Intravenous Nitroglycerin Therapy to Limit Myocardial Infarct Size, Expansion, and Complications

Effect of Timing, Dosage, and Infarct Location

Bodh I. Jugdutt, MBChB, MSc, and J. Wayne Warnica, MD

To determine 1) whether the effect of intravenous nitroglycerin (NG) therapy during acute myocardial infarction on creatine kinase infarct size is influenced by infarct location (anterior vs. inferior), timing (therapy <4 hours vs. ≥4 hours after onset of pain), and dose response (mean blood pressure ≥80 mm Hg vs. <80 mm Hg during the first 12 hours) and 2) whether NG therapy modifies infarct expansion, 310 patients were randomly allocated to NG (n = 154) and control (n = 156) groups. NG infusion was titrated to lower mean blood pressure by 10% in normotensive and 30% in hypertensive patients, but not below 80 mm Hg, and was maintained for 39 hours. Measurements included clinical variables, creatine kinase infarct size (geq) as well as left ventricular (LV) asynergy, LV ejection fraction, expansion index, and thinning ratio on serial two-dimensional echocardiography. Compared with controls, creatine kinase infarct size was less in the NG group (41 vs. 55 geq, p<0.001), in anterior (44 vs. 58 geq, p<0.05), and inferior (39 vs. 53 geq, p<0.025) NG subgroups, and in early than late NG subgroups (43% vs. 22% decrease). Other indexes of infarct size also improved (p≤0.05) with NG compared with controls. Thus, by 10 days, LV asynergy was 40% less, LV ejection fraction was 22% more, and Killip class score was 41% less. A negative effect of mean blood pressure <80 mm Hg with NG was reflected in these indexes. In addition, expansion index increased (p<0.001) by 31% and thinning ratio decreased (p<0.001) by 17% in controls by 10 days but remained unchanged with NG. Infarct-related major complications were less frequent in the NG than the control groups: infarct expansion syndrome (2% vs. 15%, p<0.0005), LV thrombus (5% vs. 22%, p<0.0005), cardiogenic shock (5% vs. 15%, p<0.005), and infarct extension (11% vs. 22%, p<0.025). Mortality was less in NG than in control groups in-hospital (14% vs. 26%, p<0.01), at 3 months (16% vs. 28%, p<0.025) and 12 months (21% vs. 31%, p<0.05), but this advantage was only found in the anterior subgroups. The results indicate that NG therapy in acute myocardial infarction limits indexes of infarct size, infarct expansion, and major infarct-related complications independent of infarct location. Greater benefit on infarct size occurs with early timing and target mean blood pressure ≥80 mm Hg. (Circulation 1988;78:906–919)

Intravenous nitroglycerin (NG) therapy during acute myocardial infarction (AMI) has the potential for limiting infarct size, infarct complications, and mortality.1-2 The combined results of four randomized clinical studies3-6 suggest that the beneficial effect on infarct size might depend on the timing of therapy and infarct location.3-6 Experimental studies suggest that the dose might be of critical importance.7,8 Thus, intravenous NG therapy in low dose during the first 6 hours after coronary artery ligation reduced the size of both inferior7 and anterior8 infarcts, but the beneficial effects on infarct size and collateral flow were abolished when hypotension was induced by higher doses of NG.8 An additional benefit of low-dose NG therapy over the first 6 hours of AMI in the canine model was a decrease of infarct expansion at 7 days.9

Despite encouraging findings in the clinical studies, such as decreased left ventricular (LV) filling...
pressure, improved global LV function, decreased electrocardiographic ST-segment elevation, decreased creatine kinase (CK) infarct size, persistently decreased endocardial surface area of LV asynergy on serial two-dimensional echocardiography, and improved perfusion and defect scores on thallium scintigraphy, the use of intravenous NG therapy in AMI for myocardial salvage has not gained general acceptance. This hesitation might be partly attributable to the lack of clear demonstration of benefit in all clinical studies, fear of NG-induced hypotension in AMI, and lack of simple guidelines for titrating the dose. Thus, Jaffe et al. treated patients within 10 hours of onset of pain and found benefit only in inferior infarcts. Bussmann et al. found benefit with therapy begun before and after 8 hours of onset of pain in anterior and inferior AMI. Flaherty et al. did not find differences between NG and placebo groups, but retrospective analysis suggested benefit in patients given NG within 10 hours of onset of pain, especially those with inferior AMI. We reported benefit with NG therapy 5.9 hours (range, 4–6 hours) of onset of anterior transmural AMI. Although there is agreement that the dose should be low, various titration endpoints were used: 1) a 10–30% decrease in LV filling pressure and not more than 10% decrease in mean blood pressure (MBP); 2) a 10% decrease in systolic blood pressure (SBP) but not below 90 mm Hg or no more than 200 μg/min and a heart rate not below 50 beats/min and an increase of no more than 20 beats/min; 3) a 10% decrease in MBP, but SBP not below 90 mm Hg and heart rate not below 50 beats/min; and 4) 10% decrease in MBP but not below 80 mm Hg. There is now agreement that therapy should be started early, probably earlier than 4 hours of onset of AMI, and continued for 24–48 hours to ensure maximum benefit.

The two primary objectives of this prospective randomized study were to determine whether 1) the effect of intravenous NG therapy over the first 48 hours of AMI on CK infarct size is significantly influenced by infarct location (anterior vs. inferior), timing (within or later than 4 hours of onset of pain), and the dose response (assessed by the level of the hypotensive response with MBP more or less than 80 mm Hg) and 2) such NG therapy to decrease preload, afterload, and infarct size might also reduce the frequency of infarct expansion. A secondary objective was to assess whether NG therapy can be given safely in the conventional clinical setting without compulsory invasive hemodynamic monitoring. With the expected sample size of 300 patients and limitation in obtaining adequate repeated two-dimensional echocardiography recordings in AMI, emphasis was placed on clinical and laboratory endpoints rather than mortality.

Materials and Methods

Patients

Between 1981 and 1983, 310 consecutive patients admitted to the coronary care unit of the University Hospital with AMI within 12 hours of onset of pain (mean, 5.0±3.9 years; range, 0–12 years) were entered into this single-blinded randomized prospective study (Table 1). Admission criteria included prolonged chest pain typical of AMI; evidence on a 12-lead electrocardiogram of persistent ST-segment elevation more than 0.2 mV in two or more adjacent precordial leads or two of three inferior leads; subsequent electrocardiographic abnormalities and cardiac enzyme evidence of AMI; clinical Killip class on admission of I, II, or III; and systolic blood pressure more than 100 mm Hg and heart rate less than 120 beats/min. Exclusion criteria included age more than 75 years, heart rate less than 55 beats/min, heart block, cardiogenic shock (Killip class 4), persistently severe hypertension (blood pressure more than 200 mm Hg systolic and 120 mm Hg diastolic) requiring alternative therapy, and the right ventricular infarction syndrome. During the first 48 hours, all patients received nasal oxygen, intravenous morphine for pain, and continuous lidocaine infusion (1 mg/min). Intramuscular injections were not used.

Protocol

Written informed consent was obtained from all patients before randomization to NG or placebo.
treatment. The study protocol was approved by the committee on human research. Patients were assigned at entry to early and late subgroups on the basis of whether timing from onset of pain was within or after 4 hours and to anterior and inferior subgroups on the basis of electrocardiographic infarct location. Patients were also stratified into subgroups with 6-hour and 10-hour cutoffs from onset of pain to therapy for comparison with other studies.3-5 At termination of NG infusion, two further subgroups were defined on the basis of the development of a hypotensive response (i.e., MBP below 80 mm Hg and MBP of 80 mm Hg or more during the first 12 hours). MBP was calculated by the formula: MBP = (2 × diastolic pressure + systolic pressure)/3. As described previously,6 NG solutions for intravenous infusion were prepared by the hospital pharmacy. NG powder (Parke-Davis) was dissolved in ethyl alcohol and sterile water, filtered (0.22 μm millipore), and transferred to glass vials, each containing 0.8 mg/ml in 10 ml. All vials were tested for sterility and pyrogen, refrigerated, protected from light, and used within 4 weeks. Before use, the solutions were diluted in 5% dextrose in water to a final concentration of 60 μg/ml in the buretrol. Infusions were made via an infusion pump through standard intravenous sets at a rate of 5 μg/min and increased by 5–20 μg/min every 5 minutes in the first 30 minutes until the MBP was reduced from its control value by 10% in normotensive patients and up to 30% in hypertensive patients (blood pressure more than 140/90 mm Hg) but not below 80 mm Hg. With these target rates, the initial decrease in MBP was 10±8% (range, −12% to +32%) in 94 normotensive patients and 19±9% (range, −1% to +37%) in 60 hypertensive patients, and MBP fell below 80 mm Hg in only 15 patients (four with anterior and 11 with inferior infarction), requiring the infusion rate to be decreased. The infusion rates were maintained at the final target levels for at least 48 hours. The infusions were slowly or temporarily stopped whenever the MBP fell below 80 mm Hg. The average infusion rate required to lower MBP to the desired level was 45±34 μg/min (range, 4–192 μg/min) for all patients, the values being 39±30 μg/min in normotensive patients and 54±39 μg/min in hypertensive patients. After 48 hours, the NG infusion was gradually tapered and discontinued. The duration of the infusion averaged 39.2±25.3 hours (range, 1–154 hours), exceeding 12 hours in 89%. It had to be stopped by 1–3 hours in five patients (or 3%) because of a MBP persistently below 80 mm Hg.

The control patients were given 5% dextrose in water intravenously without NG at a constant rate of 1 ml/min as placebo for the 48 hours.

Measurements

During the first 48 hours, all patients had the following parameters recorded at least twice over 0.5 hours before the treatments, repeated serially during the treatments (1–4/hr over the first 12 hours and 4–12/hr over the next 36 hours) and at 1 hour after treatments were stopped: heart rate, blood pressure (by sphygmomanometer), CK activity, and two-dimensional echocardiography studies for LV asynergy,6,15 for volume and ejection fraction,6,15,16 and for indexes of expansion.12,13 The two-dimensional echocardiography studies were repeated on days 4, 6, 8, and 10 and at predischarge. All patients had continuous electrocardiographic monitoring for the first 48 hours or more. Additional data, during the infusions and the subsequent interval to day 10 and predischarge, were collected on all complications and all other drugs or therapies used. Where close hemodynamic monitoring was clinically indicated (48 patients: 19 NG; 29 controls), arterial lines (for blood pressure) and thermodilution flotation catheters (for pulmonary capillary wedge pressure, right heart pressures, and cardiac output) were used. Blood samples for total CK activity were drawn in all patients before the infusions and at 2–4 hour intervals during the infusions for up to 48 hours or more until baseline levels were reached. Total CK activity values were used to compute CK-infarct size in gram-equivalents (Model 9874A, Hewlett-Packard), as described previously.6 CK-MB could not be measured on all patients.

Complete two-dimensional echocardiographic recordings (Diasonics V3400R phased-array ultrasonograph) were made in all patients6 with adequate visualization of the four cardiac chambers and ventricular walls. Standard two-dimensional echocardiographic views including parasternal long-axis, four short-axis (at mitral, chordal, midpapillary, and low papillary levels), and apical four- and two-chamber, were videotaped systematically for review in real-time, slow-motion, and single-frame format. The positions of the patients and transducer were noted for use in serial studies, as described previously.6,15

All patients were followed for at least 12 months for complications, cardiovascular events, and functional class as per questionnaire. Data collected at different stages of the study were coded (i.e., blinded for patient identity and grouping) by a nurse-technician. These codes were not broken until all data collection and analyses were completed. Members of the investigative team were not involved in the care of the patients. Other drugs or therapies were not manipulated.

The clinical syndrome of infarct expansion2,9-13 was diagnosed in patients who developed a second acute event after 48 hours of AMI associated with 1) acute hypotension (systolic blood pressure <90 mm Hg and peripheral hypoperfusion), LV failure with pulmonary congestion, evidence of LV dilatation, with or without further chest pain, no significant new ECG changes of injury, no significant new plasma CK elevation (<100 IU/l) suggesting new necrosis, and 2) two-dimensional echocardiographic evidence of regional diastolic stretching (>25% increase in asynergy-containing endocardial
Analysis of Two-dimensional Echocardiographic Data

Coded recordings (tape and log numbers) were analyzed separately in three steps by two observers, with no knowledge of patient identity or grouping. Three serial two-dimensional echocardiographic recordings from 12 normal subjects (athletes with normal histories, electrocardiogram, and exercise stress test) were also coded and analyzed with the study patients. Differences were resolved by consensus. Interobserver error in measurements was small (less than 1% in marking asynergy, segment length, and wall thickness; less than 4% in areas of outlines). First, endocardial and epicardial LV outlines were traced on plastic overlays from electrocardiogram-gated images frozen at end diastole and end systole and modified on multiple playbacks. Special attention was given to anatomic landmarks (papillary muscle markings; right ventricular and LV junctions) and shape. Second, markings of the extent of LV asynergy, defined as akinesis (no systolic inward motion and thickening) or dyskinesis (systolic outward motion and thinning) or both were made on each LV endocardial diastolic outline by careful visual assessment of wall motion and thinning on repeated real-time video playbacks, as reported from this laboratory.6,15 Care was taken to ensure that asynergic segments did not show systolic inward endocardial motion and thickening by comparing wall thicknesses in systole and diastole (light-pen system) and comparing aligned diastolic outlines.6,15,17 The endocardial diastolic outlines and asynergic segments were then digitized (Models 9874A and 9835A, Hewlett-Packard) for computing the circumferential and angular extents of asynergy in each short-axis section as percent, as well as the total extent of LV asynery as percent surface area of the endocardial shell, with the apical four-chamber and four serial short-axis data as described previously.6,15 Because regional shape distortion was present in the asynergic zones on diastolic outlines in patients with Q wave infarction, the "ideal" asynergic segment corresponding to the angular extent of "actual" asynery was used to compute total LV asynery and avoid overestimation.18,19 Global ejection fractions were calculated from LV end-diastolic and end-systolic volumes that were computed from outlines of two long-axis views (apical four- and two-chamber) and four short-axis views with the modified Simpson's rule.6,15,16 Third, topographic measurements were made on end-diastolic outlines of short-axis images at the mid-LV or papillary level.12 Expansion index was computed as the ratio of the asynergy containing endocardial segment length to that of the nonasynergy containing endocardial segment length.6,12,13 Thinning ratio was computed as the ratio of the average thickness of the asynergic zone to the average thickness of the nonasynergic zone.6,12

Statistics

All data collected and coded during the study were analyzed at the end in double-blind fashion, with no knowledge of patient identity or grouping. Statistical analysis was based on intention to treat. The following methods were used: 1) analysis of variance (ANOVA) for the significance of difference within a group and multivariate ANOVA for the significance between groups, 2) the χ² test (with ANOVA) to assess the significance of difference in event frequency between groups, and 3) repeated measures ANOVA for comparing serial data in each group. Results are given as mean ± SD. Differences were assumed significant for p≤0.05.

Results

The NG group (n = 154) and the control group (n = 156) were well matched for clinical and laboratory parameters on admission (Table 1). In all, 87% of the patients had transmural or Q wave infarcts (Q waves >40 msec wide and >0.2 mV deep), 79% had first infarcts, 45% had anterior infarcts, and 36% were hypertensive on admission (60 NG and 51 controls). The infusions were begun within 4 hours of the onset of pain in 22% of the patients, within 6 hours in 43%, and within 10 hours in 73%. The distribution of patients in the different Killip classes on admission were similar for the NG group (I, 72; II, 58; III, 24) and the control group (I, 71; II, 58; III, 27).

In the NG group, the average infusion rate was 45±34 μg/min (range, 4–192 μg/min) for all patients, similar for inferior and anterior subgroups (41±32 vs. 50±37 μg/min, p<0.2), and greater for initially hypertensive than for normotensive patients (54±39 vs. 39±30 μg/min, p<0.025). The average decrease in MAP was 13±9% for all patients, more for the initially hypertensive than for normotensive patients (19±9% vs. 10±8%, p<0.001), and more for anterior than for inferior subgroups (15±9% vs. 12±9%, p<0.05).

Hemodynamics

The hemodynamic changes at selected time intervals during and immediately after the infusions are summarized for the control and NG groups in Figure 1. Before therapy, heart rate (82 vs. 79 beats/min), MBP (100 vs. 104 mm Hg), and rate pressure product (8.1 vs. 8.2 mm Hg × beats/min × 10⁸) were similar. By 1 hour after the infusions were begun, the MBP decreased (p<0.001) by 13±9% to 96±14 mm Hg in the NG group but did not change significantly (-0.63%) in the control group; heart rate remained unchanged in both groups. Thus, the rate-pressure product also decreased (p<0.001) by 1 hour with NG and was less than for controls (7.6
controls, but there was a mild increase ($p<0.05$) in MBP (85 ± 12 vs. 88 ± 12 mm Hg) and rate-pressure product in the NG group. Hemodynamic changes were similar for anterior versus inferior and early versus late subgroups.

In the 48 patients (29 controls, 19 NG) with thermodilution flotation catheter data, NG infusion was associated with a prompt decrease in LV filling pressure, reflected by the pulmonary capillary wedge pressure (20 ± 4 to 14 ± 3 mm Hg, $p<0.001$) and a late increase in cardiac index (2.7 ± 0.6 vs. 3.1 ± 0.5 l/min/m$^2$, $p<0.01$), as reported previously. These parameters did not improve with the placebo infusion in the 29 controls.

In the NG group, the MAP of 14 patients who were clinically stable during the infusions were found to have drifted repeatedly below the 80 mm Hg target level during the first 12 hours. Five had anterior and nine had inferior infarction. Over the duration of the infusions (31 ± 19 hours) in these patients, the average blood pressures (mm Hg) were systolic, 97 ± 8 (range, 84–119); diastolic, 64 ± 5 (range, 54–69); mean, 75 ± 4 (range, 64–79). These patients were considered to have an excessive hypotensive response to NG, the average decrease in MAP being 20 ± 9% but the average NG dose being only 25 ± 4 μg/min (range, 10–35 μg/min). Over the first 12 hours, MAP was below 80 mm Hg in 48 controls.

**Creatine Kinase Infarct Size**

CK-infarct size was 27% less in the NG group than in the control group (40.6 ± 34.8 vs. 55.4 ± 42.3 geq, $p<0.001$), and this effect was seen in both anterior (43.7 ± 42.1 vs. 58.2 ± 39.7 geq, $p<0.05$) and inferior (38.9 ± 28.5 vs. 52.8 ± 44.5 geq, $p<0.025$) infarct subgroups (Figure 2). The decrease in CK-infarct size with NG was greater in early than in late subgroups (Table 2). Thus, the decrease in the early and late subgroups based on the 4-hour cutoff were 43% versus 22%, but this benefit was still found in the early subgroups with a 10-hour cutoff, the percent decrease being 32% versus 19% (Table 2).

![Figure 1](http://circ.ahajournals.org/)

**Figure 1.** Plots of hemodynamic changes in control and nitroglycerin groups during and after the infusions. *p≈0.05, difference from control. **p≈0.05, compared with value at the end of the infusion.

![Figure 2](http://circ.ahajournals.org/)

**Figure 2.** Bar charts of creatine kinase (CK)-infarct size in control (C) and nitroglycerin (NG) groups, anterior and inferior infarct subgroups, and early and late subgroups based on a 4-hour cutoff for therapy. *Significant difference comparing NG with C.
The difference between early and late NG subgroups with the 10-hour cutoff was statistically significant \((p<0.025)\). In controls, there was no difference in CK-infarct size between anterior versus inferior subgroups or between early versus late subgroups. CK-infarct size was less in the NG than the control group for patients with Q wave infarcts \((43.9 \pm 35.2 \text{ vs. } 55.7 \pm 44.1 \text{ geq, } p<0.025)\) and non-Q wave infarcts \((13.6 \pm 10.8 \text{ vs. } 29.4 \pm 31.8 \text{ geq, } p<0.05)\).

The beneficial effect of NG on CK-infarct size was less in the 14 patients whose MAP drifted below 80 mm Hg during the first 12 hours of the infusion than in those whose MAP remained consistently above 80 mm Hg during that time (Table 3). Thus, CK-infarct size was 122% larger in the NG subgroup with MAP less than 80 mm Hg than in the subgroup with MAP above 80 mm Hg \((81.3 \text{ vs. } 36.7 \text{ geq, } p<0.001)\). The latter effect was seen irrespective of anterior and inferior infarct locations (Table 3) or early and late timing of NG therapy. Although the 48 control patients who developed MAP below 80 mm Hg in the first 12 hours of placebo infusion had slightly larger CK-infarct sizes compared with the 108 patients with MAP consistently above 80 mm Hg, the difference did not reach statistical significance (Table 3).

**Left Ventricular Asynergy and Ejection Fraction by Two-dimensional Echocardiography**

On admission, the NG and control groups had similar mean total LV asynergy \((28 \pm 8\% \text{ vs. } 27 \pm 8\%)\) and mean global LV ejection fraction \((37 \pm 10\% \text{ vs. } 34 \pm 8\%)\), with no difference between subgroups based on timing of infusions or location of infarction. Of the 21% of patients with a history of old acute myocardial infarction, 35% had evidence of old acute myocardial infarction, and only 2% had persistent LV asynergy remote from the site of fresh AMI. The number of patients in the two groups with LV asynergy more than 25% \((103 \text{ of } 154 \text{ vs. } 100 \text{ of } 156, \text{ NS})\) and LV ejection fraction less than 30% \((39 \text{ of } 154 \text{ vs. } 42 \text{ of } 156, \text{ NS})\) were also similar on admission (Table 1). The data on the extent of total LV asynergy and global LV ejection fractions at five time intervals \((\text{baseline or time } 0; 6, 24, \text{ or } 48 \text{ hours}; \text{ and } 10 \text{ days})\) are summarized in Figure 3 for the 128 patients \((61 \text{ NG and } 67 \text{ controls})\) with adequate repeated two-dimensional echocardiographic recordings for this detailed analysis and no past history or evidence of old acute myocardial infarction. In the NG group, LV asynergy decreased promptly and was still 34% below baseline at 6 hours \((28 \pm 8\% \text{ vs. } 18 \pm 8\%, p<0.001)\) and 43% below baseline at 10 days \((28 \pm 8\% \text{ vs. } 16 \pm 8\%, p<0.001)\). There was a parallel increase in LV ejection frac-
tion that was still 27% above baseline at 6 hours (37 ± 10% vs. 47 ± 10%, p<0.001) and 37% above baseline at 10 days (37 ± 10% vs. 51 ± 9%, p<0.001).

In contrast, the controls showed no change in LV asynergy from baseline by 6 hours or 10 days (27 ± 8% vs. 26 ± 9% vs. 24 ± 9%). The LV ejection fraction in controls showed no change from baseline by 6 hours (34 ± 8% vs. 34 ± 8%) but showed a mild increase by 10 days (34 ± 8% vs. 42 ± 9%, p<0.005). The changes in LV asynergy and LV ejection fraction in the NG group differed significantly from those in the control group (p<0.05) by repeated measures ANOVA and LSD test (Figure 3). These differences between NG and control groups were also present in 1) anterior and inferior infarction subgroups, 2) early and late subgroups (with 4, 6, and 10-hour cutoffs), more marked with 4- than 10-hour cutoffs, and 3) the subgroup with MAP more than 80 mm Hg, but not in the subgroup with MAP less than 80 mm Hg (Table 3).

The LV end-diastolic internal dimensions, with two-dimensional echocardiographic–steered M-mode recordings, were obtained in all patients and were initially similar for NG and control groups. There was an initial decrease for the NG group over the first 48 hours (33 ± 5 vs. 48 ± 6 mm, p<0.001) followed by a return to baseline by 10 days (53 ± 5 vs. 55 ± 5 mm, NS). In the control group, there was a progressive increase in internal dimension by 48 hours (51 ± 6 vs. 56 ± 6 mm, p<0.001) and 10 days (51 ± 6 vs. 58 ± 12 mm, p<0.001). The percent change in dimension was greater in controls than the NG group (13 ± 17% vs. 2 ± 9%, p<0.001). Computed volumes reflected these changes in LV internal end-diastolic dimensions. Thus, initial, 48-hour and 10-day values for LV end-diastolic volumes were 108 ± 3 versus 90 ± 2 versus 112 ± 5 cm³, respectively, for the NG group and 103 ± 3 versus 111 ± 6 versus 138 ± 5 cm³, respectively, for the controls. The decrease in LV asynergy with NG compared with controls was still highly significant (p<0.001) when calculations were based on angular extents of asynergy in short-axis views and corrected for changes in LV internal diastolic dimension, in agreement with our previous report.6

Infarct Expansion and Thinning on Two-dimensional Echocardiography

The data on anterior and posterior endocardial segment lengths in 128 patients (with adequate repeated two-dimensional echocardiographic data and no old acute myocardial infarction) from NG and control groups are summarized in Figure 4. The data in normal subjects are based on three sets of measurements over 10 days. Data in treatment groups are those on admission, at 2–3 days, and between 7 and 10 days postinfarction. In normal subjects, initial mean segment lengths were anterior, 8.5 ± 1.2 cm (range, 6.5–12.0 cm); posterior, 5.2 ± 1.1 cm (range, 3.1–7.6 cm); there was no change over the 10 days. For anterior infarction, the initial anterior segment lengths were similar for the control and NG groups (11.2 ± 1.5 cm vs. 11.1 ± 1.7 cm); at 2–3 days, the anterior segments were longer (p<0.05) for controls (11.3 ± 3.2 cm; range, 7.5–18.0 cm) than for the NG group (11.3 ± 1.4 cm; range, 6.5–13.5 cm). There was no change in anterior segment length by 10 days for the NG group but a further increase (p<0.05) in controls to 14.5 ± 4.1 cm. For inferior infarction, the initial posterior segment lengths were similar for the control and NG groups (7.3 ± 1.0 vs. 7.4 ± 1.0 cm); at 2–3 days, the posterior segments were also longer (p<0.001) for controls (8.2 ± 1.2 cm; range, 3.8–12.5 cm) than for the NG group (7.4 ± 0.9 cm; range, 3.2–8.5 cm). There was no change in posterior segment length by 10 days for the NG group but a further increase (p<0.05) in controls to 10.3 ± 1.7 cm. The percent change in length of the infarct segment over the 10 days was greater in controls than the NG group, for all patients (26.2 ± 23.9% vs. 0.4 ± 9.2%, p<0.001) or for those with anterior infarction (30.3 ± 29.0% vs. 1.5 ± 8.6%, p<0.001) or those with inferior infarction (21.8 ± 15.9% vs. 2.4 ± 9.5%, p<0.001).
The initial and final data on expansion index and thinning ratio for the 128 patients are summarized in Figure 5. There was more expansion and thinning in the controls than the NG group. This effect was found for both anterior and inferior infarct subgroups. The percent change in thickness of the infarct segment was greater in controls than the NG groups (−17 ± 11% vs. 4 ± 9%, p < 0.001). The effect of NG on expansion index and thinning ratio was not significantly influenced by timing of therapy within 4 or 10 hours. Thus, over the first 10 days, the percent change in expansion indexes in the NG subgroups were −3% versus −1% with a 4-hour cutoff and −1% versus −1% with a 10-hour cutoff; the percent change in thinning ratios were −2% versus −6% with a 4-hour cutoff and −2 versus −3% with a 10-hour cutoff.

In-hospital Follow-up and Complications

The duration of hospitalization ranged from 9 to 38 days, with over 95% survivors being discharged 10 days (range, 9–12 days) after admission. The Killip class scores over the 10 days were significantly less (p < 0.05) in the NG than in the control group (Figure 6). The majority of infarct-related complications were less frequent in the NG than in the control group (Table 4). Apart from the hypotensive effect of NG, severe hypotension unrelated to the infusions (defined as SBP less than 90 mm Hg or MAP less than 70 mm Hg) and requiring pharmacological support was less frequent in the NG than in the control group (20% vs. 27%, χ² = 8.56, p < 0.005). Infarct extension (defined by a secondary rise of CK > 200 IU/l, new electrocardiographic changes of AMI after 24 hours) was 50% less frequent in the NG group (11% vs. 22%, χ² = 5.76, p < 0.025). More important, clinical infarct expansion9–13 was 88% less frequent in the NG group compared with controls (2% vs. 15%, χ² = 15.95, p < 0.0005). On two-dimensional echocardiography, these 27 patients had elongated infarct-containing endocardial segment lengths ranging from 13 to 18 cm for anterior infarcts and 10 to 12.5 cm for inferior infarcts, well above the upper limit in normals and nonexpanders. The expansion indexes and thinning ratio of these patients were significantly higher than for normals and nonexpanders. The percent change in infarct segment length was greater for expanders (51.5 ± 7.9% vs. 4.1 ± 2.5%, p < 0.001) as was the percent change in infarct thickness (−26.5 ± 1.5% vs. −4.9 ± 2.5%, p < 0.001).
Cardiogenic shock was 67% less frequent in the NG group (5% vs. 15%, \( \chi^2 = 8.09, p<0.005 \)). In-hospital deaths were 46% less frequent in the NG group (14% vs. 26%, \( \chi^2 = 6.33, p<0.01 \)). These deaths occurred between 1 and 38 days (mean, 9 ± 10 days), slightly sooner in the control than the NG group (7 ± 9 vs. 13 ± 10 days, NS), and were mainly associated with anterior Q wave infarcts. Of the patients who developed severe hypotension, 45% had inferior infarction (15 controls and 13 NG) and five of these (three controls and two NG) developed the right ventricular infarction syndrome associated with predominant right ventricular involvement \(^{20}\) between admission and 48 hours leading to withdrawal for alternative aggressive therapy. Three of these patients died (two controls and one NG) accounting for three in-hospital deaths. Of the patients who developed cardiogenic shock, three controls had also developed both infarct extension and expansion by day 5 and were withdrawn after 48 hours for alternative aggressive therapy but died, accounting for another three in-hospital deaths. Because analysis was based on intention to treat, these eight "withdrawals" were not excluded in comparing mortality between groups.

The frequency of cardiomegaly (assessed from portable chest radiographs) and pericarditis were not significantly different in the two groups. Interestingly, the finding of an LV thrombus on two-dimensional echocardiography was markedly less frequent in the NG than control group (5% vs. 22%, \( \chi^2 = 18.98, p<0.0005 \)). The average size of the thrombi from two views were similar for the two groups (4.5 vs. 5.3 cm\(^2\)).

**TABLE 4. Major In-Hospital Complications Related to Acute Myocardial Infarction**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Controls (%)</th>
<th>Nitroglycerin (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (n=156)</td>
<td>Anterior (n=74)</td>
</tr>
<tr>
<td>Hypotensive response*</td>
<td>. . .</td>
<td>. . .</td>
</tr>
<tr>
<td>Severe hypotension†</td>
<td>27§</td>
<td>34§</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>15§</td>
<td>20§</td>
</tr>
<tr>
<td>Infarct extension</td>
<td>22§</td>
<td>24</td>
</tr>
<tr>
<td>Infarct expansion syndrome</td>
<td>15§</td>
<td>20#</td>
</tr>
<tr>
<td>Cardiomegaly</td>
<td>30</td>
<td>36§</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>12§</td>
<td>11</td>
</tr>
<tr>
<td>Heart block</td>
<td>31§</td>
<td>34</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SVT and AF</td>
<td>22§</td>
<td>20</td>
</tr>
<tr>
<td>VT</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>VF and cardiac arrest</td>
<td>13</td>
<td>19</td>
</tr>
<tr>
<td>Ventricular septal rupture</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>LV free-wall rupture</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>LV thrombus</td>
<td>22§</td>
<td>21§</td>
</tr>
<tr>
<td>Systemic embolism</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>In-hospital deaths</td>
<td>26#</td>
<td>36#</td>
</tr>
<tr>
<td>Q wave infarction</td>
<td>25#</td>
<td>35§</td>
</tr>
<tr>
<td>Non-Q wave infarction</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

SVT, supraventricular tachycardia; AF, atrial fibrillation; VT, ventricular tachycardia; VF, ventricular fibrillation; LV, left ventricular.

*Decrease in mean arterial blood pressure below 80 mm Hg due to nitroglycerin infusion; †systolic blood pressure below 90 mm Hg or mean arterial blood pressure below 70 mm Hg unrelated to the infusions; \( \ddot{p}<0.005 \); \( \dddot{p}<0.005 \); \( \#p<0.025 \); \( \dddot{p}<0.0005 \) refer to significance of difference in event frequency comparing control and nitroglycerin groups or subgroups.

**FIGURE 6.** Plots of changes in Killip class score in control and nitroglycerin groups. Values on admission (initial), at 24 and 48 hours and the maximum between 2 and 10 days are shown. \( *p<0.05 \), significance of difference between baseline and subsequent values in all controls and control subgroups. \( **p<0.05 \), significance of difference between baseline and subsequent values in the nitroglycerin group and subgroups.
Table 5. Other Pertinent Drugs Used Acutely and During Follow-up to 12 Months

<table>
<thead>
<tr>
<th></th>
<th>Controls (%)</th>
<th>Nitroglycerin (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (n = 156)</td>
<td>Anterior (n = 74)</td>
</tr>
<tr>
<td></td>
<td>All (n = 154)</td>
<td>Anterior (n = 64)</td>
</tr>
<tr>
<td><strong>Acute in-hospital phase</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>76</td>
<td>76</td>
</tr>
<tr>
<td>Nitrate after 48 hours</td>
<td>42</td>
<td>41</td>
</tr>
<tr>
<td>Digoxin or other inotope</td>
<td>35</td>
<td>47</td>
</tr>
<tr>
<td>Furosemide or other diuretic</td>
<td>54</td>
<td>66</td>
</tr>
<tr>
<td>Ibuprofen or indomethacin</td>
<td>23</td>
<td>26</td>
</tr>
<tr>
<td><strong>Follow-up phase</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrate</td>
<td>40†</td>
<td>28†</td>
</tr>
<tr>
<td>Digoxin</td>
<td>29‡</td>
<td>32§</td>
</tr>
<tr>
<td>Diuretic</td>
<td>40</td>
<td>36</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>28‡</td>
<td>23</td>
</tr>
<tr>
<td>Calcium blocker</td>
<td>20§</td>
<td>20</td>
</tr>
<tr>
<td>Anticoagulant</td>
<td>12</td>
<td>18</td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td><strong>Follow-up and Mortality</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*In Table 5, an equal number of patients in both groups needed NG after 48 hours in the form of oral isosorbide dinitrate or nitropaste for recurrent chest pain (42% vs. 44%) and indomethacin or ibuprofen for pericarditis (23% vs. 21%). Beta-blockers and calcium blockers had been used more frequently in the acute phase in inferior controls.

The clinical characteristics of infarct expanders were similar for the control (n = 24) and NG (n = 3) groups. In both groups, the expanders tended to have anterior infarcts (63% vs. 67%), MAP more than 80 mm Hg (58% vs. 100%), Q wave infarcts (92% vs. 100%), large CK-infarct sizes (68 vs. 46 g eq), moderate initial LV asynergy (29% vs. 32%), received therapy later (71% vs. 66% after 4 hours), and treatment with indomethacin or ibuprofen for pericarditis (29% vs. 100%).

**Follow-up and Mortality**

The final follow-up of survivors ranged from 29 to 68 months (mean, 43 months or 186 weeks). Mortality was less in the NG group than the control group at 7 days (5% vs. 19%, p < 0.0005), 15 days (9% vs. 22%, p < 0.005), 1 month (14% vs. 26%, p < 0.005), 3 months (16% vs. 28%, p < 0.025), 6 months (18% vs. 28%, p < 0.05), and 12 months (21% vs. 31%, p < 0.05). Patients who died had larger mean CK-infarct size than survivors. Thus, CK-infarct sizes for patients who died by 7 days and those who survived 7 days were 84 ± 57 versus 49 ± 35 g eq (p < 0.005). The difference in mortality between the groups was not statistically significant at the final follow-up of 43 months (23% vs. 32%, p < 0.10). The beneficial effect of NG therapy on mortality was only seen in the anterior subgroup, as
shown in the actuarial survival curves (Figure 7). As for in-hospital deaths, this benefit was mainly in those with Q wave infarction. On the late follow-up, more of the survivors in the control group required therapy for cardiac failure (Table 5), but there was no difference between the groups in events such as recurrent infarction or angioplasty. However, slightly more patients in the anterior NG subgroup had angina (31% vs. 15%, p<0.05) and underwent coronary artery bypass surgery (23% vs. 5%, p<0.005). The difference (p=0.05) between NG and control groups in LV asynery, ejection fraction, and internal dimension on two-dimensional echocardiography were present in survivors studied at 3 and 6 months, the values at 6 months being LV asynery, 15 ± 8% vs. 22 ± 10%; LV ejection fraction, 55 ± 9% vs. 42 ± 9%; and LV internal dimension, 53 ± 5 vs. 59 ± 9 mm.

Discussion

The overall results of this prospective randomized single-blinded study, with double-blind analysis of results, indicate that low-dose intravenous NG therapy in acute myocardial infarction limits indexes of infarct size, infarct expansion, other infarct-related complications, and mortality up to 1 year. These beneficial early and late results appear to be related to the combined effects of NG therapy over the first 48 hours after the onset of pain on LV hemodynamics, topography, contractile function, and infarct size. There were four important new findings.

First, the beneficial effect of NG therapy on CK-infarct size was critically dependent on early timing and dosage but not on infarct location. The beneficial effect on CK-infarct size was most marked when therapy was begun less than 4 hours from the onset of pain, but significant benefit was still present in patients treated up to 10 hours from the onset of pain. Also, NG therapy was beneficial in both Q wave and non-Q wave infarction. However, the benefit was less in the few patients (9%) whose MBP drifted below 80 mm Hg within the first 12 hours of the NG infusion.

Second, the overall beneficial effect of NG therapy on CK-infarct size was associated with improved LV hemodynamics and two-dimensional echocardiographic indexes of LV regional contractile and global systolic function. Thus, compared with controls, 1) the MBP averaged 8% less and the rate-pressure product 6% less over the first 10 hours with NG; 2) the clinical Killip class score with NG was 40% less at 24 hours, 58% less at 48 hours, and 41% less at 10 days; 3) among patients in whom flotation catheters were inserted (15%), pulmonary capillary wedge pressure throughout the infusions was 30% less and cardiac index between 24 and 48 hours was 15% more with NG; and 4) in the patients with adequate serial two-dimensional echocardiographic data (41%), LV asynery decreased promptly and ejection fraction increased promptly with NG (these differences persisted at 10 days as well as at 3 and 6 months); LV asynery was 29% less at 6 hours, 29% less at 48 hours, and 40% less at 10 days; and LV ejection fraction was 40% more at 6 hours, 28% more at 48 hours, and 22% more at 10 days. Although the effects of NG on all these parameters were not significantly different for anterior and inferior infarcts, improvement in LV asynery, LV ejection fraction, and Killip class by 24 and 48 hours tended to be greater in early than in late subgroups. The negative effect of NG-induced hypotension with MBP below 80 mm Hg in the first 12 hours was also seen with the other indexes of infarct size, statistically significant with LV asynery, and not significant with LV ejection fraction.

Third, infarct expansion and thinning, from serial two-dimensional echocardiographic data in 128 patients, were less in the NG group than in controls. The expansion index increased by 14% at 2–3 days and 31% at 7–10 days in controls but did not change with NG. The thinning ratio decreased by 6% at 2–3 days and 17% at 7–10 days in controls but did not change with NG. The infarct-containing segment lengths were longer, and thicknesses of the infarct segments were less in controls than the NG group; the changes in these measurements followed closely those in expansion index and thinning ratio. Thus, the beneficial effect of NG on limiting infarct expansion was already apparent during the first 2–3 days, suggesting early remodeling. This is supported by the finding that the LV end-diastolic internal dimension was 14% less at 48 hours and 5% less at 10 days with NG compared with controls.

Fourth, the frequency of major infarct-related complications and deaths were significantly lower in the NG group. Thus, comparing the NG group with controls, the percent reduction in frequency of the complications were 87% for the infarct expansion syndrome (p<0.0005), 77% for LV thrombus on two-dimensional echocardiography (p<0.0005), 67% for cardiogenic shock (p<0.005), and 50% for infarct extension (p<0.025) and all in-hospital deaths up to 38 days (p<0.01). The percent reduction in frequency of deaths at specific time intervals were 74% by 7 days (p<0.0005), 59% by 15 days (p<0.005), 46% by 1 month (p<0.005), 43% by 3 months (p<0.025), 36% by 6 months (p<0.05), 32% by 12 months (p<0.05), and 28% by 43 months (p<0.10). However, this beneficial effect on survival was only seen with anterior infarcts.

Other studies have emphasized low dosage and early timing of NG therapy. Bussmann et al reported a 30% reduction in CK-infarct size with therapy within 8 hours of onset of pain in nine patients. Jaffe et al reported a 36% decrease in CK-infarct size in the inferior subgroup (but not anterior) given therapy within 10 hours of onset of pain. Flaherty et al found no decrease in infarct size but commented on the greater benefit in patients treated within 10 hours of onset of pain. The benefit with NG beyond 4 hours and up to 10 hours of onset of pain in this and reported studies might be attributable to a
delayed march to necrosis and gradual "reperfusion" via collateral channels opened by NG. However, none of the other studies considered the possibility that a drift in MBP slightly below 80 mm Hg to 75 mm Hg in the first 12 hours of NG therapy might significantly lessen the beneficial effect on indexes of infarct size and dilute the results. A MBP of 80 mm Hg is roughly equivalent to a BP of 100/70 mm Hg; a BP of 90/60 mm Hg translates to an MBP of about 70 mm Hg. With a target SBP of 90 mm Hg, the MBP might, therefore, have fallen below 80 mm Hg in those studies. The more modest decrease in MBP or arterial dilatation in this study and that of Bussmann et al might explain the beneficial effect on CK-infarct size. Conversely, the greater decrease in blood pressure might explain failure to demonstrate decreased CK-infarct size in either anterior or inferior subgroups by Flaherty et al or the anterior subgroup by Jaffe et al. Later timing in these studies might also have contributed to the negative findings. The number of patients randomized to NG therapy in the other studies were 31, 43, 4 and 56, less than in the present study.

The use of low-dose intravenous NG therapy for myocardial salvage has been reviewed elsewhere. A 10% decrease in MBP without allowing it to fall below 80 mm Hg was suggested as a suitable endpoint in human acute myocardial infarction. This endpoint was supported by studies in conscious dogs, where careful titration of NG infusions to decrease MBP by 10% down to a level of 90 mm Hg was associated with increased collateral flow and definite myocardial salvage, whereas a decrease of 23% or more in MBP to 83 mm Hg resulted in abolition of these beneficial effects. In these studies, myocardial salvage was dependent mainly on the increase in collateral flow and did not always require a 10% reduction in MBP; however, LV filling pressure was regularly decreased. In the absence of monitoring of LV filling pressure, a 10% fall in MBP was considered to be the minimum that could be reliably detected noninvasively but still be indicative of a significant hemodynamic effect. Because of the anticipated wide range of blood pressures in patients with acute myocardial infarction and Killip classes of I–III, the target reduction in MBP was stratified in this study and set at 10% for normotensive and 30% for hypertensive patients but still not below 80 mm Hg. With NG, MBP fell below 80 mm Hg in 15 patients (10%) during initial titration but was promptly corrected by reducing the infusion rate, fell repeatedly below 80 mm Hg in five patients (3%) resulting in discontinuation after 1–3 hours, and was found to have drifted below 80 mm Hg over the first 12 hours of therapy despite noninvasive monitoring in 14 patients (9%) in whom infusion had been continued. In two other patients (1%), hypotension developed as a result of right ventricular infarction, and the NG infusion was stopped. In all seven patients (5%) in whom NG infusion was stopped, the blood pressure returned to baseline within 5 minutes. Invasive hemodynamic monitoring was only needed in a total of 19 patients (12%) in the NG group. It should be noted that MBP also fell below 80 mm Hg within the first 12 hours of placebo infusion in 29 controls (19%). Tolerance to NG, assumed when dose had to be increased to maintain MBP at the target level, was only seen in 12% of the patients and was not a problem during the infusions. These results suggest that the regimen used for NG therapy in the present study was safe.

The potential mechanisms for myocardial salvage and remodeling in acute myocardial infarction with NG therapy have been reviewed in detail. Briefly, the factors contributing to myocardial salvage include the decrease in preload, afterload, myocardial oxygen demand, and LV internal dimension and wall stress and improved collateral blood flow related to a direct effect, less endocardial compression, and relief of coronary artery spasm. Because NG was beneficial beyond 4 hours of onset of pain, it is possible that NG delayed necrosis and extended the time for salvage beyond 6 hours. Because recovery of function with NG was prompt, it appears that an increase in perfusion via collaterals with NG differs from reperfusion by restoration of patency of an occluded epicardial vessel that is associated with reperfusion injury and delayed recovery of function. In a recent report with reperfusion combined with NG therapy in acute myocardial infarction, recovery of function after reperfusion was also prompt and persistent. The factors contributing to improved topography and decreased infarct expansion include decreased preload, afterload, LV internal dimension and wall stress, and infarct size, although collateral flow might also play a role. As suggested previously, the harmful effect of excessive NG-induced hypotension was most likely related to decreased perfusion pressure in the setting of arteriolar dilatation and compromised autoregulatory ability and less likely to be attributable to coronary steal. Thus, in the presence of NG (but not in controls), collateral flow is more sensitive to changes in perfusion pressure. These mechanisms appear to adequately explain the noted effects on infarct size and topography. The beneficial effects of NG on these parameters also adequately explain the decrease in frequency of mechanical complications, LV thrombi, and mortality. The decreased mortality with NG was predominantly seen in the anterior subgroup with Q wave infarction. The frequency of complications also decreased more in anterior than inferior subgroups: infarct expansion syndrome, 17% versus 10%; cardiogenic shock, 12% versus 8%; severe hypotension, 23% versus 7%; cardiomegaly, 17% versus 1%; LV thrombus, 15% versus –2%. The findings suggest that the greater benefit of NG in the anterior subgroup might have been because of improved topography.

However, the results on early morbidity and mortality in this study should be interpreted care-
fully in the light of the data on CK-infarct size, LV function, and topography. Mortality was not a primary endpoint because the sample size was too small to detect a reduction. The patient population was a group with large infarcts (e.g., CK-infarct size of 55 gq in controls; in-hospital mortality of 26% in controls; and 87% of patients with Q wave infarcts). On admission, ΣST averaged 17 mV, 67% of patients had LV asynergy more than 25%, 26% had LV ejection fraction less than 30%, 37% were in class II, and 16% were in class III. In hospital, 20% developed severe hypotension and 10% developed cardiogenic shock. The study was begun before the era of thrombolytic and nontrombolytic reperfusion therapy with angioplasty, streptokinase, and recombinant tissue plasminogen activator. The approach to surgery was conservative. Our hospital is a large referral center for acute care. There were no concurrent studies to skew the population. The higher mortality and morbidity in anterior Q wave infarction in this study is in agreement with the recent data of the MILIS (Multicenter Investigation of the Limitation of Infarct Size) group. The cumulative mortality for anterior and inferior subgroups in controls were 47% versus 17% at 43 months in this study, higher than corresponding values at 31 months (27% vs. 11%) in the MILIS study. However, the 3-month mortality in control and NG groups in this study (28% vs. 16%) are similar to those reported by Flaherty et al., namely, 25% versus 15%. Similar values of short-term mortality in placebo and treated groups (24% vs. 13%) were reported by Cohn et al. in a trial of nitroprusside in transmural infarction. The higher mortality found in this study was most likely related to the “high risk” population, consisting predominantly of large Q wave infarcts and a more conservative approach to therapy in an era before reperfusion became popular.

In conclusion, intravenous NG therapy, given in a low dose to reduce MBP by 13% down to 74 mm Hg for 39 hours during acute myocardial infarction, reduced CK-infarct size in both anterior and inferior locations, but benefit was greatest in the early subgroup given therapy within 4 hours of onset of pain and in the subgroup with MBP above 80 mm Hg in the first 12 hours. This effect of NG on CK-infarct size was associated with decreased LV asynergy and improved LV ejection fraction on two-dimensional echocardiography, improved LV hemodynamics, and improved clinical Killip scores. In addition, NG therapy improved LV topography with no increase in infarct expansion index, no decrease in infarct thinning ratio, and decreased LV internal diastolic dimension on two-dimensional echocardiography. More important, NG therapy markedly reduced the frequency of infarct-related in-hospital complications such as the clinical infarct expansion syndrome, infarct extension, cardiogenic shock, deaths, and LV thrombus on two-dimensional echocardiography. Finally, NG therapy decreased mortality up to 12 months, but this effect was found only with anterior Q wave infarction. Thus, low-dose intravenous NG therapy should be considered for myocardial salvage and limitation of infarct expansion.

Acknowledgments

We are grateful for the assistance of Christine Scott with typing; Catherine Jugdutt with tabulating data throughout the study; Christine Worton, BSc, with initial data collection and coding; Alison Dinwoodie, MD, of the Department of Laboratory Medicine with CK enzyme assays; Zaheer M. Lakhani, MBBS, Kathleen M. McGarry, MChB, and Cheryl Trudell, RTN, with echocardiography; and Blaine Bilton and Michael Maidens, MSc, for running computer and statistical programs.

References


19. Maidens JM, Michorowski BL, Jugdutt BI: Correction for echocardiographic overestimation of myocardial infarct size due to shape distortion in the infarct zone (abstract). Clin Res 1986;34:323A


**KEY WORDS**  
- mortality  
- two-dimensional echocardiography  
- left ventricular thrombus  
- left ventricular topography
Intravenous nitroglycerin therapy to limit myocardial infarct size, expansion, and complications. Effect of timing, dosage, and infarct location.
B I Jugdutt and J W Warnica

Circulation. 1988;78:906-919
doi: 10.1161/01.CIR.78.4.906

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1988 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/78/4/906

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/