What can fatty acids add in LBBB and to the myocardial viability issue?

TO THE EDITOR: We read with interest the articles of Sloof et al. (*1*), Zanco et al. (*2*) and the editorial of Altehoefer (*3*), (a) comparing uptake of ^{123}I-beta-methyl-p-iodophenyl-pentadecanoic acid (BMIPP) versus ^{201}Tl and ^{18}F-fluorodeoxyglucose (FDG) in chronic ischemic heart disease (CIHD) and (b) discussing glucose utilization in left bundle branch block (LBBB) (*2,3*).

In a recent study (*4*), in 21 patients with old myocardial infarctions, we compared findings from PET with both FDG and ^{18}F-fluoro-6-thiaheptadecanoic acid (FTHA) (metabolism) and from SPECT with ^{99m}Tc-hexakis-isobutyl isonitrile (MIBI) (perfusion). Out of these 21 patients, 2 patients had non–insulin-dependent diabetes, 1 of whom had complete LBBB, and 1 had complete LBBB without diabetes. Exclusively in these 3 patients [i.e., in 17% of the total myocardial region of interest (ROI) evaluated], we found reverse mismatch (FDG uptake <50%, ^{99m}Tc-MIBI uptake >70% of myocardial maximum). In these ROIs, FTHA uptake (75.5%) paralleled the MIBI uptake (78.6%) and not FDG uptake (38.1%).

If we read Table 3 of Sloof et al. (*1*) correctly, 14 of 36 (39%) ROIs displayed an FDG mismatch in old infarctions versus ^{201}Tl as the perfusion imaging agent. However, the BMIPP mismatch was more frequent (20/36 = 56%). In our study (*4*), FTHA mismatched (FTHA >70%) versus MIBI (uptake <50%) in only 15% of the ROIs with an FDG mismatch (FDG uptake >70%). Furthermore, FTHA uptake correlated well with the MIBI uptake values (r = 0.798) and less well with FDG (r = 0.571). FDG versus MIBI was r = 0.551. This is in congruence with data from Kudoh et al. (*5*) and Taki et al. (*6*), giving evidence that decreased BMIPP uptake relative to reinjection ^{201}Tl uptake occurs in chronically ischemic but viable myocardium.

Differences in the study design are obvious: Sloof et al. (*1*) used ^{201}Tl SPECT for perfusion; for FDG, Acipimox (Byk, The Netherlands) administration; and gamma-camera imaging with ultra-high-energy collimation. We used ^{99m}Tc-MIBI SPECT for perfusion, glucose load for FDG and PET with ^{67}Ge/^{68}Ga transmission correction. Fatty acids were different also (BMIPP versus FTHA). Criteria for mismatch by Sloof et al. were defined as a difference of FDG versus ^{201}Tl of only 7%; we used a difference versus ^{99m}Tc-MIBI of >20%. For the fatty acids, discriminating differences were 7.0% or 8.5% versus 20%.

The protocols used by our group have been proven to be selective and meaningful by follow-up studies after revascularization (*7,8*). Thus, we feel that some of the results of Sloof et al. (*1*) may be influenced by methods, study design and evaluation protocol. In addition, the fatty acid FTHA (*4*) performs like ^{11}C-acetate in LBBB (*2*). Therefore, as long as perfusion is preserved, both radiopharmaceuticals may be governed by this determinant. For FTHA and β-oxidation this has already been confirmed by our data (*4*).

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REPLY: We thank Dr. U. Buell et al. for their interest in our article (*1*). In this study, we compared uptake of beta-methyl-p-iodophenyl-pentadecanoic acid (BMIPP) and fluorodeoxyglucose (FDG) in chronic ischemic myocardium and found relatively increased BMIPP uptake in a substantial number of hypoperfused myocardial segments. This is different from the decreased BMIPP uptake often reported in (sub)acute myocardial ischemia.

Schulz et al. (*2*) also compared fatty acid uptake, using ^{18}F-fluoro-6-thiaheptadecanoic acid (FTHA) and FDG uptake in patients with old myocardial infarction (MI). In their letter to the editor (vide supra), Buell et al. indicate that the number of segments with increased fatty acid uptake relative to perfusion is different between both studies. However, we feel that, apart from the relative numbers, the principle observation of both studies is the same and thus confirm each other, despite differences in the methods used. The most important observation is that in both studies increased fatty acid uptake relative to perfusion is described in chronic ischemic myocardium. This is in contrast to the decreased fatty acid uptake found in (sub)acute myocardial ischemia. This latter finding is often emphasized, even when areas also containing a substantial number of segments with relatively increased fatty acid uptake are found (*3,4*). For instance, Taki et al. (*3*) also found increased BMIPP uptake relative to perfusion, using a 5-point grading scale, in 33 of 267 segments (12%). Of course, the relative number of (mis)matches largely depend on the threshold used as a criteria for (mis)match. With a 7% difference between perfusion and BMIPP uptake, as in our study, we indeed found 20/36 (56%) BMIPP-to-perfusion mismatches in areas with an old MI versus 15% in the study of Schulz et al. (*2*), using a high threshold of a 20% difference between fatty acid uptake and perfusion. Applying their threshold of 20% on our data, we found no (0%) mismatches at all in areas with an old MI and only two

(2%) in all hypoperfused segments (n = 87). These 2 segments were in ischemic but noninfarcted, remote, myocardium. Thus, even the number of segments with relatively increased fatty acid uptake was less in our study compared with the study of Schulz et al. (*2*), using their threshold, instead of more, which is the major point raised by Buell et al.

Another major resemblance between both studies is the finding that a higher correlation was found between fatty acid uptake and perfusion: BMIPP(%) = 0.75*Tl(%)+23, r = 0.87 and n = 273, than FDG versus perfusion: FDG(%) = 0.70*Tl(%)+24, r = 0.75 and n = 273.

In addition to the differences in methods pointed out by Buell et al. (vide supra), the following differences in study design should be mentioned: the myocardial segments in our study were 13 in each heart versus 33 in the study of Schulz et al. (*2*). Furthermore, we used a reference database of healthy individuals to define normal or abnormal perfusion by ^{201}Tl (*1*), whereas Schulz et al. (2) did not use a normal reference database but defined hypoperfusion by ^{99m}Tc-hexakis-isobutyl isonitrile (MIBI) uptake <70% of peak uptake. Finally, they used an oral glucose load before FDG imaging, which results in lower target-to-background ratio compared with the glucose clamp or Acipimox (Byk, The Netherlands) protocol, as we applied it (*5,6*). By coincidence, both study groups consisted of only 21 patients, and therefore one may not be surprised that the relative numbers are not exactly the same. Still, the principle finding is the same.

The protocol we used has been proven to discriminate viable from nonviable myocardial segments, hence, satisfactorally predicting functional outcome after revascularization (*7,8*). Furthermore, it has been demonstrated in our institution that there is good agreement between the detection of viability in dyssynergic myocardium with FDG/^{13}N-ammonia PET and FDG/^{201}Tl SPECT (9). Therefore, we feel that their suggestion that our results may be influenced by the study design is incorrect. Obviously, the outcomes of both studies are to some extent influenced by study design and evaluation methods.

Our study did not contain patients with a left bundle branch block (LBBB), so we cannot comment on the issue of LBBB and substrate utilization.

Thus, the differences in methods, especially the threshold of a metabolism/perfusion difference to define a matched defect or mismatch, is largely responsible for the different numerical outcomes of both studies. Nevertheless, it is an important observation that the principle outcome is the same: increased fatty acid uptake relative to perfusion can be found in chronic ischemic myocardium.

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Moyamoya Disease and Pregnancy

TO THE EDITOR: I read with great interest the article by Kume et al. (*1*) reporting on the usefulness of cerebral blood flow (CBF) mapping under hyperventilation for prediction of the risk of vaginal delivery of pregnant women with moyamoya disease.

My colleagues and I have recently reviewed the literature describing pregnant women with moyamoya disease (*2*). In the literature, there have been 53 pregnant women with moyamoya disease: 30 patients (group A) who had been diagnosed with moyamoya disease before pregnancy and were capable of delivery, and 23 patients (group B) who were symptomatic and diagnosed for the first time as having moyamoya disease associated with pregnancy. In group A, delivery could be performed safely either by cesarean or vaginal delivery, and any anesthetic method could be used, as long as special attention was given to avoid hypocapnia, hypotension and hypertension. Poor prognosis for the mother or the neonate was generally caused by cerebral hemorrhage in group B and not by cerebral ischemia in group A. In fact, neither cerebral ischemia nor cerebral hemorrhage developed during delivery in patients in group A, although only 11 patients from the group had undergone extracranial-intracranial bypass surgery when diagnosed with moyamoya disease. As Kume et al. (*1*) stated, hyperventilation challenge may be dangerous for patients with moyamoya disease. Thus, CBF mapping under hyperventilation could be dangerous and may give little information on the safety of vaginal delivery for the patients in group A. Accordingly, I do not believe that evaluation of cerebral vascular reserve using ^{99m}Tc-hexamethyl propylenamine oxime (HMPAO) is necessary even if its radiation dose to the fetus is negligible. Instead, we should find the best method of delivery (vaginal or cesarean delivery) and anesthesia (general, epidural or spinal) which are familiar to the obstetric and anesthetic teams in each hospital to avoid hypocapnia (hyperventilation), hypotension and hypertension.

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