Effects of Nitroglycerin on Left Ventricular Function in Patients with Ischemic Heart Disease

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SUMMARY

To evaluate the effects of nitroglycerin on left ventricular function in 27 patients with ischemic heart disease, ejection fraction (EF) was measured every 1 to 5 min by a nuclear stethoscope after sublingual administration of nitroglycerin (0.3 mg).

(1) There was a good correlation between EF determined by the nuclear stethoscope and EF by left ventriculography ($r=0.80$, $p<0.001$). (2) EF showed a rise after sublingual nitroglycerin, which was most marked at 4 to 7 min and returned to the control level in 20 to 25 min. (3) There were no significant differences in the maximum percent increase in EF among patients with 0, 1, 2 and 3 vessel disease. The maximum percent increases in EF were $34.0\pm10.0\%$ in the normal contraction group, $24.0\pm8.5\%$ in the hypokinesis group ($p<0.05$ vs the normal contraction group) and $15.2\pm8.5\%$ in the akinesis group ($p<0.01$ vs the normal contraction group, $p<0.05$ vs the hypokinesis group). (4) There was a weak correlation between the maximum percent increase in EF and the changes in heart rate ($r=0.49$, $p<0.05$) and there was an inverse correlation between the maximum percent increase in EF and the changes in systolic blood pressure ($r=-0.65$, $p<0.01$).

It was shown that the improvement in EF by sublingual nitroglycerin was greatest in the normal contraction group, somewhat less in the hypokinesis group and least in the akinesis group. The nuclear stethoscope is useful in monitoring changes in left ventricular function during intervention.

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NITROGLYCERIN is commonly used in patients with ischemic heart disease and its effects on cardiovascular hemodynamics[1)–3)] and coronary blood flow[4)–6)] have been studied. Recently, there has been considerable interest in the effects of nitroglycerin on left ventricular wall motion in patients with ischemic heart disease.[7)–13)] It has been reported that left ventricular wall motion abnormalities are a common result of ischemic heart disease[14),15)] and that hypokinetic wall motion improved in a majority of patients, following nitroglycerin, while dyskinetic motion was unchanged and the akinetic segments had an intermediate response.[7),10),11)]

We evaluated the effects of sublingual nitroglycerin on ejection fraction (EF) in patients with normal and abnormal wall motion, using the nuclear stethoscope[16),17)] which is an ECG-triggered, non-imaging nuclear probe. It has been shown that there is a good correlation between EF measured by the nuclear stethoscope and by the camera-computer system.[16),17)]

The present study was undertaken using the nuclear stethoscope to determine: (1) The correlation between EF measured by the nuclear stethoscope and left ventriculography, (2) serial changes in EF after sublingual administration of nitroglycerin, (3) changes in EF according to the findings of coronary angiography and left ventriculography and (4) the correlation between the changes in EF and the changes in hemodynamic parameters.

Subjects and Methods

Subjects:

Twenty-seven patients, 22 males and 5 females, with a mean age of 56 years (range 37 to 71 years) were studied. Nine patients had angina pectoris, 11 had had previous myocardial infarction and 7 had chest pain syndrome with normal coronary arteries. Coronary angiography and left ventriculography were performed in all patients and significant coronary artery disease was defined as 75% or greater stenosis of one or more of the three major coronary vessels. Eight had one-vessel disease, 9 had two-vessel disease and 3 had three-vessel disease. Seven had normal coronary arteries. According to left ventriculography, 7 had normal contraction, 10 had hypokinesis and 10 had akinesis.

None of the patients had clinical or radiological evidence of heart failure and none had used sublingual nitroglycerin, long-acting nitrates or calcium

antagonists for at least 12 hours prior to the study.

Methods:

Left ventricular function was measured with a nuclear stethoscope (Bios Inc., USA), which is a simple, mobile, non-imaging nuclear probe with an integrated microcomputer. After administration of 15 mCi of technetium-99m human serum albumin, the probe was placed in front of the chest in the 20–40° left anterior oblique position with a 10–20° caudal tilt. Ejection fraction (EF) was measured using the ventricular function mode with an acquisition period of 60 sec.

Fig. 1 shows the average left ventricular volume curve displayed after background substraction. Here, the cursors indicate end-diastolic and end-

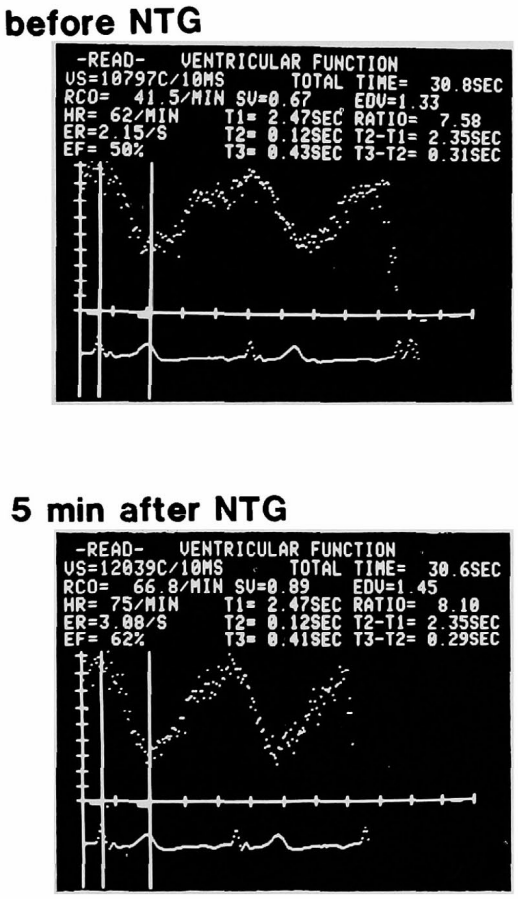

Fig. 1. The average left ventricular volume curve displayed after background substraction. Two cursors indicate end-diastolic and end-systolic count rate. EF and other parameters are shown at the upper part of the photograph. Abbreviation: NTG=nitroglycerin.

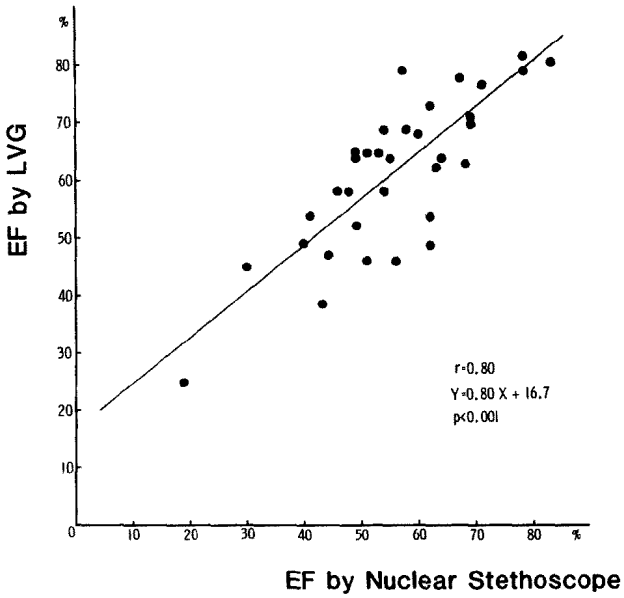

Fig. 2. The correlation between EF by the nuclear stethoscope and EF by left ventriculography in 35 patients with ischemic heart disease. Abbreviation: LVG=left ventriculography.

systolic count rates. EF and other parameters are automatically computed from this curve. As shown in this curve, EF increased from 50% to 62% 5 min after administration of sublingual nitroglycerin.

After sublingual administration of 0.3 mg of nitroglycerin, EF by the nuclear stethoscope, blood pressure and heart rate were measured serially every 1 to 5 min for 30 min.

All data are reported as mean±SD except those in Fig. 3, which are shown as mean±SEM and compared using Student's t-test. A p value of less than 0.05 was considered significant.

Results

(1) Comparison of left ventricular EF by the nuclear stethoscope and left ventriculography

EF was measured in 35 patients by both the nuclear stethoscope and left ventriculography (Fig. 2). There was a close correlation between the two methods with a correlation coefficient of 0.80 ($p<0.001$).

(2) Serial changes in EF after sublingual nitroglycerin

Fig. 3 shows the percent increase in EF after sublingual administration of nitroglycerin. Based upon ventricular contraction determined by left ven-

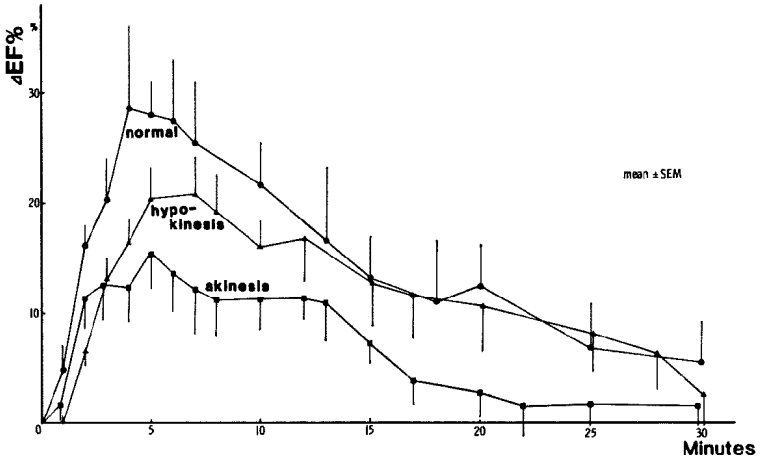

Fig. 3. The percent increase in EF (ΔEF%) after sublingual administration of nitroglycerin. Patients are divided into 3 groups according to ventricular contraction by left ventriculography.

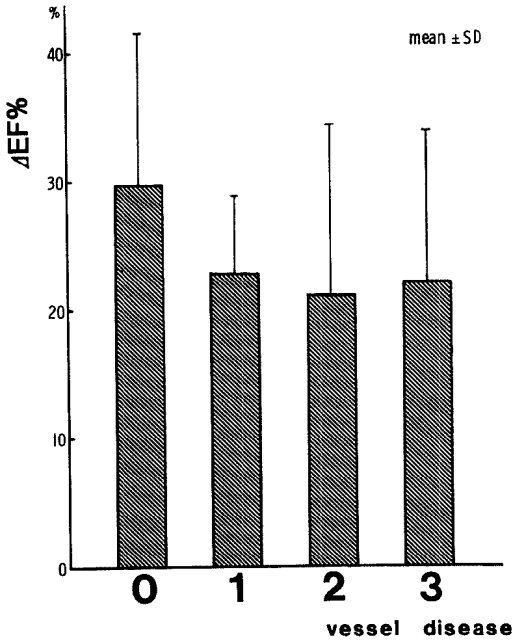

Fig. 4. The maximum percent increase in EF (ΔEF%) according to the findings of coronary angiography.

triculography, 3 groups of patients showed a rise in EF, which was most marked at 4 to 7 min. EF returned to the control level in 20 to 25 min after sublingual administration of nitroglycerin.

(3) Changes in EF according to the findings of coronary angiography

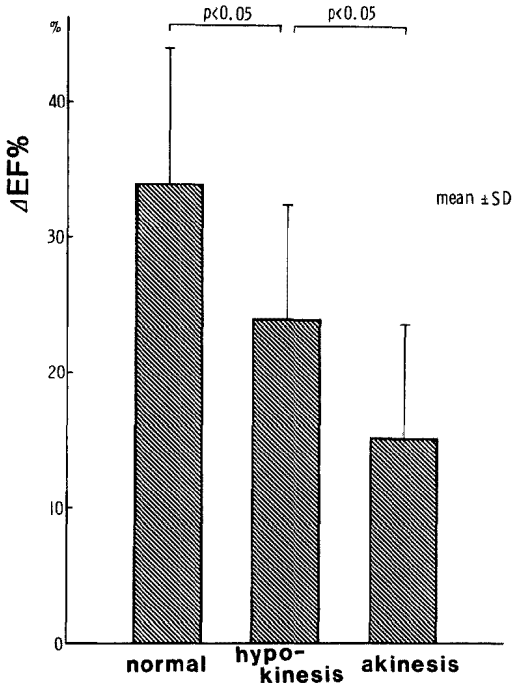

Fig. 5. The maximum percent increase in EF (ΔEF%) according to the findings of left ventriculography.

and left ventriculography

Following administration of sublingual nitroglycerin, the mean EF improved from 56.0±6.6% to 72.6±9.6% ($p<0.001$) in 0-vessel disease, from 54.6±13.9% to 67.5±18.5% ($p<0.001$) in 1-vessel disease, from 53.1±12.0% to 65.2±20.2% ($p<0.01$) in 2-vessel disease and from 46.3±5.0% to 56.3±5.1% (n.s.) in 3-vessel disease. The maximum percent increases in EF were 29.8±11.8%, 22.9±6.0%, 21.1±13.3% and 22.1±11.8%, in 0, 1, 2 and 3 vessel disease, respectively (Fig. 4). There were no significant differences in the maximum percent increase in EF.

The mean EF improved from 52.9±8.5% to 70.3±10.7% ($p<0.001$) in the normal contraction group, from 57.4±9.6% to 71.1±14.9% ($p<0.001$) in the hypokinesis group and from 48.7±11.5% to 56.8±16.4% ($p<0.01$) in the akinesis group. The maximum percent increases in EF were 34.0±10.0% in the normal contraction group, 24.0±8.5% in the hypokinesis group ($p<0.05$ vs the normal contraction group) and 15.2±8.5% in the akinesis group ($p<0.01$ vs the normal contraction group, $p<0.05$ vs the hypokinesis group) (Fig. 5).

(4) The correlation between the maximum percent increase in EF and

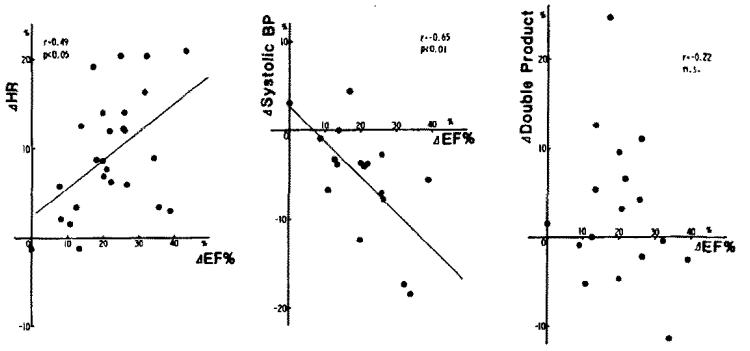

Fig. 6. The correlation between the maximum percent increase in EF (ΔEF%) and the changes in heart rate (ΔHR), systolic blood pressure (Δsystolic BP) and double product (Δdouble product).

the changes in hemodynamic parameters

There was a weak correlation between the maximum percent increase in EF and the changes in heart rate ($r=0.49$, $p<0.05$) and there was an inverse correlation between the maximum percent increase in EF and the changes in systolic blood pressure ($r=-0.65$, $p<0.01$). There was no correlation between the maximum percent increase in EF and the changes in double product ($r=-0.22$, n.s.) (Fig. 6).

Discussion

In this study, we have used the nuclear stethoscope to study the rapid sequence of events during sublingual nitroglycerin administration. The nuclear stethoscope has the obvious advantages of offering rapid bedside measurement of left ventricular function and monitoring changes in left ventricular performance non-invasively during intervention with cardiac drugs.

We have found, as have other investigators,[9),10),12),18)] that in patients with normal coronary artery and ischemic heart disease, nitroglycerin can improve EF while the patient is at rest. Our results indicate that the improvement in EF following administration of nitroglycerin was greatest in the normal contraction group, somewhat less in the hypokinesis group and least in the akinesis group. The improvement in global left ventricular ejection fraction might be a result of by the improvement in segmental wall motion, as Shah et al[19)] have reported. Helfant[7)] and others[10),11)] have also reported that most of the improvement in ventricular wall motion occurred in the hypokinetic segments and that frank dyskinesis was not improved by nitroglycerin. EF in the hypokinesis group might have improved as a result of

the remaining areas of still functionally reversible myocardium[20] possessing functional contractile reserve and being capable of responding to nitroglycerin administration. Bodenheimer et al[20] have reported that histopathologically, the improved area of myocardium after nitroglycerin showed less than 10% muscle loss.

The possible mechanisms of action of nitroglycerin have been reported as improvement in oxygen delivery to ischemic tissue by increasing total myocardial blood flow[2),4)] or producing a redistribution of flow[5),6)] and a reduction in myocardial oxygen demand by decreasing preload[1),3)] and afterload.[21),22)] The mechanism responsible for the beneficial effects of nitroglycerin[23)] cannot be elucidated from the findings of the present investigation as the myocardial blood flow and preload were not measured in this study. There was an inverse correlation between the maximum percent increase in EF and the changes in systolic blood pressure in our investigation and this observation suggests that the improved ventricular function could have been secondary, at least in part, to the effects of nitroglycerin on afterload.

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