Cardiodynamic changes during passive tilt and acute nitrate therapy

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In six patients with normal left ventricles and seven post-myocardial infarction patients cardiodynamic changes during tilt and acute nitrate medication were investigated. The conductance catheter was used for on-line registration of left ventricular volumes and a microtip manometer for high-fidelity pressure recordings. We analysed left ventricular end-diastolic volume index (EDVI) ejection fraction (EF), cardiac index (CI), heart rate (HR), end-systolic pressure (ESP) and end-diastolic pressure (EDP) in the supine position and 30 s after passive upright tilt. Supine and standing measurements were performed without medication and 2 min after acute nitrate medication (0.8 mg sublingual nitroglycerin).

After unloading by upright tilt there was a similar reduction of average EDVI in the control group (−18 ± 7 ml·m⁻²) and in the post-infarction group (−21 ± 18 ml·m⁻²). The effect of nitroglycerin on EDVI (−12 ± 4 ml·m⁻² control, −7 ± 6 ml·m⁻² post-infarction) was less than the effect of upright tilt. EF in the control group improved by +8 ± 5% (in absolute values) during passive tilt; the combined effect of tilt and nitrate was +12 ± 6% EF (p < 0.05). In the post-infarction group EF did not change significantly during tilt and/or nitrate therapy. In the patients with normal regional ventricular function, CI during tilt was maintained at a constant level. In the post-infarction group the reduction in CI was not significant.

Although the reduction in EDVI was similar in the control and infarction groups, the infarction group did not respond to the cardiodynamic change by increasing EF. The haemodynamic changes during unloading by tilt and acute nitrate medication underline that, when the contractile reserve is reduced, the Frank–Starling mechanism plays an important role in the control of pump function.

Introduction

To evaluate the pump function of the left ventricle the ventricle must be studied under different loading conditions. Of the several methods proposed as loading intervention in the intact circulation the most accepted is balloon inflation in the inferior vena cava. In order to develop a less invasive and yet physiological load intervention we analysed acute haemodynamic changes during passive upright tilt. Analysis of the cardiovascular response to passive tilt is an established method of studying the systolic and diastolic function of the heart. We compared the effects of head-up tilt to the pharmacological preload reduction achieved by acute nitrate therapy and analysed the different effects in normal patients and patients after myocardial infarction.

During upright tilt, the loading conditions change very fast, therefore we used the conductance catheter for continuous registration of the volume signal and a catheter tip-manometer for high-fidelity pressure registration. Although the accuracy of absolute volume measurements with the conductance catheter is disputed by some, it is an accepted method for the registration of relative volume changes.

Material and methods

We investigated patients with normal left ventricles (5 males, 1 female, mean age 55 ± 8 years) and patients post myocardial infarction (PI 7 males, mean age 56 ± 4 years). All patients were in sinus rhythm.

Conductance-derived volume signals were measured in the left ventricle with a pigtail single-field conductance catheter. The conductance signal was externally calibrated to absolute volume by monoplane ventriculography with the volume calculated by the integration method (Simpson’s rule); translation and angulation were corrected using the centre of gravity as a reference. The aortic region was excluded from analysis.

The tilt intervention was performed on a motorized tilt table (Siemens Orbiscope) while the catheter position in the left ventricle was under fluoroscopic control. Elevation of 90° and consecutive lowering to 0° were achieved at a constant angular speed on 10° s⁻¹ with the patient standing on a footplate.

We continuously recorded left ventricular volume, left ventricular pressure and ECG. We analysed the end-diastolic volume index (EDVI), ejection fraction (EF), cardiac index (CI), end-systolic pressure (ESP) and end-diastolic pressure in the supine position and 30 s after head-up tilt. Each tilt test consisted of a cycle of 2 min in the supine position, 2 min standing and another 2 min supine. After 5 min rest acute nitrate therapy was instituted with 0.8 mg sublingual nitroglycerin and haemodynamic measurements were repeated in the supine position. Thereafter, the measurement cycle with tilting was performed again.

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to obtain the combined effects of upright tilt and vasodilation.

All data are presented as mean ± standard deviation for the two groups. Controls and post-infarction (PI) (statistics: paired t-test, $P < 0.05$).

**Results**

Graded passive upright tilt led to a fast change in loading conditions. A cardio-acceleratory response but no syncope was observed.

**END-DIASTOLIC VOLUME INDEX (EDVI)**

At rest, end-diastolic volume index in the PI group was 17 ml.m$^{-2}$ higher than in the control group. After upright tilt, there was a significant reduction in EDVI in the control group of $-18 ± 7$ ml.m$^{-2}$ ($P < 0.05$) but not in the PI group: $-21 ± 18$ ml.m$^{-2}$ (ns).

The effect of nitroglycerin on EDVI in the control group of $-12 ± 4$ ml.m$^{-2}$ ($P < 0.05$) and in the PI group of $-7 ± 6$ ml.m$^{-2}$ (ns) was less pronounced than the effect of upright tilt. The combined effect of head-up tilt and nitroglycerin was $-24 ± 8$ ml.m$^{-2}$ ($P < 0.001$) in the control and $-27 ± 19$ ml.m$^{-2}$ (ns) in the infarction group (Fig. 1).

**STROKE VOLUME INDEX (SVI)**

Without medication SVI at rest was similar in both groups (50 ± 9 ml.m$^{-2}$ in controls, 51 ± 6 ml.m$^{-2}$ in PI). In the supine position, nitrate therapy tended to reduce SVI in the control group by $-6 ± 5$ ml.m$^{-2}$ (ns) and in the PI group by $-3 ± 5$ ml.m$^{-2}$ (ns) but the changes were not significant. Upright tilt in the control group tended to change SVI by $-7 ± 6$ ml.m$^{-2}$ (ns) without medication and by $-4 ± 7$ ml.m$^{-2}$ (ns) after acute nitrate therapy, but again without significance. In the PI group, SVI during headup tilt did not change significantly because of the inhomogeneous response of the post-infarction patients to the unloading intervention: $-10 ± 12$ ml.m$^{-2}$ without medication and $-10 ± 15$ ml.m$^{-2}$ after nitrate (Table 1).

**EJECTION FRACTION (EF)**

EF in the control group increased by $+8 ± 5$% (In absolute values, $P < 0.05$) during upright tilt. The combined effect of tilt and nitrate was $+12 ± 6$% EF ($P < 0.05$) but nitrate therapy alone had no significant effect. In the post-infarction group, EF did not increase significantly during tilt not due to nitrate therapy (Fig. 2).

**HEART RATE (HR)**

The heart rate response to tilt was $+12 ± 6$ min in the controls ($P < 0.05$), and $+5 ± 6$ min in the PI group (ns). After nitrate medication, heart rate response was $+14 ± 5$ min in controls ($P < 0.05$) and $+12 ± 11$ in the PI group (ns). The combined effect of tilt and nitrate medication was $+19 ± 6$ min in controls ($P < 0.05$) and $+13 ± 4$ min in the PI group (ns).

**CARDIAC INDEX (CI)**

In patients with normal regional ventricular function (control), CI during tilt was maintained at a constant level ($3.8 ± 0.6$ l.min.m$^{-2}$ in the supine position; $3.7 ± 0.9$ l.min.m$^{-2}$ in the upright position). After acute nitrate therapy, the tilt resulted in a stable cardiac index with an (insignificant) increase of only $+0.2 ± 0.1$ l.min.m$^{-2}$ (ns). In the post-infarction group there was no significant reduction in CI during unloading on the tilting table ($-0.5 ± 0.8$ l.min.m$^{-2}$ without medication, $-0.3 ± 1.1$ l.min.m$^{-2}$ after nitroglycerin). The combined effect of tilt and nitrate was an (insignificant) reduction in CI of $-0.5 ± 0.9$ l.min.m$^{-2}$ (ns) (Fig. 3).

**END-SYSTOLIC PRESSURE**

Without medication in the control group the end-systolic pressure (ESP) in the left ventricle did not change significantly during head-up tilt ($-7 ± 12$ mmHg), while in the PI group it tended to decrease by $-12 ± 13$ mmHg (ns), but this change was not significant either. The acute nitrate therapy did not decrease ESP ($-7 ± 6$ mmHg in controls and $-9 ± 11$ mmHg in the PI group). The com-

![Figure 1](image1.png)

**Figure 1** End-diastolic volume index (EDV) in the supine and standing positions without medication and after acute nitrate therapy in the control and post-infarction groups. The control and PI groups show a parallel shift of EDVI following upright tilt. $\bigcirc =$ post-infarction; $\bullet =$ post-infarction plus nitroglycerin; $\square =$ control; $\bigstar =$ control plus nitroglycerin.

![Figure 2](image2.png)

**Figure 2** Ejection fraction (EF) in the supine and standing positions without medication and after acute nitrate therapy in the control and post-infarction groups. EF in the control group improved after volume unloading. EF in the PI group does not change significantly. $\bigcirc =$ post-infarction; $\bullet =$ post-infarction plus nitroglycerin; $\square =$ control; $\bigstar =$ control plus nitroglycerin.
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Figure 3  Cardiac index (CI) in the supine and standing positions without medication and after acute nitrate therapy in the control and post-infarction groups. In the control group, CI is nearly constant after tilt and/or nitrate and shows no significant reduction in the PI group. ○ = post-infarction; • = post-infarction plus nitroglycerin; □ = control; ■ = control plus nitroglycerin.

bined effect of nitrate and head-up tilt was a reduction of ESP by $-15 \pm 14$ mmHg in the control group and by $-25 \pm 15$ mmHg in the PI group.

END-DIASTOLIC PRESSURE (EDP)

Head-up tilt reduced EDP by $-10 \pm 5$ mmHg in controls and by $-10 \pm 6$ mmHg in the PI group. After nitrate treatment, the respective reduction in preload on the tilting table were $-9 \pm 2$ mmHg in the controls and $-10 \pm 5$ mmHg in the PI group. The combined effect of tilt and nitrate was $-11 \pm 3$ mmHg in controls and $-12 \pm 7$ mmHg in the PI group.

Discussion

The aim of the study was to compare the cardiodynamic effects of two different load interventions which both have a predominant effect on preload: passive upright tilt and acute nitrate therapy. Upright tilt induced a significant reduction in end-diastolic volume. In accordance with non-invasive studies\(^1\), this study on the conductance catheter underlines that passive tilt is an effective tool for acute reduction of filling volume in the intact circulation. In contrast to the results of DeMey and Enterling\(^2\) we found that graded tilt led to reproducible haemodynamic changes without syncopal events.

When analysing the data separately for patients with normal and post-infarction left ventricles the reduction in EDVI at upright tilt was similar in both groups, but only the patients with normal left ventricles profited from the reduced filling volume by an improvement in ejection fraction.

The post-infarction group did not improve in response to the reduced EDVI, regardless of the method of reducing filling volume (tilt or nitrate). Nitroglycerin led to a left- and downward shift of the diastolic pressure–volume relation in accordance with other studies\(^3-15\). The combined

Table 1  Haemodynamic data in the resting position (supine) and 30 s after upright tilt (standing), in the resting position 2 min after 0.8 mg nitroglycerin sublingual (supine + nitro) and again after upright tilt (standing + nitro). All data are given for the control group (C) and the myocardial infarction group (PI).

<table>
<thead>
<tr>
<th></th>
<th>EDVI (ml.m(^{-2}))</th>
<th>SVI(ml.m(^{-2}))</th>
<th>(EF%)</th>
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<tbody>
<tr>
<td></td>
<td>C</td>
<td>PI</td>
<td>C</td>
</tr>
<tr>
<td>Supine</td>
<td>74 ± 13</td>
<td>91 ± 18</td>
<td>50 ± 9</td>
</tr>
<tr>
<td>Standing</td>
<td>56 ± 15</td>
<td>70 ± 15</td>
<td>43 ± 14</td>
</tr>
<tr>
<td>Supine + nitro</td>
<td>62 ± 14</td>
<td>84 ± 18</td>
<td>44 ± 10</td>
</tr>
<tr>
<td>Standing + nitro</td>
<td>50 ± 15</td>
<td>64 ± 12</td>
<td>40 ± 13</td>
</tr>
<tr>
<td>HR(1 min(^{-1}))</td>
<td>C</td>
<td>PI</td>
<td>C</td>
</tr>
<tr>
<td>Supine</td>
<td>76 ± 6</td>
<td>78 ± 9</td>
<td>3.8 ± 0.6</td>
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<tr>
<td>Standing</td>
<td>88 ± 9</td>
<td>83 ± 12</td>
<td>3.7 ± 0.9</td>
</tr>
<tr>
<td>Supine + nitro</td>
<td>81 ± 7</td>
<td>79 ± 10</td>
<td>3.5 ± 0.6</td>
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<tr>
<td>Standing + nitro</td>
<td>95 ± 8</td>
<td>91 ± 16</td>
<td>3.7 ± 0.9</td>
</tr>
<tr>
<td>ESP(mmHg)</td>
<td>C</td>
<td>PI</td>
<td>C</td>
</tr>
<tr>
<td>Supine</td>
<td>133 ± 12</td>
<td>145 ± 22</td>
<td>19 ± 4</td>
</tr>
<tr>
<td>Standing</td>
<td>131 ± 19</td>
<td>133 ± 31</td>
<td>9 ± 4</td>
</tr>
<tr>
<td>Supine + nitro</td>
<td>125 ± 13</td>
<td>136 ± 19</td>
<td>17 ± 4</td>
</tr>
<tr>
<td>Standing + nitro</td>
<td>118 ± 17</td>
<td>119 ± 20</td>
<td>8 ± 3</td>
</tr>
</tbody>
</table>

EDVI = End-diastolic volume index, SVI = stroke volume index, EF = ejection fraction, HR = heart rate, CI = cardiac index, ESP = end-systolic pressure, EDP = end-diastolic pressure.
The haemodynamic effect of volume unloading by nitrate therapy does not differ from unloading by upright tilt in that nitrate therapy does not shift the Starling curve, but only induces a filling volume reduction along the same Starling curve as measured during upright tilt.

When SVI is plotted against EDVI (Fig. 4), it becomes evident that the haemodynamic effect of volume unloading by nitrate therapy does not differ from unloading by upright tilt. Nitrate therapy does not shift the Starling curve but only induces a filling volume reduction along the same Starling curve as measured during upright tilt. Nitrate therapy does not shift the Starling curve, but only induces a filling volume reduction along the same Starling curve as measured during head-up tilt. The haemodynamic effect of volume unloading by nitrate therapy does not differ from unloading by upright tilt. Nitrate therapy does not shift the Starling curve, but only induces a filling volume reduction along the same Starling curve as measured during upright tilt.

The haemodynamic investigation on the tilting table is thus a non-invasive and effective method of inducing changes in loading conditions and is an alternative to balloon occlusion of the inferior vena cava, up to now the standard method for unloading in the intact circulation.