. (*1*), but the "artifact" is in the technique of quantitation not in the myocardium. In other words, regional thallium washout may be "quantitated" by a particular method as greater than normal, but actually reflect a relatively

normal clearance of tracer from a low count density area. The effect of background subtraction is most pronounced in low count regions and does cause the observed acceleration of thallium washout. This background effect may also explain the faster thallium washout noted for women in areas of soft-tissue attenuation (*10*).

If it is assumed that background subtraction in clinical studies is never precise, can potential problems in quantitation be avoided? Yes, by restricting these quantitative methods to high quality images having relatively high target to background ratio, good initial count density and careful attention to imaging angles and soft-tissue attenuation. In addition, an evaluation of the thallium decay constant for the blood over the time of the study should also be determined. Quantitative analysis of thallium scans is not a simple process and careful attention to image collection and processing must be made.

It is also important to relate the observation of reverse redistribution (*11,12*) and accelerated washout on poststreptokinase thallium studies (*13*) to this discussion. The observation that initially normal areas of thallium uptake subsequently show defects on delayed postexercise images cannot be explained by this present study in the *Journal* nor by the experimental results (*2–6*). There is no experimental model that has reproduced reverse redistribution and clinical analysis of these studies simply confirms the visual impression of accelerated regional thallium washout from initially normal myocardium. In canine experiments, regional hyperemia (*14*) and coronary reperfusion (*15*) have been reported to cause accelerated thallium clearance. Therefore, reverse redistribution may be explained, in part, by regional disparities in cellular function and flow during thallium redistribution. The observation of rapid washout in resting thallium studies performed in patient having coronary thrombolysis (*13*) may be explained by these experimental studies (*14,15*), but the study by Brown et al. (*1*) cannot be used as a comparable observation. Specifically, the present report describes rapid thallium washout in initial *defect* areas after *exercise* studies, which is in contrast to the report by Weiss et al. (*11*) which involved accelerated clearance from initially *normal* areas during *resting* studies. Although this recent observation (*1*) appears to be artifactual, the previous report (*13*) may have physiological significance. More data will need to be collected before this issue can truly be settled.

Finally, the question of the "gold standard" for thallium washout remains. It would appear that the experimental and clinical determinations of thallium kinetics suggest that homogeneous myocardial uptake means that there is little disparity in regional coronary perfusion and that normal tracer washout is fairly uniform and related to blood decay rates. Furthermore, the rate of thallium clearance is related to blood flow and also to cellular functional integrity.

This issue of the Journal provides an important lesson on the limitations of the quantitation of gamma camera imaging. Thallium washout is a fact but its analysis can sometimes be a fiction.

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