## Letters to the Editor

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### Measurement of albuminuria during acute myocardial infarction and its relation with prognosis

In the recently published study by Kragelund *et al.*,[1] fasting insulin, blood glucose, HbA1c, and microalbuminuria were measured in a large sample of non-diabetic patients with acute myocardial infarction (AMI) between the second and the fifth day after admission. All the above markers were associated with global mortality after 7 years of follow up at univariable analyses, but only insulin level remained an independent predictor of outcome at multivariable analysis. We believe that the predictive power of albumin excretion (AE) has been overlooked by the authors owing to a series of methodological problems. First, the authors measured AE on the first voided morning urine sample and expressed it as a concentration. This is not an accurate method for assessing urinary albumin, because to obtain a reliable estimate of AE, independent of urine flow rate, AE should be corrected for urinary creatinine.[2] Several studies have shown that measurement of AE rate (in overnight or 24 h samples) is more closely associated to the 'real' albumin escape than AE.[2,3] Secondly, the authors collected the urine samples 'at day 2–5 after admission'. This 4 day range in sampling AE weakened the predictive power of AE for outcome, because AE during AMI peaks at the first day and has a rapid decline throughout the first week after AMI. We showed that albumin to creatinine ratio in non-diabetic patients declined from $91.6 \pm 13.7$ on the first day to $36.5 \pm 6.7$ on the third day, and to $24.5 \pm 4.5$ mg/g on the seventh day after admission for AMI.[4] A similar trend was observed by Gosling *et al.*[5] This indicates that AE values decrease by a ratio of 2.5 and 3.7 on the third and seventh day, respectively. Therefore, in all patients AE assessment should be performed on the same day after AMI. There is another point of the article by Krakenburg *et al.*[1] that deserves a comment. The authors hypothesized that the independent association between AE and mortality previously found by our group may be due to the presence of diabetic patients in the sample.[6,7] However, the results of our recent analysis indicates that this is not the case.[4] We demonstrated that the predictive power of AE in the non-diabetic segment of our population was equal to or even greater than that in the diabetic patients.[4] Thus, the discrepancy between our results and those of Krakenburg *et al.*[1] is likely to be due to the aforementioned methodological problems.

In conclusion, the non-independent prognostic power of AE reported by Kragelund *et al.*[1] in their study is likely to be due to the inadequate assessment of urinary AE. According to our results, the best timing for urine collection in AMI patients should be set on the third day after admission.

### References

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### Measurement of albuminuria during acute myocardial infarction and its relation with prognosis: reply

We thank Berton *et al.* for the interest in our work.[1] They argue that the predictive power of albumin excretion has been overlooked due to a series of methodological problems in our study. We agree with Berton *et al.*[2] that measuring urinary albumin excretion rate in 24 h urine samples would more closely reflect the 'real' albumin excretion rate, and it is well established that albumin excretion rate decline during the first few days following acute myocardial infarction.[2] We have adequately described the methodology used, and the same weaknesses that exist for albumin excretion exist for the other markers as well. In a perfect world all samples would have been taken at the same time. Our study is a clinical study of patients admitted to hospital with acute myocardial infarction, and in this setting it is not possible always to collect samples completely homogenously. Despite this, insulin was a reliable marker of increased risk. If measurement of albumin excretion warrants more standardized and complicated methods than the ones we used, it might not have any clinical importance. The conclusion that insulin is a marker of long-term mortality independently of various other cardiovascular risk markers including urinary albumin excretion has been consistent for a long period of time of $>5$ years. An obvious explanation to the discrepancies between our study and that of Berton *et al.*[2] is the length of follow-up. All markers of risk tend to loose importance with time. Had we stopped follow-up after just 1 year as did Berton *et al.*,[2] our results would have been much more significant. It will be interesting to learn whether urinary albumin excretion rate in the population of Berton *et al.*[2] will still have prognostic importance after 5 years. We acknowledge the comment on the diabetic subpopulation; however, it is difficult to refer to a paper that at that time was not yet published.