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Original article

Non-invasively estimated left atrial stiffness is associated with short-term recurrence of atrial fibrillation after electrical cardioversion

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ABSTRACT

Background: As atrial stiffness (K_{la}) is an important determinant of cardiac pump function, better mechanical characterization of left atrial (LA) cavity would be clinically relevant. Pulmonary venous ablation is an option for atrial fibrillation (AF) treatment that offers a powerful context for improving our understanding of LA mechanical function. We hypothesized that a relation could be detected between invasive estimation of K_{la} and new non-invasive deformation parameters and traditional LA and left ventricular (LV) function descriptors, so that K_{la} can be estimated non-invasively. We also hypothesized that a non-invasive surrogate of K_{la} would be useful in predicting AF recurrence after cardioversion.
Methods: In 20 patients undergoing AF ablation, LA pressure–volume curves were derived from invasive pressure and echocardiographic images; K_{la} was calculated during ascending limb of V-loop as ΔLA pressure/ΔLA volume. 2D-speckle-tracking echocardiographic LA and LV longitudinal strains and volumes, ejection fraction (EF) and ventricular stiffness (K_{lv}), as obtained from mitral deceleration time, were tested as non-invasive K_{la} predictors. In 128 sinus rhythm patients 1 month after electrical cardioversion for persistent AF, non-invasively estimated K_{la} (*computed*-K_{la}) was tested as predictor of recurrence at 6 months.
Results: Tertiles of mean LA pressure correlated with increasing K_{la} (trend, $p = 0.06$) and decreasing LA peak strain, LVEF, and LV longitudinal strain ($p = 0.029$, $p = 0.019$, and $p = 0.024$). There were no differences in LA and LV volumes and K_{lv} across groups. Multiple regression analysis identified LV longitudinal strain as the only independent predictor of K_{la} ($p = 0.014$). Patients in highest quartile of *computed*-K_{la} (estimated as [log] = 0.735 + 0.051 × LV strain) tended to have highest AF recurrence rate (25%) as compared with remaining 3 quartiles (9%, 9%, 3%, $p = 0.09$).
Conclusion: K_{la} can be assessed invasively in patients undergoing AF ablation and it can be estimated non-invasively using LV strain. AF recurrence after cardioversion tends to be highest in highest quartile of *computed*-K_{la}.

Background

Atrial stiffness (K_{la}) is an important determinant of cardiac pump function. It has been demonstrated that a flexible atrium to the inlet of an artificial heart substantially improves the heart's output [1]. Conversely, an increase in K_{la} should reduce stroke volume and forward flow. Furthermore, left atrial (LA) wall stiffening, as assessed combining LA strain with invasively measured or noninvasively estimated mean pulmonary capillary wedge pressure, has been shown to be accurate in identifying patients with diastolic heart failure [2]. Thus, better mechanical characterization of the LA cavity would be clinically relevant [3], particularly in view of the potential association between LA stiffening and development of atrial fibrillation (AF) recurrences after AF ablation or cardioversion.

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Pulmonary venous ablation is a relatively new option for AF treatment that offers a powerful context for improving our understanding of LA mechanical function. Since transseptal puncture is most commonly performed with transesophageal echocardiographic guidance, LA dimensions and LA pressure–volume data can be obtained simultaneously. It is possible to integrate measurements of LA dimension with recordings of LA pressure, in order to generate pressure-dimension or pressure–volume curves, and from these K_{la} can be calculated during the ascending limb of the V-loop as the ratio of ΔLA pressure and ΔLA volume.

Furthermore, the special context represented by the procedure of pulmonary venous isolation for AF makes it feasible to test correlations between an invasive estimate of K_{la} and new non-invasive LA and left ventricular (LV) functional parameters describing cardiac mechanical characteristics. We hypothesized that a relation could be detected between invasive estimation of K_{la} and new non-invasive deformation parameters and traditional LA and LV function descriptors, so that K_{la} may be estimated non-invasively. We also hypothesized that a non-invasive surrogate of K_{la} would be useful in predicting AF recurrence after electrical cardioversion.

Methods

Invasive evaluation of left atrial stiffness (K_{la}) during atrial fibrillation ablation

Patients

Twenty-five consecutive patients, with no more than mild mitral regurgitation and with persistent or paroxysmal AF resistant to medical therapy, underwent NavX^{TM}-guided AF ablation (St Jude Medical, St Paul, MN, USA). Written informed consent was obtained from each patient, in accordance with Institutional Human Studies Committee Guidelines.

Transesophageal echocardiography

Transesophageal echocardiography was performed under light sedation by the imaging cardiologist just before the transseptal puncture [Vivid pro echocardiography machine (GE Medical System, Horten, Norway); 6T, KZ191683 probe, GE Medical System] [4].

Five patients were excluded from the final analysis because of suboptimal echocardiographic views or pressure artifacts, resulting in an overall feasibility of 80% (20 out of 25 patients).

Left atrial volume assessment

LA volume data were calculated from the superior-inferior dimension of the cavity, as imaged from expanded mid-esophageal four- and/or two-chamber views. Superior-inferior dimension was measured by M-mode echocardiography, directing the interrogating beam toward the mitral annulus, close to the anterior leaflet of the mitral valve. The base-to-apex dimension of the LA cavity could thus be defined, on the M-mode tracing, as the distance between a point 0.5 cm below the first echo generated from the surface of the transducer and the mitral annulus [5] and measured continuously during the entire cardiac cycle (Fig. 1A).

The superior-inferior diameter of the LA was obtained off-line by subtraction, after digitization of the superior and inferior boundaries, using a commercially available *ad hoc* software package (Sigmascan, version 5.0 for Windows, Jandel, San Rafael, CA, USA). At least 5 beats per patient were stored; ectopic and immediate post-ectopic beats were excluded from the digitization process.

Sixty-five percent of the patients were in AF at the time of the examination; in these subjects non-consecutive beats were selected to obtain recordings with comparable R-R intervals. A linear interpolation algorithm was then used to normalize each beat to a fixed number of time sampling points ($n = 200$), to enable multiple beats averaging (Fig. 1B).

The LA volume, modeled empirically as a sphere, was estimated by the formula: $V = 0.52 \times D3$, where V is LA volume and D is the superior to inferior dimension of the atrium in the M-mode tracing [6,7].

Left atrial pressure measurement

Time-adjusted LA pressure was measured simultaneously with imaging data using a fluid-filled catheter (0.5–1.3 mm in diameter and 71 cm long, BRK, St Jude Medical) that had been introduced transseptally by the electrophysiologist and sequentially connected to a strain-gauge transducer (Haemofix-Combitrans Monitoring, Braun, Melsungen, Germany). A line [6.0 mm in diameter and 150 cm long (Braun)] with a 3-way stopcock at the end was used to display the pressure tracing on the screen of a physiologic recorder (Tram-Rac A4, Mac-lab 6.0, GE Medical System). The catheter, routinely used in our institution for monitoring LA pressure during AF ablation, was placed under transesophageal guidance, filled with saline, and visually leveled to the right atrium. Continuous LA pressure signals were also visible on the screen of the echo machine (Fig. 1A).

The LA pressure monitoring system had been previously tested in an in vivo animal (pig) model, relative to a micromanometer-tipped catheter (Mikrotip model PC-350, Millar Instruments, Houston, TX, USA). The time-delay of the system relative to the micromanometer catheter (median 50 ms; range 0–60 ms) was subsequently used as a time-correction factor for the LA pressure tracing in our patients. An electrocardiographic (ECG) trace was also recorded in real-time.

The LA volume and pressure traces were then used to generate the LA pressure–volume loop using a commercially available spreadsheet, the transesophageal base-to-apex LA diastolic dimension correlating well with the derived four-chamber LA cavity area ($r = 0.56$, $y = 0.95x + 3.5$, $p = 0.01$, SEE = 0.8 cm).

Left atrial stiffness (K_{la}) was assessed using the pressure–volume loop during the ascending limb of the V-loop and computed as the ratio of ΔLA pressure – from the time of minimal to maximal systolic pressure – and ΔLA volume during this time period (Fig. 1C).

Transthoracic echocardiography

Transthoracic echocardiographic data were acquired within 15 ± 9 days from the ablation procedure using a 3.5 MHz variable-frequency transducer (GE Medical System), as in our previous studies devoted to LA mechanical function [8,9].

LA volume was calculated according to the biplane area-length method: $8/3\pi \times$ [(LA area in apical four-view chamber × LA area in apical two-chamber)/d], where d is the shorter LA long-axis diameter in apical four- and two-chamber views [10].

LV volumes were obtained by real-time three-dimensional echocardiography using three apical longitudinal planes and then by manually tracing the endocardial border using commercial software excluding the papillary muscles (EchoPAC PC version BT112, GE Healthcare). In order to estimate LV volumes this software constructs a triangular mesh by three-dimensional interpolation between the traces, and end-diastolic and end-systolic volumes are calculated by surface triangulation and summation of all triangles by the divergence theorem [11]. LV ejection fraction (EF) is calculated from the three-dimensional end-diastolic and end-systolic volumes [12]. LV mass was assessed with the two-dimensional area–length formula [13]. LA area and volume, and LV volume and mass were indexed to body surface area. Mitral deceleration time, taken as an index of diastolic

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