with hepatitis B virus infection and the efficiency of immunisation with inactivated HBsAg, it is recommended that all anaesthetists should be immunised.

We wish to thank Mrs P. C. Venter and Mr P. J. Swanepoel for excellent technical assistance, and Mrs C. Coetzee and Mrs A. H. van der Merwe for assistance in preparation of the manuscript.

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Absolute left ventricular volume changes after sublingual nitroglycerine and nifedipine intervention

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Summary
The haemodynamic effects of two vasodilators, sublingual nitroglycerine and nifedipine, on absolute end-diastolic volume, end-systolic volume, stroke volume (SV), heart rate, systolic blood pressure (SBP), cardiac output (CO) and corresponding cardiac indices were measured in two different groups, each consisting of 20 ischaemic heart disease patients, with gated blood pool scintigraphy. A control study was done in 5 ischaemic heart disease patients without intervention. Direct measurement of left ventricular (LV) volume was done by correcting LV activity for tissue attenuation utilising a geometric method.

With nifedipine intervention only SBP (125,25 ± 19,8 mmHg) showed a significant mean decrease (11 mmHg). The other measured parameters did not change significantly. With nitroglycerine all the parameters except LV ejection fraction showed significant changes. Mean CO decreased by 8% while mean SV decreased by 16%. The results in the control group showed excellent repeatability.

The absolute haemodynamic changes of future cardiac drugs might easily be measured in vivo by this non-invasive technique.

Nitroglycerine has been used for several decades in clinical medicine and has been well studied by different techniques. Nifedipine, in comparison, belongs to a relatively newer generation of vasodilators which produce smooth-muscle relaxation (especially in arterial walls) by calcium antagonism in very low plasma concentrations. Although it has been well studied in animal experiments, clinical data obtained by non-invasive techniques are relatively limited and even controversial. The purpose of our study was: (i) to determine the absolute left ventricular (LV) volume changes of sublingual nifedipine and nitroglycerine intervention with gated blood pool studies in the clinical situation; and (ii) to assess the applicability of absolute volume determination with gated blood pool scintigraphy as a drug evaluation technique.

Patients and methods
Forty-five patients with ischaemic heart disease (IHD) were evaluated in this study after informed consent had been obtained.
IHD was defined by angiography as a fixed stenosis of 50% or more in at least one major artery. The first group, who were given nifedipine, consisted of 20 patients (17 men) with a mean age of 56 years (30 - 70 years). A spectrum of LV function judged by basal ejection fraction was included (Fig. 1). Nitroglycerine (0.6 mg) was given sublingually to a second group consisting of 20 patients (19 men) with a mean age of 55 years (46 - 71 years). Fig. 2 shows LV ejection fractions at rest for this group. A third group of 5 patients with comparable LV function were chosen so that the repeatability of the technique could be evaluated.

In vivo tagging of the red blood cells was done by intravenous administration of 15 mg stannous pyrophosphate (Amerscan) followed by 99mTc-pertechnetate (740 - 925 MBq) 30 minutes later. Data were acquired with an Ohio Nuclear standard view scintillation camera and a low-energy all-purpose collimator which were connected directly to a computer for data storage. The left anterior oblique (LAO) view provided the best separation between the two ventricles. The R-R interval was divided into 32 equal parts and data were recorded for 10 minutes in a 64 x 64 byte mode matrix. A series of 32 images representing the cardiac cycle was thus obtained. On completion of a 10-minute basal scan in the LAO view, 2 x 10 mg nifedipine capsules or 0.6 mg nitroglycerine were given to the patient sublingually. After a waiting period of 30 minutes for the nifedipine and 5 minutes for the nitroglycerine to take effect, a second 10-minute scan in the LAO view was performed. A venous blood sample of 15 ml was taken with the first as well as the second scan for absolute volume determination, and blood pressure as well as mean heart rate (HR) were measured at both scans. Measurements were done in a similar way for the control group with a waiting period of 30 minutes without drug intervention.

In order to determine the depth of the LV below the thoracic wall a 57Co point source (Fig. 3) was positioned on the patient's chest to coincide with the centre of the LV in the LAO view, and the angle of rotation noted. The detector was then positioned in the anterior view and an image obtained.

Data analysis

LV regions of interest were obtained for each image by a semi-automatic method. A background region of interest 5 pixels wide was chosen automatically, 2 pixels to the left of the inferolateral border of the end-systolic region of interest. Background-corrected counts were obtained for each of the images and a time-activity curve representing the cardiac cycle was generated.

Direct measurement of LV volume was done by correcting LV activity for tissue attenuation. The time-activity curve thus obtained was corrected for attenuation with the linear attenuation coefficient of 0.15 cm⁻¹ for the 140 keV photons of 99mTc. The end-diastolic volume (EDV), end-systolic volume (ESV) and stroke volume (SV) were obtained from the corrected time activity curve. The cardiac output (CO) was determined by SV x HR. The corresponding cardiac indices were determined by correcting the specific parameters for the patient's body surface area.

An elliptical line was drawn around the LV in the anterior view to determine the centre of mass. The depth is calculated as the
quotient of the horizontal distance from the centre of the LV in
the anterior view to a similar spot in the LAO view divided by the
sine of the angle θ of rotation (Fig. 3). LV volume was then
determined by:

\[
\text{count rate of LV} \times e^{\mu_d}
\]
\[
\text{count rate/ml peripheral blood}
\]

where \(\mu\) = linear attenuation coefficient of water, i.e. 0.15 cm \(^{-1}\) for
140 keV photons of \(^{99m}\) Tc; and \(d\) = the depth of the centre of the LV
below the thoracic wall. If the activity in the peripheral blood
was obtained with the same computer and camera system,
correction for system sensitivity was not necessary, but blood
activity had to be corrected for decay. Correction for attenuation
was done by multiplying LV activity with \(e^{\mu_d}\).

The statistical analysis of the data includes the comparison
between the pre- and post-intervention values with paired \(t\)-tests.
A probability value \(P < 0.05\) was considered to be significant.

**Results**

The mean changes in the different parameters before and after
nifedipine intervention or nitroglycerine intervention and in the
control group are summarised in Tables I - III. With nifedipine
intervention only systolic blood pressure decreased significantly.
With nitroglycerine intervention all the measured parameters except
the LV ejection fraction changed significantly. In the control
group no significant change was seen except for a slight increase in
HR, which can probably be attributed to the blood sampling
procedure at the end of the first study.

**Discussion**

Radionuclide imaging offers a unique opportunity to estimate
LV volume without evoking geometric models. The most
commonly used technique employs the principle that blood
pool counts measured over the LV at the body surface are
proportional to the LV volume, when corrections are made for
the background contribution and when the count rate per
millilitre of blood is known.\(^7\) Individually measured attenuation
correction factors clearly enhance accuracy.\(^8\)

Since the patients were randomly chosen from the IHD
clinic, certain differences in mean ESV, SV and LV ejection
fractions (LVEF) exist between the two groups. The results
must, therefore, be interpreted as the effect of drug intervention
in a certain group of patients rather than a comparison between
the two drugs.

With nifedipine intervention systolic blood pressure
decreased significantly and all the other variables tended to

**TABLE I. MEAN VALUES AND CHANGES IN ABSOLUTE HAEMODYNAMIC VARIABLES BEFORE AND AFTER NIFEDIPINE INTERVENTION**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean before intervention</th>
<th>Changes</th>
<th>(t)-value</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDV (ml)</td>
<td>192.8</td>
<td>+1.3</td>
<td>1.06</td>
<td>0.5 &gt; (P &gt; 0.1)</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>133.5</td>
<td>-0</td>
<td>0</td>
<td>(P &gt; 0.5)</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>39.1</td>
<td>-0.15</td>
<td>0.16</td>
<td>(P &gt; 0.5)</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>59.3</td>
<td>+1.4</td>
<td>0.55</td>
<td>(0.5 &gt; P &gt; 0.1)</td>
</tr>
<tr>
<td>HR (c/min)</td>
<td>83.7</td>
<td>+1.7</td>
<td>1.41</td>
<td>(0.5 &gt; P &gt; 0.1)</td>
</tr>
<tr>
<td>CO (l/min)</td>
<td>4.88</td>
<td>+0.22</td>
<td>1.36</td>
<td>(0.5 &gt; P &gt; 0.1)</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>125</td>
<td>-11</td>
<td>5.46</td>
<td>(P &lt; 0.001)*</td>
</tr>
<tr>
<td>EDV index (ml/m')</td>
<td>105</td>
<td>+0.5</td>
<td>0.72</td>
<td>(0.5 &gt; P &gt; 0.1)</td>
</tr>
<tr>
<td>ESV index (ml/m')</td>
<td>73.2</td>
<td>-0.2</td>
<td>0.16</td>
<td>(P &gt; 0.5)</td>
</tr>
<tr>
<td>Cardiac index (l/min/m')</td>
<td>2.67</td>
<td>-0.12</td>
<td>0.83</td>
<td>(0.5 &gt; P &gt; 0.1)</td>
</tr>
</tbody>
</table>

*Statistically significant on the paired \(t\)-test.

**TABLE II. MEAN VALUES AND CHANGES IN ABSOLUTE HAEMODYNAMIC VARIABLES BEFORE AND AFTER NITROGLYCERINE INTERVENTION**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean before intervention</th>
<th>Changes</th>
<th>(t)-value</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDV (ml)</td>
<td>182.1</td>
<td>-25</td>
<td>6.32</td>
<td>(P &lt; 0.001)*</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>105.5</td>
<td>-13.6</td>
<td>5.63</td>
<td>(P &lt; 0.001)*</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>47.5</td>
<td>+0.6</td>
<td>0.61</td>
<td>(P &gt; 0.5)</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>76.8</td>
<td>-12.7</td>
<td>3.91</td>
<td>(P &lt; 0.001)*</td>
</tr>
<tr>
<td>HR (c/min)</td>
<td>78.8</td>
<td>+5.8</td>
<td>4.05</td>
<td>(P &lt; 0.001)*</td>
</tr>
<tr>
<td>CO (l/min)</td>
<td>5.79</td>
<td>-0.46</td>
<td>2.31</td>
<td>(P &lt; 0.05)*</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>131.8</td>
<td>-11.5</td>
<td>5.19</td>
<td>(P &lt; 0.001)*</td>
</tr>
<tr>
<td>EDV index (ml/m')</td>
<td>91.8</td>
<td>-12.8</td>
<td>6.43</td>
<td>(P &lt; 0.001)*</td>
</tr>
<tr>
<td>ESV index (ml/m')</td>
<td>53.2</td>
<td>-6.60</td>
<td>5.67</td>
<td>(P &lt; 0.001)*</td>
</tr>
<tr>
<td>Cardiac index (l/min/m')</td>
<td>2.91</td>
<td>-0.22</td>
<td>2.34</td>
<td>(P &lt; 0.05)*</td>
</tr>
</tbody>
</table>

*Statistically significant on the paired \(t\)-test.

**TABLE III. MEAN VALUES AND CHANGES IN ABSOLUTE HAEMODYNAMIC VARIABLES WITHOUT INTERVENTION**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean before tests</th>
<th>Changes</th>
<th>(t)-value</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDV (ml)</td>
<td>171.6</td>
<td>-0.8</td>
<td>0.40</td>
<td>(P &gt; 0.5)</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>112</td>
<td>+1.2</td>
<td>0.60</td>
<td>(P &gt; 0.5)</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>38</td>
<td>+0.6</td>
<td>0.52</td>
<td>(P &gt; 0.05)</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>58.6</td>
<td>+1.6</td>
<td>0.63</td>
<td>(P &gt; 0.5)</td>
</tr>
<tr>
<td>HR (c/min)</td>
<td>72.6</td>
<td>+2</td>
<td>7.45</td>
<td>(0.01 &gt; P &gt; 0.001)*</td>
</tr>
<tr>
<td>CO (l/min)</td>
<td>4.23</td>
<td>+0.23</td>
<td>1.28</td>
<td>(0.5 &gt; P &gt; 0.1)</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>136</td>
<td>-4</td>
<td>1.82</td>
<td>(0.5 &gt; P &gt; 0.1)</td>
</tr>
<tr>
<td>EDV index (ml/m')</td>
<td>90</td>
<td>-0.4</td>
<td>0.40</td>
<td>(P &gt; 0.5)</td>
</tr>
<tr>
<td>ESV index (ml/m')</td>
<td>59.6</td>
<td>+0.6</td>
<td>0.62</td>
<td>(P &gt; 0.5)</td>
</tr>
<tr>
<td>Cardiac index (l/min/m')</td>
<td>2.16</td>
<td>+0.11</td>
<td>1.29</td>
<td>(0.5 &gt; P &gt; 0.1)</td>
</tr>
</tbody>
</table>

*Statistically significant on the paired \(t\)-test.
increase slightly. The mean ESV, however, showed no change. The fact that the mean EDV did not change significantly in this group, implies that preload was within normal limits at the time of the study, as described previously. There are three possible explanations for the non-significant changes in mean ESV, SV, CO and LVEF in this group. Firstly, most patients had received nifedipine 10 mg 8-hourly as part of their treatment for IHD. Although the last oral dosage of the drug was stopped at least 8 hours before the study, the relatively long plasma half-life of the drug might have masked the acute effects. This has been noted previously. The second possibility is that patients with decreased LV function were being treated for cardiac failure and were therefore under fairly good haemodynamic control. Furthermore, the study was done under basal conditions and this group was therefore comparable with a relatively normal population. As shown before, SV, CO and LVEF did not change after nifedipine intervention in a group of normal volunteers.

A third possibility is as follows: peripheral resistance is the difference between arterial and venous pressure divided by flow, i.e. CO; thus flow is pressure difference divided by resistance. If the ratio of decrease in resistance and decrease in arterial and venous pressure difference remains the same, the CO (i.e. flow) will not change. The mean blood pressure, however, will decrease with reduction of the workload of the heart without significant changes in CO.

In contrast with nifedipine, nitroglycerine intervention produced significant changes in all the variables except LVEF. HR increased significantly while all the other variables decreased significantly. The mean CO decreased by 8% while the mean SV decreased by almost 16%. The ratio of the decrease in mean SV and mean EDV stayed almost constant and therefore LVEF did not change significantly.

Results obtained from the control group showed excellent repeatability. The slightly significant increase in HR without intervention could be ascribed to the blood sampling procedure at the end of the first recording. The HR increased by 2/min in these 5 patients.

Conclusions

The radionuclide technique for measuring absolute cardiac volume changes after drug intervention was found to be effective and highly applicable in the clinical situation.

Nitroglycerine intervention significantly decreases pre- and afterload of the heart as well as CO, as has been reported previously. Nifedipine decreases systolic blood pressure significantly, thereby reducing the workload of the heart with a non-significant increase in CO. The effect on preload is probably limited. Nifedipine can be used in addition to other vasodilators, not only for symptomatic treatment of angina but also when increased CO is required.

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