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Non-invasive ultrasound-based assessment of ventricular–arterial interaction in vascular Ehlers–Danlos syndrome patients

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Abstract The role of ventricular–arterial hemodynamic interaction in the occurrence of arterial dissection and rupture in vascular Ehlers–Danlos syndrome (vEDS) is unknown. We recently introduced an ultrasound-based method to extract, from common carotid artery (CCA) diameter waveforms, central arterial properties and left ventricular (LV) systolic time intervals. We obtained CCA diameters, compliance and distensibility coefficients, and LV isovolumic contraction and ejection periods (ICP and EP) of 19 vEDS patients (aged 27–65 yrs) and 19 age-matched healthy controls. CCA distension and compliance tended to be lower in vEDS subjects ($p = 0.062$ and $p = 0.073$), especially in younger patients. ICP (−12 ms) and EP (−24 ms) were shorter ($p < 0.001$), while heart rate was increased (+10 bpm; $p < 0.001$) in vEDS. The ICP/EP ratio and estimated isovolumic dP_{LV}/dt indicated increased LV contractility in vEDS. In conclusion, vascular EDS patients tend to have a lower CCA compliance but a normal pulse pressure, most likely reflecting reduced physical fitness.

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Introduction

Vascular type (IV) Ehlers—Danlos syndrome (vEDS) is a genetic disorder (mutations in COL3A1), leading to abnormalities in type III procollagen which affect connective tissue development and wound healing. Affected patients suffer from rupture and dissection of large arteries due to fragility of arterial wall structure and increased wall stress.[1—3] However, the role of ventricular—arterial interaction in the occurrence of vascular complications of vEDS is still unknown. A normal stroke volume ejected into a less compliant arterial system will produce a greater pulse pressure; similarly, an increased stroke volume into a normal compliant load will also increase pulsatile load on the arterial wall.

We recently developed a method to derive both central arterial and LV function parameters from non-invasively recorded carotid artery diameter waveforms by means of ultrasonography,[4,5] giving the opportunity to study ventricular and arterial function, and their interaction. We retrospectively analysed existing M-mode ultrasound recordings of 19 vEDS patients and 19 age-matched controls. We hypothesized that in vEDS arterial distensibility may be lower than normal, because stiff structures are more prone to disintegrate than elastic structures when put under stress. Furthermore, we expected to observe normal LV function because, to the best of our knowledge, cardiac events are rather uncommon in vEDS.[3]

Methods

Study population

Vascular Ehlers—Danlos syndrome (vEDS) patients were diagnosed as reported previously[1] and following the guidelines defined in the nosology for Ehlers—Danlos syndromes.[3,6] The patients were apparently in good health at the time of measurement. None of them were taking any anti-hypertensive drugs and none of the patients had a history of diabetes or hypercholesterolemia. An age-matched control group was randomly selected from an existing ultrasound recording database of normal healthy subjects. None of the controls had a history of cardiovascular disease, diabetes or hypercholesterolemia, and all of them were normotensive and not taking any medication affecting cardiovascular function. The medical ethical committees of Saint-Germain-en-Laye (France) and Maastricht University Medical Centre (the Netherlands) approved the study. All subjects gave written informed consent prior to enrolment.

Measurement protocol

Ultrasound and blood pressure measurements were performed under controlled conditions, as described previously.[1,7] Briefly, measurements were done in a quiet and temperature-controlled room (20—22 °C), after subjects were allowed to acclimatize for 10 min in supine position. Patients remained in this position during subsequent measurements. Brachial artery blood pressures were measured by automated oscillometry (Dinamap model 845, Critikon) in all subjects. Per subject, a total of six measurements of systolic (SBP) and diastolic blood pressures (DBP) were taken before, in between, and after the ultrasound M-mode recordings and averaged subsequently. After localizing the right common carotid artery (CCA) with a medical ultrasound scanner in B-mode, M-mode recordings were obtained (7.5 MHz linear array, P350 system, Esaote Europe, Maastricht, the Netherlands). The ultrasound probe was positioned with the M-line intersecting the CCA perpendicularly, 2—3 cm proximal to the carotid artery bifurcation. A minimum of three (range 3—7) repeated measurements was obtained per subject. Recording length was 5 s and thus each measurement covered 4—7 consecutive heartbeats. Radiofrequency data were directly recorded on a dedicated acquisition system, with a single ECG tracing (lead II) acquired simultaneously as a time reference.

Radiofrequency processing and timing analysis

The radiofrequency signals from the anterior and posterior artery walls were tracked automatically to obtain the diameter waveform,[8] utilizing spatial and temporal estimation windows of 600 μm and 10 ms, respectively. Temporal estimation windows were half-overlapping, resulting in an effective sample interval of 5 ms for the diameter waveforms. Left ventricular (LV) isovolumic contraction (ICP) and ejection periods (EP), and CCA diastolic diameter (Dd), and distension (ΔD; systolic minus diastolic diameter) were obtained as previously described.[4,8] Second-derivative and post-processing filters had cut-off frequencies of 60 Hz and 30 Hz, respectively. These enable detection of time intervals down to 20 ms with less phase distortion than the previously employed 40 and 20 Hz cut-offs.[4] Figure 1 (left panel) illustrates extraction of ICP and EP from the CCA distension waveform on the basis of the second time-derivative/acceleration waveform.[4,5]

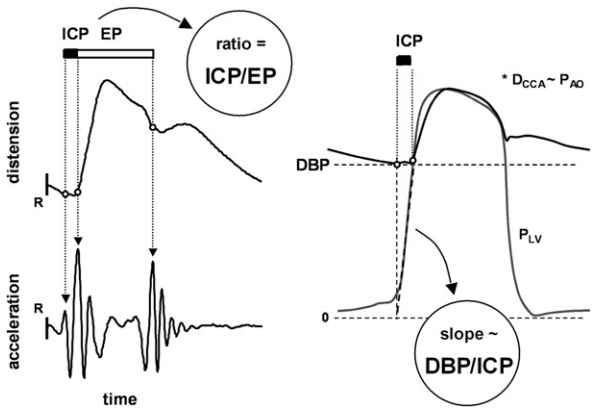

Figure 1 Left: Extraction of left ventricular isovolumic contraction period (ICP) and ejection period (EP) from the common carotid artery (CCA) diameter waveform, enabling calculation of ICP-to-EP ratio. R indicates the ECG R-wave. Right: Approximation of left ventricular isovolumic dP/dt by the DBP/ICP index. P_{LV}, left ventricular pressure. *It is assumed that CCA diameter (D_{CCA}) and aortic pressure (P_{AO}) waveforms are similar in terms of relative timing.