**Online Supplemental Materials**

# Capillary rarefaction associates with albuminuria: The Maastricht Study

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## Supplemental Methods

### *Kidney function*

GFR was estimated using the CKD-EPI equation based on both serum creatinine and serum cystatin C.[1] Serum creatinine was measured with a Jaffé method traceable to isotope dilution mass spectrometry (Beckman Synchron LX20, Beckman Coulter Inc., Brea, USA). Serum cystatin C was measured with a particle enhanced immunoturbidimetric assay standardized against ERM-DA471/IFCC reference material (Roche Cobas 8000, F. Hoffman-La Roche Ltd, Basel, Switzerland).

To assess urinary albumin excretion, participants were requested to collect two 24h urine collections. Urinary albumin concentration was measured with a standard immunoturbidimetric assay by an automatic analyzer (Beckman Synchron LX20, Beckman Coulter Inc., Brea, USA) and multiplied by collection volume to obtain the 24h urinary albumin excretion. A urinary albumin concentration below the detection limit of the assay (2 mg/l) was set at 1.5 mg/l before multiplying by collection volume. Only urine collections with a collection time between 20h and 28h were considered valid. If needed, urinary albumin excretion was extrapolated to a 24h excretion.

Albuminuria was defined as an albumin excretion ≥ 30 mg/24h,[2] which is used in clinical practice to guide cardiovascular disease prevention, particularly in individuals with type 2 diabetes.[3] In an additional analysis, albuminuria was defined as an albumin excretion ≥ 15 mg/24h (the upper level of daily albumin excretion in healthy individuals[4]), in agreement with the fact that an association with (cardiovascular) mortality already exists below the clinical cut off value of 30 mg/24h.[5] These definitions were preferably based on the average of two (available in 89.9% of the participants) 24h urine collections.

***Potential confounders***

We assessed glucose metabolism status, body mass index, waist circumference, hip circumference, office blood pressure, 24h average ambulatory blood pressure, fasting glucose, HbA1c, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, medication use, smoking behavior, alcohol consumption, educational level and prevalent cardiovascular disease as described previously.[6,7] Glucose metabolism status was classified according to the World Health Organization 2006 criteria[8] into normal glucose metabolism, impaired fasting glucose, impaired glucose tolerance, and diabetes mellitus. Participants with diabetes mellitus and participants using glucose-lowering medication were considered as having type 2 diabetes if they had no (self-reported) type 1 or other specific type of diabetes. Prevalent cardiovascular disease was defined as a self-reported history of myocardial infarction, and(or) cerebrovascular infarction or hemorrhage, and(or) percutaneous artery angioplasty of, or vascular surgery on, the coronary, abdominal, peripheral or carotid arteries. Alcohol consumption was classified into three categories: non-consumption, low-consumption ($\leq$7 glasses per week for women and $\leq$14 glasses per week for men) and high-consumption (>7 glasses per week for women and >14 glasses per week for men). Waist-to-hip ratio was calculated by dividing waist circumference by hip circumference. Total-to-HDL cholesterol ratio was calculated by dividing total cholesterol by HDL cholesterol. Hypertension was defined as an office systolic blood pressure ≥ 140 mmHg, an office diastolic blood pressure ≥ 90 mmHg and(or) the use of antihypertensive medication. Office pulse pressure was defined as office systolic blood pressure minus office diastolic blood pressure and office mean arterial pressure as office diastolic blood pressure plus 0.412 times office pulse pressure.[9] Similar equations were used to calculate 24h average ambulatory pulse

pressure and 24h average ambulatory mean arterial pressure, respectively. Educational level was assessed during the cognitive assessment and was classified into three groups: low (none, primary, or lower vocational education only), intermediate (intermediate general secondary, intermediate vocational or higher general secondary education) and high (higher vocational education or university level of education).[7,10]

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## Supplemental Tables

Supplemental Table 1. Clinical characteristics of the study population according to tertiles of the percentage recruitment during venous congestion

| | **Tertiles of the percentage recruitment during venous congestion** | | |
|---|---|---|---|
| | **T1 (high)** n = 247 | **T2 (middle)** n = 247 | **T3 (low)** n = 247 |
| Recruitment during venous congestion (%) | 75.6 [55.8-253.3] | 39.0 [27.6-55.7] | 16.2 [-2.9-27.5] |
| Demographics | | | |
| Age (years) | 59.4 ±8.5 | 59.9 ±8.6 | 59.9 ±8.5 |
| Men | 122 (49.4) | 131 (53.0) | 159 (64.4) |
| Educational level | | | |
| Low | 32 (13.0) | 29 (11.7) | 59 (23.9) |
| Middle | 96 (38.9) | 101 (40.9) | 109 (44.1) |
| High | 119 (48.2) | 117 (47.4) | 79 (32.0) |
| Prior cardiovascular disease | 43 (17.4) | 41 (16.6) | 50 (20.2) |
| Lifestyle variables | | | |
| Smoking behavior | | | |
| Never smoker | 80 (32.4) | 78 (31.6) | 72 (29.1) |
| Former smoker | 130 (52.6) | 132 (53.4) | 134 (54.3) |
| Current smoker | 37 (15.0) | 37 (15.0) | 41 (16.6) |
| Alcohol consumption | | | |
| Non | 30 (12.1) | 44 (17.8) | 49 (19.8) |
| Low (women ≤ 7 glasses/week; men ≤ 14 glasses/week) | 127 (51.4) | 127 (51.4) | 138 (55.9) |
| High (women > 7 glasses/week; men > 14 glasses/week) | 90 (36.4) | 76 (30.8) | 60 (24.3) |
| Metabolic variables | | | |
| BMI categories | | | |
| Normal weight (< 25 kg/m$^2$) | 86 (34.8) | 86 (34.8) | 62 (25.1) |
| Overweight (25-30 kg/m$^2$) | 115 (46.6) | 112 (45.3) | 118 (47.8) |
| Obesity (≥ 30 kg/m$^2$) | 46 (18.6) | 49 (19.8) | 67 (27.1) |
| Waist circumference (cm) | | | |
| Men | 100.0 ±11.9 | 101.3 ±11.4 | 103.6 ±11.4 |
| Women | 89.4 ±11.6 | 90.1 ±12.8 | 94.5 ±15.6 |
| Waist-to-hip-ratio | | | |
| Men | 0.99 ±0.07 | 1.00 ±0.06 | 1.01 ±0.07 |

| | | | |
|---|---|---|---|
| Women | 0.87 ±0.07 | 0.88 ±0.07 | 0.90 ±0.08 |
| Office systolic blood pressure (mmHg) | 136.4 ±18.3 | 136.0 ±18.6 | 139.6 ±20.0 |
| Office diastolic blood pressure (mmHg) | 76.7 ±10.4 | 75.7 ±10.4 | 78.1 ±10.7 |
| 24h average ambulatory systolic blood pressure (mmHg)* | 118.6 ±11.7 | 119.1 ±12.4 | 120.8 ±12.3 |
| 24h average ambulatory diastolic blood pressure (mmHg)* | 73.9 ±7.3 | 74.1 ±7.4 | 74.6 ±7.2 |
| Hypertension | 135 (54.7) | 137 (55.5) | 158 (64.0) |
| Glucose metabolism status | | | |
| Normal glucose metabolism | 153 (61.9) | 144 (58.3) | 107 (43.3) |
| Impaired fasting glucose | 7 (2.8) | 12 (4.9) | 21 (8.5) |
| Impaired glucose tolerance | 44 (17.8) | 26 (10.5) | 16 (6.5) |
| Type 2 diabetes | 43 (17.4) | 65 (26.3) | 103 (41.7) |
| Fasting glucose (mmol/l) | | | |
| Without type 2 diabetes | 5.4 ±0.5 | 5.3 ±0.6 | 5.5 ±0.6 |
| With type 2 diabetes | 7.9 ±1.6 | 7.7 ±1.5 | 7.6 ±1.9 |
| HbA1C (%)** | | | |
| Without type 2 diabetes | 5.7 ±0.4 | 5.6 ±0.4 | 5.6 ±0.4 |
| With type 2 diabetes | 6.9 ±0.8 | 6.8 ±0.7 | 6.8 ±0.9 |
| Total cholesterol (mmol/l) | 5.5 ±1.2 | 5.2 ±1.1 | 5.0 ±1.1 |
| HDL cholesterol (mmol/l) | | | |
| Men | 1.2 ±0.5 | 1.2 ±0.3 | 1.1 ±0.3 |
| Women | 1.5 ±0.4 | 1.5 ±0.4 | 1.5 ±0.5 |
| LDL cholesterol (mmol/l) | 3.5 ±1.1 | 3.3 ±1.0 | 3.1 ±1.0 |
| Triglycerides (mmol/l) | 1.20 [0.79-1.76] | 1.19 [0.86-1.66] | 1.31 [0.90-1.92] |
| Total-to-HDL cholesterol ratio | 4.2 ±1.2 | 4.2 ±1.3 | 4.3 ±1.2 |
| Kidney function | | | |
| Estimated GFR (ml/min/1.73m$^2$) | 89.1 ±14.1 | 87.3 ±15.4 | 87.8 ±15.7 |
| Albumin excretion rate (mg/24h) | 8.2 [5.4-11.1] | 7.4 [5.4-11.4] | 7.9 [5.5-16.6] |
| Albumin excretion ≥ 15 mg/24h | 31 (12.6) | 38 (15.4) | 66 (26.7) |
| Albumin excretion ≥ 30 mg/24h | 9 (3.6) | 16 (6.5) | 32 (13.0) |
| Medication | | | |
| Antihypertensive medication | 91 (36.8) | 88 (35.6) | 117 (47.4) |
| Renin-angiotensin system inhibitor | 73 (29.6) | 59 (23.9) | 92 (37.2) |
| Lipid-modifying medication | 85 (34.4) | 75 (30.4) | 111 (44.9) |

Data are presented as n (%), mean ±standard deviation, median [interquartile range] or (only for the percentage recruitment during venous congestion) median [range]. * 24h average ambulatory blood pressure measurements were missing in n = 76 participants (n=23 for T1, n=28 for T2 and n=25 for T3). ** To convert to HbA1c values in mmol/mol: (10.93 * HbA1c [%]) - 23.5.

Supplemental Table 2A. Association between the percentage recruitment during post-occlusive peak reactive hyperemia as well as venous congestion and the presence of albuminuria (albumin excretion ≥ 30 mg/24h) in participants without type 2 diabetes

| Model | Recruitment during post-occlusive peak reactive hyperemia (%) | OR (95% CI) | P value | Recruitment during venous congestion (%) | OR (95% CI) | P value |
|---|---|---|---|---|---|---|
| 1 | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 0.92 (0.24; 3.48) | 0.903 | T2 (middle) | 2.68 (0.68; 10.52) | 0.158 |
| | T3 (low) | 4.13 (1.45; 11.73) | 0.008 | T3 (low) | 6.65 (1.86; 23.78) | 0.004 |
| 2 | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 0.85 (0.22; 3.25) | 0.817 | T2 (middle) | 2.67 (0.68; 10.57) | 0.161 |
| | T3 (low) | 3.86 (1.35; 11.10) | 0.012 | T3 (low) | 6.16 (1.71; 22.26) | 0.006 |
| 3a | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 0.97 (0.25; 3.85) | 0.970 | T2 (middle) | 2.69 (0.66; 11.01) | 0.169 |
| | T3 (low) | 4.49 (1.50; 13.49) | 0.007 | T3 (low) | 6.73 (1.79; 25.34) | 0.005 |
| 3b | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 1.15 (0.27; 4.96) | 0.852 | T2 (middle) | 3.80 (0.74; 19.66) | 0.111 |
| | T3 (low) | 4.93 (1.47; 16.51) | 0.010 | T3 (low) | 8.41 (1.75; 40.48) | 0.008 |

Odds ratios represent the odds of having albuminuria (defined as an albumin excretion ≥ 30 mg/24h) in the respective tertile of the percentage recruitment during post-occlusive peak reactive hyperemia or venous congestion compared with the odds of having albuminuria in the reference tertile. Model 1: unadjusted model; Model 2: age, sex; Model 3a: model 2 + waist circumference, total-to-HDL cholesterol ratio, triglycerides, use of lipid-modifying drugs, office systolic blood pressure, use of antihypertensive medication, estimated GFR, prevalent cardiovascular disease, smoking behavior, alcohol consumption, educational level; Model 3b: as model 3a but adjusted for 24h average ambulatory systolic blood pressure instead of office systolic blood pressure (n=477). CI: confidence interval, OR: odds ratio, T: tertile.

Supplemental Table 2B. Association between the percentage recruitment during post-occlusive peak reactive hyperemia as well as venous congestion and the presence of albuminuria (albumin excretion ≥ 30 mg/24h) in participants with type 2 diabetes

| Model | Recruitment during post-occlusive peak reactive hyperemia (%) | OR (95% CI) | P value | Recruitment during venous congestion (%) | OR (95% CI) | P value |
|---|---|---|---|---|---|---|
| 1 | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 0.76 (0.26; 2.21) | 0.613 | T2 (middle) | 0.99 (0.33; 3.02) | 0.987 |
| | T3 (low) | 1.16 (0.44; 3.02) | 0.765 | T3 (low) | 1.40 (0.52; 3.78) | 0.513 |
| 2 | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 0.67 (0.23; 1.99) | 0.472 | T2 (middle) | 0.94 (0.30; 2.91) | 0.911 |
| | T3 (low) | 1.12 (0.42; 2.97) | 0.823 | T3 (low) | 1.38 (0.50; 3.79) | 0.538 |
| 3a | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 0.82 (0.26; 2.59) | 0.731 | T2 (middle) | 1.19 (0.36; 3.95) | 0.779 |
| | T3 (low) | 1.16 (0.41; 3.30) | 0.781 | T3 (low) | 1.41 (0.48; 4.15) | 0.530 |
| 3b | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 1.16 (0.34; 3.97) | 0.817 | T2 (middle) | 1.04 (0.29; 3.67) | 0.957 |
| | T3 (low) | 0.92 (0.28; 3.01) | 0.889 | T3 (low) | 1.07 (0.34; 3.40) | 0.908 |

Odds ratios represent the odds of having albuminuria (defined as an albumin excretion ≥ 30 mg/24h) in the respective tertile of the percentage recruitment during post-occlusive peak reactive hyperemia or venous congestion compared with the odds of having albuminuria in the reference tertile. Model 1: unadjusted model; Model 2: age, sex; Model 3a: model 2 + waist circumference, total-to-HDL cholesterol ratio, triglycerides, use of lipid-modifying drugs, office systolic blood pressure, use of antihypertensive medication, estimated GFR, prevalent cardiovascular disease, smoking behavior, alcohol consumption, educational level; Model 3b: as model 3a but adjusted for 24h average ambulatory systolic blood pressure instead of office systolic blood pressure (n=188). CI: confidence interval, OR: odds ratio, T: tertile

Supplemental Table 3A. Association between the absolute number of capillaries during post-occlusive peak reactive hyperemia as well as venous congestion and the presence of albuminuria (albumin excretion ≥ 30 mg/24h) in participants without type 2 diabetes

| Model | Post-occlusive peak reactive hyperemia (n/mm$^2$) | OR (95% CI) | P value | Venous congestion (n/mm$^2$) | OR (95% CI) | P value |
|---|---|---|---|---|---|---|
| 1 | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 2.71 (0.71; 10.39) | 0.145 | T2 (middle) | 1.82 (0.52; 6.33) | 0.346 |
| | T3 (low) | 4.71 (1.31; 17.00) | 0.018 | T3 (low) | 3.64 (1.15; 11.52) | 0.028 |
| 2 | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 2.49 (0.65; 9.62) | 0.185 | T2 (middle) | 1.57 (0.45; 5.53) | 0.479 |
| | T3 (low) | 4.08 (1.12; 14.86) | 0.033 | T3 (low) | 2.96 (0.92; 9.49) | 0.068 |
| 3a | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 2.48 (0.63; 9.81) | 0.196 | T2 (middle) | 1.84 (0.51; 6.62) | 0.352 |
| | T3 (low) | 3.85 (1.03; 14.40) | 0.045 | T3 (low) | 2.82 (0.86; 9.28) | 0.089 |
| 3b | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 2.16 (0.52; 8.86) | 0.287 | T2 (middle) | 2.48 (0.60; 10.29) | 0.212 |
| | T3 (low) | 4.17 (1.10; 15.78) | 0.035 | T3 (low) | 4.03 (1.06; 15.31) | 0.041 |

Odds ratios represent the odds of having albuminuria (albumin excretion ≥ 30 mg/24h) in the respective tertile of the absolute number of capillaries during post-occlusive peak reactive hyperemia or venous congestion compared with the odds of having albuminuria in the reference tertile. Model 1: unadjusted model; Model 2: age, sex; Model 3a: model 2 + waist circumference, total-to-HDL cholesterol ratio, triglycerides, use of lipid-modifying drugs, office systolic blood pressure, use of antihypertensive medication, estimated GFR, prevalent cardiovascular disease, smoking behavior, alcohol consumption, educational level; Model 3b: as model 3a but adjusted for 24h average ambulatory systolic blood pressure instead of office systolic blood pressure (n=477). CI: confidence interval, OR: odds ratio, T: tertile.

Supplemental Table 3B. Association between the absolute number of capillaries during post-occlusive peak reactive hyperemia as well as venous congestion and the presence of albuminuria (albumin excretion ≥ 30 mg/24h) in participants with type 2 diabetes

| Model | Post-occlusive peak reactive hyperemia (n/mm$^2$) | OR (95% CI) | P value | Venous congestion (n/mm$^2$) | OR (95% CI) | P value |
|---|---|---|---|---|---|---|
| 1 | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 2.47 (0.88; 6.92) | 0.085 | T2 (middle) | 0.81 (0.31; 2.14) | 0.669 |
| | T3 (low) | 1.75 (0.63; 4.85) | 0.282 | T3 (low) | 1.22 (0.51; 2.94) | 0.653 |
| 2 | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 2.19 (0.77; 6.23) | 0.142 | T2 (middle) | 0.68 (0.25; 1.84) | 0.449 |
| | T3 (low) | 1.60 (0.57; 4.51) | 0.372 | T3 (low) | 1.20 (0.49; 2.93) | 0.697 |
| 3a | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 2.84 (0.91; 8.88) | 0.073 | T2 (middle) | 0.76 (0.26; 2.25) | 0.626 |
| | T3 (low) | 1.92 (0.63; 5.88) | 0.255 | T3 (low) | 1.24 (0.47; 3.27) | 0.668 |
| 3b | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 2.16 (0.60; 7.71) | 0.237 | T2 (middle) | 0.78 (0.23; 2.71) | 0.700 |
| | T3 (low) | 1.60 (0.48; 5.33) | 0.442 | T3 (low) | 1.48 (0.49; 4.50) | 0.491 |

Odds ratios represent the odds of having albuminuria (albumin excretion ≥ 30 mg/24h) in the respective tertile of the absolute number of capillaries during post-occlusive peak reactive hyperemia or venous congestion compared with the odds of having albuminuria in the reference tertile. Model 1: unadjusted model; Model 2: age, sex; Model 3a: model 2 + waist circumference, total-to-HDL cholesterol ratio, triglycerides, use of lipid-modifying drugs, office systolic blood pressure, use of antihypertensive medication, estimated GFR, prevalent cardiovascular disease, smoking behavior, alcohol consumption, educational level; Model 3b: as model 3a but adjusted for 24h average ambulatory systolic blood pressure instead of office systolic blood pressure (n=188). CI: confidence interval, OR: odds ratio, T: tertile

Supplemental Table 4A. Descriptive information of the tertiles of the respective capillaroscopy measures

| | Percentage recruitment during post-occlusive peak reactive hyperemia (%) | | Percentage recruitment during venous congestion (%) | | Absolute number of capillaries during post-occlusive peak reactive hyperemia (n/mm$^2$) | | Absolute number of capillaries during venous congestion (n/mm$^2$) | |
|---|---|---|---|---|---|---|---|---|
| Tertile | Range | ≥ 30 mg/24h (n (%)) | Range | ≥ 30 mg/24h (n (%)) | Range | ≥ 30 mg/24h (n (%)) | Range | ≥ 30 mg/24h (n (%)) |
| 1 | 55.0-186.7 | 12 (4.9%) | 55.8-253.3 | 9 (3.6%) | 111.5-161.0 | 9 (3.7%) | 111.5-170.0 | 14 (5.6%) |
| 2 | 27.0-54.9 | 13 (5.3%) | 27.6-55.7 | 16 (6.5%) | 97.0-111.0 | 22 (8.8%) | 97.0-111.0 | 16 (6.4%) |
| 3 | 0.0-26.9 | 32 (13.0%) | -2.9-27.5 | 32 (13.0%) | 43.0-96.5 | 26 (10.4%) | 48.0-96.5 | 27 (11.2%) |

Supplemental Table 4B. Descriptive information of the quintiles of the respective capillaroscopy measures

| | Percentage recruitment during post-occlusive peak reactive hyperemia (%) | | Percentage recruitment during venous congestion (%) | | Absolute number of capillaries during post-occlusive peak reactive hyperemia (n/mm$^2$) | | Absolute number of capillaries during venous congestion (n/mm$^2$) | |
|---|---|---|---|---|---|---|---|---|
| Quintile | Range | ≥ 30 mg/24h (n (%)) | Range | ≥ 30 mg/24h (n (%)) | Range | ≥ 30 mg/24h (n (%)) | Range | ≥ 30 mg/24h (n (%)) |
| 1 | 68.8-186.7 | 5 (3.4%) | 69.8-253.3 | 6 (4.1%) | 118.5-161.0 | 7 (4.8%) | 119.5-170.0 | 5 (3.4%) |
| 2 | 49.1-68.7 | 11 (7.4%) | 47.7-69.6 | 6 (4.1%) | 108.0-118.0 | 8 (5.2%) | 108.5-119.0 | 12 (7.9%) |
| 3 | 31.7-49.0 | 6 (4.0%) | 32.3-47.6 | 12 (8.1%) | 99.5-107.5 | 12 (8.5%) | 100.0-108.0 | 8 (5.5%) |
| 4 | 18.9-31.4 | 11 (7.4%) | 18.7-32.2 | 10 (6.8%) | 89.5-99.0 | 16 (10.5%) | 91.0-99.5 | 19 (12.7%) |
| 5 | 0.0-18.7 | 24 (16.2%) | -2.9-18.6 | 23 (15.5%) | 43.0-89.0 | 14 (9.5%) | 48.0-90.5 | 13 (8.8%) |

Supplemental Table 4C. Descriptive information of the deciles of the respective capillaroscopy measures

| | Percentage recruitment during post-occlusive peak reactive hyperemia (%) | | Percentage recruitment during venous congestion (%) | | Absolute number of capillaries during post-occlusive peak reactive hyperemia (n/mm$^2$) | | Absolute number of capillaries during venous congestion (n/mm$^2$) | |
|---|---|---|---|---|---|---|---|---|
| Decile | Range | ≥ 30 mg/24h (n (%)) | Range | ≥ 30 mg/24h (n (%)) | Range | ≥ 30 mg/24h (n (%)) | Range | ≥ 30 mg/24h (n (%)) |
| 1 | 88.6-186.7 | 2 (2.7%) | 89.0-253.3 | 2 (2.7%) | 125.5-161.0 | 3 (3.9%) | 126.5-170.0 | 2 (2.7%) |
| 2 | 68.8-88.3 | 3 (4.1%) | 69.8-88.3 | 4 (5.4%) | 118.5-125.0 | 4 (5.6%) | 119.5-126.0 | 3 (4.2%) |
| 3 | 59.1-68.7 | 4 (5.4%) | 59.2-69.6 | 2 (2.7%) | 113.0-118.0 | 2 (2.5%) | 113.0-119.0 | 6 (7.4%) |
| 4 | 49.1-58.8 | 7 (9.5%) | 47.7-59.0 | 4 (5.4%) | 108.0-112.5 | 6 (8.1%) | 108.5-112.5 | 6 (8.5%) |
| 5 | 39.5-49.0 | 2 (2.7%) | 39.1-47.6 | 3 (4.1%) | 104.0-107.5 | 5 (6.8%) | 103.5-108.0 | 1 (1.4%) |
| 6 | 31.7-39.0 | 4 (5.3%) | 32.3-39.0 | 9 (12.0%) | 99.5-103.5 | 7 (10.3%) | 100.0-103.0 | 7 (9.3%) |
| 7 | 24.8-31.4 | 5 (6.8%) | 25.4-32.3 | 5 (6.8%) | 95.5-99.0 | 10 (12.8%) | 96.0-99.5 | 5 (6.8%) |
| 8 | 18.9-24.6 | 6 (8.1%) | 18.7-25.3 | 5 (6.8%) | 89.5-95.0 | 6 (8.1%) | 91.0-95.5 | 14 (18.4%) |
| 9 | 12.8-18.7 | 11 (14.9%) | 12.7-18.6 | 14 (18.9%) | 82.0-89.0 | 7 (9.5%) | 82.0-90.5 | 6 (8.2%) |
| 10 | 0.0-12.7 | 13 (17.6%) | -2.9-12.7 | 9 (12.2%) | 43.0-81.5 | 7 (9.6%) | 48.0-81.5 | 7 (9.5%) |

Supplemental Table 5A. Association between the percentage recruitment during post-occlusive peak reactive hyperemia as well as venous congestion and the presence of albuminuria (albumin excretion ≥ 30 mg/24h)

| Model | Recruitment during post-occlusive peak reactive hyperemia (%) | OR (95% CI) | P value | Recruitment during venous congestion (%) | OR (95% CI) | P value |
|---|---|---|---|---|---|---|
| 1 | Q1 | Reference | | Q1 | Reference | |
| | Q2 | 2.30 (0.78; 6.78) | 0.132 | Q2 | 1.00 (0.32; 3.18) | 1.000 |
| | Q3 | 1.20 (0.36; 4.02) | 0.768 | Q3 | 2.07 (0.76; 5.68) | 0.156 |
| | Q4 | 2.30 (0.78; 6.78) | 0.132 | Q4 | 1.72 (0.61; 4.85) | 0.309 |
| | Q5 | 5.54 (2.05; 14.94) | 0.001 | Q5 | 4.36 (1.72; 11.04) | 0.002 |
| 2 | Q1 | Reference | | Q1 | Reference | |
| | Q2 | 2.03 (0.67; 6.14) | 0.209 | Q2 | 0.92 (0.29; 3.00) | 0.895 |
| | Q3 | 0.95 (0.28; 3.24) | 0.928 | Q3 | 1.59 (0.56; 4.46) | 0.382 |
| | Q4 | 1.62 (0.53; 4.94) | 0.394 | Q4 | 1.33 (0.46; 3.85) | 0.601 |
| | Q5 | 3.51 (1.26; 9.79) | 0.016 | Q5 | 2.74 (1.04; 7.20) | 0.041 |
| 3a | Q1 | Reference | | Q1 | Reference | |
| | Q2 | 2.23 (0.70; 7.09) | 0.176 | Q2 | 0.98 (0.29; 3.34) | 0.974 |
| | Q3 | 1.20 (0.34; 4.25) | 0.782 | Q3 | 1.78 (0.60; 5.26) | 0.295 |
| | Q4 | 1.74 (0.55; 5.52) | 0.348 | Q4 | 1.40 (0.46; 4.24) | 0.548 |
| | Q5 | 4.08 (1.40; 11.86) | 0.010 | Q5 | 3.11 (1.14; 8.50) | 0.027 |
| 3b | Q1 | Reference | | Q1 | Reference | |
| | Q2 | 1.59 (0.47; 5.44) | 0.460 | Q2 | 0.89 (0.24; 3.32) | 0.857 |
| | Q3 | 1.23 (0.34; 4.45) | 0.752 | Q3 | 1.64 (0.53; 5.03) | 0.391 |
| | Q4 | 1.49 (0.45; 4.90) | 0.514 | Q4 | 1.18 (0.37; 3.80) | 0.782 |
| | Q5 | 3.14 (1.03; 9.52) | 0.044 | Q5 | 2.74 (0.96; 7.82) | 0.059 |

Odds ratios represent the odds of having albuminuria (defined as an albumin excretion ≥ 30 mg/24) in the respective quintile of the percentage recruitment during post-occlusive peak reactive hyperemia or venous congestion compared with the odds of having albuminuria in the reference quintile. Model 1: unadjusted model; Model 2: age, sex, type 2 diabetes; Model 3a: model 2 + waist circumference, total-to-HDL cholesterol ratio, triglycerides, use of lipid-modifying drugs, office systolic blood pressure, use of antihypertensive medication, estimated GFR, prevalent cardiovascular disease, smoking behavior, alcohol consumption, educational level; Model 3b: as model 3a but adjusted for 24h average ambulatory systolic blood pressure instead of office systolic blood pressure (n=665). CI: confidence interval, OR: odds ratio, Q: quintile.

Supplemental Table 5B. Association between the absolute number of capillaries during post-occlusive peak reactive hyperemia as well as venous congestion and the presence of albuminuria (albumin excretion ≥ 30 mg/24h)

| Model | Post-occlusive peak reactive hyperemia (n/mm$^2$) | OR (95% CI) | P value | Venous congestion (n/mm$^2$) | OR (95% CI) | P value |
|---|---|---|---|---|---|---|
| 1 | Q1 | Reference | | Q1 | Reference | |
| | Q2 | 1.10 (0.39; 3.10) | 0.863 | Q2 | 2.42 (0.83; 7.04) | 0.106 |
| | Q3 | 1.86 (0.71; 4.87) | 0.206 | Q3 | 1.64 (0.52; 5.12) | 0.399 |
| | Q4 | 2.35 (0.94; 5.90) | 0.068 | Q4 | 4.09 (1.49; 11.27) | 0.006 |
| | Q5 | 2.11 (0.82; 5.38) | 0.120 | Q5 | 2.74 (0.95; 7.88) | 0.062 |
| 2 | Q1 | Reference | | Q1 | Reference | |
| | Q2 | 0.96 (0.33; 2.79) | 0.940 | Q2 | 1.95 (0.65; 5.85) | 0.235 |
| | Q3 | 1.56 (0.58; 4.20) | 0.384 | Q3 | 1.18 (0.37; 3.80) | 0.785 |
| | Q4 | 2.20 (0.85; 5.68) | 0.105 | Q4 | 3.40 (1.20; 9.69) | 0.022 |
| | Q5 | 1.50 (0.57; 3.95) | 0.413 | Q5 | 1.90 (0.64; 5.65) | 0.247 |
| 3a | Q1 | Reference | | Q1 | Reference | |
| | Q2 | 0.86 (0.28; 2.65) | 0.799 | Q2 | 1.76 (0.56; 5.54) | 0.331 |
| | Q3 | 1.67 (0.59; 4.74) | 0.336 | Q3 | 1.37 (0.41; 4.67) | 0.605 |
| | Q4 | 2.12 (0.78; 5.72) | 0.139 | Q4 | 3.23 (1.07; 9.79) | 0.038 |
| | Q5 | 1.55 (0.57; 4.26) | 0.392 | Q5 | 1.86 (0.60; 5.81) | 0.283 |
| 3b | Q1 | Reference | | Q1 | Reference | |
| | Q2 | 0.85 (0.26; 2.73) | 0.779 | Q2 | 1.45 (0.43; 4.91) | 0.552 |
| | Q3 | 1.23 (0.40; 3.80) | 0.715 | Q3 | 1.33 (0.37; 4.78) | 0.661 |
| | Q4 | 1.92 (0.68; 5.42) | 0.216 | Q4 | 3.33 (1.04; 10.59) | 0.042 |
| | Q5 | 1.45 (0.51; 4.15) | 0.489 | Q5 | 1.98 (0.61; 6.39) | 0.252 |

Odds ratios represent the odds of having albuminuria (defined as an albumin excretion ≥ 30 mg/24h) in the respective quintile of the absolute number of capillaries during post-occlusive peak reactive hyperemia or venous congestion compared with the odds of having albuminuria in the reference quintile. Model 1: unadjusted model; Model 2: age, sex, type 2 diabetes; Model 3a: model 2 + waist circumference, total-to-HDL cholesterol ratio, triglycerides, use of lipid-modifying drugs, office systolic blood pressure, use of antihypertensive medication, estimated GFR, prevalent cardiovascular disease, smoking behavior, alcohol consumption, educational level; Model 3b: as model 3a but adjusted for 24h average ambulatory systolic blood pressure instead of office systolic blood pressure (n=665). CI: confidence interval, OR: odds ratio, Q: quintile.

Supplemental Table 6A. Association between the percentage recruitment during post-occlusive peak reactive hyperemia as well as venous congestion and the presence of albuminuria (albumin excretion ≥ 30 mg/24h)

| Model | Recruitment during post-occlusive peak reactive hyperemia (%) | OR (95% CI) | P value | Recruitment during venous congestion (%) | OR (95% CI) | P value |
|---|---|---|---|---|---|---|
| 1 | D1 | Reference | | D1 | Reference | |
| | D2 | 1.52 (0.25; 9.38) | 0.651 | D2 | 2.06 (0.37; 11.59) | 0.414 |
| | D3 | 2.06 (0.37; 11.59) | 0.414 | D3 | 1.00 (0.14; 7.29) | 1.000 |
| | D4 | 3.76 (0.76; 18.75) | 0.106 | D4 | 2.06 (0.37; 11.59) | 0.414 |
| | D5 | 1.00 (0.14; 7.29) | 1.000 | D5 | 1.52 (0.25; 9.38) | 0.651 |
| | D6 | 2.02 (0.36; 11.43) | 0.423 | D6 | 4.91 (1.02; 23.55) | 0.047 |
| | D7 | 2.61 (0.49; 13.90) | 0.261 | D7 | 2.61 (0.49; 13.90) | 0.261 |
| | D8 | 3.18 (0.62; 16.28) | 0.166 | D8 | 2.61 (0.49; 13.90) | 0.261 |
| | D9 | 6.29 (1.34; 29.44) | 0.020 | D9 | 8.40 (1.84; 38.43) | 0.006 |
| | D10 | 7.67 (1.67; 35.34) | 0.009 | D10 | 4.99 (1.04; 23.82) | 0.045 |
| 2 | D1 | Reference | | D1 | Reference | |
| | D2 | 1.46 (0.23; 9.24) | 0.689 | D2 | 1.91 (0.33; 11.05) | 0.472 |
| | D3 | 1.98 (0.34; 11.49) | 0.445 | D3 | 0.91 (0.12; 6.77) | 0.924 |
| | D4 | 2.96 (0.57; 15.26) | 0.195 | D4 | 1.80 (0.31; 10.40) | 0.512 |
| | D5 | 0.75 (0.10; 5.59) | 0.776 | D5 | 1.16 (0.18; 7.40) | 0.873 |
| | D6 | 1.16 (0.28; 9.35) | 0.594 | D6 | 3.50 (0.71; 17.33) | 0.125 |
| | D7 | 1.64 (0.30; 9.01) | 0.572 | D7 | 1.94 (0.35; 10.64) | 0.445 |
| | D8 | 2.45 (0.46; 13.03) | 0.293 | D8 | 1.96 (0.36; 10.81) | 0.439 |
| | D9 | 3.92 (0.81; 19.07) | 0.091 | D9 | 4.70 (0.98; 22.50) | 0.053 |
| | D10 | 4.75 (1.00; 22.61) | 0.050 | D10 | 3.35 (0.68; 16.60) | 0.139 |

Odds ratios represent the odds of having albuminuria (defined as an albumin excretion ≥ 30 mg/24) in the respective decile of the percentage recruitment during post-occlusive peak reactive hyperemia or venous congestion compared with the odds of having albuminuria in the reference decile. Model 1: unadjusted model; Model 2: age, sex, type 2 diabetes. CI: confidence interval, OR: odds ratio, D: decile.

Supplemental Table 6B. Association between the absolute number of capillaries during post-occlusive peak reactive hyperemia as well as venous congestion and the presence of albuminuria (albumin excretion ≥ 30 mg/24h)

| Model | Post-occlusive peak reactive hyperemia (n/mm$^2$) | OR (95% CI) | P value | Venous congestion (n/mm$^2$) | OR (95% CI) | P value |
|---|---|---|---|---|---|---|
| 1 | D1 | Reference | | D1 | Reference | |
| | D2 | 1.45 (0.31; 6.73) | 0.633 | D2 | 1.57 (0.25; 9.66) | 0.629 |
| | D3 | 0.62 (0.10; 3.84) | 0.611 | D3 | 2.88 (0.56; 14.74) | 0.204 |
| | D4 | 2.15 (0.52; 8.93) | 0.293 | D4 | 3.32 (0.65; 17.05) | 0.150 |
| | D5 | 1.79 (0.41; 7.77) | 0.438 | D5 | 0.51 (0.05; 5.80) | 0.591 |
| | D6 | 2.79 (0.69; 11.26) | 0.140 | D6 | 3.71 (0.74; 18.47) | 0.110 |
| | D7 | 3.58 (0.95; 13.56) | 0.061 | D7 | 2.61 (0.49; 13.90) | 0.261 |
| | D8 | 2.15 (0.52; 8.93) | 0.293 | D8 | 8.13 (1.78; 37.17) | 0.007 |
| | D9 | 2.54 (0.63; 10.23) | 0.189 | D9 | 3.22 (0.63; 16.53) | 0.160 |
| | D10 | 2.58 (0.64; 10.39) | 0.182 | D10 | 3.76 (0.76; 18.75) | 0.106 |
| 2 | D1 | Reference | | D1 | Reference | |
| | D2 | 1.83 (0.38; 8.92) | 0.452 | D2 | 2.04 (0.32; 13.16) | 0.452 |
| | D3 | 0.59 (0.09; 3.78) | 0.581 | D3 | 2.60 (0.49; 13.81) | 0.261 |
| | D4 | 2.16 (0.50; 9.38) | 0.304 | D4 | 3.08 (0.58; 16.51) | 0.188 |
| | D5 | 1.49 (0.33; 6.75) | 0.606 | D5 | 0.45 (0.04; 5.20) | 0.521 |
| | D6 | 2.96 (0.70; 12.54) | 0.142 | D6 | 2.88 (0.56; 14.94) | 0.208 |
| | D7 | 3.92 (0.99; 15.61) | 0.053 | D7 | 2.57 (0.46; 14.24) | 0.280 |
| | D8 | 2.12 (0.49; 9.23) | 0.316 | D8 | 7.42 (1.56; 35.41) | 0.012 |
| | D9 | 1.98 (0.49; 8.78) | 0.349 | D9 | 2.67 (0.50; 14.79) | 0.249 |
| | D10 | 2.08 (0.49; 8.78) | 0.319 | D10 | 2.85 (0.55; 14.79) | 0.213 |

Odds ratios represent the odds of having albuminuria (defined as an albumin excretion ≥ 30 mg/24h) in the respective decile of the absolute number of capillaries during post-occlusive peak reactive hyperemia or venous congestion compared with the odds of having albuminuria in the reference decile. Model 1: unadjusted model; Model 2: age, sex, type 2 diabetes. CI: confidence interval, OR: odds ratio, D: decile.

Supplemental Table 7A. Association between the percentage recruitment during post-occlusive peak reactive hyperemia as well as venous congestion and the presence of albuminuria (albumin excretion ≥ 15 mg/24h)

| Model | Recruitment during post-occlusive peak reactive hyperemia (%) | OR (95% CI) | P value | Recruitment during venous congestion (%) | OR (95% CI) | P value |
|---|---|---|---|---|---|---|
| 1 | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 1.10 (0.67; 1.83) | 0.700 | T2 (middle) | 1.27 (0.76; 2.11) | 0.364 |
| | T3 (low) | 2.19 (1.38; 3.47) | 0.001 | T3 (low) | 2.54 (1.59; 4.07) | < 0.001 |
| 2 | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 0.86 (0.50; 1.46) | 0.571 | T2 (middle) | 1.09 (0.64; 1.86) | 0.751 |
| | T3 (low) | 1.62 (0.99; 2.65) | 0.055 | T3 (low) | 1.88 (1.14; 3.10) | 0.014 |
| 3a | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 0.92 (0.53; 1.60) | 0.775 | T2 (middle) | 1.10 (0.63; 1.91) | 0.743 |
| | T3 (low) | 1.59 (0.96; 2.64) | 0.075 | T3 (low) | 1.75 (1.05; 2.95) | 0.033 |
| 3b | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 1.03 (0.57; 1.84) | 0.931 | T2 (middle) | 1.16 (0.65; 2.08) | 0.622 |
| | T3 (low) | 1.67 (0.97; 2.88) | 0.067 | T3 (low) | 1.79 (1.03; 3.11) | 0.040 |

Odds ratios represent the odds of having albuminuria (defined as an albumin excretion ≥ 15 mg/24) in the respective tertile of the percentage recruitment during post-occlusive peak reactive hyperemia or venous congestion compared with the odds of having albuminuria in the reference tertile. Model 1: unadjusted model; Model 2: age, sex, type 2 diabetes; Model 3a: model 2 + waist circumference, total-to-HDL cholesterol ratio, triglycerides, use of lipid-modifying drugs, office systolic blood pressure, use of antihypertensive medication, estimated GFR, prevalent cardiovascular disease, smoking behavior, alcohol consumption, educational level; Model 3b: as model 3a but adjusted for 24h average ambulatory systolic blood pressure instead of office systolic blood pressure (n=665). CI: confidence interval, OR: odds ratio, T: tertile.

Supplemental Table 7B. Association between the absolute number of capillaries during post-occlusive peak reactive hyperemia as well as venous congestion and the presence of albuminuria (albumin excretion ≥ 15 mg/24h)

| Model | Post-occlusive peak reactive hyperemia (n/mm$^2$) | OR (95% CI) | P value | Venous congestion (n/mm$^2$) | OR (95% CI) | P value |
|---|---|---|---|---|---|---|
| 1 | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 1.71 (1.05; 2.79) | 0.031 | T2 (middle) | 1.31 (0.81; 2.14) | 0.274 |
| | T3 (low) | 1.88 (1.17; 3.04) | 0.011 | T3 (low) | 1.99 (1.25; 3.18) | 0.004 |
| 2 | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 1.57 (0.94; 2.63) | 0.084 | T2 (middle) | 1.15 (0.69; 1.93) | 0.594 |
| | T3 (low) | 1.54 (0.92; 2.56) | 0.098 | T3 (low) | 1.72 (1.05; 2.83) | 0.031 |
| 3a | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 1.75 (1.02; 2.99) | 0.042 | T2 (middle) | 1.28 (0.75; 2.18) | 0.372 |
| | T3 (low) | 1.64 (0.96; 2.80) | 0.071 | T3 (low) | 1.78 (1.06; 2.99) | 0.029 |
| 3b | T1 (high) | Reference | | T1 (high) | Reference | |
| | T2 (middle) | 1.45 (0.82; 2.57) | 0.205 | T2 (middle) | 1.17 (0.66; 2.09) | 0.591 |
| | T3 (low) | 1.61 (0.92; 2.80) | 0.095 | T3 (low) | 1.92 (1.11; 3.33) | 0.019 |

Odds ratios represent the odds of having albuminuria (defined as an albumin excretion ≥ 15 mg/24h) in the respective tertile of the absolute number of capillaries during post-occlusive peak reactive hyperemia or venous congestion compared with the odds of having albuminuria in the reference tertile. Model 1: unadjusted model; Model 2: age, sex, type 2 diabetes; Model 3a: model 2 + waist circumference, total-to-HDL cholesterol ratio, triglycerides, use of lipid-modifying drugs, office systolic blood pressure, use of antihypertensive medication, estimated GFR, prevalent cardiovascular disease, smoking behavior, alcohol consumption, educational level; Model 3b: as model 3a but adjusted for 24h average ambulatory systolic blood pressure instead of office systolic blood pressure (n=665). CI: confidence interval, OR: odds ratio, T: tertile.