Whole-body MR Imaging for Risk Stratification in Patients with Diabetes Mellitus

Diabetes mellitus is a serious systemic illness that affects an ever-increasing number of people. A recent survey of national health in Germany showed that the prevalence of diabetes rises markedly and continuously from the age of 50 years onwards, reaching over 20% in the 70-79 years of age group in the general population [1]. According to another recent international meta-analysis study, an average 50 years old male diabetic patient has a life expectancy of 5.8 years shorter than that of a man without diabetes of the same age. The corresponding estimate for diabetic women is 6.4 years shorter life expectancy than non-diabetic women [2].

These significantly reduced life expectancies can largely be attributed to an increased likelihood of cardiovascular events in diabetic subjects. The risk of myocardial infarction is four times greater in diabetic males, and six times greater in diabetic females, than in otherwise comparable non-diabetic subjects. However, it should not be forgotten that, despite being on average at higher risk, diabetics are a heterogeneous population with varying individual disease status and risks. These are influenced by several clinical, angiographic and biological features [3].

Thus, advanced risk stratification and evaluation of disease burden appears warranted.

In particular, given its non-invasive nature and the absence of ionizing radiation, MRI appears well suited as a tool for risk assessment in diabetics. With substantial technological developments having been introduced in MRI over the last few decades, the modality is now in routine clinical use. The application of the MRI techniques of T2-, T2*-, diffusion-weighted, fluid-attenuated inversion-recovery and time-of-flight angiography enables detection and stratification of cerebral vascular disease [4]. With the introduction of steady-state free precession pulse and inversion recovery sequences, cardiac MR has become the standard of reference for noninvasive evaluation of cardiac function and, with the use of gadolinium (Gd) contrast, cardiac MR imaging also can characterize ischemic and infarcted myocardium [5]. Extracellular matrix expansion in myocardium caused by various diseases can be quantified by measuring the extracellular volume fraction (ECV) based on T1 analyses of blood and myocardium before and after Gd contrast with hematocrit reference [6]. Whole-body 3D MR angiograms obtained using continuous table movement with an integrated phased-array torso surface coil yield improved image quality and permit assessment of the entire vascular tree from the carotid to the tibial arteries [7].

A number of previous studies in the diabetes field have focused on the value of dedicated organ imaging, particularly cardiac imaging. Basically, such work investigated the relevance of late Gd enhancement (LGE) of the myocardium in the prognosis of major adverse cardiovascular events (MACE). Interestingly, LGE in the left ventricular wall as measured by cardiac MR was present in about 21% (72 out of 337) of diabetic patients with unrecognized myocardial infarction [8]. Furthermore, according to the study of Kwong et al [9] in a cohort of 109 diabetic patients without any clinical evidence of myocardial infarction, LGE was present in up to 28% of the patients. The presence of LGE was the strongest multivariable predictor of MACE and death by stepwise selection, and gave a 4-fold hazards increase. Similar findings were reported by Yoon et al [10] in a prospective cohort study of 181 patients with impaired fasting glucose (IFG) and 151 patients with diabetes. In this study, the prevalence of LGE was 25% in patients with IFG and 38% in diabetic patients. Compared to left ventricular ejection fraction and the presence of wall motion abnormalities, LGE was the strongest predictor of MACE in the IFG group (unadjusted hazards ratio (HR): 6.1) and diabetic group (unadjusted HR:

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FIGURE 1. Whole-body MR images show multiple findings in a 74-year-old man with type 2 diabetes for 21 years. Left Panel. Cardiac acquisitions in short-axis (top image) and four-chamber (middle image) views show impaired function with anterolateral hypokinesia (arrows). Late gadolinium-enhanced image (bottom image) shows enhancement of anterolateral myocardium (arrowhead), indicative of myocardial infarction. Middle Panel. Cerebral acquisitions reveal normal cerebral arteries on time-of-flight angiogram (top image), axial T2-weighted brain image (middle image), and coronal fluid-attenuated inversion-recovery image (bottom image). Right Panel. Vascular acquisitions on contrast-enhanced MR angiograms demonstrate 50% stenosis of left internal carotid artery (arrowhead) and multisegmental luminal irregularities of abdomen (upper arrow), thighs, and lower leg with severe atherosclerotic disease and vessel occlusion (lower arrow). Images already published in ref. 13, reproduced courtesy of the publishers of Radiology.
in a multivariate model. When adding the extent of atherosclerotic vessel score to the model, the corresponding C-statistic increased significantly [13].

While these early results are encouraging, further research is necessary to establish whole-body MR imaging as a justified alternative to the currently accepted tools for risk stratification. Generally, these include ultrasonographic measurement of carotid intima-media thickness, exercise electrocardiogram, dobutamine stress echocardiography, nuclear myocardial perfusion imaging, or cardiac CT for the assessment of accurate anatomic information and functional significance of coronary artery disease [15]. Each of these techniques has its own advantages and disadvantages. These latter include cost, sensitivity, radiation dose, technical complexity and acquisition time. It can be anticipated that, if the early promising results of whole-body MR imaging are confirmed, the assessment of the systemic burden of disease by MRI could contribute to better risk stratification in diabetic patients.

CONCLUSION
Whole-body MR imaging has the potential to be an optimal tool for the non-invasive low risk evaluation of the subclinical degree of systemic disease states. This may be particularly relevant in the diabetic patient population in which, although at high risk as a group, on an individual basis, the degree of subclinical disease burden and likelihood of major adverse events vary significantly.

To date, the available scientific evidence for the whole-body MRI approach is very encouraging but is based on relatively few patients. Further dedicated research in larger patient cohorts is needed.

REFERENCES.