Supplementary material

In HARVEST-Malmö, fasting blood samples were collected at admission in 4.5 ml EDTA-tubes and centrifuged at 1,950 g for 10 minutes. Plasma was then aliquoted in 200μl fractions into bar coded tubes (REMP, Brooks, Life Sciences, USA) and stored at -80°C until analysis. In GREAT Network Rome, blood samples were collected at admission in 4.5 ml EDTA-tubes and centrifuged to 3,500 g for 15 minutes. Plasma of each patient was divided in tubes of 1 ml and stored at -80°C until analyses.

Bioactive adrenomedullin

In both cohorts, bio-ADM was measured using a chemiluminescence immunoassay (sphingotest® bio-ADM®, sphingotec GmbH, Hennigsdorf, Germany) as previously described.[1, 2] The analytical assay sensitivity was 2 pg/mL. Using this assay, the median bio-ADM concentration of healthy adults was 20.7 pg/mL, with a 99th percentile of 43.0 pg/mL.[1] Bio-ADM was successfully analysed in 324 subjects in the HARVEST-Malmö cohort, and in 209 subjects in GREAT Network Rome.

Proenkephalin

In both cohorts, Proenkephalin A 119-159 (penKid) was determined by a chemiluminescence immunoassay (sphingotest® penKid®, sphingotec GmbH, Hennigsdorf, Germany) as described previously.[3] The limit of quantification was 17.3 pmol/L. In a reference population the mean ± standard deviation (SD) was 46.6 ± 14.1 pmol/L, the median [range] was 45 [9–518] pmol/L, with a 99th percentile of 80 pmol/L.[4] PenKid was successfully analysed in 323 subjects in the HARVEST-Malmö cohort, and in 209 subjects in GREAT Network Rome.

Natriuretic B-type peptide

In HARVEST-Malmö, N-terminal pro B-type natriuretic peptide (NT-proBNP) was analysed at the Department of Clinical Chemistry, Skåne University Hospital in Malmö, participating in a national standardization and quality control system using a sandwich assay based on ElectroChemiLuminiscence Immunoassay (Cobas, Roche Diagnostic, Basel, Switzerland). NT-proBNP was successfully analysed in 317 subjects.

In GREAT Network Rome, mature BNP was measured in 218 subjects, and NT-proBNP in 20 subjects. Seven subjects did not have data on neither mature BNP nor NT-proBNP. Both BNP and NT-proBNP were measured in Architect assays (Abbott Laboratories Diagnostics Division, Abbott Park, IL 60064 USA).

Plasma creatinine

In HARVEST-Malmö, plasma creatinine was analysed at the Department of Clinical Chemistry, Skåne University Hospital in Malmö, participating in a national standardisation and quality control system using an enzymatic colorimetric assay (Cobas, Roche Diagnostic, Basel, Switzerland). Creatinine at admission and creatinine after 48h was successfully analysed in 293 subjects.

In GREAT Network Rome, plasma creatinine was measured by Architect assays (Abbott Laboratories Diagnostics Division, Abbott Park, IL 60064 USA). Creatinine at admission and creatinine after 48h was successfully analysed in 211 subjects.

**REFERENCES**

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