Further evidence for the robustness of regadenoson stress myocardial perfusion SPECT: its predictive value for cardiac events in chronic renal failure

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In recent years, regadenoson has increasingly penetrated the clinical market as a novel pharmacologic stress agent for myocardial perfusion imaging (MPI).¹ Regadenoson has favourable features such as a rapid onset of vasodilation with sustained action, enabling injection as a slow bolus,¹ and a preferable side-effect profile when compared with adenosine due to adenosine A2A receptor subtype selectivity.² Another advantage is that it can be used in obstructive pulmonary disease, when the traditional agents dypridamole and adenosine may be unsafe.³

Many studies investigating regadenoson in different risk groups, using various imaging protocols and nuclear tracers, demonstrated safety and efficacy comparable with adenosine for the detection of reversible myocardial perfusion defects.² More recently, regadenoson, despite its predominantly renal clearance, was also shown to be well tolerated in patients with chronic renal failure (CRF).⁴ Because CRF patients are generally at a higher risk for cardiovascular events, the value of MPI in this group has been actively investigated in recent years. Using exercise or adenosine stress, left ventricular ejection fraction (LVEF), ischaemic burden, scar burden, and left ventricular dysynchrony, as measured with phase analysis of gated single-photon-emission computed tomography (SPECT), all are strong predictors of outcome.⁵ Similar data for regadenoson as a stress agent, however, have not yet been obtained so far.

This issue has been successfully addressed by Bhatti et al.⁶ in this issue of European Heart Journal– Cardiovascular Imaging where the authors aimed at assessing the prognostic value of regadenoson MPI in patients with different degrees of kidney dysfunction. The authors retrospectively evaluated 1107 patients, among whom 426 had CRF, defined as the presence of glomerular filtration rate < 60 mL/min/1.73 m². Noticeably, it was found that CRF is a major predictor of cardiac events, and that event rates increased with increasing perfusion defect on MPI across the entire spectrum of renal function. In a set of multi-variate analyses, however, only LVEF < 50%, the presence of transient ischaemic dilatation and the inability to perform low-level exercise during regadenoson stress were predictors of cardiac events besides the non-imaging parameters of age and renal function. At the same time, a very low-risk group was identified, consisting of patients with normal renal function, with normal perfusion, and with preserved ability to undergo concomitant low-level exercise.

The importance of the functional response to a pharmacological stress test has been previously confirmed. For example, by Hage et al.,⁷ who evaluated 879 patients with CRF and found that a blunted heart rate response to adenosine is a strong predictor of mortality and may also provide additional prognostic data to MPI. Also in a paper by Hsiao et al.,⁸ LVEF reserve during regadenoson stress was found to be inversely related to the extent of inducible perfusion abnormalities and to angiographic jeopardized myocardium, thus highlighting the important incremental value of the response to stress. Similarly, Bhatti et al. show the importance of LVEF in regadenoson MPI to predict outcome.

The authors fail, however, to observe an incremental value of perfusion defects over the other variables in their patient group. These findings could be due to the relatively short follow-up, or due to censoring of patients with early revascularization, which was probably driven by most severe ischaemia and removed those cases. They emphasize the need for further analyses of the prognostic value of regadenoson in the setting of CRF.

Some additional factors should be considered as follows:

First, the study was a single-centre, retrospective study, which may have been influenced by loco-regional referral patterns and therapy strategies. Secondly, regional perfusion analysis was based on assignment to subgroups based on different summed scores. This group analysis may not allow for detection of detailed relationships.

Thirdly, absolute flow may be globally impaired in CRF due to adverse effects on micro-vascular function.⁹ This may attenuate the presence of regional defects and influence the prognostic value. The possibility of obtaining a truly quantitative measure of myocardial perfusion abnormalities and to angiographic jeopardized myocardium, thus highlighting the important incremental value of the response to stress. Similarly, Bhatti et al. show the importance of LVEF in regadenoson MPI to predict outcome.

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perfusion with SPECT may emerge from new gamma cameras with increased sensitivity and improved spatial resolution, or from the use of PET imaging. In fact, the incremental value of absolute flow quantification is supported by an increasing amount of evidence, suggesting that this parameter should also be tested in CRF with regards to its possible prognostic importance.

Nevertheless, the article by Bhatti et al. provides valuable further support for a broader use of regadenoson stress MPI, including patients with CRF. Further studies with an extended follow-up and with myocardial perfusion evaluated more quantitatively are highly anticipated, in order to assess the precise contribution of this important technique to the prognostic assessment of renal failure-related coronary heart disease.

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**References**


