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# THE METABOLIC-MICROVASCULAR DYSREGULATION SYNDROME

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## CENTRAL BP MEASUREMENT AND VALIDATION: THE ENGINEER'S POINT OF VIEW

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The non-invasive assessment of aortic (central) pressure evolved as an emerging clinical research area over the last two decades. Several non-invasive methods and devices were developed to support these investigations. A variety of technical approaches and sites of peripheral signal acquisition have been established to non-invasively estimate aortic pressure, but interchangeability of results was limited due to the lack of standardization. To overcome this threatening situation, an ARTERY Society task force was set up to provide a consensus document with recommendations regarding appropriate protocols to assess and report the evaluation of accuracy of devices measuring aortic pressure.

This presentation aims to provide background information about the genesis of the actual ARTERY consensus document and discusses resulting strengths and opportunities. Furthermore, it reviews the document from an engineering viewpoint, focusing on several novel and strong statements that have been proposed in the published consensus document, e.g. for the first time ever invasive (preferably solid state) catheter measurements as the sole reference (gold) standard for comparison have been defined. Amongst other relevant topics, particular focus is brought to issues of waveform calibration and subsequent effects leading to differences between measures of brachial and aortic pressures.

### Focus update

#### ARTERIAL HEMODYNAMICS AND WAVE REFLECTIONS

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Despite years of research, there are still some contentious aspects of arterial hemodynamics that have remained unresolved. These were discussed during a workshop entitled Arterial hemodynamics: past, present and future held in London on June 14 and 15, 2016, with keynote contributions by Nico Westerhof, Kim Parker and Michael O'Rourke. In follow-up of that meeting, we formulated a list of potential consensus statements informed by discussion at the meeting in London and quantified the degree of agreement and invited comments from the participants of the workshop. The survey was set up making use of Google forms.

Overall the responses and comments show a high measure of quantitative agreement with the various proposed 'consensus' statements. There is a large consensus on the nature and role of wave reflections in arterial hemodynamics, while consensus gets more blunted when it comes to methods and paradigms for the analysis of hemodynamics.

The followed methodology provided an elegant way to collect input from a broad scientific community, but we also learned that statements were too broadly formulated, making it harder to obtain clear-cut positions on specific topics. Also, it is highly unlikely that all participants to the poll had the same degree of expertise on all of the topics. As we did not want to weigh answers according to a presumed level of competence (what may also be another source of bias), all answers were equally valued.

Taken together, these statements seem a useful basis for proceeding with a more detailed and comprehensive consensus document on the current understanding and approaches to analysis of the pulse waveform. Future

efforts should be directed at identifying remaining areas of dispute and future topics for research.

### Debate

#### CON: GLUCOSE IS THE MOST IMPORTANT TARGET FOR CARDIOVASCULAR PREVENTION IN DIABETES

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The overall impact of glucose-lowering on vascular complications and major clinical outcomes, including mortality, in type 2 diabetes is still an open issue. While intensive glucose control has undoubtedly benefit for microvascular endpoints, the relationship between glucose-lowering approaches and reduced incidence and/or progression of macrovascular complications is less clear. This presentation will discuss the effect of glucose-lowering per se as well as the effects of specific glucose-lowering therapies on vascular outcomes in type 2 diabetes. Recent analyses from large cardiovascular outcome studies (ACCORD, ADVANCE, VADT) provide new information on factors that modulate the impact of intensive glucose-lowering on outcomes, helping to identify the specific clinical characteristics of the patients receiving the intervention that would show better response. Several studies on cardiovascular outcomes with diabetes drugs are now available, and they highlight cardiovascular benefits from using specific medications, as for the SGLT-2 blockers and some GLP-1 receptor agonists.

### McDonald lecture

#### THE METABOLIC-MICROVASCULAR DYSREGULATION SYNDROME

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Microvascular and metabolic physiology are inextricably linked. Thus, metabolic dysfunction impairs microvascular function and microvascular dysfunction impairs normal metabolism. The relationship is therefore reciprocal, justifying the concept of a 'Metabolic-Microvascular Dysregulation Syndrome'. For example, metabolic dysregulation (hyperglycaemia) causes microvascular dysfunction, diabetic retinopathy and diabetic nephropathy. Conversely, microvascular dysregulation impairs insulin-mediated glucose disposal, i.e. causes insulin resistance, impairs insulin secretion, and is associated with onset of type 2 diabetes in prospective studies. Obesity is a key driver of the Metabolic-Microvascular Dysregulation Syndrome, as it impairs insulin signal transduction in endothelial cells through adverse changes in adipokines such as adiponectin, free fatty acids and tumour necrosis factor- $\alpha$ . Microvascular dysfunction in obesity appears reversible by diet-induced weight loss. Next to obesity, other factors are also likely to play a role. Examples are microvascular dysfunction of adipose tissue as a primary cause of adipose tissue dysfunction; early life exposures, both antenatal and postnatal; and large artery stiffening. Large artery stiffening is unquestionably important for microvascular function in susceptible organs such as the brain, the eye and the kidney but whether it can cause microvascular dysfunction in metabolically crucial tissues such as skeletal muscle, pancreas and adipose tissue has not been studied. It is therefore not clear that arterial stiffening in and of itself is sufficient to cause the Metabolic-Microvascular Dysregulation Syndrome.

**Keywords:** Microcirculation; microvascular function; endothelium; metabolism; hyperglycaemia; insulin resistance; obesity