Supplementary Material

Methods

Exercise training regimen
Subjects in the ICE group were instructed to join indoor cycling classes at a local gym, 3 sessions per week over 12 weeks. Subjects were encouraged to reach a sense of high effort (rate of perceived exertion 17 on the Borg scale) during their work out session without using heart rate monitors to imitate a realistic scenario. The workout intensity was, however, checked during one of their first exercise sessions using a heart rate monitor (Polar S610), showing an average heart rate that corresponded to 75–88 % of their individual heart rate response (HRR), which was defined as \((HR_{exerc}-HR_{rest}) / (HR_{max}-HR_{rest})\), taking \(HR_{max}\) from the baseline ergometer test. At each indoor cycling session, an instructor guided them through a 45–60 min program consisting of a warm-up phase followed by more challenging interval phases where resistance and cadence were altered until a period of peak effort was reached, followed by a cool-down phase. Each subject self-registered completed exercise sessions in a log book and printouts of their registered visits at the gym were later collected.

Additional description of the vascular methods

Vascular ultrasound
A digital ultrasound system (HDI 5000, Philips Medical Systems, ATL Ultrasound, Bothell, WA, USA) equipped with an ECG module was used with a phased array (P4-2) transducer for determination of the end-diastolic diameter of the tubular ascending aorta and sinuses of Valsalva, using B-mode guided M-mode measurements in the parasternal view (Supplementary Fig. 15). The intra-observer in-between session coefficient of variation was 1.2 % for tubular ascending aortic diameter measurements.

Linear array broadband transducers were used for scanning the CCA and BA (L12-5), and AA (L9-4). Frozen end-diastolic, magnified B-mode images were saved for later analysis on a PC with software (Artery Measurement System II, Image and Data Analysis, Gothenburg, Sweden) for off-line measurement of lumen diameter (LD) and intima-media thickness (IMT). Calibration and subsequent measurement was performed by manually tracing a cursor along the leading edge of the intima-lumen echo of the near wall, leading edge of the lumen-intima echo and media-adventitia echo of the far wall to obtain mean LD and far wall IMT along a 10 mm long section of the artery (Supplementary Fig. 15c). During analysis, the measurement window was hidden for the operator and values were saved in a text file.

Arterial wall tracking
An ultrasound system (Esaote AU5, Esaote Biomedica, Florence, Italy) equipped with a 7.5 MHz linear array, and a 3.5 MHz curved array transducer was used for real-time imaging of CCA, BA (7.5 MHz) and AA (3.5 MHz). The system was connected to a PC, with the Wall Track System software (WTS2, Pie Medical, Maastricht, The Netherlands). In short, ECG leads were connected to the subject and after visualization of the artery in a B-mode longitudinal section, the scanner was switched to M-mode, and the M-mode line was positioned perpendicular to the anterior and posterior vessel wall. A window of sufficient width to include the envelope from both anterior and posterior wall was chosen, and the radio frequency signal was transferred to the PC for storage. A sample volume was automatically positioned on the media-adventitia transition of the anterior and posterior wall and tracked the positions over 4 s,
followed by calculation of the diameter distension curve (Supplementary Fig. 2s).

Blood pressure measurement

A blood pressure cuff of appropriated size was wrapped around the subject’s upper arm. The cuff was connected to an oscillometric blood pressure device (Dinamap PRO 200 Monitor, Critikon, Tampa, FL, U.S.A) that automatically calculates systolic, diastolic and mean arterial blood pressure together with heart rate with the aid of an implemented algorithm.

Applanation tonometry

The SphygmoCor system (Model MM3, AtCor Medical, Sydney, Australia) equipped with a Millar pressure tonometer was used to sample pulse waves during ten seconds to a commercially available software for online analysis (SphygmoCor version 7.0). The average central pressure waveform was obtained by a transfer function, calculated from the radial artery pressure waveform that was calibrated by taking the brachial systolic and diastolic pressures (Supplementary Fig. 2sb). Time to reflection (Tr), augmentation index (AI) and augmentation pressure (Aug) were automatically calculated from the aortic waveform. Each file was given a quality index from 0 to 100 by the software, where the value 100 indicates regular heart rhythm and similar pressure wave configuration for all cardiac cycles. In most saved files, an index > 90 was obtained, while the files with a quality index below 75 were rejected. Further prerequisites for accepting a file were; a true arterial pressure wave configuration and reasonable automatic identification of the 2 peaks, P1 and P2, during systole.

Carotid artery pressure waveform was calibrated by taking mean arterial pressure (MAP) from the integrated radial artery pressure curve in combination with diastolic brachial pressure (DBP).

Calculations and data analysis

The distensibility coefficient (DC, unit 10⁻³/kPa) is the relative increase of arterial cross-section area for a given increase in pressure [49].

\[
DC = \frac{D \cdot D + \Delta D^2}{\Delta P \cdot D^2}
\]

where D is the minimum diastolic diameter in mm, \(\Delta D\) is pulsatile diameter change, \(\Delta D^2\) is the square of the pulsatile diameter change in mm and \(\Delta P\) is pulse pressure in kPa. The arm pulse pressure (PP) was used as a surrogate measure for local pulse pressure when DC of the AA was calculated, whereas the tonometer derived local PP was used in the calculation of CCA DC. The inter-session coefficients of variation for distensibility coefficients calculated from measurements in the CCA and the BA were 10 % and 14 %, respectively, in a previous methodological evaluation at our laboratory.

The radial augmentation index (RA AI) is defined as the pressure at the second systolic shoulder (P2), divided by pressure at the first peak (P1)

\[
RA AI\% = \frac{P2}{P1} \times 100
\]
The aortic augmentation index (AI) is defined as the increase of pressure over the first systolic shoulder (P1) due to wave reflection (Aug), divided by pulse pressure (ΔP).

\[ AI (\%) = \frac{\text{Aug}}{\text{PP}} \times 100 \]

To account for differences in heart rate, AI@75 is also presented as the AI normalized to a heart rate of 75 min⁻¹.

References