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Regional cardioprotection by subselective intracoronary nifedipine is not due to enhanced collateral flow during coronary angioplasty

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Twelve patients with proximal stenosis of the left anterior descending artery, normal myocardial wall motion but without angiographically demonstrable collateral circulation, were studied during transluminal occlusion. Prior to the first transluminal occlusion before crossing the lesion with the balloon, patients were randomly given 0.2 mg nifedipine or its solvent in the left mainstem. The same dose was repeated via the balloon catheter, positioned across the lesion, immediately prior to the second transluminal occlusion. In all patients great cardiac venous flow and ST-elevation were monitored during and after each transluminal occlusion. The lactate extraction ratio A-GCV / A (A = arterial, GCV = great cardiac vein) was determined prior to the angioplasty procedure, 10–15 seconds after each transluminal occlusion and 10 minutes after the third transluminal occlusion. Great cardiac venous flow rose significantly to an average of 160% of basal flow when nifedipine was administered into the mainstem before the angioplasty procedure while its solvent had no effect. During each transluminal occlusion, great cardiac venous flow diminished on average by 30% in those who received nifedipine and by 28% in those who received only its solvent. This difference was statistically not significant. After angioplasty great cardiac venous flow was slightly, but not significantly, increased in both groups with

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respect to basal flow (104% resp. 120% of control). Patients who received nifedipine in the post-stenotic area just before the second transluminal occlusion, had significantly lower lactate production, measured immediately after the transluminal occlusion compared with the patients who received only its solvent ($P < 0.01$). The ST-elevation during the second transluminal occlusion was significantly lower in the nifedipine group (0.1 mm in nifedipine group versus 1.4 mm in solvent group; $P < 0.05$, unpaired t-test).

Nifedipine given intracoronary in the post-stenotic area just before coronary angioplasty reduces lactate release and electrocardiographic signs of myocardial ischemic injury. This regional cardioprotective effect seems not due to an enhanced collateral flow, but to a regional cardioplegic effect, which precedes the ischemic event.

Key words: Coronary angioplasty; Intracoronary nifedipine; Regional cardioprotection; Collateral flow

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Introduction

Nifedipine is known to have a number of actions, which can be beneficial during a period of acute ischemia. The drug was introduced as a coronary dilator [1,2], increasing coronary flow by reducing coronary arteriolar resistance. In the peripheral circulation its effect is mainly directed toward the arterial circulation by reducing resistance [2]. Studies in our laboratory [3,4] have shown that by its calcium antagonist properties, nifedipine also exerts a negative inotropic effect on the myocardium when injected in the local circulation. It is partly because of this negative inotropic effect that calcium-antagonists are used as a cardioplegic agent in cardiac surgery [5,6]. A prolonged direct effect on cardiac metabolism has also been postulated [2,6,7] which is exerted through a powerful effect on myocardial adenine nucleotide metabolism, possibly by increasing the efficiency of oxygen utilization [8].

Percutaneous transluminal coronary angioplasty provides a unique opportunity to study the effects of acute coronary occlusion on coronary hemodynamics [9], on myocardial metabolism [10,11] and on the electrocardiographic signs of myocardial ischemia [12,13] in the human. Considering the different potentially beneficial effects of nifedipine in acute ischemia, we investigated the possible cardioprotective effect of intracoronary nifedipine before and during coronary angioplasty. We also tried to elucidate the mechanism(s) which might be responsible for the cardioprotection by nifedipine. Cardioprotection during angioplasty is of importance as both the number of occlusive episodes and the duration of the occlusion have increased progressively, especially in multivessel dilatations. Recent studies suggest that prolonged balloon inflations may enhance plaque molding and reduce the restenosis rate [14]. On the other hand, Braunwald and Kloner found evidence that even short periods of acute ischemia can cause prolonged, postischemic, ventricular dysfunction [15]. Repetitive transluminal occlusions may in this sense provoke a "stunned"

TABLE 1

Clinical characteristics of the study group.

	Group N ($n = 6$)	Group S ($n = 6$)
Age (years) average	60.8	58
range	51–69	49–66
Male/female	4/2	4/2
Patients in NYHA		
Class III	5	4
Class IV	1	2
Average severity of stenosis		
before PTCA (%)	80	78
after PTCA (%)	45	44
Average ejection fraction (%)	60	66
Mean aortic pressure during		
3×TO (mm Hg)	101	104
Mean heart rate during		
3×TO (beats/minute)	72	62

N = nifedipine; S = solvent; NYHA = New York Heart Association; PTCA = percutaneous transluminal coronary angioplasty; TO = transluminal occlusion.

myocardium. It seems appropriate, therefore, to look for a useful pharmacological agent which can diminish or prevent this undesired effect of a potentially useful intervention.

Materials and Methods

Patients

Twelve patients, who underwent percutaneous transluminal coronary angioplasty and who met the following criteria were studied: (1) presence of an isolated proximal stenosis of less than 1 cm in length in the left anterior descending artery; (2) no collateral filling seen angiographically in the region supplied by the anterior ventricular artery; (3) preserved myocardial wall motion in the region perfused by the left anterior descending artery; (4) no need for nitrate perfusion during coronary angioplasty. In all patients vasoactive substances were discontinued at least 12 hours before study. The age of the patients varied between 49 and 69 years (Table 1) and all of them were in New York Heart Association functional class III to IV. All patients gave their informed consent and there were no complications directly related to the investigational procedure. Coronary angioplasty was indicated because of persistence of angina pectoris despite maximal oral therapy.

Coronary angioplasty technique

Percutaneous transluminal coronary angioplasty was performed by the same technique in all patients. Via a 9F, 16 cm introducing sheath, a balloon catheter was

directed into the stenotic area under fluoroscopic and pressure control. Coronary angioplasty was performed according to the technique of Simpson et al. [16] using a steerable long guide wire (high torque floppy, 0.018 inch), via the femoral route. Angioplasty balloons with diameters of 3.0 or 3.4 mm were used. The maximal inflation pressure ranged from 10–12 atmospheres. Dilation times for each individual patient were the same and ranged from 45 to 60 seconds. Attempts to dilate the lesion were repeated as long as the stenosis persisted by more than 50%. Only measurements of the first three consecutive occlusions were included in this study. Coronary angiography with non-ionic contrast medium was performed immediately before and after coronary angioplasty. Lateral, anteroposterior, oblique and hemiaxial angiographic views were obtained in virtually all patients. Premedication consisted of aspirin and heparin intravenously. In addition, low molecular weight dextran was administered during the procedure.

Lactate measurements

Blood (2 ml) for lactate measurements was taken 10 minutes prior to the first transluminal occlusion simultaneously from the femoral artery via the sheath, and from the great cardiac vein via the distal opening of a Webster flow catheter. The samples were repeated immediately after drug administration, 10–15 seconds after each transluminal occlusion and 10 minutes after the last transluminal occlusion. The blood for lactate measurements was rapidly deproteinized with an equal volume of cold 8% perchloric acid ($HClO_4$) and centrifuged. After centrifugation, the supernatant fluids were stored at $-20\,^{\circ}C$. Lactate in the supernatant was analyzed enzymatically according to Gutmann and Wahlefeld [17] on a Gilford 2600. Standard curves were made with lithium lactate in 4% $HClO_4$.

Flow measurements

A Webster thermodilution coronary sinus blood flow catheter [18] was introduced into the coronary sinus by way of the right femoral vein. The tip of the catheter was positioned under fluoroscopic control in the great cardiac vein. The location of the distal thermistor in the great cardiac vein was confirmed by injection of 3 ml contrast material. Great cardiac venous flow was measured prior to coronary angioplasty, after drug administration, during each transluminal occlusion and 10 minutes after the last transluminal occlusion. Each recording of blood flow during coronary angioplasty began a minute before balloon inflation and was interrupted at the moment of balloon deflation. Mean aortic pressure obtained through the guiding catheter was monitored continuously during the procedure.

Electrocardiographic measurements

Two electrocardiographic standard leads (I, III) and one precordial lead (V4) were monitored throughout the study. Each lead was calibrated before the procedure (10 mm = 1 mVolt). The magnitude (mVolts) of maximal ST-elevation at the

end of balloon inflation was measured, as an index of myocardial ischemia [19–21]. The measurements were taken 0.80 seconds after the J-point, with the T wave–P wave interval as the isoelectric line.

Protocol of drug administration

Prior to the first transluminal occlusion, before crossing the lesion with the balloon, patients were randomly assigned to either 0.2 mg nifedipine or its solvent, which was administered slowly within 30 seconds in the left main stem. Following the drug administration the lesion was crossed as soon as possible and the balloon inflated. The times taken for this procedure are listed in Table 2. The same dose was repeated also within 30 seconds via the balloon catheter, positioned across the lesion, just prior to the second transluminal occlusion. There was a third control occlusion without prior administration of nifedipine. No other vasoactive drugs were given during the coronary angioplasty.

Statistical analysis

Results are expressed as mean ± standard error of the mean. Comparison between pre-angioplasty, post-angioplasty and occlusion conditions was evaluated using analysis of variance for repeated measurements. When overall significance was found, multiple comparisons were considered statistically significant at the 0.05 level (paired *t*-test). Comparisons between nifedipine-treated patients and those treated with the solvent only were statistically evaluated using the unpaired *t*-test. A *P*-value less than 0.05 was considered statistically significant.

Results

Clinical characteristics of the patients

The characteristics of the groups assigned to nifedipine (group N) and its solvent (group S) are listed in Table 1. The average ages, the New York Heart Association functional class, severity of stenosis of the left anterior descending artery and ejection fraction in the two groups were not significantly different. There was no difference in inflation time and inflation pressure during the first three consecutive inflations between nifedipine group (56 seconds and 8.6 atmospheres) and solvent group (54 seconds and 9.5 atmospheres). The mean cross sectional area of the stenosis before coronary angioplasty did not differ in both groups (80% in nifedipine group versus 78% in solvent group).

Coronary hemodynamic measurements

The coronary hemodynamic values are summarized in Table 2 and are displayed in Fig. 1. Great cardiac vein blood flow increased on average by 160% of basal flow after the first administration of nifedipine in the left main stem ($P < 0.05$). This is

TABLE 2

Coronary hemodynamic measurements. Great cardiac vein flow is expressed in ml/minute and percentage of basal flow is given in parentheses.

Group N		Basal flow	After N	T_1 *	TO 1	TO 2	T_2 *	TO 3	Recovery
Patient	1	68 (100)	68 (100)	50	27 (40)	26 (38)	15	29 (43)	71 (104)
	2	51 (100)	119 (232)	28	56 (109)	24 (46)	20	48 (93)	53 (102)
	3	84 (100)	180 (214)	26	67 (80)	66 (79)	21	72 (86)	84 (100)
	4	56 (100)	74 (132)	3	58 (103)	52 (93)	10	54 (96)	68 (121)
	5	50 (100)	82 (164)	6	43 (86)	ND	11	44 (88)	75 (150)
	6	81 (100)	97 (120)	8	45 (56)	28 (35)	18	33 (41)	36 (44)
Mean		65.0 (100)	103.3 (160)		49.3 (79)	39.2 (58)		46.6 (74)	64.5 (104)
Group S		Basal flow	After S	T_1	TO 1	TO 2	T_2	TO 3	Recovery
Patient	7	36 (100)	42 (117)	15	38 (106)	33 (92)	15	33 (92)	54 (150)
	8	68 (100)	48 (71)	9	21 (31)	19 (28)	11	20 (29)	87 (128)
	9	55 (100)	52 (94)	10	43 (79)	18 (33)	12	31 (56)	57 (103)
	10	43 (100)	41 (95)	11	25 (58)	ND	10	28 (65)	42 (97)
	11	29 (100)	36 (124)	8	29 (100)	32 (110)	12	40 (137)	43 (148)
	12	19 (100)	17 (89)	14	13 (68)	13 (68)	14	15 (79)	17 (89)
Mean		41.6 (100)	39.3 (98)		28.2 (74)	23 (66)		27.8 (77)	50 (120)

ND = not determined. *, T_1 = time-interval (min) between nifedipine/solvent administration and first transluminal occlusion; T_2 = time-interval (min) between last nifedipine/solvent administration and third transluminal occlusion. N = nifedipine; S = solvent; TO = transluminal occlusion.

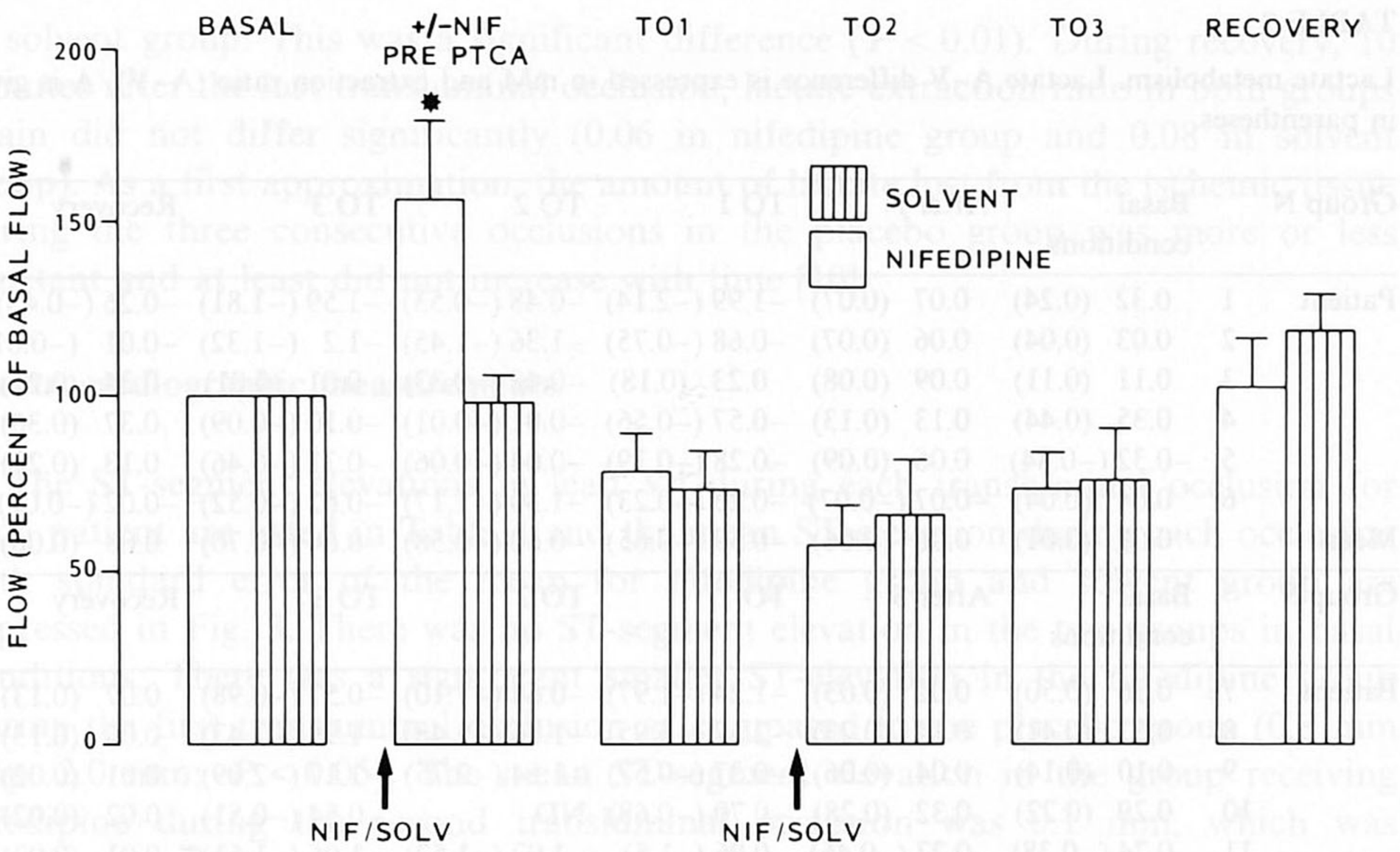

Fig. 1. Effect of nifedipine on flow measured in the great cardiac vein before and during angioplasty. Nifedipine (NIF) or solvent (SOLV) were given before the first transluminal occlusion (TO) in the main stem and just prior to the second transluminal occlusion in the post-stenotic area. After the first administration, control measurements were done before the transluminal occlusion. * $P < 0.05$ versus solvent. PTCA = percutaneous transluminal coronary angioplasty.

consistent with results of earlier studies [2,3]. Flow within the great cardiac vein did not change after injection of the solvent. During the transluminal occlusion, venous flow decreased on average in both groups by the same extent, i.e. to 70% of basal flow in the nifedipine group and to 72% of basal flow in the control group. There was no significant difference in reduction of flow between the two groups during transluminal occlusion. Ten minutes after last transluminal occlusion, flow returned to 104% of its basal state in the nifedipine group and 120% in solvent group; this difference was not statistically significant. Nifedipine 0.2 mg given slowly within 30 seconds selectively in the left mainstem and subselectively in the post-stenotic area produced a slight transient decrease of aortic pressure which subsided after 3 minutes and which did not affect the heart rate.

Lactate metabolism

The arteriovenous lactate measurements are expressed in terms of extraction rate (A–V)/A (A = arterial lactate concentration, V = venous lactate concentration) [22] and are listed for each patient in Table 3. Mean extractions of lactate with standard error of the mean for both groups during each transluminal occlusion are shown in Fig. 2. Extraction of lactate under basal conditions was similar in both groups (0.01 in nifedipine group and 0.17 in solvent group). The mean lactate extraction ratio during the second transluminal occlusion was −0.58 in nifedipine group and −1.88

TABLE 3

Lactate metabolism. Lactate A–V difference is expressed in mM and extraction ratio (A–V)/A is given in parentheses.

Group N		Basal conditions	After N	TO 1	TO 2	TO 3	Recovery
Patient	1	0.32 (0.24)	0.07 (0.07)	−1.99 (−2.14)	−0.48 (−0.53)	−1.59 (−1.81)	−0.26 (−0.43)
	2	0.03 (0.04)	0.06 (0.07)	−0.68 (−0.75)	−1.36 (−1.45)	−1.2 (−1.32)	−0.01 (−0.01)
	3	0.11 (0.11)	0.09 (0.08)	0.23 (0.18)	−0.42 (−0.33)	0.01 (0.01)	0.24 (0.22)
	4	0.35 (0.44)	0.13 (0.13)	−0.57 (−0.56)	−0.01 (−0.01)	−0.10 (−0.09)	0.37 (0.36)
	5	−0.32 (−0.84)	0.06 (0.09)	−0.28 (−0.39)	−0.04 (−0.06)	−0.31 (−0.46)	0.13 (0.22)
	6	0.04 (0.04)	−0.07 (−0.07)	−0.25 (−0.23)	−1.30 (−1.17)	−0.62 (−0.52)	−0.02 (−0.02)
Mean		0.09 (0.01)	0.06 (0.06)	−0.59 (−0.65)	−0.60 (−0.58)	−0.64 (−0.70)	0.08 (0.06)
Group S		Basal conditions	After S	TO 1	TO 2	TO 3	Recovery
Patient	7	0.36 (0.50)	0.02 (0.03)	−1.24 (−1.97)	−0.64 (−1.10)	−0.57 (−0.98)	0.07 (0.13)
	8	0.33 (0.41)	0.14 (0.23)	−2.57 (−3.95)	−1.66 (−2.48)	−1.99 (−2.43)	0.09 (0.13)
	9	0.10 (0.14)	0.04 (0.06)	−0.37 (−0.57)	−1.54 (−2.75)	−1.17 (−2.09)	0.01 (0.02)
	10	0.29 (0.22)	0.32 (0.28)	−0.70 (−0.68)	ND	−0.54 (−0.51)	0.02 (0.02)
	11	−0.24 (−0.38)	−0.27 (−0.46)	−0.96 (−1.5)	−1.02 (−1.52)	−1.06 (−1.61)	0.01 (0.02)
	12	0.12 (0.15)	0.05 (0.07)	−1.16 (−1.38)	−1.21 (−1.53)	−0.85 (−1.09)	0.09 (0.13)
Mean		0.16 (0.17)	0.05 (0.04)	−1.17 (−1.68)	−1.21 (−1.88)	−1.03 (−1.45)	0.05 (0.08)

A = arterial; V = great cardiac venous; for other abbreviations see legend to Table 2.

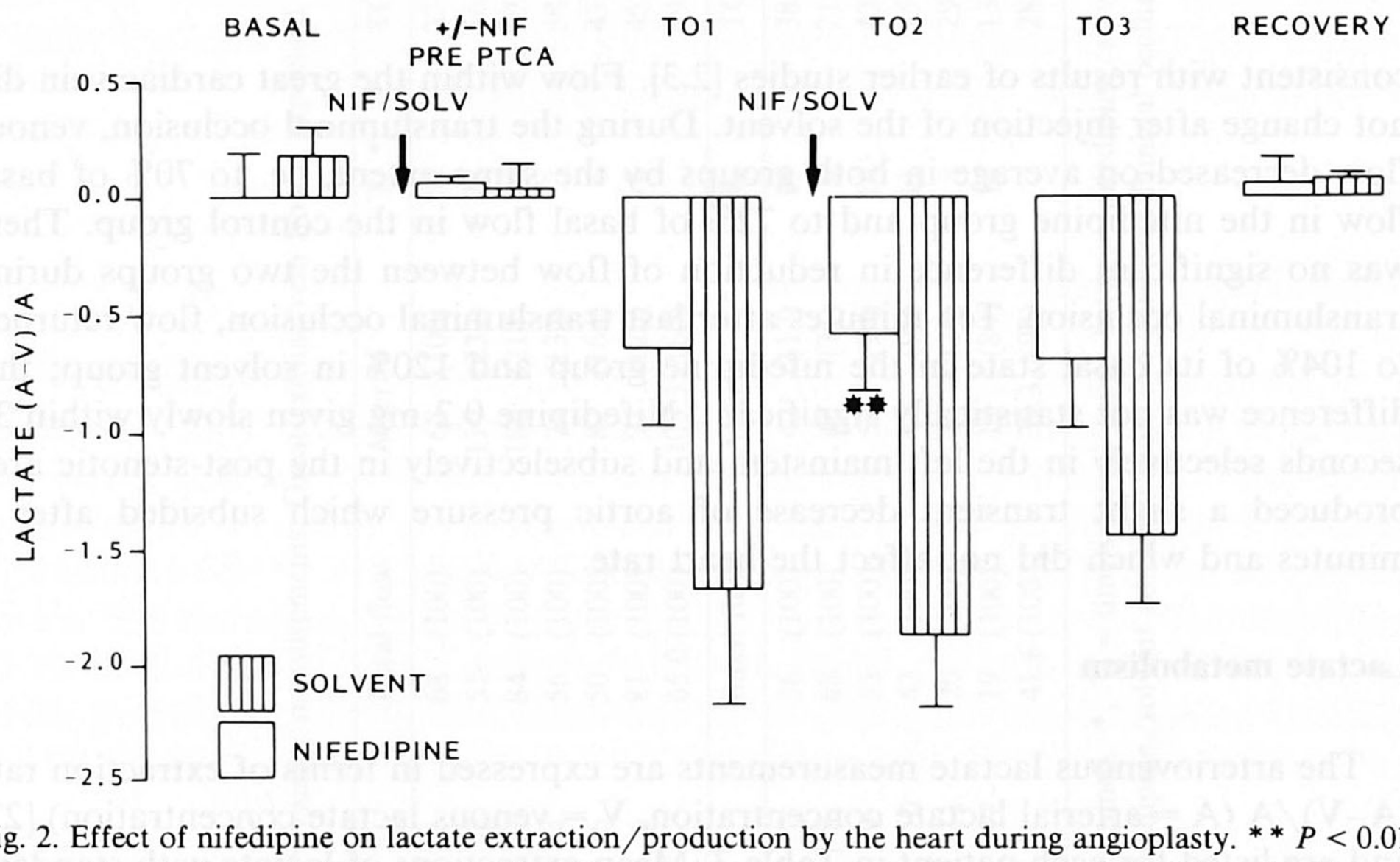

Fig. 2. Effect of nifedipine on lactate extraction/production by the heart during angioplasty. ** $P < 0.01$ versus solvent. A = arterial concentration, V = great cardiac venous concentration. Other details, see legend to Fig. 1.

in solvent group. This was a significant difference ($P < 0.01$). During recovery, 10 minutes after the last transluminal occlusion, lactate extraction ratio in both groups again did not differ significantly (0.06 in nifedipine group and 0.08 in solvent group). As a first approximation, the amount of lactate lost from the ischemic tissue during the three consecutive occlusions in the placebo group was more or less constant and at least did not increase with time [10].

Electrocardiographic measurements

The ST-segment elevations in lead V4 during each transluminal occlusion for each patient are listed in Table 4 and the mean ST-elevation during each occlusion with standard error of the mean for nifedipine group and solvent group are expressed in Fig. 3. There was no ST-segment elevation in the two groups in basal conditions. There was a significant smaller ST-elevation in the nifedipine group during the first transluminal occlusion as compared to the placebo group (0.8 mm resp. 2.0 mm; $P < 0.05$). The mean ST-segment elevation in the group receiving nifedipine during the second transluminal occlusion was 0.1 mm, which was significantly different from the 1.4 mm ST-segment elevation in those receiving placebo ($P < 0.05$). During the third transluminal occlusion there was no significant difference in ST-elevation between the groups. During recovery, 10 minutes after the last transluminal occlusion, the ST-segment elevation in both groups disappeared. In some patients of the two groups no ST-segment elevation was seen during one transluminal occlusion, although a few had some T-wave alterations during transluminal occlusion. Minimal ST-segment depression was seen in only one patient

TABLE 4

Electrocardiographic measurements. ST-segment elevation in mm.

Group N		TO 1	TO 2	TO 3	Recovery
Patient	1	1.7	0.0	1.3	−0.2
	2	1.4	0.0	0.8	0.0
	3	0.5	0.0	0.2	0.0
	4	−0.3	0.0	0.2	0.0
	5	0.5	0.2	0.4	0.0
	6	0.7	0.6	0.9	0.0
Mean		0.8	0.1	0.6	0.0
Group S		**TO 1**	**TO 2**	**TO 3**	**Recovery**
Patient	7	2.3	0.0	0.5	0.0
	8	3.2	3.0	3.0	0.0
	9	0.0	1.5	0.0	0.0
	10	2.7	0.0	0.0	0.0
	11	2.6	2.4	2.0	0.0
	12	1.5	1.5	1.0	0.0
Mean		2.0	1.4	1.1	0.0

Abbreviations: see legend to Table 2.

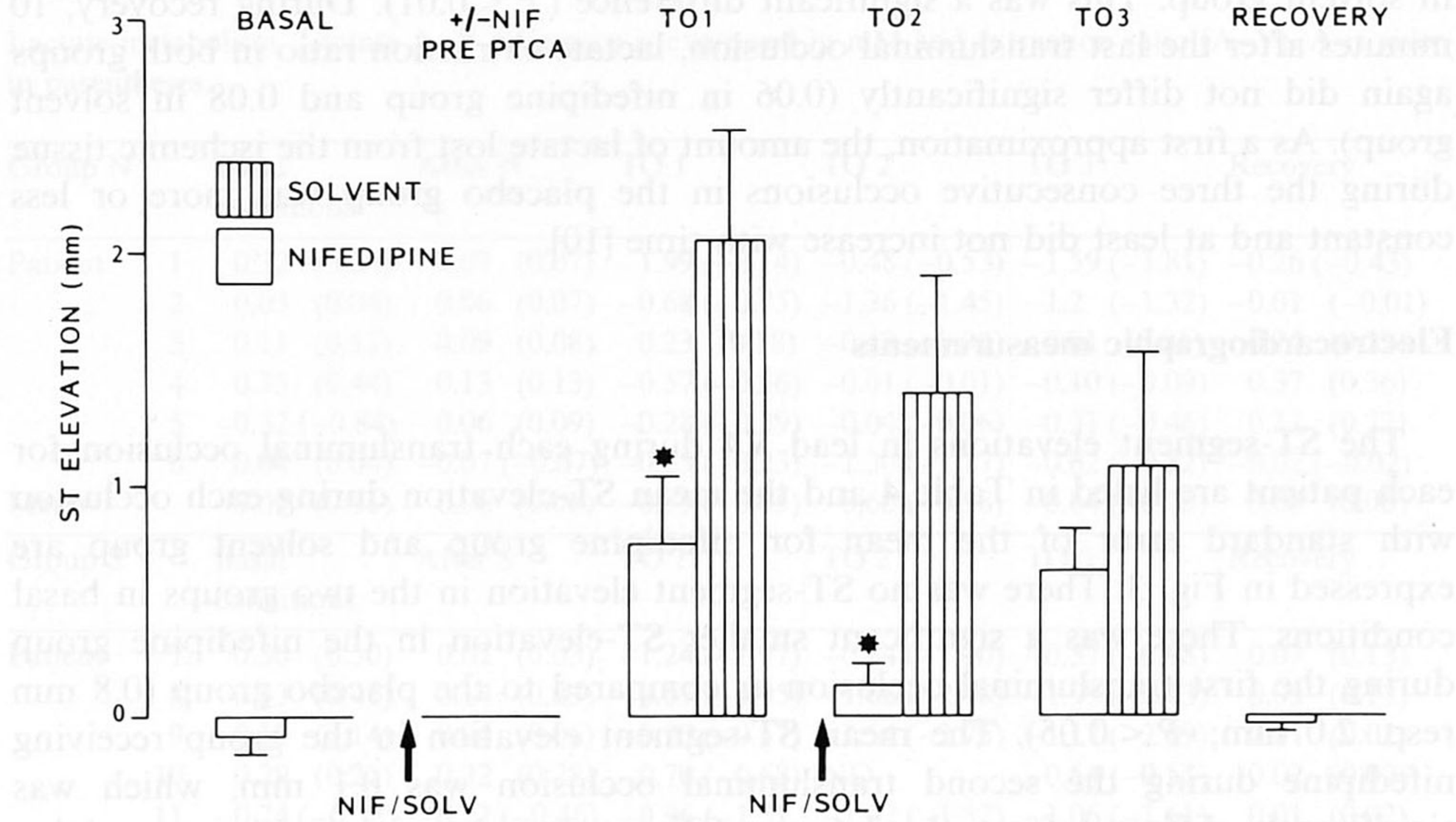

Fig. 3. Effect of nifedipine on ST-segment elevation during angioplasty. * $P < 0.05$ versus solvent. For other details see legend to Fig. 1.

during the first occlusion. The extent of the ST-elevation has been correlated to the lack of collateral filling of the region supplied by the left anterior descending artery [23].

Discussion

The coronary dilating effect of nifedipine when given within the coronary arteries is well established [1,2]. The initial action lasts for about 5 minutes [2,24]. Forman and Kirk [25] have suggested that the vasodilator acts predominantly on the small resistance vessels of the coronary system and not as nitroglycerine does [26,27], on the larger epicardial vessels. The negative inotropic effect of nifedipine given in this fashion was described by Serruys et al. [3] and Amende et al. [24], who showed that the duration of this effect lasted approximately 5 minutes after administration. The systemic effect of vasodilation by nifedipine seems to be negligible when it is given within the coronary arteries [3,24]. Yet a fourth biochemical effect was postulated by Kaltenbach et al. [2], and proved by Serruys et al. and others [6,8]. These studies suggest a direct effect of nifedipine on cardiac metabolism. The significance of this effect is still uncertain. It has been suggested that the drug increases the efficiency of oxygen utilization by the ischemic myocardium. This effect appears prolonged, lasting for at least 60 minutes [7,8] and may be related to intracellular action.

The limitations of this study are several. Flow within the great cardiac vein, as measured by thermodilution, is a mixture of flow coming predominantly from the region supplied by the left anterior descending artery but also from the region

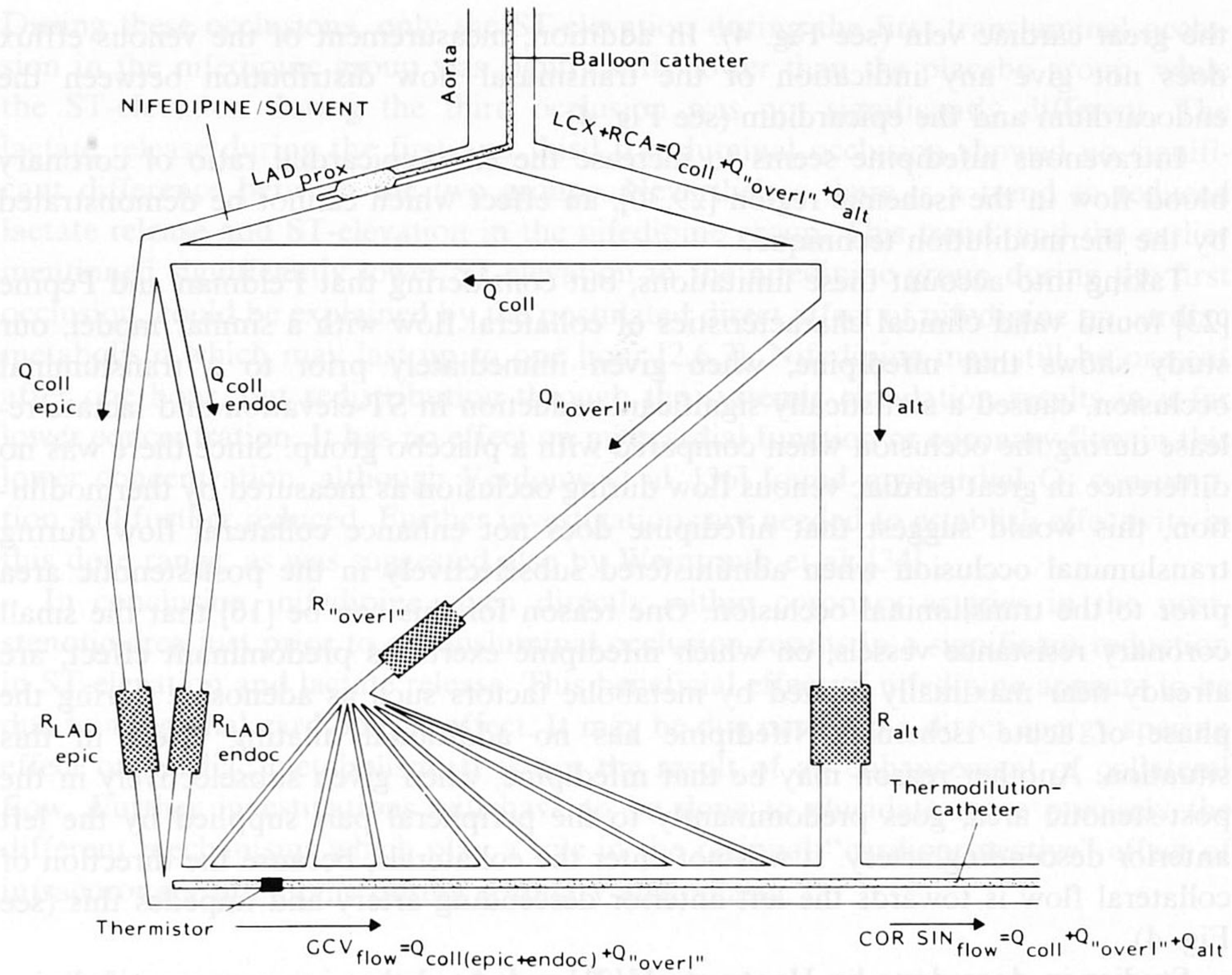

Fig. 4. An illustration of the assumptions made in our study. During transluminal occlusion of the proximal left anterior descending coronary artery (LAD_{prox}), collateral flow (Q_{coll}) is shown coming from the circumflex (LCX) and to a lesser extent from the right coronary artery (RCA). This collateral flow passes through epicardial ($Q_{coll\ epic}$) and endocardial ($Q_{coll\ endoc}$) zones supplied by the left descending coronary artery region. The thermodilution catheter (Webster) is shown located distally in the great cardiac vein, the more proximal thermistor measuring collateral flow ($Q_{coll\ (epic+endoc)}$) as well as some "overlap flow" ($Q_{\text{"overl"}}$). True collateral flow therefore is not completely separated from overlap flow, but under ideal conditions great cardiac venous (GCV) flow measured by thermodilution is a reliable approximation of true collateral flow. Coronary sinus flow consists of collateral flow, overlap flow and alternative vessel flow (Q_{alt}). Alternative vessel flow is flow from the left circumflex artery and right coronary artery of which the venous efflux is not drained into the great cardiac vein (nor in the Thebesian veins), but directly in the coronary sinus. The sign R in the figure stands for resistance in the respective vascular capillary beds. COR SIN = coronary sinus.

supplied by the circumflex artery and to a lesser extent from the region supplied by the right coronary artery [23]. During transluminal occlusion, the venous flow consists of "true collateral flow" and "overlap flow" (see Fig. 4). Overlap flow is blood delivered to the non-ischemic zone by nonoccluded vessels, whereas collateral flow is blood delivered to the ischemic zone by the non-occluded vessels [28]. Failure, as Marcus [28] states, to distinguish "overlap flow" from "true collateral flow" yields results which are misleading. In our study we tried to avoid "overlap flow" by positioning the tip of the thermodilution catheter as distally as possible in

the great cardiac vein (see Fig. 4). In addition, measurement of the venous efflux does not give any indication of the transmural flow distribution between the endocardium and the epicardium (see Fig. 4).

Intravenous nifedipine seems to increase the endo-epicardial ratio of coronary blood flow in the ischemic region [29,30], an effect which cannot be demonstrated by the thermodilution technique.

Taking into account these limitations, but considering that Feldman and Pepine [23] found valid clinical characteristics of collateral flow with a similar model, our study shows that nifedipine, when given immediately prior to a transluminal occlusion, caused a statistically significant reduction in ST-elevation and lactate-release during the occlusion when compared with a placebo group. Since there was no difference in great cardiac venous flow during occlusion as measured by thermodilution, this would suggest that nifedipine does not enhance collateral flow during transluminal occlusion when administered subselectively in the post-stenotic area prior to the transluminal occlusion. One reason for this can be [16] that the small coronary resistance vessels, on which nifedipine exerts its predominant effect, are already near maximally dilated by metabolic factors such as adenosine during the phase of acute ischemia. Nifedipine has no additional dilating effect in this situation. Another reason may be that nifedipine, when given subselectively in the post-stenotic area, goes predominantly to the peripheral part supplied by the left anterior descending artery. It will not enter the collaterals, because the direction of collateral flow is towards the left anterior descending artery and impedes this (see Fig. 4).

Studies in dogs done by Henry et al. [31] suggested that intravenous nifedipine does increase collateral flow to the acute ischemic myocardium, but also, by its systemic vasodilating effect, decreases afterload. The increased cardiac output with decrease in wall tension could explain the overall enhanced coronary flow [30,32]. On the other hand Feldman et al. [33] showed that nifedipine given buccally in patients had no beneficial effect on collateral flow to the ischemic region in pacing-induced angina. Weintraub et al. [34] gave nifedipine directly within the coronary arteries in dogs and neither they nor Lamping and Gross [30] or Probst [35] found an increase of myocardial flow in the ischemic zone, these findings being consistent with our results.

As the beneficial effect of intracoronary nifedipine, when given subselectively in the post-stenotic area, is not due to enhanced collateral flow in our study, it may better be explained by the negative inotropic effect of the drug [3]. This causes a regional cardioplegia just before the onset of ischemia which occurs during transluminal occlusion. This cardioplegia results in a reduced demand for oxygen and could attenuate the detrimental effect of acute ischemia. The extent to which a direct effect of nifedipine on cardiac metabolism plays a role in the beneficial effect of nifedipine when given just prior to a transluminal occlusion remains to be elucidated by further investigations.

Any effect of nifedipine on coronary flow during the first and third transluminal occlusions and on the inotropic state of the myocardium is absent. In both situations nifedipine was administered more than 5 minutes before occlusion [3,24].

During these occlusions, only the ST-elevation during the first transluminal occlusion in the nifedipine group was significantly lower than the placebo group, while the ST-elevation during the third occlusion was not significantly different. The lactate release during the first and third transluminal occlusion showed no significant difference between the two groups. Nevertheless there is a trend to reduced lactate release and ST-elevation in the nifedipine group. This trend, and the earlier mentioned significantly lower ST-elevation in the nifedipine group during the first occlusion, could be explained by the postulated direct effect of nifedipine on cardiac metabolism which may last up to one hour [2,6,7]. Nifedipine may still be present after one hour, but redistribution through the systemic circulation results in a far lower concentration. It has no effect on myocardial function or coronary flow in this lower concentration, although Verdouw et al. [36] found myocardial O_2 consumption still further reduced. Further investigations are needed to establish effectivity in this dose range, as was suggested also by Weintraub et al. [34].

In conclusion, nifedipine given directly within coronary arteries in the poststenotic area just prior to a transluminal occlusion results in a significant reduction in ST-elevation and lactate release. This beneficial effect of nifedipine appears to be due to a regional cardioplegic effect. It may be due partly to a direct energy sparing effect on cardiac metabolism. It is not the result of an enhancement of collateral flow. Further investigations will have to be done to elucidate more precisely the different mechanisms which play a role in the regional "cardioprotective" effect of intracoronary nifedipine during coronary angioplasty.

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