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EDITORIAL COMMENTARY

Coronary endothelial function: a clinical role for PET?

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Coronary endothelial dysfunction is the earliest abnormality in the development of coronary atherosclerosis and is also independently associated with future cardiac events. Quantification of myocardial blood flow (MBF) can assist in the diagnosis of diffuse coronary artery disease (CAD), heart failure and microvascular disease [1, 2]. In the absence of coronary stenoses, a reduced coronary flow reserve (CFR) reflects dysfunction of the coronary microcirculation.

Positron emission tomography (PET) plays an important role in the assessment of MBF due to four major characteristics: (1) high sensitivity, (2) excellent temporal resolution, (3) the possibility to label molecules without altering their chemical properties and (4) the short half-life of isotopes. The most common method of quantifying MBF involves the acquisition of dynamic images with the cyclotron-produced radiopharmaceuticals ^{13}N-ammonia and ^{15}O-water. An alternative method is the generator-produced ^{82}Rb.

In this issue of the *European Journal of Nuclear Medicine and Molecular Imaging*, Yoshinaga and colleagues present some interesting data comparing the quantitative analysis of coronary endothelial function with ^{82}Rb and ^{15}O-water PET [3]. MBF was assessed at rest and during a cold pressor test (CPT) with ^{82}Rb and ^{15}O-water PET in controls and smokers. They found a reduced CPT to rest ratio in smokers compared with controls for both radiopharmaceuticals. They concluded that ^{82}Rb is a reliable method in comparison to ^{15}O-water PET and that ^{82}Rb may be applicable for risk assessment in subjects with coronary risk factors.

The usefulness of ^{82}Rb is proven in this study; however, the study included in total 19 subjects, and there will be a need for studies with larger sample sizes. A wide pallet of pathological disorders like hyperlipidaemia, hypertension, diabetes and smoking attenuate the vasomotor response to NO and reveals the widespread distribution of underlying causes that can result in endothelial dysfunction. In other words, MBF assessment provides a way to document how risk factors translate into measurable damage to the coronary circulation.

In my opinion, it is time to get MBF PET ready for the future, because of the open access to ^{82}Rb now in Europe. The use of ^{82}Rb would give advantages compared to ^{13}N-ammonia and ^{15}O-water PET: no need for a cyclotron, 24-h/day access, fast acquisition protocols allowing high throughput, evaluation of stunning by using rest and stress gating modality and a better visual quality compared to ^{15}O-water. Also absolute quantification of MBF is possible with ^{82}Rb and validated [4, 5] and the important parameter of CFR for prognosis can be calculated [6]. Due to the wide range of the ^{82}Rb positron, the resolution is reduced. An important issue of concern is the cost-effectiveness of ^{82}Rb, especially compared to the widely used SPECT technique. The ^{82}Rb generator needs to be replaced every 4–6 weeks, rendering this technique relatively expensive, with a price in the region of 25,000 euros. Industry should put maximal effort into reducing the price of the generator, so that ^{82}Rb may finally facilitate a breakthrough of cardiac PET myocardial perfusion imaging (MPI) for routine clinical practice in Europe.

The first studies on the clinical utility of ^{82}Rb MPI were reported almost 25 years ago [7], and accurate data of ^{82}Rb MPI are available in the literature linked to outcomes [8, 9].

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Although ^{82}Rb is now widely available in the USA, this tracer is moderately available in Europe; however, a dawn is coming. Industrial ^{82}Rb supply for Europe is growing and may lead to a wider implementation of ^{82}Rb. Nevertheless, and although the use of ^{82}Rb has been already described in a number of reports in the literature, the merit of the present study is that it encourages us to benefit from the substantial superiority of the PET technique for instance over SPECT, resulting in good image quality even in obese patients. The superiority over SPECT can be expected regarding accuracy, study duration, staff radiation exposure, reduced patient dose, patient discomfort and potentially economic benefit. These are all important implications, which may not have been fully appreciated in Europe so far. A clinical role of MBF PET should be highlighted now, because of the easier access to ^{82}Rb.

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