Cardiac adaptations to 60 day head-down-tilt bed rest deconditioning. Findings from the AGBRESA study

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Abstract

Aims Reduced physical activity increases the risk of heart failure; however, non-invasive methodologies detecting subclinical changes in myocardial function are not available. We hypothesized that myocardial, left ventricular, systolic strain measurements could capture subtle abnormalities in myocardial function secondary to physical inactivity.

Methods and results In the AGBRESA study, which assessed artificial gravity through centrifugation as potential countermeasure for space travel, 24 healthy persons (eight women) were submitted to 60 day strict –6° head-down-tilt bed rest. Participants were assigned to three groups of eight subjects: a control group, continuous artificial gravity training on a short-arm centrifuge (30 min/day), or intermittent centrifugation (6 × 5 min/day). We assessed cardiac morphology, function, strain, and haemodynamics by cardiac magnetic resonance imaging (MRI) and echocardiography. We observed no differences between groups and, therefore, conducted a pooled analysis. Consistent with deconditioning, resting heart rate (Δ8.3 ± 6.3 b.p.m., P < 0.0001), orthostatic heart rate responses (Δ22.8 ± 19.7 b.p.m., P < 0.0001), and diastolic blood pressure (Δ8.8 ± 6.6 mmHg, P < 0.0001) increased, whereas cardiac output (Δ−0.56 ± 0.94 L/min, P = 0.096) decreased during bed rest. Left ventricular mass index obtained by MRI did not change. Echocardiographic left ventricular, systolic, global longitudinal strain (Δ1.8 ± 1.83%, P < 0.0001) decreased, whereas left ventricular, systolic, global MRI circumferential strain increased not significantly (Δ−0.68 ± 1.85%, P = 0.0843). MRI values rapidly returned to baseline during recovery.

Conclusion Prolonged head-down-tilt bed rest provokes changes in cardiac function, particularly strain measurements, that appear functional rather than mediated through cardiac remodelling. Thus, strain measurements are of limited utility in assessing influences of physical deconditioning or exercise interventions on cardiac function.

Keywords Cardiac atrophy; Heart failure; Myocardial strain; Bed rest; Immobilization

Background and aims

Reduced physical activity increases the risk of heart failure later in life.¹,² Conversely, exercise interventions reverse cardiac changes associated with sedentary ageing, as determined by right heart catheterization and three-dimensional echocardiography.³ To guide exercise interventions in patients, less invasive methodology is required. Echocardiographic left ventricular, systolic, global longitudinal strain predicts cardiovascular morbidity and mortality.⁴ Left ventricular, systolic, global circumferential strain analysis by magnetic resonance imaging (MRI) may further improve risk prediction.⁵ Head-down-tilt bed rest models cardiovascular deconditioning in weightlessness.⁶ The response resembles cardiovascular adaptation to sedentary ageing⁷ and provides a highly standardized model to assess deconditioning influences on cardiac function. We tested the hypothesis that left ventricular, systolic, myocardial strain measurements,
obtained through echocardiography or MRI, could detect subclinical changes in myocardial function secondary to bed rest deconditioning. Furthermore, we determined whether artificial gravity through short-arm centrifugation would ameliorate the response.

**Methods**

This study is part of the NASA/ESA/DLR 60 day –6° head-down-tilt bed rest study ‘Artificial Gravity Bed Rest with European Space Agency’ (AGBRESA) conducted at the DLR: envihab. The study enrolled 24 healthy persons (23–54 years, 24.3 ± 2 kg/m²). The study was approved by the North Rhine Medical Association Ethics Committee and prospectively registered (DRKS00015677).

The study comprised 14 day baseline, 60 day strict –6° head-down-tilt bed rest, and 15 day recovery. Participants were pseudorandomly distributed to a control group, daily 6 x 5 min short-arm centrifugation with 3 min breaks, or daily continuous 30 min short-arm centrifugation, each with 1 Gz at the centre of mass. Participants did not exercise, were on a controlled sodium diet, and maintained a constant body weight.

We performed echocardiographic and Doppler imaging (Vivid-IQ with M5SC-RS sector probe, GE Healthcare, Boston, Massachusetts, USA) at baseline (supine, 6 days before bed rest) and at the end of bed rest (–6° head-down-tilt, 1 day before recovery) to assess biplane end-diastolic and end-systolic volumes; mitral annulus plane systolic excursion; left ventricular, systolic, global longitudinal peak strain by speckle tracking; transmitral filling patterns [E wave, A wave, E/A, and tissue Doppler of the lateral mitral annulus (e’lat) velocities and ratio]; and stroke volume index (derived from pulse-wave Doppler velocity–time integral of the left ventricular outflow tract, its diameter, and body surface area).

Cardiac MRI (3-T Biograph, PET/MR, Siemens, Munich, Germany) was performed at baseline (5 days before bed rest), on 56th day of bed rest, and on 4th day of recovery. We recorded two-chamber, three-chamber, and 4-chamber cine loops (1.6 x 1.6 x 6 mm; TE 1.43 ms, TR 39.24 ms, 25 phases) and a complete short-axis stack (1.6 x 1.6 x 7 mm; TE 1.43 ms, TR 45.78 ms, 25 phases) with retrospective electrocardiogram gating and analysed cardiac output; left ventricular mass index; ejection fraction; left ventricular, systolic, global circumferential strain and strain rate; and time to peak (cmr42 Siemens Integration, version 5.9.3, Circle Cardiovascular Imaging Inc.) (see Appendix 1).

During passive orthostatic testing at the last day of baseline and on the last day of bed rest, we recorded resting heart rate and blood pressure.

Results are reported as mean ± standard deviation. We calculated group and time point effects using linear mixed-effect

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**Table 1 Cohort analysis**

| Parameter                          | Baseline  | Bed rest  | Recovery | P       |
|-----------------------------------|-----------|-----------|----------|---------|
| Heart rate (b.p.m.)               | 64 ± 9.6  | 72.3 ± 10.6 | 69.6 ± 10.5 | <0.0001 |
| Systolic blood pressure (mmHg)    | 125 ± 11.1 | 124.3 ± 8.9  | 122.7 ± 70.6 | 0.561   |
| Diastolic blood pressure (mmHg)   | 69.6 ± 7.3  | 78.5 ± 6.9  | 70.3 ± 6.3  | <0.0001 |
| Upright–supine heart rate (b.p.m.)| 22.8 ± 10.5 | 6 ± 1       | 6.8 ± 1.2   | 0.015   |
| Ejection fraction a,b,c (%)       | 68.3 ± 3.9  | 66.4 ± 4.8  | 63.9 ± 4.7  | 0.005   |
| LV mass index c (g/m²)            | 66.6 ± 11.3 | 64.5 ± 11.7 | 65.8 ± 9.8  | 0.792   |
| LV stroke volume index d (mL)     | 51.5 ± 10   | 44.1 ± 6.3  |           | 0.001   |
| LV EDV d (mL)                     | 100.1 ± 28.2 | 79.7 ± 17.6 |           | <0.0001 |
| MAPSE e (mm)                      | 18.5 ± 2.7  | 16.6 ± 3.1  |           | 0.013   |
| Global longitudinal PS d (%)      | –19.9 ± 2.1 | –18.1 ± 2.1 |           | <0.0001 |
| Global circumferential Ps a,c (%) | –18.6 ± 1.7 | –19.1 ± 1.6 | –18.1 ± 1.7 | 0.049   |
| Global circumferential t2p c (%)   | –0.97 ± 0.1 | –1.14 ± 0.18 | –1 ± 0.11 | <0.0001 |
| E-wave velocity a (cm/s)          | 79.4 ± 14.1 | 65.3 ± 12.5 |           | <0.0001 |
| A-wave velocity a (cm/s)          | 52.7 ± 13   | 53.3 ± 12.1 |           | 0.796   |
| E/A d                             | 1.58 ± 0.39 | 1.25 ± 0.24 |           | 0.015   |
| e' lateral d (cm/s)               | 15.5 ± 2.9  | 12.3 ± 2.7  |           | <0.0001 |
| E/e lateral ratio d               | 5.25 ± 1.17 | 5.68 ± 1.66 |           | 0.0889  |

LV, left ventricular; LV EDV, left ventricular end-diastolic volume; MAPSE, mitral annulus plane systolic excursion; PS, peak strain; sSR, systolic strain rate; t2p, time to systolic peak strain.

Absolute mean values ± standard deviation of the whole cohort for all three time points (baseline, bed rest, and recovery). P-values for linear mixed-effect model analysis. P < 0.05 indicates significance. All strain measurements refer to the left ventricle in systole. All strain values refer to the left ventricle in systole.

1In pairwise comparison of baseline vs. bed rest and baseline vs. recovery, values do not differ significantly.
2In pairwise comparison of baseline vs. recovery, results differ significantly (P = 0.005).
3Parameters obtained by cardiac magnetic resonance imaging.
4Parameters obtained by echocardiography.

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model analysis. \( P < 0.05 \) indicated statistical significance. The data supporting the reported results are available from the corresponding author upon reasonable request.

**Results**

Because baseline characteristics and cardiac responses did not differ between groups (Appendix 1), we conducted a pooled analysis in all 24 participants (Table 1). Compared with baseline, supine heart rate increased 8.3 ± 6.3 b.p.m. \(( P < 0.0001)\), systolic blood pressure did not change, and diastolic blood pressure increased 8.8 ± 6.6 mmHg \(( P < 0.0001)\) at the end of bed rest. On Day 4 of recovery, blood pressure had returned to baseline, while resting heart rate remained elevated by 5.6 ± 8.4 b.p.m. \(( P < 0.001)\). With standing, heart rate increased 22.8 ± 10.5 b.p.m. at baseline and 45.6 ± 21.4 b.p.m. following bed rest \(( P < 0.0001; Figure 1)\).

Following bed rest, cardiac output and left ventricular stroke volume index had decreased 8.2% \((-0.54 \pm 0.94 \text{ L/min}, P = 0.0096)\) and 14.4% \((-7.4 \pm 8.3 \text{ mL/m}^2, P = 0.0168)\), respectively. Left ventricular end-diastolic volume determined by echocardiography decreased 20.3 ± 15.4% \(( P = 0.0001)\) together with ejection fraction \((6.4 \pm 5.1\%)\). Left ventricular mass index did not change \((Figure 2)\). Left ventricular mass index by MRI, which was significantly greater in men compared with women \((P = 0.0001)\), did not change in men \((baseline: \text{70.4 \pm 10.7; recovery: 68.7 \pm 8.6 \text{ g/m}^2, P = 0.69})\) or in women \((baseline: \text{59 \pm 8.6; recovery: 59.8 \pm 9.9 \text{ g/m}^2, P = 0.968})\). Mitral annulus plane systolic excursion and global longitudinal peak strain were reduced following bed rest \((Table 1)\).

Left ventricular, systolic global circumferential peak strain by cardiac MRI did not change significantly with bed rest \((Figure 3)\). However, following 4 day recovery, global circumferential peak strain tended to decrease compared with bed rest \((P = 0.05; Figure 4)\). Circumferential contraction expressed as systolic strain rate and time to peak was significantly augmented at Day 56 of bed rest compared with baseline with increases in strain rate and shortened time to peak. While peak values for transmitral A wave did not change with bed rest, E was reduced such that the E/A ratio decreased. We observed a similar pattern for e’/lat, whereas E/e’lat remained unchanged.

Artificial gravity through intermittent or continuous centrifugation did not abolish cardiovascular adaptations to head-down-tilt bed rest \((Appendix 1)\).

**Discussion**

Sixty days of strict head-down-tilt bed rest elicited cardiovascular deconditioning indicated by increases in resting and upright heart rate with reductions in left ventricular end-diastolic volume, cardiac output, and stroke volume. Yet bed rest did not lead to clinical apparent heart failure. Previous studies showed worsened cardiopulmonary fitness and orthostatic tolerance.\(^{8}\) Yet we did not observe sustained reductions in left ventricular function assessed by systolic strain analysis in line with shorter duration bed rest studies.\(^{9}\)

Finally, myocardial mass did not change significantly, suggesting that cardiac atrophy is not a general feature during physical deconditioning and cannot be seen as risk factor for developing chronic heart failure. While we cannot exclude modest improvements in cardiovascular deconditioning, artificial gravity failed to abolish the response.

**Figure 1** Cardiac deconditioning. Supine and upright heart rate, left ventricular (LV) stroke volume index, and cardiac output at baseline and after 60 day bed rest. \(*P < 0.05\).
Strain can be affected by intrinsic myocardial properties, cardiac loading conditions, and sympathetic drive. We and others observed reductions in left ventricular end-diastolic volume with predominant long-axis diameter shortening following bed rest deconditioning. The phenomenon may result from plasma volume reductions during bed rest. Plasma volume reductions are at least in part explained by cephalad volume shifts promoting natriuretic peptide release through atrial stretch. The left ventricle seems less compliant with a smaller stroke volume independent of the volume loss. The asymmetric change in left ventricular shape likely explains differential global circumferential and longitudinal strain responses. Normalization of strain and left ventricular volumes within days of recovery is consistent with loading-dependent functional changes rather than cardiac remodelling that might lead to persistent cardiac dysfunction. Left ventricular diastolic filling, which is also preload dependent, changed as well. Similar volume

**Figure 2** Left ventricular (LV) function and morphology. LV ejection fraction, LV mass index derived from cardiac magnetic resonance imaging at baseline, after 60 day bed rest, and recovery. LV end-diastolic volume by echocardiography at baseline and after 60 day bed rest. *P < 0.05.

**Figure 3** Cardiac strain. Cardiac strain measurements at baseline and after 60 day bed rest (56 days for circumferential strain). *P < 0.05. MAPSE, mitral annulus plane systolic excursion.
alterations have been reported during 5 and 35 days of bed rest.\textsuperscript{13,20} Altered loading conditions may also explain the significant albeit small reduction in left ventricular ejection fraction upon recovery.

Cardiac function measurements could be confounded by sympathetic activation, which is an expected physiological response to plasma volume reductions. Indeed, increases in resting heart rate and diastolic blood pressure, which we observed at the end of bed rest similar to others,\textsuperscript{13} often occur in conditions associated with increased sympathetic drive.\textsuperscript{21,22} Previous findings in bed rest studies support the idea that sympathetic activity is, indeed, increased.\textsuperscript{23–25} Furthermore, after 21 day bed rest, plasma norepinephrine increased more with orthostasis compared with baseline.\textsuperscript{26} We speculate that sympathetic activation may have increased circumferential strain with bed rest.

\textbf{Figure 4} Global circumferential peak strain. Circumferential peak strain measurements at baseline, end of bed rest, and end of recovery in a representative study participant. Upper panel: end-systolic cross-sectional short-axis cardiac magnetic resonance imaging images at the level just above the papillary muscles with circumferential strain overlay. Middle panel: Bull’s eye view of the 16 American Heart Association (AHA) myocardial segments model with circumferential peak strain values and colour coding, where deeper blue resembles higher strain values. Lower panel: Circumferential peak strain time course over one heartbeat for the 16 AHA myocardial segments model.
The main limitation of our study is the relatively small sample size limiting statistical power and detailed subgroup analyses. Yet rigorous standardization including controlled sodium intake and caloric adjustment to maintain body weight made it possible observing small but relevant physiological changes in cardiovascular function. Furthermore, participants were relatively young with low heart failure risk. Finally, longer periods of limited physical activity may be required to alter intrinsic myocardial properties and to promote interstitial fibrosis.

We conclude that 60 days of –6° head-down-tilt bed rest provoke changes in cardiac function that appear functional rather than mediated through cardiac remodelling. Additional risks such as older age or concomitant cardiovascular disease may be required to express cardiac dysfunction and consecutive chronic heart failure. Because –6° head-down-tilt bed rest is a model for weightless conditions, our findings are reassuring for human space travel. While in weightlessness, cardiopulmonary fitness and orthostatic tolerance will deteriorate in the absence of sufficient countermeasures, overt cardiac disease appears unlikely. Furthermore, our findings might have implications for patients undergoing forced bed rest in, for example, intensive care settings. Finally, our study suggests that strain measurements, as preload-dependent analysis, may be of limited utility in prospectively guiding exercise interventions in the prevention of heart failure. While deconditioning elicits plasma volume reductions and sympathetic activation, physical exercise, particularly endurance training, elicits the opposite response.27,28 Thus, intrinsic changes in myocardial functional properties cannot be discerned.

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**Conflict of interest**

None.

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### Baseline Characteristics

|                          | Total          | Control        | Continuous AG | Intermittent AG | P     |
|--------------------------|---------------|---------------|---------------|----------------|-------|
| **Weight (kg)**          | 74 ± 10.1     | 79.5 ± 12.7   | 71.3 ± 9.9    | 71.3 ± 4.8     | 0.1709|
| **Height (cm)**          | 174.4 ± 8.7   | 176.9 ± 7.3   | 172.1 ± 8.1   | 174.1 ± 10.7   | 0.566 |
| **Body surface area (m²)**| 1.89 ± 0.169  | 1.96 ± 0.19   | 1.84 ± 0.17   | 1.85 ± 0.14    | 0.2874|
| **Age (years)**          | 33.3 ± 9.3    | 33.8 ± 8.2    | 31.4 ± 9.9    | 34.6 ± 10.6    | 0.7855|
| **Heart rate (b.p.m.)**  | 64 ± 9.6      | 63.8 ± 7      | 63.4 ± 13.2   | 63.4 ± 9       | 0.9752|
| **Systolic blood pressure (mmHg)** | 125 ± 11.1 | 125.2 ± 8.2 | 127 ± 14.9 | 122.9 ± 10.2 | 0.78  |
| **Diastolic blood pressure (mmHg)** | 69.6 ± 7.3    | 71 ± 8.2      | 70.3 ± 6.4    | 67.5 ± 7.6     | 0.6187|
| **Cardiac output (L/min)** | 6.59 ± 0.89   | 6.75 ± 0.85   | 6.57 ± 0.89   | 6.44 ± 1       | 0.7935|
| **Ejection fraction (%)** | 68.3 ± 3.9    | 66.6 ± 3.4    | 70.5 ± 4      | 67.8 ± 3.5     | 0.11  |
| **LV mass index (g/m²)**  | 100.1 ± 28.2  | 109.2 ± 34.9  | 98.5 ± 29.3   | 92.6 ± 19.5    | 0.5095|
| **LV stroke volume index (mL/²)** | 51.5 ± 10     | 50.5 ± 14.3   | 50.8 ± 9.8    | 53.2 ± 4.7     | 0.8566|
| **MAPSE (mm)**           | 18.5 ± 2.7    | 17.5 ± 3      | 18.3 ± 2.8    | 19.7 ± 2.1     | 0.276 |
| **Global longitudinal PS (%)** | −19.9 ± 2.1  | −19.7 ± 2.2   | −19.8 ± 1.7   | −20.2 ± 2.6    | 0.8966|
| **Global circumferential PS (%)** | −18.6 ± 1.7 | −18.6 ± 1.6  | −18.3 ± 2    | −18.8 ± 1.6    | 0.8181|
| **Global circumferential sSR (1/s)** | −0.97 ± 0.1  | −0.98 ± 0.11  | −0.97 ± 0.12  | −0.99 ± 0.08   | 0.958 |
| **Global circumferential t²p (ms)** | 315 ± 35.1  | 312.3 ± 34.7  | 323.3 ± 47.1  | 303 ± 19.6     | 0.5296|
| **E-wave velocity (cm/s)** | 79.4 ± 14.8   | 79.6 ± 17.1   | 80.9 ± 9.6    | 77.6 ± 16.4    | 0.9053|
| **A-wave velocity (cm/s)** | 52.7 ± 13     | 56.5 ± 15.1   | 53 ± 15.7     | 48.6 ± 6.2     | 0.4993|
| **E to A ratio**         | 1.58 ± 0.39   | 1.5 ± 0.45    | 1.62 ± 0.38   | 1.61 ± 0.39    | 0.8078|
| **e’lateral (cm/s)**     | 15.5 ± 2.9    | 14.8 ± 2.5    | 16.3 ± 3.8    | 15.1 ± 2.3     | 0.561 |
| **E to e’lateral ratio** | 5.25 ± 1.17   | 5.47 ± 1.48   | 5.17 ± 1.17   | 5.17 ± 0.97    | 0.8646|

LV, left ventricular; LV EDV, left ventricular end-diastolic volume; MAPSE, mitral annulus plane systolic excursion; PS, peak strain; sSR, systolic strain rate; t²p, time to systolic peak strain.

Baseline characteristics: Absolute mean values ± standard deviation of the whole cohort and three subgroups [control, continuous artificial gravity (AG) and intermittent AG] at baseline. P-values for linear mixed-effect model analysis. P < 0.05 indicates significance. All strain measurements refer to the left ventricle in systole.


|                              | Bed rest—Baseline |  | Recovery—Baseline |  |
|------------------------------|-------------------|---|-------------------|---|
|                              | Control           | Continuous AG | Intermittent AG | P  | Control             | Continuous AG | Intermittent AG | P  |
| Heart rate (b.p.m.)          | 8.2 ± 7.6         | 9 ± 4.6        | 7.6 ± 7.1       | 0.9021 | 7.7 ± 5.3         | 9.4 ± 8      | 0.2 ± 9.2      | 0.0616 |
| Systolic blood pressure (mmHg)| 3.4 ± 7.2         | -3.1 ± 13.5    | -2.5 ± 6.7      | 0.3459 | -1.5 ± 7.6        | 6 ± 7.9      | 6 ± 8.9        | 0.3729 |
| Diastolic blood pressure (mmHg)| 9.1 ± 6.8       | 8.6 ± 5.9      | 8.8 ± 8.0       | 0.8677 | -1 ± 4.7          | 2.5 ± 2.4    | 6 ± 6.8        | 0.3882 |
| Cardiac output (L/min)       | -0.51 ± 0.81      | -0.41 ± 1.1    | -0.76 ± 0.99    | 0.7657 | 0.07 ± 0.77       | 0.54 ± 1.1   | 0.18 ± 1.02    | 0.3729 |
| Ejection fraction (%)        | -2.06 ± 5.19      | -1.69 ± 5.06   | -2.08 ± 5.1     | 0.985  | -4.36 ± 3.09      | -4.3 ± 3.8   | -4.43 ± 3.93   | 0.988  |
| LV mass index (g/m²)         | -0.58 ± 6.43      | -5 ± 3.97      | -0.84 ± 5.82    | 0.222  | -1.95 ± 5.21      | -2.59 ± 6.05 | 2.04 ± 7.56    | 0.308  |
| LV stroke volume index (mL/L) | -7.3 ± 12.3       | -8.3 ± 6.2     | -6.6 ± 6        | 0.926  |                     |              |               |       |
| LV EDV (mL)                  | -26.8 ± 29.2      | -16.1 ± 15     | -18.1 ± 10      | 0.3181 |                     |              |               |       |
| MAPSE (mm)                   | -0.69 ± 3.06      | -3.28 ± 3      | -1.72 ± 4.12    | 0.335  |                     |              |               |       |
| Global longitudinal PS (%)   | -2.03 ± 1.54      | -2.36 ± 1.28   | -1.01 ± 2.42    | 0.3181 |                     |              |               |       |
| Global circumferential PS (%)| 0.15 ± 2.21       | -1.34 ± 1.77   | -0.86 ± 1.38    | 0.2676 | 1.7 ± 1.59         | -0.39 ± 1.53 | -0.05 ± 1.91   | 0.054  |
| Global circumferential sSR (1/s) | -0.16 ± 0.16   | -0.25 ± 0.2   | -0.18 ± 0.12    | 0.5263 | 0.01 ± 0.14        | -0.08 ± 0.15 | -0.03 ± 0.15   | 0.4863 |
| Global circumferential t2p (ms) | -23.2 ± 33.7     | -38.8 ± 40    | 24.3 ± 31.1     | 0.6181 | 0.0 ± 21.6         | -23.1 ± 40.8 | -3.1 ± 37.6    | 0.3897 |
| E-wave velocity (cm/s)       | -2 ± 18           | -11.3 ± 13.7   | -11 ± 10.2      | 0.3867 |                     |              |               |       |
| A-wave velocity (cm/s)       | -7.5 ± 12.3       | 3.5 ± 18.6     | 5.9 ± 14.3      | 0.1992 |                     |              |               |       |
| E to A ratio                 | -0.26 ± 0.34      | -0.34 ± 0.54   | -0.36 ± 0.42    | 0.883  |                     |              |               |       |
| e′lateral (cm/s)             | -4.3 ± 2.3        | -3.1 ± 2.3     | -2.4 ± 1.8      | 0.8168 |                     |              |               |       |
| E to e′lateral ratio         | 0.33 ± 2.65       | 0.25 ± 1.33    | 0.42 ± 2.10     | 0.741  |                     |              |               |       |

LV, left ventricular; LV EDV, left ventricular end-diastolic volume; MAPSE, mitral annulus plane systolic excursion; PS, peak strain; sSR, systolic strain rate; t2p, time to systolic peak strain. Intergroup comparison: Differences of bed rest—baseline and recovery—baseline ± standard deviation of the whole cohort and three subgroups [control, continuous artificial gravity (AG), and intermittent AG]. All strain measurements refer to the left ventricle in systole. P < 0.05 indicates significance.
Cardiac magnetic resonance imaging
acquisition parameters

Two-chamber, three-chamber, and four-chamber views and right ventricular long-axis view—cine

| CINE_3CV_4CV_RV_2CV |
|----------------------|
| TA: 3.2 ± PM: REF voxel size: 1.6 × 1.6 × 6.0 mm PAT: 2 Rel. SNR: 1.00: tff |
| Properties |
| Prior recon: Off |
| Load images to viewer: On |
| Inline movie: On |
| Auto store images: On |
| Load images to stamp segments: On |
| Load images to graphic segments: On |
| Auto open inline display: Off |
| Auto close inline display: Off |
| Start measurement without further preparation: Off |
| Wait for user to start: Off |
| Start measurements: Single measurement |
| Routine |
| Slice group: 1 |
| AutoAlign: |
| Phase oversampling: 50% |
| FoV read: 340 mm |
| FoV phase: 83.7% |
| Slice thickness: 6.0 mm |
| TR: 39.24 ms |
| TE: 1.43 ms |
| Averages: 1 |
| Concatenations: 1 |
| Filter: Distortion corr. (2D) |
| Prescan normalize: |
| Image filter: |
| Coil elements: BP1, 2; SP1-3 |
| Slices: 1 |
| Dist. factor: 20% |
| Position: L4.2 A1.0 H24.6 mm |
| Orientation: T > C3.2 > S-12.2 |
| Phase enc. dir.: A >> P |
| Contrast—Common |
| TR: 39.24 ms |
| TE: 1.43 ms |
| Magn. preparation: None |
| Flip angle: 40° |
| Fat suppr.: None |
| Wrap-up magn.: Restore |
| Contrast—Dynamic |
| Averages: 1 |
| Averaging mode: Short term |
| Reconstruction: Magnitude |
| Measurements: 1 |
| Multiple series: Each slice |
| Resolution—Common |
| FoV read: 340 mm |
| FoV phase: 83.70% |
| Slice thickness: 6.0 mm |
| Base resolution: 208 |
| Phase resolution: 80% |
| Phase partial Fourier: Off |
| Trajectory: Cartesian |
| View sharing: Off |
| Interpolation: Off |
| Resolution—iPAT |
| PAT mode: GRAPPA |
| Accel. factor PE: 2 |
| Ref. lines PE: 24 |

(Continues)
| **CINE_3CV_4CV_RV_2CV** |
|--------------------------|
| **Matrix coil mode**     | Auto (triple)               |
| **Reference scan mode**  | Integrated                  |
| **Resolution—Filter image** |                            |
| **Image filter**         | On                         |
| **! Intensity**           | Medium                     |
| **Edge enhancement**     | 1                          |
| **Smoothing**            | 3                          |
| **Unfiltered images**    | Off                        |
| **Distortion corr.**     | On                         |
| **Mode**                 | 2D                         |
| **Unfiltered images**    | Off                        |
| **Prescan normalize**    | On                         |
| **Unfiltered images**    | Off                        |
| **Normalize**            | Off                        |
| **B1 filter**            |                            |
| **Resolution—Filter raw data** |                    |
| **Raw filter**           | Off                        |
| **Elliptical filter**    | Off                        |
| **POCS**                 | Off                        |
| **Geometry—Common**      |                            |
| **Slice group 1**        | 340 mm                     |
| **FoV read**             | 83.7%                      |
| **FoV phase**            | 6.0 mm                     |
| **Slice thickness**      | 39.24 ms                   |
| **TR**                   | Sequential                 |
| **Multi-slice mode**     | Descending                 |
| **Series**               | 1                          |
| **Concatenations**       |                            |
| **Slices 1**             |                            |
| **Dist. factor 20%**     |                            |
| **Position L4.2 A1.0 H24.6 mm** |                        |
| **Orientation T > C32.0 > S-12.2** |                 |
| **Phase enc. dir. A >> P** |                            |
| **Geometry—AutoAlign**   |                            |
| **Slice group 1**        | 1                          |
| **AutoAlign**            | __                         |
| **Position**             | L4.2 A1.0 H24.6 mm         |
| **Orientation**          | T > C32.0 > S-12.2         |
| **Phase enc. dir.**      | A >> P                     |
| **Initial position**     | Isocentre                  |
| **L**                    | 0.0 mm                     |
| **P**                    | 0.0 mm                     |
| **H**                    | 0.0 mm                     |
| **Initial rotation**     | 0.00°                      |
| **Initial orientation**  | Transversal                |
| **Geometry—Saturation**  |                            |
| **Fat suppr.**           | None                       |
| **Wrap-up magn.**        | Restore                    |
| **Special sat.**         | None                       |
| **Geometry—Navigator**   |                            |
| **Geometry—Tim planning suite** |                   |
| **Set-n-Go protocol**   | Off                        |
| **Table position**       | H                          |
| **Table position**       | 0 mm                       |
| **Inline composing**     | Off                        |
| **System—Miscellaneous** |                            |
| **Positioning mode REF** |                            |
| **Table position H**     |                            |
| **Table position 0 mm**  |                            |
| **MSMA S-C-T**           |                            |
| **Sagittal R >> L**      |                            |
| **Coronal A >> P**       |                            |
| **Transversal F >> H**   |                            |
| **Coil combine mode sum of squares** |                  |
| **Save uncombined off**  |                            |
| **Matrix coil mode auto (triple)** |                |
| **AutoAlign**            |                            |
| **Coil select mode off—AutoCoilSelect** |                |
System—Adjustments
B0 Shim mode Cardiac
B1 Shim mode TrueForm
Adjust with body coil Off
Confirm freq. adjustment Off
Assume dominant fat Off
Assume silicone Off
Adjustment tolerance Auto
System—Adjust volume
Position L4.2 A1.0 H24.6 mm
Orientation T > C32.0 > S-12.2
Rotation A >> P 7.56°
R >> L 285 mm
F >> H 340 mm
Reset 6 mm Off
System—Tx/Rx
Frequency 1H 123.197081 MHz
Correction factor 1 High
Gain 1.000
Reset Off
Physio—Signal1
1st signalemode ECG/retro
Average cycle 290 ± 23 ms
Average cycle No signal ms
Calculated phases 25
TR 39.24 ms
Concatenations 1
Segments 12
Arrhythmia detection None
Physio—Cardiac
Tagging None
Magn. preparation None
Fat suppr. None
Dark blood Off
FoV read 340 mm
FoV phase 83.70%
Phase resolution 80%
Cine
Cine On
Physio—Cardiac
Trajectory Cartesian
View sharing Off
Dummy heartbeats 1
Physio—PACE
Resp. control Breath-hold
Concatenations 1
Inline—Common
Subtract Off
Measurements 1
StdDev Off
Save original images On
Inline—Cardiac
Inline evaluation Off
Mgn. preparation Ventricular function
Contrasts None
TE 1.43 ms
TR 39.24 ms
Save original images On
Inline—MIP
MIP-Sag Off
MIP-Cor Off
MIP-Tra Off
MIP-Time Off
Save original images On
Inline—Composing
Inline composing Off
(Continues)
Cardiac deconditioning

CINE_3CV_4CV_RV_2CV

- Distortion corr.: On
- Mode: 2D
- Unfiltered images: Off

Sequence—Part 1
- Introduction: Off
- Dimension: 2D
- Reordering: Linear
- Asymmetric echo: Weak
- Contrasts: 1
- Optimization: Min. TE TR
- Multi-slice mode: Sequential
- Echo spacing: 3.3 ms
- Sequence type: Tru
- Bandwidth: 962 Hz/Px

Sequence—Part 2
- Define: Segments
- Segments: 12
- Trufl delta freq.: 0 Hz
- RF pulse type: Normal
- Gradient mode: Fast
- Excitation: Slice-sel.
- Flip angle mode: Constant
- Cine: On
- Sequence—Assistant
  - Mode: Min flip angle
  - Min flip angle: 45°
  - Allowed delay: 5 s

Left ventricular short-axis stack—cine

CINE_segmented_SAX*

- TA: 2.0 s PM: REF voxel size: 1.6 × 1.6 × 7.0 mm PAT: 3 Rel. SNR: 1.00: tfi
- Properties
  - Prio recon: Off
  - Load images to viewer: On
  - Inline movie: On
  - Auto store images: On
  - Load images to stamp segments: On
  - Load images to graphic segments: On
  - Auto open inline display: Off
  - Auto close inline display: Off
  - Start measurement without further preparation: Off
  - Wait for user to start: Off
  - Start measurements: Single measurement
- Routine
  - Slice group: 1
  - AutoAlign
  - Phase oversampling: 50%
  - FoV read: 340 mm
  - FoV phase: 80.8%
  - Slice thickness: 7.0 mm
  - TR: 45.78 ms
  - TE: 1.43 ms
  - Averages: 1
  - Concatenations: 1
  - Filter
  - Distortion corr. (2D)
  - Prescan normalize
  - Image filter
  - Coil elements: BP1, 2; SP1–3
  - Slices: 1
  - Dist. factor: 20%
  - Position: L4.2 A1.0 H24.6 mm
  - Orientation: T > C32.0 > S-12.2
  - Phase enc. dir: A >> P

(Continues)
### CINE_segmented_SAX*

| Parameter                      | Value                        |
|--------------------------------|------------------------------|
| TR                             | 45.78 ms                     |
| TE                             | 1.43 ms                      |
| Magn. preparation              | None                         |
| Flip angle                     | 40°                           |
| Fat suppr.                     | None                         |
| Wrap-up magn.                  | Restore                      |
| Contrast—Common                |                              |
| Averages                       | 1                            |
| Averaging mode                 | Short term                   |
| Reconstruction Measurements    | 1                            |
| Multiple series                | Each slice                   |
| Resolution—Common              |                              |
| FoV read                       | 340 mm                       |
| FoV phase                      | 80.80%                       |
| Slice thickness                | 7.0 mm                       |
| Base resolution                | 208                          |
| Phase resolution               | 70%                          |
| Phase partial Fourier          | Off                          |
| Trajectory                     | Cartesian                     |
| View sharing                   | Off                          |
| Interpolation                  | Off                          |
| Resolution—Dynamic             |                              |
| Averages                       | 1                            |
| Averaging mode                 | Short term                   |
| Measurements                   | 1                            |
| Multiple series                | Each slice                   |
| Resolution—Common              |                              |
| FoV read                       | 340 mm                       |
| FoV phase                      | 80.80%                       |
| Slice thickness                | 7.0 mm                       |
| Base resolution                | 208                          |
| Phase resolution               | 70%                          |
| Phase partial Fourier          | Off                          |
| Trajectory                     | Cartesian                     |
| View sharing                   | Off                          |
| Interpolation                  | Off                          |
| Resolution—ipAT                |                              |
| PAT mode                       | GRAPPA                       |
| Accel. factor PE               | 3                            |
| Ref. lines PE                  | 24                           |
| Matrix coil mode               | Auto (triple)                |
| Reference scan mode            | Integrated                   |
| Resolution—Filter image        |                              |
| Image filter                   | On                           |
| Intensity                      | Medium                       |
| Edge enhancement               | 1                            |
| Smoothing                      | 3                            |
| Unfiltered images              | Off                          |
| Distortion corr.               | On                           |
| Mode                           | 2D                           |
| Unfiltered images              | Off                          |
| Prescan Normalize              | On                           |
| Unfiltered images              | Off                          |
| Normalize                      | Off                          |
| B1 filter                      | Off                          |
| Resolution—Filter raw data     |                              |
| Raw filter                     | Off                          |
| Elliptical filter              | Off                          |
| POCS                           | Off                          |
| Geometry—Common                |                              |
| Slice group 1                  | 340 mm                       |
| FoV read                       | 80.8%                        |
| FoV phase                      | 7.0 mm                       |
| Slice thickness                | 45.78 ms                     |
| TR                             | Sequential                   |
| Multi-slice mode               | To apex                      |
| Series base                    | 1                            |
| Concatenations                 | 1                            |
| Slices                         | 20%                          |
| Dist. factor                   | L4.2 A1.0 H24.6 mm           |
| Position                       | T > C32.0 > S-12.2           |
| Orientation                    | A >> P                       |
| Phase enc. dir.                |                              |
| Geometry—AutoAlign             |                              |
| Slice group                    | L4.2 A1.0 H24.6 mm           |
| AutoAlign                      | T > C32.0 > S-12.2           |
| Position                       | A >> P                       |
| Orientation                    | Isocentre                    |
| Phase enc. dir.                | 0.0 mm                       |
| Initial position               |                              |

(Continues)
| Parameter                     | Value                                      |
|-------------------------------|--------------------------------------------|
| P                             | 0.0 mm                                     |
| H                             | 0.0 mm                                     |
| Initial rotation              | 0.0°                                       |
| Initial orientation           | Transversal                                |
| Geometry—Saturation           |                                            |
| Fat suppr.                    | None                                       |
| Wrap-up magn.                 | Restore                                    |
| Special sat.                  | None                                       |
| Geometry—Navigator            |                                            |
| Geometry—Tim planning suite   |                                            |
| Set-n-Go protocol             | Off                                        |
| Table position                | H                                          |
| Table position                | 0 mm                                       |
| Inline composing              | Off                                        |
| System—Miscellaneous          |                                            |
| Positioning mode              | REF                                        |
| Table position                | H                                          |
| Table position                | 0 mm                                       |
| MSMA                          | S-C-T                                      |
| Sagittal                      |                                            |
| Coronal                       |                                            |
| Transversal                   |                                            |
| Coil combine mode             | Sum of squares                             |
| Save uncombined               | Off                                        |
| Matrix coil mode              | Auto (triple)                              |
| AutoAlign                     |                                            |
| Coil select mode              | Off—AutoCoilSelect                         |
| System—Adjustments            |                                            |
| B0 Shim mode                  | Cardiac                                    |
| B1 Shim mode                  | TrueForm                                   |
| Adjust with body coil         | Off                                        |
| Confirm freq. adjustment      | Off                                        |
| Assume dominant fat           | Off                                        |
| Assume silicone               | Off                                        |
| Adjustment tolerance          | Auto                                       |
| System—Adjust volume          |                                            |
| Position                      | L4.2 A1.0 H24.6 mm                         |
| Rotation                      | T > C32.0 > S-12.2                         |
| A >> P                        | 7.56°                                      |
| R >> L                        | 275 mm                                     |
| F >> H                        | 340 mm                                     |
| Reset                         | 7 mm                                       |
| Reset                         | Off                                        |
| System—Tx/Rx                  |                                            |
| Frequency 1H                  | 123.197081 MHz                             |
| Correction factor             | 1                                          |
| Gain                          | High                                       |
| Img. scale cor.               | 1.000                                      |
| Reset                         | Off                                        |
| ? Ref. amplitude 1H           | 0.000 V                                    |
| Physio—Signal1                |                                            |
| 1st signal/mode              | ECG/retro                                  |
| Average cycle                 | 290 ± 23 ms                                |
| Average cycle                 | No signal ms                               |
| Calculated phases             | 25                                         |
| TR                            | 45.78 ms                                   |
| Concatenations                | 1                                          |
| Segments                      | 14                                         |
| Arrhythmia detection          | None                                       |
| Physio—Cardiac                |                                            |
| Tagging                       | None                                       |
| Magn. preparation             | None                                       |
| Fat suppr.                    | None                                       |
| Dark blood                    | Off                                        |
| FoV read                      | 340 mm                                     |
| FoV phase                     | 80.80%                                     |
| Phase resolution              | 70%                                        |
| Cine                          | On                                         |

(Continues)
| CINE_segmented_SAX*                          |
|---------------------------------------------|
| **Physio—Cardiac**                          |
| Trajectory | Cartesian |
| View sharing | Off |
| Dummy heartbeats | 1 |
| **Physio—PACE**                              |
| Resp. control | Breath-hold |
| Concatenations | 1 |
| **Inline—Common**                            |
| Subtract | Off |
| Measurements | 1 |
| StdDev | Off |
| Save original images | On |
| **Inline—Cardiac**                           |
| Inline evaluation | Ventricular function |
| Magn. preparation | None |
| TE | 1.43 ms |
| TR | 45.78 ms |
| Save original images | On |
| **Inline—MIP**                               |
| MIP-Sag | Off |
| MIP-Cor | Off |
| MIP-Tra | Off |
| MIP-Time | Off |
| Save original images | On |
| **Inline—Composing**                         |
| Inline composing | Off |
| Distortion corr. | On |
| Mode | 2D |
| Unfiltered images | Off |
| **Sequence—Part 1**                          |
| Introduction | Off |
| Dimension | 2D |
| Reordering | Linear |
| Asymmetric echo | Weak |
| Contrasts | 1 |
| Optimization | Min. TE TR |
| Multi-slice mode | Sequential |
| Echo spacing | 3.3 ms |
| Sequence type | Trufl |
| Bandwidth | 962 Hz/Px |
| **Sequence—Part 2**                          |
| Define | Segments |
| Segments | 14 |
| Trufl delta freq. | 0 Hz |
| RF pulse type | Normal |
| Gradient mode | Fast |
| Excitation | Slice-sel. |
| Flip angle mode | Constant |
| Cine | On |
| **Sequence—Assistant**                       |
| Mode | Min flip angle |
| Min flip angle | 45° |
| Allowed delay | 5 s |