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Objective evaluation of changes in left ventricular and atrial volumes during parabolic flight using real-time three-dimensional echocardiography

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Caiani, E. G., L. Sugeng, L. Weinert, A. Capderou, R. M. Lang, and P. Vaïda. Objective evaluation of changes in left ventricular and atrial volumes during parabolic flight using real-time three-dimensional echocardiography. *J Appl Physiol* 101: 000–000, 2006. First published April 6, 2006; doi:10.1152/jappphysiol.00014.2006.—We tested the feasibility of real-time three-dimensional (3D) echocardiographic (RT3DE) imaging to measure left heart volumes at different gravity during parabolic flight and studied the effects of lower body negative pressure (LBNP) as a countermeasure. Weightlessness-related changes in cardiac function have been previously studied during spaceflights using both 2D and 3D echocardiography. Several technical factors, such as inability to provide real-time analysis and the need for laborious endocardial definition, have limited its usefulness. RT3DE imaging overcomes these limitations by acquiring real-time pyramidal data sets encompassing the entire ventricle. RT3DE data sets were obtained (Philips 7500, X3) during breath hold in 16 unmedicated normal subjects in upright standing position at different gravity phases during parabolic flight (normogravity, 1 G_z; hypergravity, 1.8 G_z; microgravity, 0 G_z), with LBNP applied (–50 mmHg) at 0 G_z in selected parabolas. RT3DE imaging during parabolic flight was feasible in 14 of 16 subjects. Data were analyzed (Tomtec) to quantify left ventricular (LV) and atrial (LA) volumes at end diastole and end systole, which significantly decreased at 1.8 G_z and increased at 0 G_z. While ejection fraction did not change with gravity, stroke volume was reduced by 16% at 1.8 G_z and increased by 20% at 0 G_z, but was not significantly different from 1 G_z values with LBNP. RT3DE during parabolic flight is feasible and provides the basis for accurate quantification of LV and LA volume changes with gravity. As LBNP counteracted the increase of LV and LA volumes caused by changes in venous return, it may be effectively used for preventing cardiac dilatation during 0 G_z.

weightlessness; countermeasures

DURING SPACEFLIGHT, CHANGES in gravity (G_z, head-to-foot acceleration) affect the cardiovascular system by causing fluid shifts from the lower extremities toward the head and thorax, thus altering central filling volumes (FVs) and pressures (15, 16, 23, 31). These hemodynamic alterations, which directly influence heart chamber dimensions and function, are responsible for many of the adverse effects associated with the postflight orthostatic intolerance observed in astronauts (20–22).

The potential for commercial spaceflight has made a precise understanding of the early cardiovascular adaptation to weightlessness important. As more individuals have the opportunity

to fly in space, standards will need to be set to decide what level of cardiovascular function is needed to tolerate the acute headward fluid shift that occurs in weightlessness. Some individuals with nondistensible ventricles potentially could develop pulmonary edema upon entering weightlessness. Measurements of the expected changes in ventricular volumes, atrial volumes, and peak filling rate (PFR) upon entering weightlessness are needed to help set appropriate standards. In addition, certain countermeasures, like lower body negative pressure (LBNP) devices (24, 38), could be used to reduce the fluid shift and prevent or treat adverse events.

Moreover, the evaluation of cardiovascular physiology under different gravitational loads may provide some crossover benefits to clinical medicine on Earth. Ground-based studies represent an invaluable opportunity to investigate human physiology during simulated microgravity (0 G_z) conditions. Among them, parabolic flight presents a unique opportunity to study the immediate physiological adaptations of the cardiovascular system to different gravity conditions.

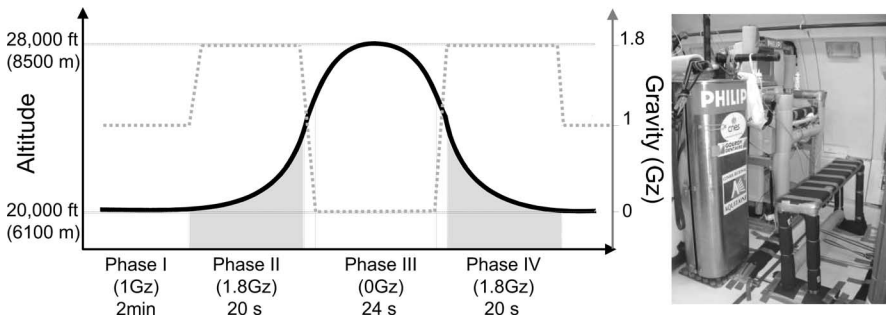
Two-dimensional (2D) echocardiography (2DE) has been the principal imaging modality used in space programs to evaluate changes in the cardiovascular system and to test the effectiveness of countermeasures employed to alleviate these changes (34). Using 2DE, patterns of adaptation of left ventricular (LV) dimensions to 0 G_z during short- and long-term missions have been previously described (3, 10, 11, 25, 37, 41). However, although 2DE is routinely used in clinical practice to measure heart chamber dimensions, wall thickness, and function, this imaging technique is limited because it relies on correct probe positioning to avoid acquisition of foreshortened apical views. In addition, derivation of volumetric parameters from multiple 2D views requires the use of geometric models, which may introduce additional errors (19, 43, 49).

In an attempt to circumvent these constraints, Zoghbi et al. (50) have developed a nongeometric three-dimensional (3D) echocardiographic (3DE) method by acquiring multiple short-axis 2DE images of the LV from a single pivoting point and reconstructing the volume offline. Using this approach, 3DE was previously used in space (Spacelab Life Sciences-1 and -2 missions) to measure LV volumes (8). However, this methodology is limited by several factors, such as cumbersome data acquisition required for offline 3D reconstruction and the need for tedious offline manual tracings of endocardial borders in multiple planes.

AQ: 6 Address for reprint requests and other correspondence: E. G. Caiani, Politecnico di Milano, Dipartimento di Bioingegneria, Piazza L. da Vinci, 32, 20133 Milano, Italy (e-mail: caiani@biomed.polimi.it).

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AQ: 7 Fig. 1. *Left*: parabolic flight trajectory (solid line) and corresponding gravity (G_z) along the parabola (shaded dashed line). *Right*: experimental setup onboard the Airbus. On the *left*, in the foreground, is the lower body negative pressure (LBNP) chamber and, in the background, the ultrasound equipment embedded into a safety rack. On the *right* are a bench and straps on the floor utilized to stabilize the sonographer to prevent free floating during microgravity ($0\ G_z$). $1\ G_z$, normogravity; $1.8\ G_z$, hypergravity.



The recent development of second-generation full-matrix array transducers, capable of high spatial resolution and near real-time acquisition of wide-angled pyramidal 3DE data sets, has overcome many of the limitations of 2DE, and thus provided the basis for accurate estimates of LV volumes (13, 26, 30), mass (36), and function (18).

We hypothesized that real-time 3DE (RT3DE) could be used in a weightlessness environment for accurate quantification of the adaptations in LV and left atrial (LA) dimensions in response to changes in gravity. Accordingly, the aims of this study were 1) to test the feasibility of RT3DE imaging of the LV and LA in a weightlessness environment; 2) to evaluate the changes in LV and LA volumes occurring with changes in gravity during parabolic flight; and 3) to test the effectiveness of the LBNP device in reducing LV and LA volumes during $0\ G_z$ by counteracting the decrease in hydrostatic pressure in the lower body.

METHODS

Subjects. Eighteen normal volunteers (13 men and 5 women, mean age 38 ± 14 yr) without a history of cardiovascular disease were enrolled in the study, after providing written, informed consent. All subjects were screened before participation to ensure adequate acoustic windows, even when imaging in the upright position. After completion of the preliminary screening, 16 out of the 18 volunteers (12 men and 4 women, mean age 36 ± 13 yr) were selected. None of the subjects were taking medication before and/or during the flights. This study was approved by both the French [Centre National d'Etudes Spatiales (CNES)] and the European Space Agency (ESA).

Equipment and protocol. The study was conducted during two parabolic flight campaigns (CNES: November 2004, ESA: October 2005), on board of the ESA-CNES ZeroG Airbus A300 aircraft,

performed in Bordeaux, France. Each flight lasted 2.5–3 h and included 31 parabolas.

Instantaneous gravity was continuously measured using the aircraft's accelerometer. Gravity variations during a parabolic flight trajectory include four consecutive phases (Fig. 1, *left*): normogravity (phase I: head-to-foot acceleration, $1\ G_z$) before parabola initiation; mild hypergravity (phase II: $1.8\ G_z$, 20 s) during the ascending phase of the parabola; microgravity (phase III: $0\ G_z$, 24 s) at the top of the parabola; and a second period of mild hypergravity (phase IV: $1.8\ G_z$, 20 s) during the descending phase of the parabola. Between consecutive parabolas, a period of steady state (at $1\ G$) persisted for a minimum of 2 min.

Each subject was imaged in the upright standing position during a maximum of 12 consecutive parabolas, with the abdomen and lower extremities placed inside a LBNP chamber (Fig. 1, *right*). To allow the lower limbs to stay relaxed (to maximize blood and fluid movement to/from the lower body), subjects were placed on a saddle within the LBNP chamber with the arms secured to the structure by straps. To test the effectiveness of LBNP in counteracting the effects of $0\ G_z$ by reducing venous return, a negative pressure of -50 mmHg was applied during the $0\ G_z$ phase in selected parabolas (from 3 to 5) in random order.

RT3DE imaging. Transthoracic RT3DE was performed from the apical window, with a full-matrix array transducer (X3, 2–4 MHz) in the harmonic mode using a SONOS 7500 (Philips Medical Systems, Andover, MA). To avoid body movement during acquisition, both subject and sonographer were stabilized against free floating. A second operator aided in optimizing image quality (gain and compression) and completing data acquisition.

For each gravity phase of the parabola, one RT3DE data set representing one cardiac cycle (frame rate 20 Hz) was acquired during a breath hold, while avoiding Mueller or Valsalva maneuvers, and thus trying to minimize changes in intrathoracic pressure. Image acquisition was performed using the wide-angled acquisition mode, in

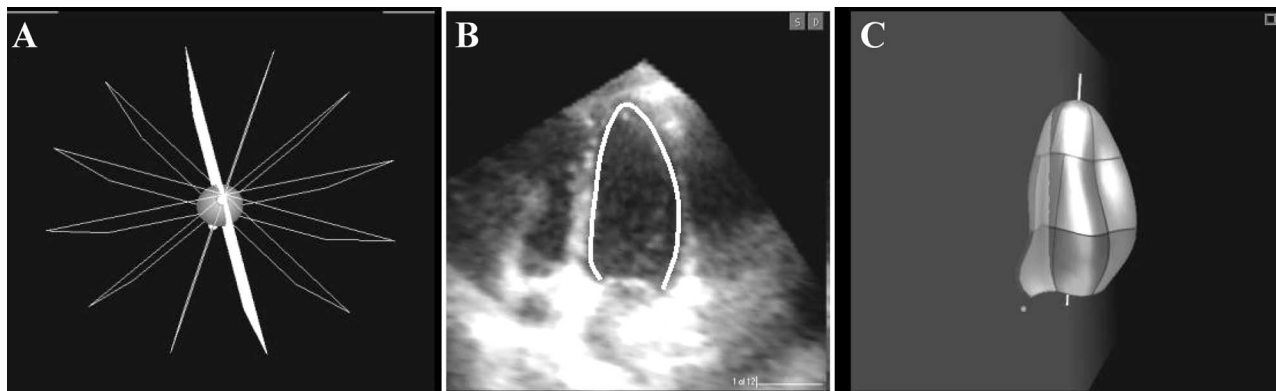


Fig. 2. Left ventricular (LV) volume analysis procedure (see text for details). A: LV long-axis and 6 equi-angled two-dimensional (2D) cut-planes selection; B: semiautomatic tracing of the LV endocardial contour in each cut-plane; C: automated computation of the three-dimensional (3D) cast representing the LV cavity volume.

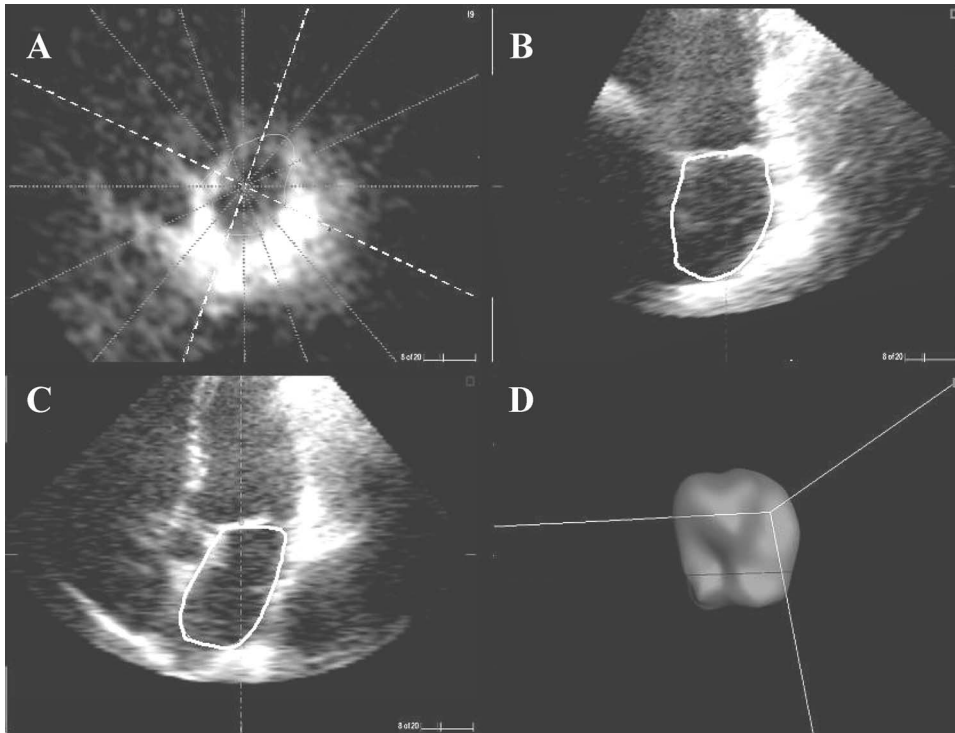


Fig. 3. Left atrial (LA) volume analysis procedure. A: LA long-axis and 8 equi-angled 2D cut-planes selection; B and C: semiautomatic tracing of the LV endocardial contour in each set of two orthogonal cut-planes; D: automated computation of the 3D cast representing LA cavity volume.

which four wedge-shaped subvolumes ($93^\circ \times 21^\circ$) were obtained over eight cardiac cycles with ECG gating. In this mode, each subvolume acquisition is triggered to the R-wave of every other heartbeat to allow sufficient time for the probe to be recalibrated and each subvolume stored. Particular care was taken to include the entire LV and atrium within the pyramidal 3D scan volume.

Image acquisition at 1 G_z was performed 10 s before the initiation of phase II, while image acquisition at 1.8 G_z, 0 G_z, and final 1.8 G_z was performed 5 s after the beginning of phases II, III, and IV, respectively, to avoid data acquisition during the short initial transition during which abrupt changes in cardiac volumes and heart rate may occur.

RT3DE volume analysis. The RT3DE data sets acquired in each subject during each phase of the parabola (i.e., I, II, III and IV) were first visually inspected. Only parabolas with proper LV and LA endocardial visualization in each gravity phase, assessed in two orthogonal cut-planes, corresponding to apical two- and four-chamber views, were selected for analysis. The RT3DE data sets were analyzed in random order by an expert reader, blinded to the subject's identity and to the gravity phase.

To quantify LV dimensions, each data set was analyzed offline using commercially available software (4D LV Analysis, TomTec), previously described in detail (30). Briefly, after identifying the LV long axis, six equi-angled long-axis cut-planes were automatically generated (Fig. 2A). To define the mitral valve plane in each of these cut-planes, the mitral valve annulus was identified in the end-diastolic (ED) and end-systolic (ES) frames. An ellipse was then placed in the ED and ES frames in each of the six selected long-axis cut-planes, manually adapting its shape and angular position to fit as close as possible to the endocardial border. Following this initialization phase, the semiautomatic endocardial contour detection procedure was applied, resulting in a detected endocardial contour for each cut-plane and for each consecutive frame throughout the cardiac cycle (Fig. 2B). To verify the correctness of the border detection, each cut-plane was then visualized in the cine mode with the detected contour overimposed, to allow the operator to perform manual adjustments, when necessary. Finally, for each frame, the contours of the six cut-planes

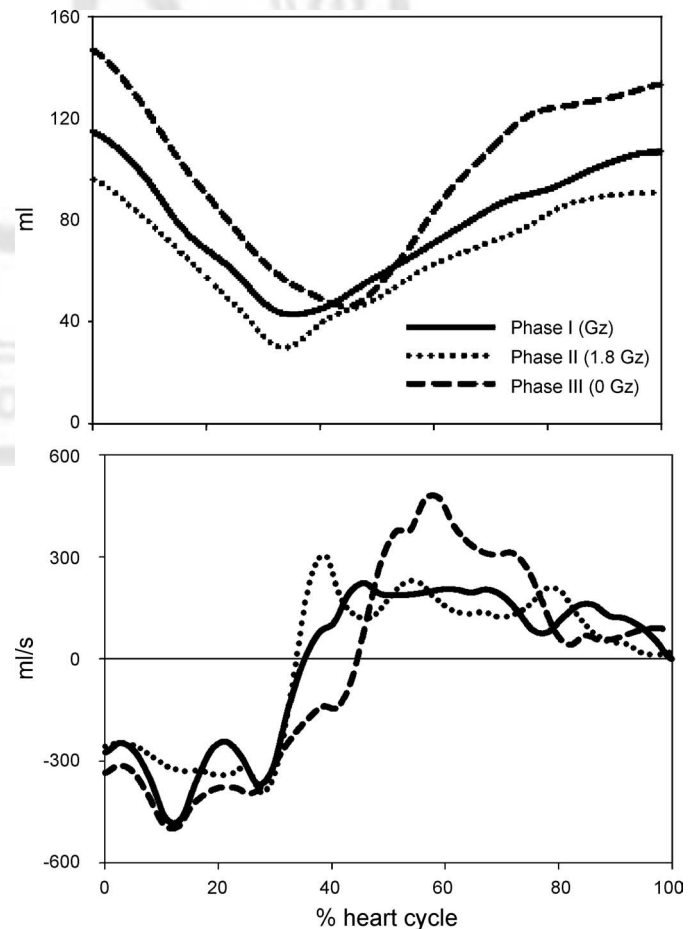


Fig. 4. LV volume vs. time curves (top) and corresponding first derivatives (bottom), both expressed in percentage of the heart cycle, obtained from a subject during the first three G_z phases of the parabola.

were then interpolated and displayed as a wire-frame model in the 3D space (Fig. 2C), from which the enclosed LV volume was computed using Gaussian quadrature formulas.

Global LV volume vs. time curves were obtained, from which ED (EDV) and ES volumes (ESV), defined as the maximum and the minimum volume, respectively, were measured. Stroke volume (SV) was computed as the difference between EDV and ESV, and ejection fraction (EF) was derived as $100 * SV/EDV$. Moreover, the first derivative of LV volume vs. time was computed, and the PFR and peak ejection rates (PER) were calculated.

To quantify the LA volumes in the ED and ES frames, the same RT3DE data sets were analyzed offline using commercial software (EchoView, TomTec). After selecting the LA long axis, eight equi-angled 2D long-axis cut-planes were generated (Fig. 3A), and, in each pair of orthogonal planes, manual tracing of the atrial endocardial borders was performed using an interactive spline interpolation algorithm (Fig. 3, B and C). After interpolation of the traced contours in a 3D wire-frame model (Fig. 3D), the LA cavity volume was calculated automatically (29).

The LA volume computed in the ES frame was defined as LA_{max} , whereas the LA volume computed in the ED frame was defined as LA_{min} . The LA reservoir function was assessed using FV, defined as $(LA_{max} - LA_{min})$, and the expansion index (EI), defined as $100 * FV/LA_{min}$. The overall diastolic emptying index (DEI) was calculated as $100 * FV/LA_{max} * 100$ (44). Moreover, to evaluate possible asymmetries in LA shape changes with 0 G_z , the LA diameters along its major (D2, antero-posterior dimension) and minor (D1, medial-lateral dimension) axes were computed at 1 G_z and 0 G_z .

Statistical analysis. LV and LA volumes and derived parameters, normalized by their value at 1 G_z , were averaged for all subjects in each gravity phase. Data were displayed as means \pm SD. One-way ANOVA with repeated measures ($P < 0.05$, Tukey test) was used to test the differences between gravity phases. The effectiveness of LBNP in reducing changes in LV, LA volumes, and derived parameters at 0 G_z was tested by paired Student's *t*-test. Differences were

considered significant for $P < 0.05$ compared with the results at 0 G_z obtained without LBNP.

RESULTS

RT3DE imaging during parabolic flight was feasible in 14 of 16 subjects (87.5% of success), in which RT3DE data sets were acquired for each gravity phase (1 G_z , first 1.8 G_z , 0 G_z , second 1.8 G_z). In the remaining two subjects, adequate visualization of the LV during all gravity phases of the parabola was difficult due to unpredictable shifting of the heart within the chest cavity. In these subjects, repositioning of the probe required more time than the 20 s available for image acquisition during each phase of the parabola.

Of these 14 subjects, only 10 had also the RT3DE data sets acquired during 0 G_z with LBNP activated. In the remaining 4 of 14 subjects, this data acquisition was not possible due to subjects experiencing motion sickness (3 of 14), and due to flight interruption caused by weather conditions (1 of 14).

Quantitative analysis of LV and LA chambers was feasible in all RT3DE data sets selected for analysis. The time required to analyze a complete RT3DE data set to compute the LV volume was ~ 15 min, whereas the time required to analyze a single frame to measure the LA volume was ~ 3 min. Results obtained from the analysis of up to three parabolas in each subjects were averaged to take into account intrasubject variability.

Figure 4 shows LV volume vs. time curves with the corresponding first derivatives computed in a same subject during 1 G_z , 1.8 G_z , and 0 G_z . Compared with the 1 G_z curve, an upward shift of the LV volume curve was noted at 0 G_z . In contrast, a downward shift of the LV volume curve was seen at 1.8 G_z . Also, an increase in PFR was evident during 0 G_z . Figure 5 shows an example of the LV (top) and LA (bottom) 3D ED and

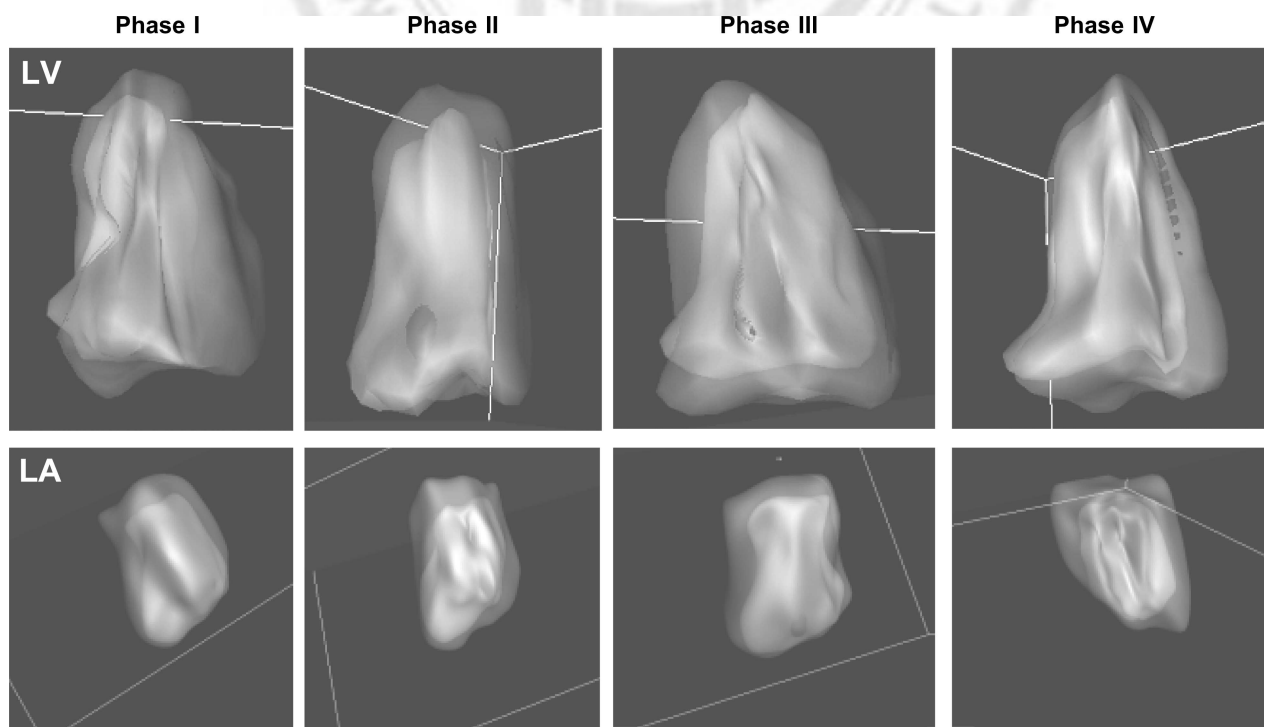


Fig. 5. LV and LA 3D casts obtained from the same subject, visualized using the same zooming scale and orientation, during the different gravity phases of the parabola. In each cast, end-diastolic (light gray) and end-systolic (white shaded) volumes are shown contemporaneously using transparency.

Table 1. Left ventricular and atrial function parameters computed in 14 normal subjects during the four phases of the parabola

	Phase I (1 G _z)	Phase II (1.8 G _z)	Phase III (0 G _z)	Phase IV (1.8 G _z)
LV EDV, ml	87±22	72±29† (−19%)	105±32‡ (+19%)	81±29 (−9%)
LV ESV, ml	29±9	23±13* (−24%)	35±13* (+23%)	24±13 (−21%)
LV SV, ml	58±19	49±21* (−16%)	69±25‡ (+20%)	57±23 (−2%)
LV EF, %	66±8	68±10 (+4%)	66±8 (0%)	70±10 (+6%)
LV PFR, ml/s	255±65	221±70 (−13%)	335±102* (31%)	278±89 (+8%)
LV PER, ml/s	−325±120	−289±122 (−5%)	−417±128* (37%)	−431±192 (+30%)
LA _{max} , ml	40±12	26±9* (−34%)	58±14‡ (+41%)	34±17 (−16%)
LA _{min} , ml	18±5	13±4‡ (−29%)	23±9‡ (+26%)	15±7 (−17%)
LA _{max} − LA _{min} , ml	21±8	13±5* (−36%)	35±7‡ (+59%)	19±12 (−18%)
DEI, %	53±8	49±8 (−5%)	60±7* (+16%)	51±19 (−5%)
EI, %	117±42	101±35 (−6%)	158±44* (+31%)	133±92 (+6%)

Values are means ± SD. In parentheses, the mean percentage of variation with respect to normogravity (1 G_z) value is reported. 1.8 G_z, hypergravity; 0 G_z, microgravity; LV, left ventricular; EDV, end-diastolic volume; ESV, end-systolic volume; SV, stroke volume; EF, ejection fraction; PFR, peak filling rate; PER, peak ejection rate; LA_{max}, left atrial volume at ventricular end-systole; LA_{min}, left atrial volume at ventricular end-diastole; DEI, diastolic emptying index; EI, expansion index. **P* < 0.05 vs. 1 G_z. ‡*P* < 0.01 vs. 1 G_z.

ES casts obtained in the same subject during the different phases of the parabola: during 1.8 G_z, a shrinking of both the LV and atrium was observed compared with 1 G_z, while an enlargement was seen during the 0 G_z phase.

Significant changes in both LV and LA volumes were measured during the different phases of the parabola (Table 1). Compared with 1 G_z values, both ED and ES LV volumes decreased by 19 and 24%, respectively, during 1.8 G_z, and

increased of 19 and 23%, respectively, during 0 G_z. These changes resulted in a reduction of SV of 16% during 1.8 G_z and an increase of 20% during 0 G_z, while EF did not change with gravity. Though PFR and PER did not change at 1.8 G_z, these parameters increased by 31 and 37%, respectively, during 0 G_z, compared with 1 G_z values (Fig. 6).

Compared with 1 G_z, both LA_{max} and LA_{min} volumes decreased by 34 and 29%, respectively, during 1.8 G_z, and

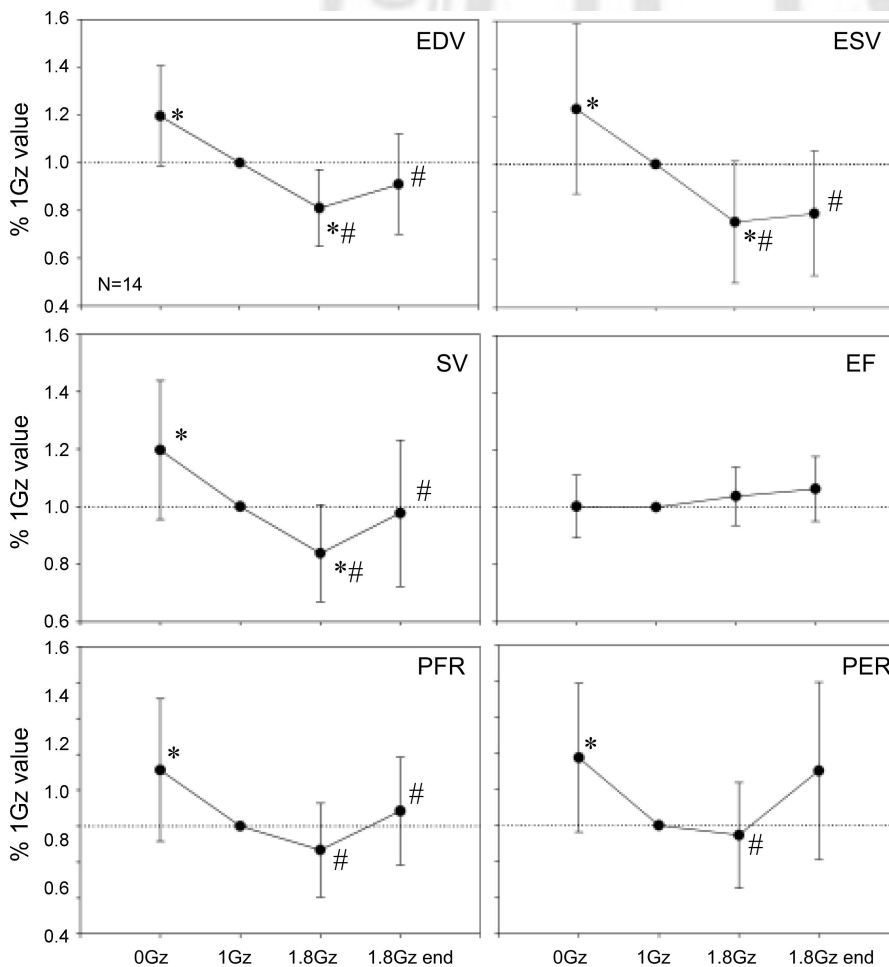


Fig. 6. Average ± SD of LV parameters measured in 14 subjects during the different gravity phases [0 G_z, 1 G_z, 1.8 G_z, 1.8 G_z end (second hypergravity phase)] along the parabola. **P* < 0.05 vs. 1 G_z. #*P* < 0.05 vs. 0 G_z. All data in each subject have been normalized to the corresponding 1 G_z value. EDV, end-diastolic volume; ESV, end-systolic volume; SV, stroke volume; EF, ejection fraction; PFR, peak filling rate; PER, peak ejection rate.

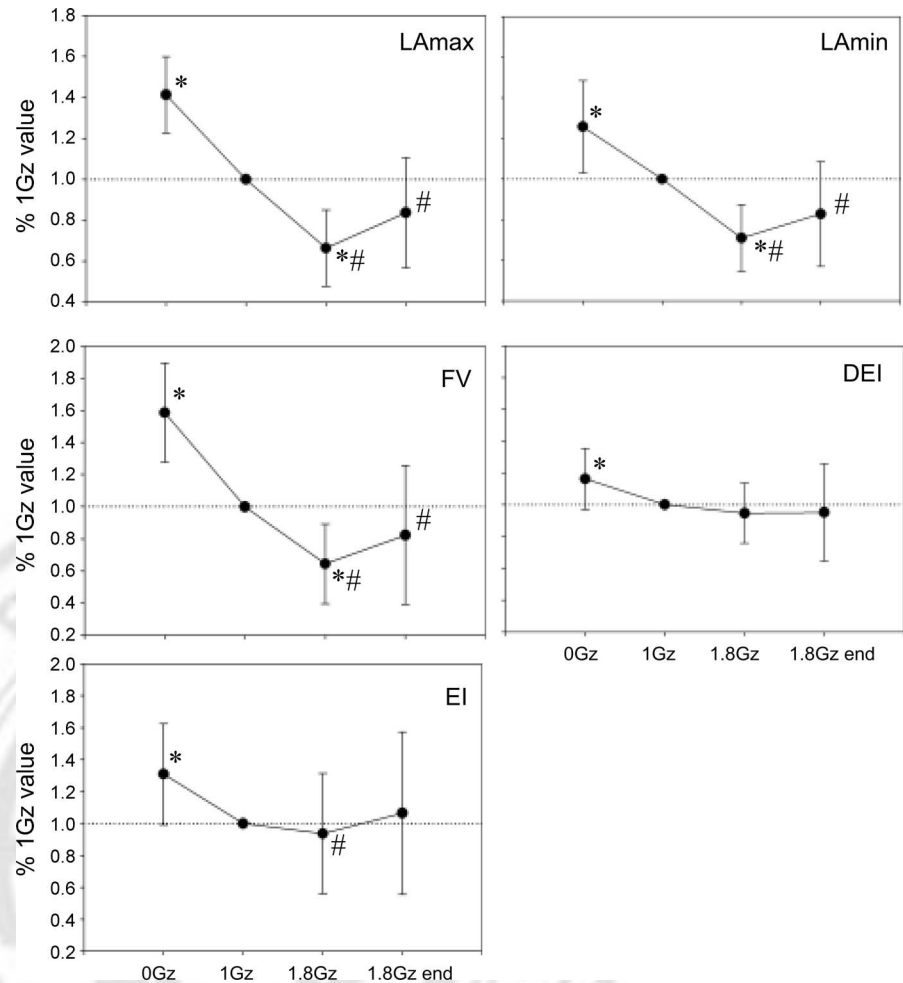


Fig. 7. Average \pm SD of LA parameters measured in 14 subjects during the different gravity phases along the parabola. * $P < 0.05$ vs. 1 Gz. # $P < 0.05$ vs. 0 Gz. All data in each subject have been normalized to the corresponding 1 Gz value. LA_{max}, LA volume at end-systole; LA_{min}, LA volume at end-diastole; FV, filling volume; DEI, diastolic emptying index; EI, expansion index.

increased by 41 and 26%, respectively, during 0 Gz. As a consequence, FVs were reduced by 36% and increased by 59% at 1.8 Gz and 0 Gz, respectively. Both DEI and EI increased during 0 Gz by 12 and 31%, respectively (Fig. 7). LA D1 and D2 diameters at ES were increased by 28 and 18% at 0 Gz, while at ED only D2 was found augmented by 25% compared with 1 Gz (Table 2).

With the activation of the LBNP countermeasure during 0 Gz, LV and LA volumes were quantified in 10 subjects. All LV and LA parameters trended toward 1 Gz values (Fig. 8), resulting in an attenuation of the changes noted at 0 Gz without LBNP. In particular, EDV and PFR were found reduced and restored to 1 Gz values. Also, LA_{max}, FV, and DEI were reduced and not different from their values at 1 Gz.

Table 2. Left atrial diameters computed in 14 normal subjects at 1 Gz and during 0 Gz

	Phase I (1 Gz)	Phase III (0 Gz)
LA _{max} D1, mm	26 \pm 5	33 \pm 6* (28%)
LA _{max} D2, mm	42 \pm 7	49 \pm 8* (22%)
LA _{min} D1, mm	18 \pm 4	21 \pm 9 (32%)
LA _{min} D2, mm	32 \pm 8	39 \pm 9* (25%)

Values are means \pm SD. In parentheses, the mean percentage of increase in respect of 1 Gz value is reported. D1, medial-lateral dimension; D2, antero-posterior dimension. * $P < 0.05$ vs. 1 Gz.

DISCUSSION

This study is the first to provide 3DE data sets from complete cardiac cycles in weightlessness, allowing for the calculation of LV and LA volumes and performance data.

Cardiac ultrasound has been the only medical imaging modality used in space to evaluate cardiovascular function. However, its use for scientific purposes during spaceflights has been limited due to operational constraints and technical factors (34). Despite these limitations, 2DE has been used to measure changes in cardiac size and function during weightlessness (3, 5, 37) and to assess the time course of postflight recovery (2, 6, 10, 25, 35).

Parabolic flights are the only way to reproduce in humans the weightlessness (or free-falling) state that characterizes spaceflights, thus representing a unique experimental condition to study reversible and repeatable acute nonpharmacologically induced variations in venous return in the same subject. We demonstrated the feasibility of acquiring 3D data sets suitable for analysis for each gravity phase of the parabola, despite the relatively short period of time available for image acquisition. The methodology used in this study allowed us to overcome many of the limitations of 2DE imaging. In particular, the availability of a 3D pyramidal data set allowed offline selection of the anatomically correct LV long axis, from which the equi-angled long-axis cut-planes were obtained for endocardial

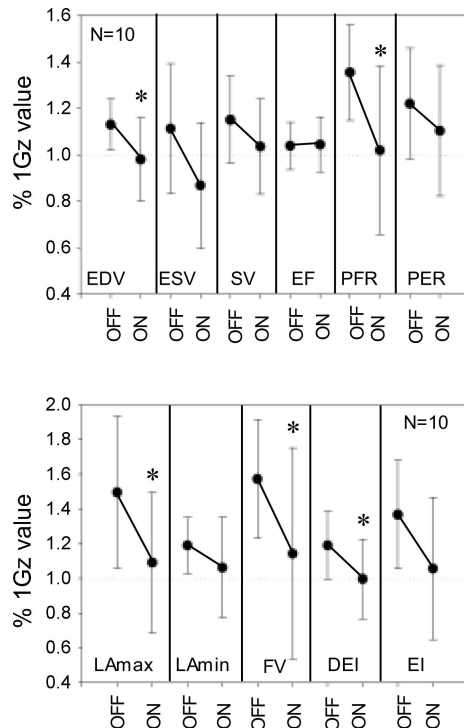


Fig. 8. Average \pm SD of LV (top) and LA (bottom) parameters measured in 10 subjects during the 0 G_z phase of the parabola without (OFF) and with (ON) LBPN at -50 mmHg activated. * $P < 0.05$.

contour detection. This minimized LV apical foreshortening, thus preventing the underestimation of LV volumes. Also, the frame-by-frame analysis throughout the cardiac cycle allowed computation of LV volume vs. time curves, from which clinical parameters, such as PFR and PEF, were derived. From the same data sets, we also measured the effects of 0 G_z on LA volumes, to obtain new insights into the physiology of this chamber at 0 G_z .

In contrast to other studies (27, 42, 48), imaging the subjects in the standing position allowed us both to maximize the effects of abrupt gravitational fluid shift on LV and LA volumes and to study, for the first time during parabolic flight, the effects induced by LBPN.

Our results demonstrate that, when a subject experiences a higher gravitational stress (phase II, 1.8 G_z), both LV and LA volumes become smaller compared with 1 G_z values, due to a decrease in venous return, resulting in a reduction of SV and LA FV. Interestingly, during the second 1.8 G_z phase (phase IV), these parameters were also significantly reduced compared with 0 G_z but not different from 1 G_z values. As the left heart is more dilated at the beginning of phase IV compared with the onset of phase II, the 1.8 G_z induced reduction in LV and LA volumes appears to be independent from the gravity gradient (+0.8 G_z in phase II and +1.8 G_z in phase IV) and more directly related to the magnitude of the preexisting LV and LA volumes when entering the 1.8 G_z phase.

In contrast, when the subject is in 0 G_z , both ED and ES LV volumes augment by $\sim 20\%$ compared with 1 G_z values, resulting in an increase in SV, while EF remains unchanged. These LV volume changes have been previously shown to be due to the increase in central blood volume that occurs in

weightlessness. The increase in cardiac volumes occurs, despite a decrease in central venous pressure (48), potentially due to a reduction in intrathoracic pressure and/or to the loss of compressive forces that occurs throughout the body in weightlessness.

In a previous study, where we measured LV area changes from 2DE in the apical four-chamber view using a similar experimental setting, we reported an increase in LV area at 0 G_z of only 12% (17). Compared with the current results, the underestimation found with 2DE was probably due to apical foreshortening, caused by the difficulties in continuously acquiring the correct anatomical 2D plane during the parabola. Our observations on LV volume changes at 0 G_z induced by parabolic flight closely resemble the short-term effects of 0 G_z on LV dimensions occurring in astronauts during the initial 2–3 days of spaceflight (9). These data reinforce the notion that parabolic flight represents a unique setting to study the short-term effects of weightlessness on Earth.

The observed increase in the rapid LV filling during 0 G_z is in agreement with our laboratory's previous observation that a significant increase in the peak mitral E wave occurs in standing subjects during 0 G_z (12) due to increased LV preload. The observed increase in PER could be explained by both increased LV ED pressure caused by the EDV augmentation, and by probable afterload reduction due to decreased blood pressure with 0 G_z (7, 42).

With regard to the LA, we found that, at 0 G_z , both the ED and ES LA volumes increased considerably compared with 1 G_z values, resulting in an increase in both the LA reservoir function (i.e., FV and EI) and in the overall DEI. Previously, Videbaek and Norsk (48) studied the ES LA diameter by M-mode from the parasternal long-axis view in subjects in the supine position during parabolic flight, reporting a 15% increase at 0 G_z compared with 1 G_z . The measurement of only a single diameter of the LA represented a limitation of that study, because it assumed that a consistent relationship is maintained between the anteroposterior and all other LA dimensions as the atrium enlarges, which is often not the case (32, 33). Our results obtained with RT3DE measured the true atrial volume and demonstrated that the magnitude of LA distension at 0 G_z appears to be larger (approximately doubled) than previously reported. Moreover, changes in LA D1 and D2 diameters at 0 G_z evidenced a similar increase of ~ 7 mm in D1 and D2 at ES, demonstrating a symmetric distension of the LA following an abrupt increase in venous return.

These findings could be considered for the formulation of new qualification criteria for commercial space travel. Since the increase in venous return induced by 0 G_z generates a considerable increase in LA and LV volumes, a compliant LV is required to avoid any abrupt increase in filling pressures. Noninvasive maneuvers resulting in significant preload augmentation (i.e., -40° head-down tilt) could be used in the future to ensure LV compliance. In fact, we can hypothesize that, when entering weightlessness, individuals with compromised LV compliance could develop pulmonary edema, resulting in different clinical scenarios, which could range from a reduction of in-flight performance to a life-threatening condition.

LBPN has been used as a test of orthostatic tolerance both on Earth and during long-term spaceflights, and as an in-flight countermeasure prior to reentry, associated with fluid intake, to

prevent postflight orthostatic intolerance. Although previous studies investigated the effects of LBNP on LV dimensions in various experimental conditions using 2DE (4, 28, 39, 45, 46), this is the first time that LBNP has been studied during parabolic flight, to assess in a weightlessness environment its counterbalancing effects on LV and LA volumes in a normal heart. In ground experiments, performed in subjects in the supine position, a reduction in LV volumes and SV with LBNP at different pressures (from -10 to -40 mmHg) have been previously reported using M-mode echocardiography (28, 39). Our results obtained in subjects in standing position during $0\text{ }G_z$ showed that LBNP at -50 mmHg was able to restore LV and LA dimensions to $1\text{ }G_z$ values, in particular LV EDV, LA_{\max} , and LA FV. Since LBNP is known to increase the pooling of blood in the lower body, leading to decreases in both central blood volume and cardiac filling pressures (1, 14, 40, 47), and since $0\text{ }G_z$ has been shown to increase central blood volume and atrial distension (48), the combined effect of $0\text{ }G_z$ and LBNP appears to counterbalance each other, resulting in minimal change in central blood volume.

This study had several limitations. First, 3DE using a full-matrix array transducer has been previously described as being a “real-time” technique. However, data were acquired in the full volume mode, which is a “near” real-time technique that requires temporal registration of a number of subsegments acquired from consecutive beats. Accordingly, it was not possible to acquire data sets representative of consecutive cardiac cycles along the whole parabola, but only one data set for each gravity phase. However, after the short transient when entering in a new gravity phase, the LV and LA volumes can be considered stabilized and representative of the corresponding parabolic phase. Furthermore, in the interpretation of the results, when the effects of $1\text{ }G_z$ are compared with those of weightlessness, it is important to consider the effects of the $1.8\text{ }G_z$ phase occurring in between.

The semiautomated segmentation procedure requires the manual initialization of the endocardial borders in multiple, evenly rotated long-axis views, which is a time-consuming and subjective procedure. Nevertheless, this technique, applied to the LV, was found to be highly reproducible and accurate (30). As no standard analysis methods for LA volume quantification from RT3DE data exist, our measurements of absolute LA dimensions could be affected by biases or inaccuracies. However, as these errors should be of the same magnitude for each gravity phase, and since results were normalized in each subject for the corresponding $1\text{ }G_z$ values, the resulting change in LA volumes should not be affected by the method of analysis.

In conclusion, the result of this study indicates that RT3DE imaging during parabolic flight is feasible and provides the basis for accurate quantification of LV volume changes with gravity, thus providing pyramidal data sets from which correct non-foreshortened apical views can be obtained. Moreover, also, LA volume changes during weightlessness can be quantified by RT3DE. In $0\text{ }G_z$, we reported an increase of both LV and LA volumes, due to changes in venous return, which was counteracted by LBNP.

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