EuroIntervention 2019;14:e1621-e1622 published online e-edition February 2019

Reply to the letter to the editor regarding the article "Prediabetes and its impact on clinical outcome after coronary intervention in a broad patient population"

Marlies M. Kok[1], MD; Naveed Sattar[2], MD, PhD; Clemens von Birgelen[1,3]*, MD, PhD

1. Thoraxcentrum Twente, Medisch Spectrum Twente, Enschede, the Netherlands; 2. Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, Scotland, United Kingdom; 3. Health Technology and Services Research, MIRA - Institute of Technical Medicine and Biomedical Technology, University of Twente, Enschede, the Netherlands

We welcome the opportunity of responding to Dr Chattopadhyay et al and elaborating on the rationale for using HbA1c and fasting plasma glucose (FPG) assessments in this study[1].

HbA1c has increasingly been used as a diagnostic test for diabetes mellitus (DM) and a screening test to identify subjects at high risk of DM[2]. HbA1c measurement can be performed at any time of the day and does not require the patient to be fasting, making it an appropriate test in routine clinical settings. Although the oral glucose tolerance test (OGTT) is said to be more sensitive than HbA1c for diagnosing DM, the difficulty of test performance and interpretation in an acute illness makes HbA1c an appropriate, albeit not ideal, test in patients with acute coronary syndromes (ACS). Our report describes our experience with utilising HbA1c or FPG in all-comer patients with ACS and stable coronary artery disease to diagnose incident DM and prediabetes in this cohort, reflective of routine clinical care.

It is well known that subjects with DM remain asymptomatic for years, and often their first clinical presentation is an ACS or a stroke. The current HbA1c threshold for diagnosing overt DM was established primarily from outpatient data, and studies have suggested a lower threshold for diagnosing DM in patients with ACS[3]. It is likely that a proportion of patients with prediabetes, based on HbA1c, may actually have overt DM, if retested through a more sensitive diagnostic test (such as OGTT). However, for OGTT to be proven more accurate or cost-effective than HbA1c testing would also require data showing that patients with cardiovascular disease and newly diagnosed type 2 diabetes based on OGTT (but not HbA1c) had greater risk reduction from any potential interventions; such evidence does not exist[4]. This issue has been subject to debate over recent decades, resulting in strong believers in OGTT as well as supporters of HbA1c. Both tests are able to identify subjects at risk of (developing) DM and may complement each other. Unfortunately, OGTT is more time-consuming and costly, and definitely not a standard diagnostic tool in daily cardiology practice.

The purpose of our present study[1] was not to assess whether one diagnostic test trumps the other. Our main goal was to assess, in a broad patient population, the relation between prediabetes and

**Corresponding author: Thoraxcentrum Twente, Medisch Spectrum Twente, Koningsplein 1, 7512 KZ Enschede, the Netherlands. E-mail: c.vonbirgelen@mst.nl*

DOI: 10.4244/EIJ-D-18-00235R

adverse event risk after percutaneous coronary intervention with contemporary drug-eluting stents. For that purpose, we used clinical and laboratory data of all-comer patients who were treated at four clinical sites and participated in a randomised clinical trial[5]. Our findings show that patients with abnormal glucose metabolism deserve much more medical attention with the prospect of potentially improving their outcome. The majority of patients in our study were diagnosed based on HbA1c. Only in the absence of HbA1c were FPG levels used solely. The vast majority of prediabetic patients were diagnosed based on abnormal HbA1c levels (70%). Discordance was seen in only 3% of the prediabetic patients; in such patients, an abnormal finding by at least one approach was considered sufficient for classifying.

The GRACE risk score estimates the mortality risk of patients with ACS. Approximately one third of our population had stable coronary disease and, for these patients, the GRACE score is unsuitable. As a consequence, it made no sense to include this score in the model. However, we did include the clinical presentation and various other well-known risk factors in our Cox proportional hazards analyses. It also made no sense to include the stent type, as stent types were randomly assigned and one-year clinical outcome was similar for the three stent groups[5].

We agree that more research on abnormal glucose metabolism is needed in patients with obstructive coronary disease. However, we would rather see that all patients had at least HbA1c testing than attempting more complex diagnostic approaches, limited to a small subpopulation.

Conflict of interest statement

C. von Birgelen reports receiving institutional research grants from Biotronik, Boston Scientific, and Medtronic. N. Sattar reports receiving personal fees from Boehringer Ingelheim, and Janssen, and grants/personal fees from AstraZeneca. The other author has no conflicts of interest to declare.

References

1. Kok MM, von Birgelen C, Sattar N, Zocca P, Lowik MM, Danse PW, Schotborgh CE, Scholte M, Hartmann M, Kant GD, Doelman C, Tjon Joe Gin M, Stoel MG, van Houwelingen G, Linssen GCM, IJzerman MJ, Doggen CJM, van der Heijden LC. Prediabetes and its impact on clinical outcome after coronary intervention in a broad patient population. *EuroIntervention.* 2018;14: e1049-56.

2. International Expert Committee. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. *Diabetes Care.* 2009;32:1327-34.

3. Silverman RA, Thakker U, Ellman T, Wong I, Smith K, Ito K, Graff K. Hemoglobin A1c as a screen for previously undiagnosed prediabetes and diabetes in an acute-care setting. *Diabetes Care.* 2011;34:1908-12.

4. Sattar N, Preiss D. Screening for diabetes in patients with cardiovascular disease: HbA1c trumps oral glucose tolerance testing. *Lancet Diabetes Endocrinol.* 2016;7:560-2.

5. von Birgelen C, Kok MM, van der Heijden LC, Danse PW, Schotborgh CE, Scholte M, Gin RMTJ, Somi S, van Houwelingen KG, Stoel MG, de Man FHAF, Louwerenburg JHW, Hartmann M, Zocca P, Linssen GCM, van der Palen J, Doggen CJM, Löwik MM. Very thin strut biodegradable polymer everolimus-eluting and sirolimus-eluting stents versus durable polymer zotarolimus-eluting stents in allcomers with coronary artery disease (BIO-RESORT): a three-arm, randomised, non-inferiority trial. *Lancet.* 2016;388:2607-17.