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LETTER

Electrical atrial vulnerability and renal complications in type 2 diabetes. Reply to Montaigne D, Coisne A, Sosner P et al [letter]

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Abbreviations
AF Atrial fibrillation
NDR Swedish National Diabetes Register

To the Editor: We thank David Montaigne and colleagues for their letter to the Editor [1] commenting on our recent publication [2] on risk factors for atrial fibrillation (AF) in type 2 diabetes. We also thank the Editor of *Diabetologia* for the opportunity to respond to this letter.

The aim of our study was to assess various risk factors associated with the development of AF in an observational cohort of patients with type 2 diabetes obtained from the Swedish National Diabetes Register (NDR). We included 83,162 female and male patients with a mean follow-up of 6.8 years. Register data in the NDR are obtained nationwide with high coverage throughout Sweden. The longitudinal design and large number of patients included in our study enabled us to investigate exposure by outcome relations, including multivariable analyses, and allowed us to present robust results. To our knowledge, a longitudinal study of this kind in diabetic patients with AF as the outcome has not been presented previously. In their letter, Dr Montaigne et al argue that we claim that microalbuminuria and macroalbuminuria have not been described previously in the literature as risk factors for AF in diabetes, and that this is incorrect in their opinion. We assume that they refer to the wording of a single sentence in the Discussion section of our paper, taken out of context, and perhaps they missed where we stated in the Introduction that it is an 'important task to estimate risk factors for AF in patients with diabetes', and further 'to our knowledge, such studies have not been presented previously'; in addition, elsewhere in the Discussion, we reiterated 'to the best of our knowledge, this is the first study of risk factors for AF in type 2 diabetes patients'.

Interestingly they refer in their letter to several articles that were not referenced in our study. However, only one of these articles reported a longitudinal observational study: the Atherosclerosis Risk in Communities (ARIC) study, including 15,792 patients at baseline, which found albuminuria to be a predictor of incident AF during long-term follow-up [3]. However, this was a study in the general population, and only approximately 20–21% (total numbers of diabetic patients in the ARIC study were not clearly stated in the article) were diabetic, and this subgroup was not presented separately. Thus, we still find it reasonable to say that, to the best of our knowledge, no study estimating albuminuria as a risk factor for incident AF in diabetes has been published previously, although the ARIC study [3] could have been cited in our article [2] as a reference to the general population.

Another report referred to by Montaigne et al concerns post hoc observational analyses in the Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) study [4], in which AF at study entry

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was analysed as an exposure and not as an outcome, and hence the risk of AF on cardiovascular disease was studied, rather than the risk for incident AF per se. In addition, they also refer to two reports of cross-sectional studies, the International Survey Evaluating Microalbuminuria Routinely by Cardiologists in patients with Hypertension (I-SEARCH) study [5] and the SURDAIGNE (Survie, Diabete de type 2 et Genetique) and DIAB2NEPHROGENE (Diabete de type 2, Nephropathie et Genetique) study [6] by Montaigne et al. Cross-sectional studies on prevalent disease are generally regarded as describing associations between sets of variables without defining the predictor, while longitudinal studies allow us to analyse risk factors as predictors of incident disease. Nevertheless, we do find cross-sectional studies to be interesting and valuable, mainly as hypothesis-generating exercises.

Previously we have reported, using NDR data including 66,065 patients followed up for 5.7 years in a longitudinal study [7], that albuminuria and renal impairment are independent risk factors for cardiovascular outcomes and mortality in type 2 diabetes and where albuminuria was a relevant cardiovascular risk factor at all levels of renal function. We agree with David Montaigne and his colleagues that albuminuria should be monitored in patients with diabetes and more stringently in diabetic patients with renal damage.

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References

1. Montaigne D, Coisne A, Sosner P, Lacroix D, Hadjadj S (2015) Electrical atrial vulnerability and renal complications in type 2 diabetes. Diabetologia. doi:10.1007/s00125-015-3840-0
2. Zethelius B, Gudbjörnsdottir S, Eliasson B, Eeg-Olofsson K, Svensson A-M, Cederholm J (2015) Risk factors for atrial fibrillation in type 2 diabetes: report from the Swedish National Diabetes Register (NDR). Diabetologia 58:2259–2268
3. Alonso A, Lopez FL, Matsushita K et al (2011) Chronic kidney disease is associated with the incidence of atrial fibrillation: the Atherosclerosis Risk in Communities (ARIC) study. Circulation 123:2946–2953
4. Du X, Ninomiya T, de Galan B et al (2009) Risks of cardiovascular events and effects of routine blood pressure lowering among patients with type 2 diabetes and atrial fibrillation: results of the ADVANCE study. Eur Heart J 30:1128–1135
5. Böhm M, Thoenes M, Neuberger HR et al (2009) Atrial fibrillation and heart rate independently correlate to microalbuminuria in hypertensive patients. Eur Heart J 30:1364–1371
6. Montaigne D, Bailloeuil O, Hulin-Delmotte C et al (2012) DIAB2NEPHROGENE and SURDIAGENE study groups. Renal complications correlate with electrical atrial vulnerability hallmarks in type 2 diabetic patients. Int J Cardiol 159: 63–66
7. Svensson MK, Cederholm J, Eliasson B, Zethelius B, Gudbjörnsdottir S, Swedish National Diabetes Register (2013) Albuminuria and renal function as predictors of cardiovascular events and mortality in a general population of patients with type 2 diabetes: a nationwide observational study from the Swedish National Diabetes Register. Diab Vasc Dis Res 10:520–529