* Supplementary material (online only) −

**Reference intervals for local arterial stiffness. Part A: carotid artery**

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Table S1: Contributing centres (in order of decreasing number of participating individuals) and respective carotid properties measurement techniques used

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Total n** | **Healthy subpopulation n** | | **Centre** | **Study name/acronym** | **Echotracking system** | **Anatomical location\*** | **(Local) PP measurement** | **MAP calculation for local PP** |
| 4,892 | - |  | Rotterdam (NL) | Rotterdam Study | WTS | Centred at 1 cm | Brachial PP | - |
| 4,772 | 1,053 | 810  193  50 | Paris-HEGP (F) | PPS3 (*n*=3,762)  HEGP studies (*n*=622)  CASHMERE (*n*=388) | ART.LABa  WTSb  WTS | Centred at 1 cm  Centred at 2 cm  Centred at 2 cm | Distension waveforms  Carotid tonometry/brachial PP (338/281) Carotid tonometry | Distension waveforms  Radial tonometry  Radial tonometry |
| 3,423 | 14 | 14  - | Utrecht (NL) | SMART (*n*=3,296)  Whistler Cardio (*n*=127) | WTS  ART.LAB | Centred at 2 cm  Centred at 1 cm | Brachial PP  Brachial PP | -  - |
| 2,027 | 742 |  | Ghent (BE) | ASKLEPIOS | Echopac | 1-2 cm | Carotid tonometry | Brachial tonometry |
| 1,597 | 279 | 45  192  42 | Maastricht/Amsterdam (NL) | Hoorn study (*n*=717)  AGAHLS (*n*=406)  CODAM 1 (*n*=474) | WTS  WTS  WTS | Centred at 1 cm  Centred at 1 cm  1-2 cm | Distension waveforms  Distension waveforms  Brachial PP | Distension waveforms  Distension waveforms  - |
| 1,367 | 340 |  | Leuven (BE) | FLEMENGHO | WTS | Centred at 2 cm | Carotid tonometry | Maximal oscillometry |
| 854 | 398 |  | Shanghai (CN) | Ningbo Working place | ART.LAB | 0-1 cm | Radial tonometryf | Constant |
| 664 | 157 | 36  121 | Pisa (I) | CATOD (*n*=369)  Other (*n*=295) | Carotid Studioe | Centred at 1 cm | Carotid tonometry  Carotid tonometry | Radial tonometry  Radial tonometry/Constant (241/54) |
| 570 | 74 |  | Mannheim (D) | MIPH Industrial Cohort Study | ART.LAB | Centred at 1 cm | Brachial PP | - |
| 472 | 83 |  | Vilnius (LT) | LitHir | ART.LAB | Centred at 1 cm | Carotid tonometry/brachial PP (249/223) | Radial tonometry |
| 355 | 10 |  | Antwerp (BE) |  | WTS | Centred at 2 cm | Brachial PP | - |
| 307 | 65 |  | São Paulo (BR) | CHEST-BR, GeneHy | WTS | Centred at 1 cm | Brachial PP | - |
| 300 | 31 |  | Nancy (F) | ARTEOS study | WTS | Centred at 2 cm | Brachial PP | - |
| 248 | 70 |  | Bern (CH) |  | ART.LAB | Centred at 1 cm | Carotid tonometry | Brachial tonometry |
| 223 | 29 |  | Milano (I) |  | ART.LAB | Centred at 2 cm | Radial tonometry | Constant |
| 222 | 43 |  | Maastricht-VitaK (NL) |  | ART.LAB | Centred at 2 cm | Brachial PP | - |
| 176 | 126 |  | Budapest (H) |  | ART.LAB | Centred at 1 cm | Carotid tonometry | Radial tonometry |
| 136 | 36 |  | Rouen (F) |  | ART.LAB | Centred at 1 cm | Carotid tonometry | Radial tonometry |
| 121 | 2 |  | Paris-Foch (F) |  | ART.LAB | Centred at 1 cm | Carotid tonometry | Maximal oscillometry |
| 100 | 49 | 49 | Maastricht/Leuven (NL/BE) | Migraine | WTS | 1-2 cm | Carotid tonometry | Brachial tonometry |
| 85 | - |  | Gdansk (PL) | CareNorth | ART.LAB | Centred at 1 cm | Carotid tonometry | Constant (MAP=SBP+1/3\*PP) |
| 43 | - |  | Pilsen (CZ) | SAS study | ART.LAB | Centred at 1 cm | Brachial PP | - |
| 32 | - |  | Québec (CDN) |  | ART.LAB | Centred at 1 cm | Carotid tonometry | Radial tonometry |
| 21 | - |  | Montreal (CDN) |  | ART.LAB | Centred at 1 cm | Carotid tonometry | Brachial tonometry |

\*Anatomical location of the measurement is expressed as distance (in cm) proximal to the carotid bifurcation;aART.LABechotracking system (ESAOTE, Maastricht, the Netherlands); bWall Track System [WTS (former version of ART.LAB), ESAOTE, Maastricht, the Netherlands][24](#_ENREF_24); cVivid-7 US system (GE Vingmed Ultrasound, Horten, Norway) with Echopac post-processing; dAloka SSD-650 US system (Aloka, Tokyo, Japan) with post-processing in dedicated software (M’ATHS, Metris, France)[49](#_ENREF_49); eCarotid Studio (Institute of Clinical Physiology, National Research Council, Pisa, Italy)[25](#_ENREF_25); fRadial tonometry plus transfer function (Sphygmocor, Atcor Medical, Australia).

Table S2: Calibration factors for carotid diameter and distension values as obtained with different measurement devices and locations

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Carotid diameter** | | |  | **Carotid distension** | | |
|  | β | 95% CI | *p* |  | β | 95% CI | *p* |
| Echotracking system [reference=ART.LAB\* (n=6,841)] |  |  |  |  |  |  |  |
| Wall Track system (n=13,176) | 0.220 | 0.191; 0.250 | <0.001 |  | 0.019 | 0.014; 0.024 | <0.001 |
| Vivid-7 (n=2,027) | 0.191 | 0.109; 0.273 | <0.001 |  | 0.185 | 0.172; 0.198 | <0.001 |
| Carotid studio (n=664) | -0.082 | -0.149; -0.015 | 0.016 |  | 0.113 | 0.102; 0.123 | <0.001 |
| Anatomical location [reference=centred at 1 cm\*\* (n=12,528)] |  |  |  |  |  |  |  |
| 0-1 cm (n=854) | 0.910 | 0.849; 0.970 | <0.001 |  | -0.015 | -0.024; -0.005 | 0.002 |
| 1-2 cm (n=2,601) | -0.068 | -0.139; 0.003 | 0.062 |  | -0.115 | -0.126; -0.103 | <0.001 |
| Centred at 2 cm (n=6,725) | -0.125 | -0.155; -0.095 | <0.001 |  | 0.004 | -0.001; 0.009 | 0.105 |

Regression coefficients β represent the mean difference in carotid artery diameter (in mm) or distension (in mm) when using each of the echotracking systems, and/or anatomical locations vs. the reference one (as indicated above) at mean levels of age, sex, MAP, total-HDL cholesterol ratio, smoking, diabetes, BMI, history of CVD, and use of BP- and/or lipid-lowering medication in the total reference population (n=22,812).

\*In contrast to the Wall Track system, Vivid-7 and Carotid Studio, which select a single M-line, ART.LAB takes measures over an arterial width of >10 mm, comprising multiple M-lines, which may yield considerably more precise measurements.

\*\*Anatomical location is expressed as distance (in cm) proximal to the carotid bifurcation.

On the basis of this equation, to rescale diameter values obtained by, for instance, the Wall Track System (WTS) to values of

ART.LAB (i.e. to the values presented in the paper), 0.220 mm needs to be *subtracted* from the original WTS values. Likewise, if values were obtained at 0-1 cm proximal to the carotid bifurcation, then to rescale these to values of measurements centred at 1 cm proximal to the carotid bifurcation (i.e. to the values presented in the paper), 0.910 mm needs to be *subtracted* from the original 0-1 cm values.

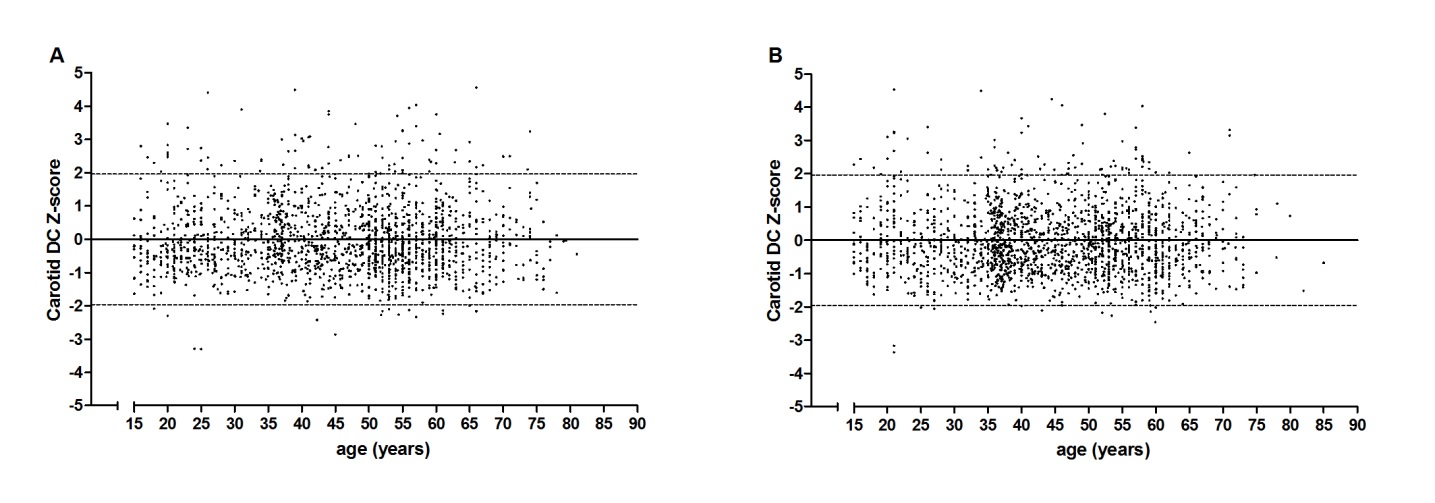


Figure S1: Scatter plot of carotid DC Z-scores by age, showing the mean (horizontal line) and +/- 1.96 SD (dotted lines), from the fitted model for carotid DC data for men (***A***) and women (***B***)

**Results S1:**

*Age- and sex-specific reference intervals for carotid PWV in the healthy subpopulation*

The best fitting FPs’ powers (*p*, *q*, …) for the meanPWV curves were *p*=1 for both men andwomen and for the SDPWV curves were *p*=1 for men and *p*=2women. Accordingly, the equations derived on the basis of the estimated coefficients were, for men:

* *MeanPWV*(in m/s)*= 3.914 + 0.069\*age*  [eq. 7]
* *SDPWV*(in m/s) *= 0.317 + 0.017\*age* [eq. 8]

and, for women:

* *MeanPWV*(in m/s) *= 3.310 + 0.080\*age* [eq. 9]
* *SDPWV*(in m/s) *= 0.624 + 0.021\*(age/10)2* [eq. 10]

Figure S2: Age-specific percentiles of carotid PWV in the healthy subpopulation. ***A***, men; ***B***, women.

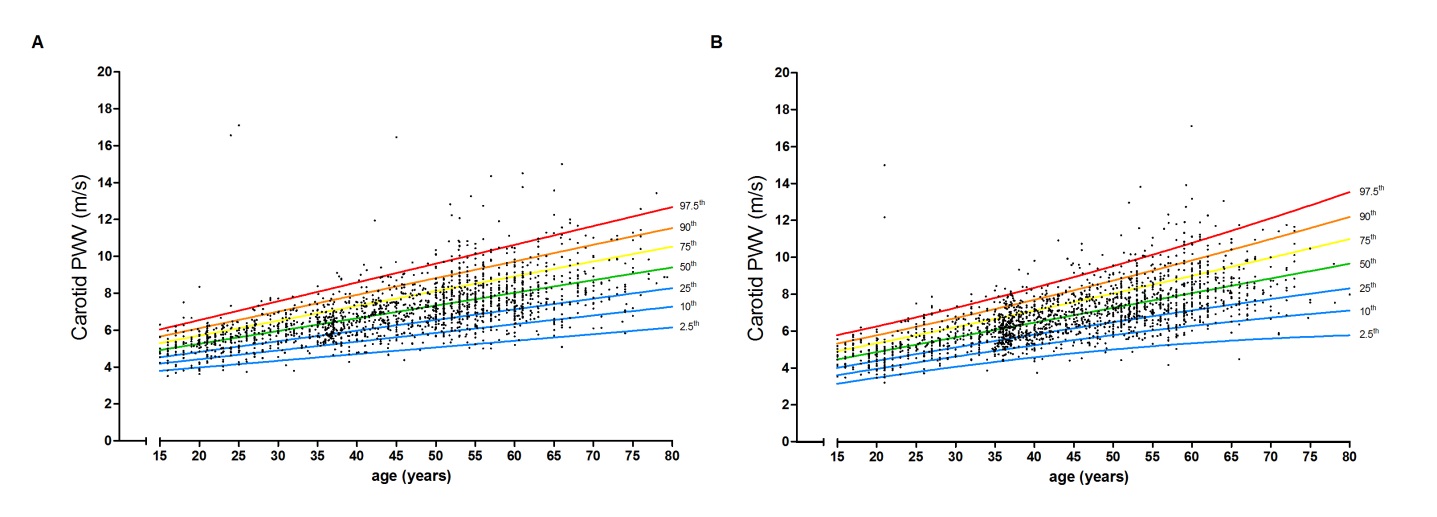


Table S3: Age- and sex-specific percentiles of carotid PWV (in m/s) in the healthy subpopulation

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **percentiles** | | | | | | |
|  | **Age (years)** | 2.5th | 10th | 25th | 50th | 75th | 90th | 97.5th |
| *Men (n=1,724)* | *20* | 4.0 | 4.5 | 4.9 | 5.3 | 5.7 | 6.1 | 6.6 |
|  | *30* | 4.4 | 4.9 | 5.4 | 6.0 | 6.5 | 7.0 | 7.6 |
|  | *40* | 4.7 | 5.4 | 6.0 | 6.7 | 7.3 | 7.9 | 8.6 |
|  | *50* | 5.1 | 5.9 | 6.6 | 7.4 | 8.1 | 8.8 | 9.6 |
|  | *60* | 5.5 | 6.4 | 7.2 | 8.1 | 8.9 | 9.7 | 10.7 |
|  | *70* | 5.8 | 6.8 | 7.7 | 8.7 | 9.8 | 10.7 | 11.7 |
|  |  |  |  |  |  |  |  |  |
| *Women (n=1,877)* | *20* | 3.5 | 4.0 | 4.4 | 4.9 | 5.4 | 5.8 | 6.3 |
|  | *30* | 4.1 | 4.7 | 5.2 | 5.7 | 6.3 | 6.8 | 7.3 |
|  | *40* | 4.6 | 5.3 | 5.9 | 6.5 | 7.2 | 7.7 | 8.4 |
|  | *50* | 5.1 | 5.8 | 6.5 | 7.3 | 8.1 | 8.8 | 9.6 |
|  | *60* | 5.4 | 6.3 | 7.2 | 8.1 | 9.0 | 9.9 | 10.8 |
|  | *70* | 5.7 | 6.8 | 7.8 | 8.9 | 10.0 | 11.0 | 12.1 |

**Results S2:**

*Age- and sex-specific reference intervals for carotid diameter in the healthy subpopulation*

The best fitting FPs’ powers (*p, q, …*) for the meandiameter curves were *p*=-2 *q*=-2 for men and *p*=0.5 for women and for the SDdiameter curves were *p*=3 for men and *p*=3 women. Accordingly, the equations derived on the basis of the estimated coefficients were, for men:

* *Meandiameter*(in mm)*= 7.661 + 0.087\*(age/10)-2 – 8.250\*(age/10)-2\*ln(age/10)* [eq. 11]
* *SDdiameter*(in mm) *= 0.514 + 0.001\*(age/10)3* [eq. 12]

and, for women:

* *Meandiameter*(in mm) *= 4.783 + 0.780\*(age/10)0.5* [eq. 13]
* *SDdiameter*(in mm) *= 0.555 + 0.001\*(age/10)3* [eq. 14]

*Age- and sex-specific reference intervals for carotid distension in the healthy subpopulation*

The best fitting FPs’ powers (*p*, *q*, …) for the meandistension curves were *p*=0 for men and *p*=-0.5 for women and for the SDdistension curves were *p*=-2 for men and *p*=-1 women. Accordingly, the equations derived on the basis of the estimated coefficients were, for men:

* *Meandistension*(mm)*= 0.962 - 0.326\*ln(age/10)* [eq. 15]
* *SDdistension*(in mm) *= 0.118 + 0.221\*(age/10)-2* [eq. 16]

and, for women:

* *Meandistension*(in mm) *= -0.137 + 1.163\*(age/10)-0.5*[eq. 17]
* *SDdistension*(in mm) *= 0.089 + 0.114\*(age/10)-1* [eq. 18]

*Age- and sex-specific reference intervals for brachial PP in the healthy subpopulation*

The best fitting FPs’ powers (*p*, *q*, …) for the meanPP curves were *p*=3 *q*=3 for men and *p*=-2 *q*=-0.5 for women and for the SDPP curves were *p*=1 for men and *p*=1 women. Accordingly, the equations derived on the basis of the estimated coefficients were, for men:

* *MeanPP*(in mm Hg)*= 53.64 - 0.133\*(age/10)3 + 0.067\*(age/10)3 \* ln(age/10)* [eq. 19]
* *SDPP*(in mm Hg) *= 9.940 - 0.035\*age* [eq. 20]

and, for women:

* *MeanPP*(in mm Hg) *= 72.83 + 55.88\*(age/10)-2 - 59.22\*(age/10)-0.5* [eq. 21]
* *SDPP*(in mm Hg) *= 6.266 + 0.052\*age* [eq. 22]

|  |  |  |
| --- | --- | --- |
|  |  |  |
| Figure S3: Age-specific percentiles of *carotid diameter* in the healthy subpopulation. ***A***, men; ***B***, women. | Figure S4: Age-specific percentiles of *carotid distension* in the healthy subpopulation. ***A***, men; ***B***, women. | Figure S5: Age-specific percentiles of *brachial pulse pressure* in the healthy subpopulation. ***A***, men; ***B***, women. |

**Methods S1:**

*Calibration between different techniques to determine local carotid pulse pressure*

Different methods to determine local carotid PP were used. First, carotid distension waveforms were obtained and rescaled using brachial distension waveforms (*n*=4,807). Second, carotid tonometry was performed and the obtained pressures were rescaled with brachial MAP calculated using brachial tonometry (*n*=2,276), radial tonometry (*n*=1,857), maximal oscillometry (n=1,384) or the equation MAP=DBP+1/3\*PP (n=125). Third, radial tonometry was performed to obtain carotid pressures using a transfer function (Sphygmocor, Atcor Medical, Australia; n=1,009) (Supplemental material, Table S1).

Similar to the calibration analyses for diameter and distension as described in the main manuscript, we performed multiple linear regression analyses that included dummy variables for each method (with carotid distension waveforms + brachial distension waveforms as reference) as independent determinants of carotid PP. These analyses were conducted in all individuals that had any measurement of local carotid PP (n=11,458; i.e. individuals with brachial PP only were excluded) and included adjustments for all CV-RFs, history of CVD and use of BP- and/or lipid-lowering medication. The regression coefficients (β) for the dummy variables hereby obtained were used as ‘calibration factors’ to rescale individual carotid PP values to the reference technique (Table S4). We used these rescaled carotid PP values in all further analyses.

Table S4: Calibration factors for local carotid pulse pressure values as obtained with different methods

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Local carotid PP** | | |
|  | β | 95% CI | *p* |
| Carotid tonometry + brachial tonometry | 7.2 | 6.5; 7.8 | <0.001 |
| Carotid tonometry + radial tonometry | 0.4 | -0.2; 1.1 | 0.218 |
| Carotid tonometry + maximal oscillometry | 2.1 | 1.3; 2.8 | <0.001 |
| Carotid tonometry + constant | -0.4 | -2.5; 1.6 | 0.687 |
| Radial tonometry + transfer function | -5.6 | -6.4; -4.8 | <0.001 |

Regression coefficients β represent the mean difference in local carotid pulse pressure (in mm Hg) when using each of the local PP measurement techniques vs. the reference one (carotid distension waveforms + brachial distension waveforms) at mean levels of age, sex, MAP, heart rate, total-HDL cholesterol ratio, BMI, history of CVD, and use of BP- and/or lipid-lowering medication only in individuals in whom a measure of local carotid PP was performed (n=11,458).

On the basis of this equation, to rescale local carotid PP values obtained by for instance radial tonometry + transfer function to values of carotid distension waveforms + brachial distension waveforms (i.e. to the values presented in the Supplemental material), to the original radial tonometry + transfer function values 5.6 mm Hg needs to be *added*.

**Results S3:**

*Age- and sex-specific reference intervals for carotid DC (calculated using local carotid PP) in the healthy subpopulation*

The best fitting FPs’ powers (*p*, *q*, …) for the meanDC curves were *p*=-0.5 for men and *p*=-2 *q*=-2 for women and for the SDDC curves were *p*=-2 for both men and women. Accordingly, the equations derived on the basis of the estimated coefficients were, for men:

* *MeanDC*(in 10-3\*kPa-1)*= -17.38 + 89.86\*(age/10)-0.5* [eq. 23]
* *SDDC*(in 10-3\*kPa-1) *= 5.293 + 41.40\*(age/10)-2* [eq. 24]

and, for women:

* *MeanDC*(in 10-3\*kPa-1) *= 8.391 + 122.3\*(age/10)-2 + 143.4\*(age/10)-2 \* ln(age/10)*  [eq. 25]
* *SDDC*(in 10-3\*kPa-1) *= 3.033 + 101.1\*(age/10)-2*  [eq. 26]

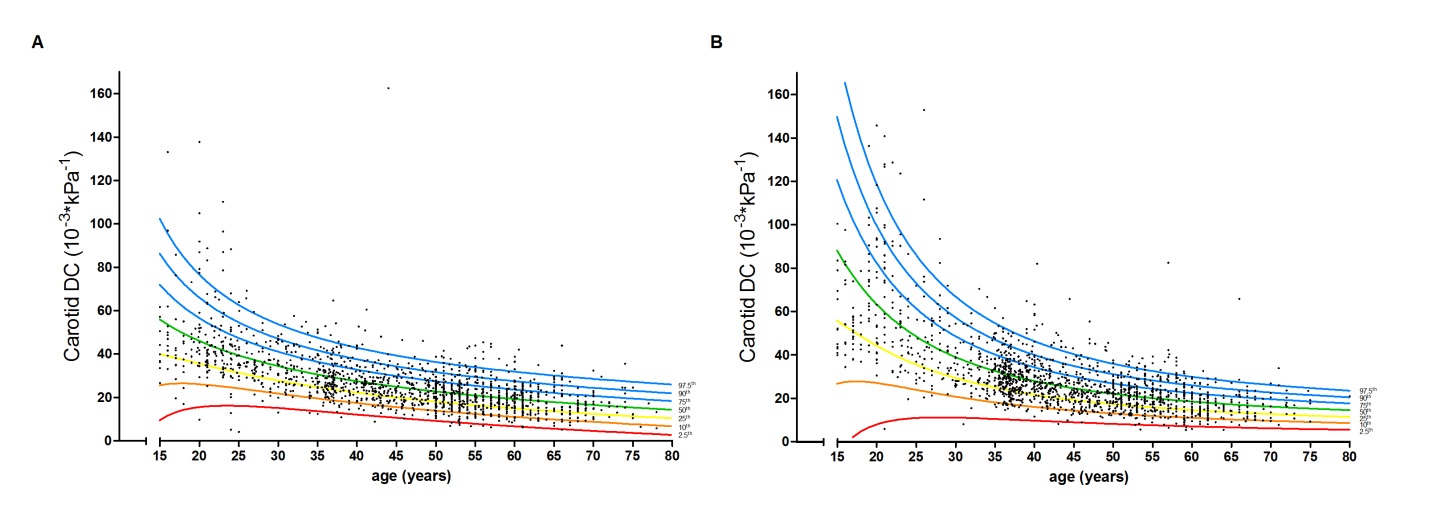


Figure S6: Age-specific percentiles of carotid DC calculated with local carotid PP in the healthy subpopulation. ***A***, men; ***B***, women.

Table S5: Age- and sex-specific percentiles of carotid DC (in 10-3\*kPa-1) calculated with local carotid PP in the healthy subpopulation

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **percentiles** | | | | | | |
|  | **Age (years)** | 2.5th | 10th | 25th | 50th | 75th | 90th | 97.5th |
| *Men (n=1,532)* | *20* | 15.5 | 26.1 | 35.6 | 46.2 | 56.7 | 66.2 | 76.8 |
|  | *30* | 15.1 | 21.8 | 27.8 | 34.5 | 41.2 | 47.2 | 53.9 |
|  | *40* | 12.1 | 17.5 | 22.2 | 27.6 | 32.9 | 37.6 | 43.0 |
|  | *50* | 9.2 | 13.9 | 18.1 | 22.8 | 27.5 | 31.7 | 36.4 |
|  | *60* | 6.7 | 11.1 | 15.0 | 19.3 | 23.7 | 27.6 | 31.9 |
|  | *70* | 4.6 | 8.7 | 12.4 | 16.6 | 20.7 | 24.4 | 28.6 |
|  |  |  |  |  |  |  |  |  |
| *Women (n=1,591)* | *20* | 8.3 | 27.6 | 44.7 | 63.8 | 82.9 | 100.0 | 119.3 |
|  | *30* | 11.5 | 21.2 | 29.9 | 39.5 | 49.1 | 57.7 | 67.4 |
|  | *40* | 10.1 | 16.5 | 22.1 | 28.5 | 34.8 | 40.4 | 46.8 |
|  | *50* | 8.6 | 13.5 | 17.7 | 22.5 | 27.3 | 31.6 | 36.4 |
|  | *60* | 7.5 | 11.4 | 15.0 | 18.9 | 22.9 | 26.4 | 30.4 |
|  | *70* | 6.6 | 10.1 | 13.1 | 16.6 | 20.0 | 23.1 | 26.6 |

Table S6:Associations between known cardiovascular risk factors and carotid DC Z-scores *calculated using local pulse pressure* in the reference subpopulations in *men*

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Subpopulation *without* CVD** | | | | | | |  | **Subpopulation *with* CVD**  **(n=596)** | | |
|  |  | ***without* treatmenta**  **(n=4,458)** | | |  | ***with*treatmenta**  **(n=1,117)** | | |  |
| Risk factor | Model | ß | 95%CI | *P-value* |  | ß | 95%CI | *P-value* |  | ß | 95%CI | *P-value* |
| Mean arterial pressure (10 mm Hg)b | 1 | -0.263 | -0.290; -0.235 | <0.001 |  | -0.353 | -0.403; -0.303 | <0.001 |  | -0.290 | -0.350; -0.231 | <0.001 |
|  | 2 | - | - | - |  | - | - | - |  | - | - | - |
|  | 3 | -0.221 | -0.250; -0.191 | <0.001 |  | -0.331 | -0.382; -0.280 | <0.001 |  | -0.251 | -0.313; -0.190 | <0.001 |
| Smoking |  |  |  |  |  |  |  |  |  |  |  |  |
| Previous smoking (vs. never smoking) | 1 | -0.083 | -0.156; -0.011 | 0.024 |  | -0.054 | -0.193; 0.086 | 0.452 |  | -0.230 | -0.402; -0.057 | 0.009 |
|  | 2 | 0.006 | -0.064; 0.077 | 0.856 |  | -0.018 | -0.147; 0.111 | 0.785 |  | -0.147 | -0.309; 0.015 | 0.074 |
|  | 3 | 0.025 | -0.045; 0.095 | 0.481 |  | -0.007 | -0.136; 0.122 | 0.913 |  | -0.094 | --0.255; 0.067 | 0.252 |
| Current smoking (vs. never smoking) | 1 | -0.016 | -0.102; 0.070 | 0.713 |  | -0.053 | -0.233; 0.127 | 0.562 |  | -0.184 | -0.420; 0.052 | 0.127 |
|  | 2 | 0.022 | -0.061; 0.105 | 0.607 |  | -0.054 | -0.221; 0.112 | 0.524 |  | -0.129 | -0.350; 0.092 | 0.254 |
|  | 3 | 0.040 | -0.044; 0.124 | 0.351 |  | -0.030 | -0.197; 0.137 | 0.728 |  | -0.064 | -0.285; 0.157 | 0.570 |
| Diabetes (yes) | 1 | -0.437 | -0.682; -0.193 | <0.001 |  | -0.246 | -0.406; -0.085 | 0.003 |  | -0.612 | -0.822; -0.402 | <0.001 |
|  | 2 | -0.269 | -0.505; -0.033 | 0.025 |  | -0.174 | -0.323; -0.025 | 0.022 |  | -0.445 | -0.646; -0.244 | <0.001 |
|  | 3 | -0.208 | -0.444; 0.028 | 0.084 |  | -0.144 | -0.295; 0.007 | 0.062 |  | -0.447 | -0.706; -0.188 | 0.001 |
| Total-to-HDL cholesterol ratio (unit) | 1 | -0.094 | -0.135; -0.052 | <0.001 |  | -0.052 | -0.140; 0.036 | 0.196 |  | -0.137 | -0.203; -0.072 | <0.001 |
|  | 2 | -0.063 | -0.106; -0.019 | 0.009 |  | -0.038 | -0.103; 0.027 | 0.207 |  | -0.110 | -0.170; -0.051 | <0.001 |
|  | 3 | -0.039 | -0.087; 0.009 | 0.098 |  | -0.033 | -0.089; 0.023 | 0.215 |  | -0.100 | -0.161; -0.039 | 0.001 |
| Body mass index (kg/m2) | 1 | -0.062 | -0.072; -0.053 | <0.001 |  | -0.046 | -0.062; -0.030 | <0.001 |  | -0.039 | -0.061; -0.017 | 0.001 |
|  | 2 | -0.038 | -0.047; -0.028 | <0.001 |  | -0.027 | -0.042; -0.012 | <0.001 |  | -0.020 | -0.041; 0.001 | 0.062 |
|  | 3 | -0.032 | -0.043; -0.021 | <0.001 |  | -0.022 | -0.038; -0.006 | 0.007 |  | -0.004 | -0.027; 0.018 | 0.707 |
| Use of BP-lowering medication (yes) | 1 | - | - | - |  | - | - | - |  | -0.213 | -0.373; -0.053 | 0.009 |
|  | 2 | - | - | - |  | - | - | - |  | -0.086 | -0.238; 0.066 | 0.267 |
|  | 3 | - | - | - |  | - | - | - |  | -0.032 | -0.191; 0.127 | 0.694 |
| Use of lipid-lowering medication (yes) | 1 | - | - | - |  | - | - | - |  | 0.034 | -0.056; 0.124 | 0.707 |
|  | 2 | - | - | - |  | - | - | - |  | -0.024 | -0.189; 0.140 | 0.772 |
|  | 3 | - | - | - |  | - | - | - |  | 0.019 | -0.153; 0.192 | 0.826 |
| Use of glucose-lowering medication (yes) | 1 | - | - | - |  | - | - | - |  | -0.403 | -0.719; -0.086 | 0.013 |
|  | 2 | - | - | - |  | - | - | - |  | -0.320 | -0.615; -0.024 | 0.034 |
|  | 3 | - | - | - |  | - | - | - |  | 0.093 | -0.277; 0.463 | 0.623 |

The regression coefficient ß represents the increase in carotid DC (in SD from the healthy population mean among *men* of the same age) per unit increase in each risk factor. Model 1: unadjusted; Model 2: adjusted for MAP; Model 3: adjusted for MAP and all other risk factors.aBP-, lipid- and glucose-lowering treatment; bmean arterial pressure was calculated by DBP+0.4\*PP.

Table S7:Associations between known cardiovascular risk factors and carotid DC Z-scores *calculated using local pulse pressure* in the reference subpopulations in *women*

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Subpopulation *without* CVD** | | | | | | |  | **Subpopulation *with* CVD**  **(n=630)** | | |
|  |  | ***without* treatmenta**  **(n=3,716)** | | |  | ***with*treatmenta**  **(n=941)** | | |  |
| Risk factor | Model | ß | 95%CI | *P-value* |  | ß | 95%CI | *P-value* |  | ß | 95%CI | *P-value* |
| Mean arterial pressure (10 mm Hg)b | 1 | -0.296 | -0.324; -0.269 | <0.001 |  | -0.355 | -0.408; -0.302 | <0.001 |  | -0.448 | -0.520; -0.375 | <0.001 |
|  | 2 | - | - | - |  | - | - | - |  | - | - | - |
|  | 3 | -0.277 | -0.308; -0.246 | <0.001 |  | -0.334 | -0.388; -0.280 | <0.001 |  | -0.364 | -0.440; -0.288 | <0.001 |
| Smoking |  |  |  |  |  |  |  |  |  |  |  |  |
| Previous smoking (vs. never smoking) | 1 | -0.004 | -0.097; 0.089 | 0.932 |  | 0.046 | -0.157; 0.250 | 0.657 |  | -0.214 | -0.453; 0.024 | 0.078 |
|  | 2 | 0.009 | -0.079; 0.098 | 0.834 |  | 0.026 | -0.161; 0.213 | 0.786 |  | -0.136 | -0.352; 0.080 | 0.218 |
|  | 3 | 0.017 | -0.071; 0.106 | 0.700 |  | 0.030 | -0.157; 0.217 | 0.751 |  | -0.156 | -0.369; 0.056 | 0.149 |
| Current smoking (vs. never smoking) | 1 | 0.104 | 0.004; 0.203 | 0.041 |  | 0.194 | -0.027; 0.416 | 0.085 |  | 0.461 | 0.143; 0.780 | 0.005 |
|  | 2 | 0.073 | -0.022; 0.167 | 0.131 |  | 0.051 | -0.153; 0.256 | 0.623 |  | 0.393 | 0.105; 0.682 | 0.008 |
|  | 3 | 0.078 | -0.016; 0.173 | 0.105 |  | 0.042 | -0.161; 0.246 | 0.684 |  | 0.333 | 0.049; 0.618 | 0.022 |
| Diabetes (yes) | 1 | -0.419 | -0.949; 0.110 | 0.113 |  | -0.303 | -0.499; -0.108 | 0.002 |  | -1.059 | -1.345; -0.773 | <0.001 |
|  | 2 | -0.130 | -0.579; 0.319 | 0.556 |  | -0.232 | -0.413; -0.051 | 0.012 |  | -0.691 | -0.963; -0.419 | <0.001 |
|  | 3 | -0.050 | -0.503; 0.403 | 0.822 |  | -0.178 | -0.362; 0.006 | 0.058 |  | -0.686 | -1.015; -0.357 | <0.001 |
| Total-to-HDL cholesterol ratio (unit) | 1 | -0.102 | -0.148; -0.057 | <0.001 |  | -0.088 | -0.147; -0.028 | 0.004 |  | -0.037 | -0.126; 0.052 | 0.418 |
|  | 2 | -0.052 | -0.098; -0.006 | 0.028 |  | -0.040 | -0.095; 0.014 | 0.146 |  | -0.011 | -0.092; 0.069 | 0.781 |
|  | 3 | -0.043 | -0.093; 0.006 | 0.084 |  | -0.010 | -0.069; 0.048 | 0.726 |  | 0.053 | -0.032; 0.137 | 0.223 |
| Body mass index (kg/m2) | 1 | -0.042 | -0.051; -0.033 | <0.001 |  | -0.040 | -0.054; -0.026 | <0.001 |  | -0.078 | -0.101; -0.054 | <0.001 |
|  | 2 | -0.015 | -0.024; -0.006 | 0.002 |  | -0.024 | -0.037; -0.011 | <0.001 |  | -0.042 | -0.064; -0.019 | <0.001 |
|  | 3 | -0.011 | -0.021; -0.001 | 0.037 |  | -0.021 | -0.035; -0.006 | 0.006 |  | -0.032 | -0.057; -0.007 | 0.011 |
| Use of BP-lowering medication (yes) | 1 | - | - | - |  | - | - | - |  | -0.572 | -0.789; -0.355 | <0.001 |
|  | 2 | - | - | - |  | - | - | - |  | -0.303 | -0.507; -0.098 | 0.004 |
|  | 3 | - | - | - |  | - | - | - |  | -0.127 | -0.345; 0.090 | 0.252 |
| Use of lipid-lowering medication (yes) | 1 | - | - | - |  | - | - | - |  | -0.193 | -0.483; 0.097 | 0.192 |
|  | 2 | - | - | - |  | - | - | - |  | -0.043 | -0.306; 0.220 | 0.750 |
|  | 3 | - | - | - |  | - | - | - |  | 0.024 | -0.244; 0.291 | 0.863 |
| Use of glucose-lowering medication (yes) | 1 | - | - | - |  | - | - | - |  | -0.656 | -1.178; -0.135 | 0.014 |
|  | 2 | - | - | - |  | - | - | - |  | -0.326 | -0.801; 0.149 | 0.179 |
|  | 3 | - | - | - |  | - | - | - |  | 0.404 | -0.137; 0.945 | 0.144 |

The regression coefficient ß represents the increase in carotid DC (in SD from the healthy population mean among *women* of the same age) per unit increase in each risk factor. Model 1: unadjusted; Model 2: adjusted for MAP; Model 3: adjusted for MAP and all other risk factors.aBP-, lipid- and glucose-lowering treatment; bmean arterial pressure was calculated by DBP+0.4\*PP.

**Results S3:**

*Age- and sex-specific reference intervals for carotid DC in the healthy subpopulation used in* ***part B****: the femoral artery*

The best fitting FPs’ powers (*p*, *q*, …) for the meanDC curves were *p*=-2 *q*=-2 for men and *p*=0 for women and for the SDDC curves were *p*=1 for both men and women. Accordingly, the equations derived on the basis of the estimated coefficients were, for men:

* *MeanDC*(in 10-3\*kPa-1)*= 4.875 - 11.47\*(age/10)-2 + 222.5\*(age/10)-2\*ln(age/10)*  [eq. 27]
* *SDDC*(in 10-3\*kPa-1) *= 11.47 - 0.119\*age* [eq. 28]

and, for women:

* *MeanDC*(in 10-3\*kPa-1) *= 58.85 - 24.37\*ln(age/10)*  [eq. 29]
* *SDDC*(in 10-3\*kPa-1) *= 12.12 - 0.128\*age* [eq. 30]

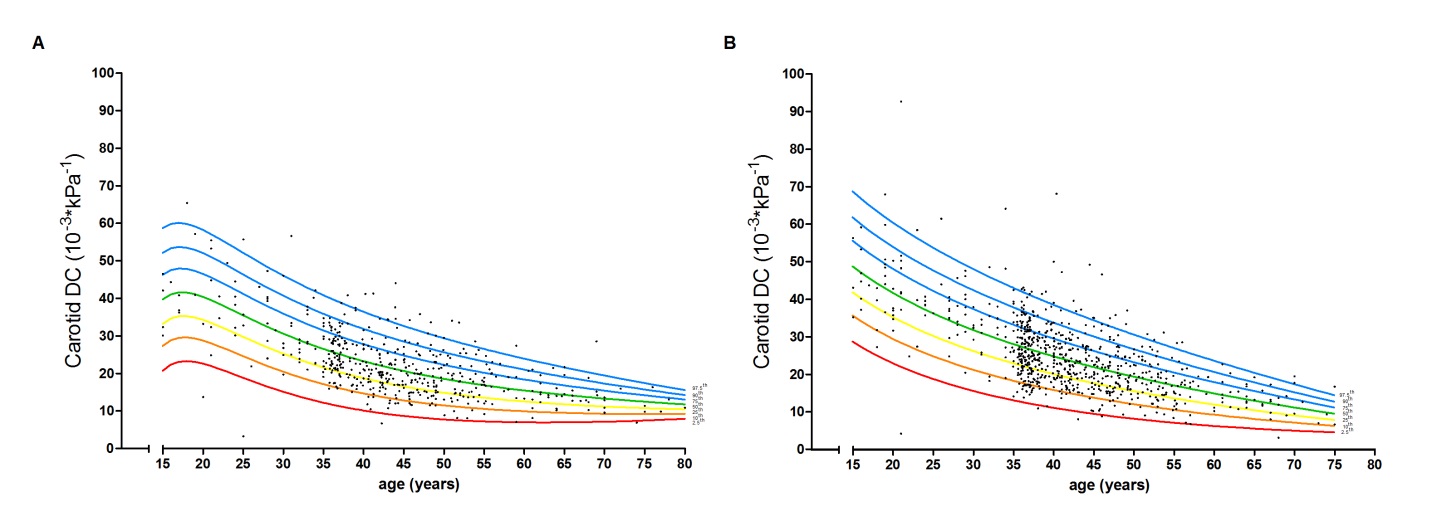


Figure S7: Age-specific percentiles of carotid DC in the subpopulation used in ***part B***: the femoral artery. ***A***, men; ***B***, women.

Table S8: Age- and sex-specific percentiles of carotid DC (in 10-3\*kPa-1) in the healthy subpopulation used in ***part B***: the femoral artery

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **percentiles** | | | | | | |
|  | **Age (years)** | 2.5th | 10th | 25th | 50th | 75th | 90th | 97.5th |
| *Men (n=488)* | *20* | 22,7 | 28,9 | 34,4 | 0,6 | 46,7 | 52,2 | 58,4 |
|  | *30* | 15,3 | 20,6 | 25,4 | 30,8 | 36,1 | 40,9 | 46,2 |
|  | *40* | 10,3 | 14,8 | 18,9 | 23,4 | 28,0 | 32,0 | 36,6 |
|  | *50* | 7,9 | 11,7 | 15,0 | 18,7 | 22,5 | 25,8 | 29,6 |
|  | *60* | 7,1 | 10,1 | 12,7 | 15,6 | 18,6 | 21,2 | 24,1 |
|  | *70* | 7,3 | 9,5 | 11,4 | 13,5 | 15,6 | 17,5 | 19,6 |
|  |  |  |  |  |  |  |  |  |
| *Women (n=775)* | *20* | 23,2 | 29,7 | 35,5 | 42,0 | 48,4 | 54,2 | 60,7 |
|  | *30* | 15,8 | 21,5 | 26,5 | 32,1 | 37,7 | 42,7 | 48,3 |
|  | *40* | 11,3 | 16,1 | 20,3 | 25,1 | 29,8 | 34,0 | 38,8 |
|  | *50* | 8,4 | 12,3 | 15,8 | 19,6 | 23,5 | 26,9 | 30,8 |
|  | *60* | 6,5 | 9,5 | 12,2 | 15,2 | 18,2 | 20,9 | 23,9 |
|  | *70* | 5,2 | 7,4 | 9,3 | 11,4 | 13,6 | 15,5 | 17,6 |

Table S9:Associations between known cardiovascular risk factors and carotid DC Z-scores in the reference subpopulations used in ***part B***: the femoral artery in *men*

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Subpopulation *without* CVD** | | | | | | |  | **Subpopulation *with* CVD**  **(n=262)** | | |
|  |  | ***without* treatmenta**  **(n=1,672)** | | |  | ***with*treatmenta**  **(n=268)** | | |  |
| Risk factor | Model | ß | 95%CI | *P-value* |  | ß | 95%CI | *P-value* |  | ß | 95%CI | *P-value* |
| Mean arterial pressure (10 mm Hg)b | 1 | -0.318 | -0.363; -0.274 | <0.001 |  | -0.392 | -0.487; -0.297 | <0.001 |  | -0.190 | -0.261; -0.119 | <0.001 |
|  | 2 | - | - | - |  | - | - | - |  | - | - | - |
|  | 3 | -0.274 | -0.321; -0.228 | <0.001 |  | -0.360 | -0.458; -0.262 | <0.001 |  | -0.152 | -0.226; -0.077 | <0.001 |
| Smoking |  |  |  |  |  |  |  |  |  |  |  |  |
| Previous smoking(vs. never smoking) | 1 | -0.045 | -0.160; 0.071 | 0.448 |  | -0.050 | -0.328; 0.228 | 0.724 |  | -0.286 | -0.530; 0.042 | 0.022 |
|  | 2 | 0.065 | -0.045; 0.176 | 0.247 |  | 0.024 | -0.227; 0.275 | 0.850 |  | -0.228 | -0.463; 0.006 | 0.056 |
|  | 3 | 0.092 | -0.019; 0.203 | 0.103 |  | 0.086 | -0.164; 0.337 | 0.501 |  | -0.189 | -0.425; 0.048 | 0.118 |
| Current smoking (vs. never smoking) | 1 | 0.246 | 0.123; 0.369 | <0.001 |  | 0.123 | -0.231; 0.477 | 0.495 |  | -0.179 | -0.468; 0.109 | 0.222 |
|  | 2 | 0.249 | 0.132; 0.366 | <0.001 |  | 0.066 | -0.253; 0.385 | 0.685 |  | -0.202 | -0.477; 0.074 | 0.151 |
|  | 3 | 0.250 | 0.133; 0.367 | <0.001 |  | 0.129 | -0.188; 0.447 | 0.424 |  | -0.201 | -0.476; 0.074 | 0.153 |
| Diabetes (yes) | 1 | -0.549 | -0.865; -0.234 | 0.001 |  | -0.574 | -0.867; -0.281 | <0.001 |  | -0.381 | -0.575; -0.187 | <0.001 |
|  | 2 | -0.310 | -0.611; -0.010 | 0.043 |  | -0.437 | -0.704; -0.170 | 0.001 |  | -0.303 | -0.493; -0.114 | 0.002 |
|  | 3 | -0.259 | -0.558; 0.040 | 0.089 |  | -0.423 | -0.696; -0.151 | 0.002 |  | -0.272 | -0.496; -0.047 | 0.018 |
| Total-to-HDL cholesterol ratio (unit) | 1 | -0.055 | -0.096; -0.013 | 0.010 |  | -0.083 | -0.186; 0.020 | 0.111 |  | -0.055 | -0.138; 0.028 | 0.192 |
|  | 2 | -0.022 | -0.061; 0.017 | 0.265 |  | -0.048 | -0.136; 0.040 | 0.283 |  | -0.039 | -0.114; 0.035 | 0.292 |
|  | 3 | -0.002 | -0.043; 0.038 | 0.904 |  | -0.025 | -0.116; 0.067 | 0.591 |  | -0.011 | -0.087; 0.064 | 0.766 |
| Body mass index (kg/m2) | 1 | -0.064 | -0.079; -0.050 | <0.001 |  | -0.047 | -0.084; -0.010 | 0.012 |  | -0.046 | -0.074; -0.018 | 0.001 |
|  | 2 | -0.037 | -0.052; -0.022 | <0.001 |  | -0.014 | -0.048; 0.020 | 0.416 |  | -0.036 | -0.063; -0.009 | 0.008 |
|  | 3 | -0.034 | -0.050; -0.019 | <0.001 |  | -0.009 | -0.044; 0.025 | 0.597 |  | -0.029 | -0.058; 0.000 | 0.047 |
| Use of BP-lowering medication (yes) | 1 | - | - | - |  | - | - | - |  | -0.192 | -0.374; -0.010 | 0.039 |
|  | 2 | - | - | - |  | - | - | - |  | -0.131 | -0.307; 0.045 | 0.143 |
|  | 3 | - | - | - |  | - | - | - |  | -0.118 | -0.301; 0.066 | 0.209 |
| Use of lipid-lowering medication (yes) | 1 | - | - | - |  | - | - | - |  | 0.078 | -0.127; 0.282 | 0.457 |
|  | 2 | - | - | - |  | - | - | - |  | 0.014 | -0.183; 0.211 | 0.890 |
|  | 3 | - | - | - |  | - | - | - |  | 0.093 | -0.114; 0.301 | 0.378 |
| Use of glucose-lowering medication (yes) | 1 | - | - | - |  | - | - | - |  | -0.196 | -0.495; 0.104 | 0.201 |
|  | 2 | - | - | - |  | - | - | - |  | -0.232 | -0.518; 0.053 | 0.111 |
|  | 3 | - | - | - |  | - | - | - |  | 0.048 | -0.285; 0.381 | 0.776 |

The regression coefficient ß represents the increase in carotid DC (in SD from the healthy population mean among *men* of the same age) per unit increase in each risk factor. Model 1: unadjusted; Model 2: adjusted for MAP; Model 3: adjusted for MAP and all other risk factors.aBP-, lipid- and glucose-lowering treatment; bmean arterial pressure was calculated by DBP+0.4\*PP.

Table S10:Associations between known cardiovascular risk factors and carotid DC Z-scores in the reference subpopulations used in ***part B***: the femoral artery in *women*

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Subpopulation *without* CVD** | | | | | | |  | **Subpopulation *with* CVD**  **(n=199)** | | |
|  |  | ***without* treatmenta**  **(n=1,709)** | | |  | ***with*treatmenta**  **(n=278)** | | |  |
| Risk factor | Model | ß | 95%CI | *P-value* |  | ß | 95%CI | *P-value* |  | ß | 95%CI | *P-value* |
| Mean arterial pressure (10 mm Hg)b | 1 | -0.294 | -0.313; -0.274 | <0.001 |  | -0.270 | -0.351; -0.190 | <0.001 |  | -0.267 | -0.361; -0.173 | <0.001 |
|  | 2 | - | - | - |  | - | - | - |  | - | - | - |
|  | 3 | -0.279 | -0.320; -0.238 | <0.001 |  | -0.250 | -0.332; -0.168 | <0.001 |  | -0.229 | -0.328; -0.131 | <0.001 |
| Smoking |  |  |  |  |  |  |  |  |  |  |  |  |
| Previous smoking (vs. non-smoking) | 1 | 0.054 | -0.061; 0.170 | 0.358 |  | 0.076 | -0.185; 0.337 | 0.570 |  | 0.092 | -0.182; 0.366 | 0.511 |
|  | 2 | 0.052 | -0.058; 0.161 | 0.355 |  | 0.060 | -0.184; 0.304 | 0.629 |  | 0.112 | -0.144; 0.367 | 0.391 |
|  | 3 | 0.057 | -0.053; 0.166 | 0.312 |  | 0.059 | -0.190; 0.390 | 0.466 |  | 0.119 | -0.139; 0.377 | 0.368 |
| Current smoking (vs. non-smoking) | 1 | 0.251 | 0.130; 0.371 | <0.001 |  | 0.401 | 0.106; 0.696 | 0.008 |  | 0.242 | -0.148; 0.633 | 0.224 |
|  | 2 | 0.171 | 0.056; 0.285 | 0.003 |  | 0.288 | 0.010; 0.566 | 0.042 |  | 0.218 | -0.146; 0.583 | 0.240 |
|  | 3 | 0.184 | 0.067; 0.301 | 0.002 |  | 0.266 | -0.016; 0.548 | 0.065 |  | 0.163 | -0.203; 0.530 | 0.382 |
| Diabetes (yes) | 1 | -0.398 | -0.904; 0.106 | 0.117 |  | -0.298 | -0.574; -0.023 | 0.034 |  | -0.066 | -0.907; -0.409 | <0.001 |
|  | 2 | -0.126 | -0.559; 0.307 | 0.561 |  | -0.190 | -0.452; 0.071 | 0.153 |  | -0.538 | -0.779; -0.297 | <0.001 |
|  | 3 | -0.096 | -0.548; 0.356 | 0.669 |  | -0.189 | -0.456; 0.077 | 0.163 |  | -0.531 | -0.806; -0.256 | <0.001 |
| Total-to-HDL cholesterol ratio (unit) | 1 | -0.087 | -0.149; -0.025 | 0.007 |  | 0.000 | -0.108; 0.109 | 0.995 |  | -0.034 | -0.127; 0.059 | 0.476 |
|  | 2 | -0.029 | -0.090; 0.032 | 0.341 |  | 0.018 | -0.079; 0.116 | 0.708 |  | -0.035 | -0.122; 0.053 | 0.441 |
|  | 3 | -0.033 | -0.102; 0.035 | 0.324 |  | 0.041 | -0.064; 0.146 | 0.439 |  | -0.006 | -0.100; 0.088 | 0.897 |
| Body mass index (kg/m2) | 1 | -0.037 | -0.050; -0.025 | <0.001 |  | -0.024 | -0.036; -0.012 | 0.049 |  | -0.022 | -0.053; 0.008 | 0.147 |
|  | 2 | -0.006 | -0.019; 0.006 | 0.322 |  | -0.013 | -0.036; 0.010 | 0.264 |  | 0.000 | -0.030; 0.029 | 0.991 |
|  | 3 | -0.003 | -0.017; 0.011 | 0.680 |  | -0.011 | -0.036; 0.014 | 0.380 |  | 0.011 | -0.019; 0.041 | 0.470 |
| Use of BP-lowering medication (yes) | 1 | - | - | - |  | - | - | - |  | -0.347 | -0.591; -0.103 | 0.005 |
|  | 2 | - | - | - |  | - | - | - |  | -0.192 | -0.431; 0.046 | 0.114 |
|  | 3 | - | - | - |  | - | - | - |  | -0.076 | -0.339; 0.186 | 0.570 |
| Use of lipid-lowering medication (yes) | 1 | - | - | - |  | - | - | - |  | -0.052 | -0.351; 0.248 | 0.735 |
|  | 2 | - | - | - |  | - | - | - |  | -0.005 | -0.285; 0.275 | 0.972 |
|  | 3 | - | - | - |  | - | - | - |  | -0.036 | -0.327; 0.255 | 0.807 |
| Use of glucose-lowering medication (yes) | 1 | - | - | - |  | - | - | - |  | -0.559 | -1.118;-0.000 | 0.050 |
|  | 2 | - | - | - |  | - | - | - |  | -0.269 | -0.805; 0.266 | 0.324 |
|  | 3 | - | - | - |  | - | - | - |  | 0.085 | -0.325; 0.495 | 0.761 |

The regression coefficient ß represents the increase in carotid DC (in SD from the healthy population mean among *women* of the same age) per unit increase in each risk factor. Model 1: unadjusted; Model 2: adjusted for MAP; Model 3: adjusted for MAP and all other risk factors.aBP-, lipid- and glucose-lowering treatment; bmean arterial pressure was calculated by DBP+0.4\*PP.

Table S11: Funding of the included datasets

|  |  |
| --- | --- |
| **Centre** | **Origin of funding** |
| Rotterdam (the Netherlands) | The Rotterdam Study is funded by the Erasmus Medical Center and the Erasmus University, Rotterdam, Netherlands Organization for the Health Research and Development (ZonMw), the Research Institute for Diseases in the Elderly (RIDE), The Netherlands Heart Foundation, the Ministry of Education, Culture and Science, the Ministry for Health, Welfare and Sports, the European Commission (DG XII), and the Municipality of Rotterdam. Maryam Kavousi is supported by the AXA Research Fund. Oscar H. Franco works in ErasmusAGE, a center for aging research across the life course funded by Nestlé Nutrition (Nestec Ltd.); Metagenics Inc.; and AXA. Nestlé Nutrition (Nestec Ltd.); Metagenics Inc.; and AXA had no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review or approval of the manuscript. |
| Paris-HEGP/APHP-St Antoine Hospital (France) | HEGP studies: PHRC-APHP 2003 [AOM 03023P030439], INSERM [ANR-05-PCOD-004-01; Grants 2008-2011]; APHP-St Antoine Hospital, CASHMERE study: Pfizer [NCT00163163]; PPS3 study: French Foundation for Research in Hypertension [0607-10], Institute for Research in Public Health [grant 2008], grants from the Paris area, France [CCODIM 2009-2013]. |
| Utrecht (the Netherlands) | The SMART study was made possible by a grant from the University Medical Center Utrecht (UMCU, the Netherlands) and the echotracking measurements were made possible by a grant from the Netherlands Organization for Scientific Research (NOW) [904-61-154]; The WHISTLER birth cohort was supported with a grant from the Netherlands Organization for Health Research and Development (2100.0095), WHISTLER-Cardio was supported with an unrestricted strategic grant from the UMCU, the Netherlands. |
| Ghent (Belgium) | Funded by Research Foundation – Flanders [FWO; FWO G.0427.03, FWO G.0838.10N and 3G013109] |
| Maastricht/ Amsterdam (the Netherlands) | Hoorn study: Dutch Diabetes Research Foundation [DFN 98901], the Dutch Organization for Scientific Research (NWO) [940-35-034) and The Netherlands Heart Foundation (NHS) [98154]; Amsterdam Growth and Health Longitundinal Study (AGAHLS): Dutch Prevention Fund (ZON) and NHS [2006T050 to I.F.]; CODAM: Netherlands Organization for Scientific Research [940-35-034], the Dutch Diabetes Research Foundation [98.901] and NHS [2006T050 to I.F.]. |
| Leuven (Belgium) | The European Union ([IC15-CT98-0329-EPOGH, LSHM-CT-2006-037093 InGeniousHyperCare, HEALTH-F4-2007-201550 HyperGenes, HEALTH-F7-2011- 278249 EU-MASCARA] and the European Research Council Advanced Researcher Grant [294713 EPLORE]), the FondsvoorWetenschappelijkOnderzoekVlaanderen, Ministry of the Flemish Community, Brussels, Belgium [G.0575.06 and G.0734.09], and the KatholiekeUniversiteit Leuven, Belgium [OT/00/25 and OT/05/49] supported the Studies Coordinating Centre (Leuven, Belgium). |
| Shanghai (China) | The Ningbo workplace study: The National Natural Science Foundation of China [30871360, 30871081, and 81170245], the Ministry of Science and Technology [2006BAI01A03], the Shanghai Commissions of Science and Technology [07JC14047 and 06QA14043] and Education [07ZZ32 and 08SG20], and the Shanghai Shenkang Hospital Development Centre [SHDC12007318] |
| Pisa (Italy) | - |
| Mannheim (Germany) | The Mannheim Study was funded by an internal grant from the Mannheim Medical Faculty, Heidelberg University |
| Vilnius (Lithuania) | This research was funded by the European Social Fund under the Global Grant measure [VP1-3.1-SMM-07-K-03-041] |
| Antwerp (Belgium) | - |
| São Paulo (Brazil) | FundaçãoZerbini, Instituto do Coração  FAPESP, Fundação de Amapro a Pesquisa do Estado de São Paulo |
| Nancy (France) | ERA study: FRM [DCV-2007-0409250]; ARTEOS study: University of Nancy [CPRC 2005]. |
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| Maastricht-VitaK (the Netherlands) | - |
| Budapest (Hungary) | - |
| Rouen (France) | - |
| Paris-Foch (France) | - |
| Maastricht/Leuven (the Netherlands/Belgium) | - |
| Gdansk (Poland) | Polish Norwegian Research Found, Norway Grants, CareNorth Project, PNRF - A213 |
| Pilsen (Czech Republic) | Charles University Research Fund [P36] |
| Québec (Canada) | Canadian Institutes of Health Research |
| Montreal (Canada) | - |

**Appendix**

Table A1: Author list and participating centres/studies

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| Centre | Authors | Affiliations |
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*BE*, Belgium; *BR*, Brazil; *CDN*, Canada; *CH*, Switzerland; *CN*, China; *CZ*, Czech Republic; *D*, Germany; *F*, France; *H*, Hungary; *I*, Italy; *LT*, Lithuania; *N*, Norway; *NL*, the Netherlands; *PL*, Poland.