Recovery from Circulatory Depression after Coronary Artery Bypass Surgery[1]

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Abstract. The direct traumatic effects of coronary artery bypass surgery may counterbalance the expected improvement of myocardial function in the early postoperative period. In 55 patients, the regional shortening fraction was measured over 12 months using radiopaque epicardial marker pairs implanted during surgery in the newly perfused regions. The time course of cardiothoracic ratio, heart rate and cuff blood pressure was documented. All patients were catheterized before surgery and 1 year afterwards. There is an initial depression in myocardial function lasting up to 3 months after surgery which is not directionally related to changes in loading conditions or chronotropic state, but most likely to recovery of the myocardium from perioperative injury. At 1 year after surgery the overall ventricular function is unchanged. The evaluation of ventricular function after coronary artery bypass grafting should be performed no sooner than 3 months after surgery to avoid this transient period of depressed myocardial performance.

After coronary artery bypass surgery, graft closure as well as its functional consequences remain, to some extent, unpredictable. There is ample evidence that the majority of grafts that occlude do so within a few weeks after surgery. Afterwards, graft occlusion occurs less frequently. This also parallels the cumulative survival statistics. There appears to be an early postoperative period during which both the graft and patient are at a greater risk than in any later period.

Even in the absence of manifest perioperative myocardial infarction, a great deal of clinical evidence (*Bolook*, 1973; *Sung* et al., 1977; *Righetti* et al., 1977a, b; *Boudoulas* et al., 1976; *Dixon* et al., 1973; *Oldham* et al., 1973) demonstrates beyond doubt the presence of myocardial trauma after coronary surgery, which, fortunately, most patients tolerate well. In view of this trauma, it would appear necessary to examine more closely myocardial function, especially regional function in the vicinity of the graft, in the early postoperative period. At least the magnitude and duration of the expected myocardial depression should be better defined. This information may prove to be useful in the clinical management of these patients, but the basis for this needs to be further developed.

Direct and serial measurements of regional myocardial function in the postoperative phase have been greatly facilitated by the recent introduction of a direct method utilizing radiopaque epicardial markers implanted during surgery (*Brower* et al., 1978). With this technique we examined regional shortening and conventional clinical variables over a 1-year period in 55 patients with coronary artery bypass grafting. The aim being to better define the presence and time course of any depression in myocardial function after coronary artery surgery.

Material and Methods

The study group consisted of 55 consecutive adult patients (51 men, 4 women) scheduled for elective coronary bypass grafting and followed for 1 year after operation. Ages ranged from 41 to 62 years. The majority (27/55) had stable angina pectoris and 23/55 presented either an increasing frequency or an increasing severity of attacks in spite of medical therapy. 4 presented a decreasing severity of angina pectoris, and 1 patient was classified as unstable. The majority 32/55 had a previous myocardial infarction; 29 were in NYHA class III, 23 in class II and 3 in class I. Regional wall motion (RAO and LAO cineangiography) abnormalities of dyskinesia were found in 6 patients, akinesia in 8 and hypokinesia in 31. All myocardial segments were scored normal in 12 patients. Markers were not placed in regions observed to be dyskinetic during surgery. Hemodynamic and functional data are given in tables I and II.

Cardiac catheterization was performed 3 months before surgery and 1 year after surgery. Cardiac output was determined by the thermodilution technique. Left ventricular pressure was recorded by tip manometry, and V_{max}, using an on-line computer system (*Meester* et al., 1975; *Brower* et al., 1977), was used to estimate the contractile state. The coronary arteries were studied by the Sones technique and filmed at 50 frames per second. Left ventricular volume and wall motion were quantified (*Brower* et al., 1975).

Routine clinical measurements, including cardiothoracic ratio, heart rate, and cuff blood pressure were documented at 3 months and 1 day prior to surgery, and at 1 week and

1, 3, 6 and 12 months after surgery. In 40 patients, the cardiothoracic ratio was available for follow-up over 1 year, as chest X-rays with pleural or pericardial effusion, as assessed by echocardiography, were excluded from this analysis.

Epicardial Markers

The method used for quantifying regional epicardial shortening has been described in detail elsewhere (*Brower* et al., 1978, 1979). In brief, radiopaque markers of different shapes were implanted on the epicardium during surgery in all bypassed regions and, if possible, in control regions. The controls were primarily near the base of the heart on the anterior surface, which were apparently well perfused and normally contracting, as seen in the preoperative angiogram.

All markers were placed in pairs, aligned transverse to the major axis, 2 cm apart, and located from 0 to 3 cm distal to the coronary anastomosis of the graft. The fact that there are marked differences in regional shortening with position and direction on the myocardium, as demonstrated by *LeWinter* et al. (1975), is not a significant limitation in this study as each marker pair served as its own control in all follow-up examinations. A total of 120 marker pairs were placed in bypass regions and 31 pairs were placed as controls.

In the follow-up studies, all marker pairs were filmed individually with the conventional C-arm single-plane cinefluoroscopy used for coronary artery studies. Individual marker pair filming with the image intensifier aligned perpendicular to the axis of shortening was necessary to achieve minimal foreshortening. From biplane studies (*Brower* et al., 1978; *Serruys* et al., in press), the measurement error in shortening fraction from single-plane cinefluoroscopy has been shown to be less than 1% when the image intensifier is correctly aligned as described above. This small error was due to the fact that the measured rotation perpendicular to the viewing plane averaged $\pm$ 4.5°, the error in normalized shortening is proportional to cos Θ, or $\pm$ 0.5%. These results are entirely consistent with the studies of *Leshin* et al. (1972) on the standard deviation obtained from minor axis markers using biplane filming.

The marker separation starting from the onset of the Q wave of the ECG to minimum separation was measured and plotted. Shortening fraction was determined by shortening fraction = $(L_{max} - L_{min})/L_{max}$, and expressed as a percentage. L_{max} and L_{min} denote the maximum and minimum marker separation, respectively. For a normal shortening pattern, this shortening fraction is identical to the shortening fraction achieved during ejection. To verify this condition, the time to onset of shortening (T = time from Q wave of ECG to L_{max}) (*Brower* et al., 1978, 1979; *Serruys* et al., in press) was determined. The occurrence of paradoxical systolic expansion was determined from the pattern of marker shortening and was usually associated with T $\geqslant$ 200 ms. The occurrence of paradoxical systolic expansion is treated separately in the data analysis.

Surgical Procedure

Anesthesia was induced with fentanyl, pancuronium, and thiopentone, and subsequently maintained with fentanyl, pancuronium and 60% N_2 in O_2. Total cardiopulmonary bypass with whole blood and hemacel (hematocrit 32% was utilized under moderate hypothermia. The myocardium was cooled by topical hypothermia. In 48 cases, fibrillation occurred spontaneously with hypothermia or cross-clamping, but electrical fibrillation was used in 8 patients. Intermittent aortic cross-clamping was used during grafting. Shortly

Table I. Results (mean ± SD) at 3 months before and 1 year after surgery

Measurement	3 months preoperatively	1 year postoperatively
HR, beats/min	72 ± 12	74 ± 12
EF, %	55 ± 10	55 ± 13
V_{max}, s^{-1}	49 ± 9	48 ± 9
LVEDP, mm Hg	14 ± 7	18 ± 7*
LVEDV, ml/m²	74 ± 16	89 ± 26*
mean AoP, mm Hg	106 ± 17	115 ± 21*
CI, $l \cdot min^{-1} \cdot m^{-2}$	3.2 ± 0.6	2.9 ± 0.5*
R, $dyn \cdot s \cdot cm^{-5}$	1,430 ± 340	1,700 ± 460*

HR = Heart rate; EF = ejection fraction; V_{max} = extrapolated isovolumic dP/dt/P to P = 0 (P = left ventricular pressure); LVEDP = left ventricular end-diastolic pressure; LVEDV = left ventricular end-diastolic volume; AoP = mean aortic pressure; CI = cardiac index; R = systemic resistance. * Difference significant at the 0.0025 level, paired Student's t test.

after cardiopulmonary bypass, blood flow in each graft was measured using an electromagnetic flowmeter (*Brower* et al., 1979). 4 patients had aneurysmectomy.

A twelve-lead ECG was obtained 2 days before surgery and daily afterwards. Perioperative infarction was diagnosed when new Q waves appeared within 48 h after surgery. Classes I-1 and I-2 of the Minnesota code were used (*Blackburn* et al., 1960). ST-T changes in the absence of Q waves were not accepted as evidence of infarction.

Results

Cardiac Catheterization

The cardiac catheterization results at 3 months before surgery and 1 year afterwards are summarized in table I. Heart rate at both times was unchanged: 72 vs. 74 beats/min. Ejection fraction and resting V_{max} were identical: ejection fraction 55 vs. 55% postoperatively and V_{max} 49 vs. 48 s^{-1} postoperatively. End-diastolic pressure and volume were slightly but significantly increased at 1 year after surgery. The pericardium was not closed at the end of surgery. From the increase in mean aortic pressure of 106 to 115 mm Hg, and the increase in systemic resistance of 1,430 to 1,700 $dyn \cdot s \cdot cm^{-5}$, an increase in afterload is clear. 1 year after surgery, usage of β-blockers dropped from 55% of patients to 13%, while usage of
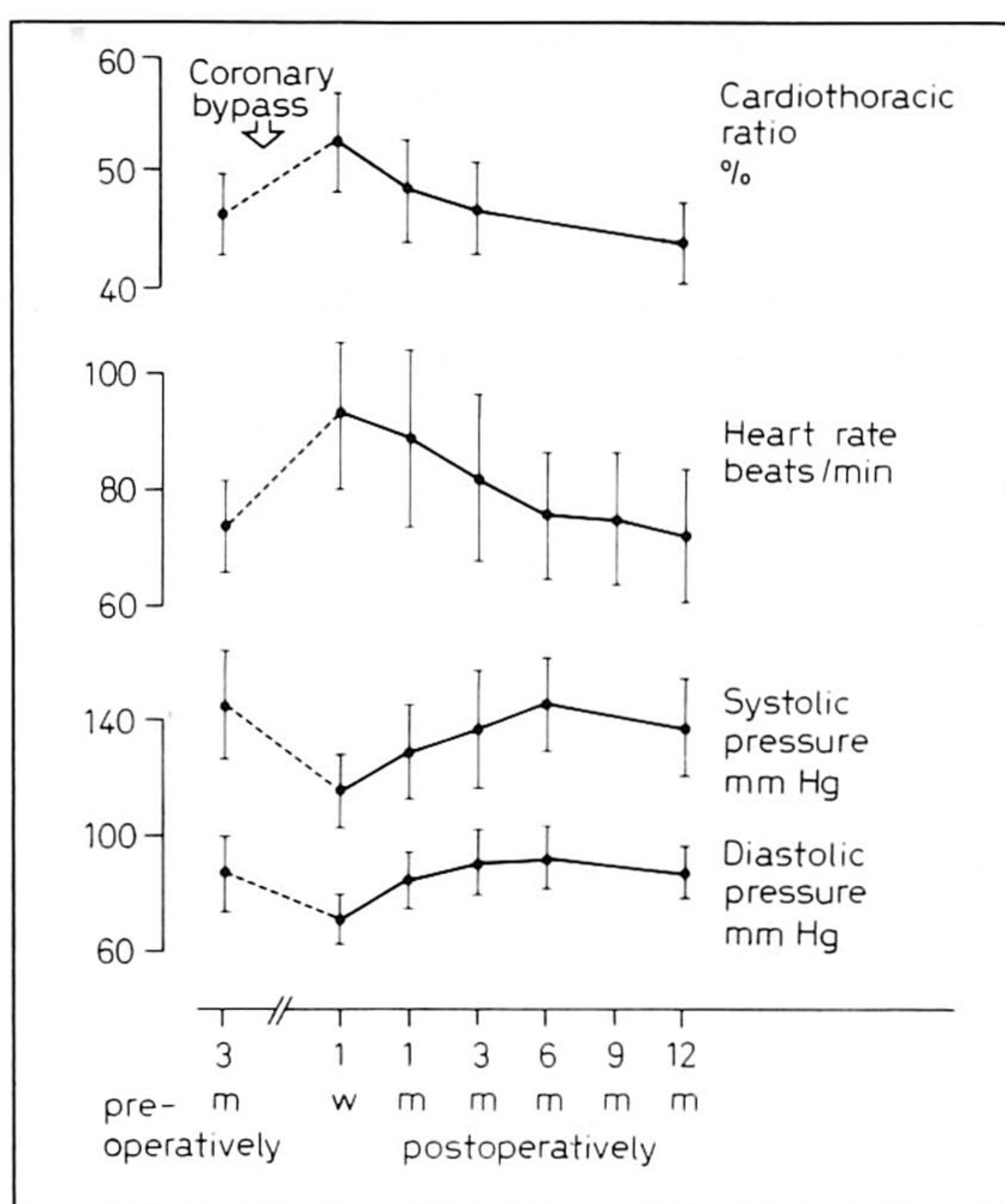
Fig. 1. Conventional clinical measurements from 3 months before surgery to 12 months after surgery.

diuretics dropped from 32 to 11%. Thus, at 1 year after surgery, left ventricular function, as judged by the above variables, remained unchanged on average in the face of increased afterload, slightly increased preload and constant heart rate.

Clinical Findings

The 1st-year mortality was 4%, and in 3 of 4 patients with persistent new Q waves, myocardial infarction was confirmed by SGOT, LDH and CPK levels exceeding those observed in uncomplicated bypass surgery (*Kansal* et al., 1975; *Hultgren* et al., 1973). 1 year after surgery, the majority of patients (79%) showed an improvement in the NYHA class of at least one grade while 19% were unchanged. Pertinent clinical findings over the 1-year follow-up period are summarized in table II and figure 1. 1 week after surgery, the average heart rate was considerably higher than before surgery, with a mean difference of 22 beats/min, and it returned to the

preoperative rate between 6 and 9 months after surgery. Without exception there was a consistent enlargement of heart size from before surgery to 1 month after surgery. The cardiothoracic ratio was significantly increased from a mean of 46% preoperatively, to 53% at 1 week after surgery. At 1 month, cardiothoracic ratio remained abnormally large, but by 3 months postoperatively it returned to preoperative values. Finally, at 1 week, the cuff blood pressure also showed a significant reduction from 141 to 116 mm Hg (systolic), and from 87 to 72 mm Hg (diastolic). The blood pressure was still decreased at 1 month, but returned to preoperative values between 1 and 3 months.

Regional Shortening

Of the 151 marker pairs implanted on the epicardium, four subgroups have been identified: group 1, 23 control regions located on the anterior surface near the base; group 2, 8 'nonnormal' regions similarly located as the controls, but perfused by a nonnormal coronary artery which was not grafted; group 3, 18 bypass regions showing a paradoxical systolic expansion; group 4, 102 bypass regions with normal or slightly delayed onset of shortening over the entire 12-month follow-up period.

The shortening fraction data are presented in table II and figure 2. In the event of paradoxical systolic expansion developing in a region, the data up to but not including the moment of this occurrence are included. For paradoxical systolic expansion, apparent shortening begins at end systole, thus the shortening fraction then denotes a reduction in length following removal of pressure loading and cannot be compared with shortening occurring at end diastole as a result of myocardial contraction (*Brower* et al., 1979). At 1 week after surgery, the shortening fraction in the control regions exceeded that in the 102 bypassed regions taken as a whole (11.5 vs. 9.7%), but this just failed to reach statistical significance at the 0.05 level. At 1 month, the original difference between controls and bypass regions had completely disappeared. However, over a 6-month period, both groups showed a slow and highly significant ($p < 0.001$) rise in shortening fraction. After 6 months, the shortening fraction in both groups remained stable at 13.7%.

Relation to Surgical Technique

The possibility that regional function, as determined 1 week after surgery, was directly related to some aspect of surgical technique was explored in this group of patients. As a whole, the cardiopulmonary bypass duration

Table II. Heart rate (HR) during marker measurements, cardiothoracic ratio, systolic blood pressure, diastolic blood pressure and shortening fraction in the follow-up period

Measurement	Pre-operatively (1 week)	Postoperatively					
		1 week	1 month	3 months	6 months	9 months	1 year
Heart rate							
Mean	74.0	96.4	92.0	83.2	78.9	75.7	73.0
SD	8	15	16	14	14	12	12
Significance							
WRT preop.	–	10^{-6}	10^{-6}	10^{-4}	0.02	NS	NS
Cardiothoracic ratio, %							
Mean	46.5	52.8	48.8	47.1	–	–	43.5
SD	3.7	4.4	4.5	4.2	–	–	3.7
Significance							
WRT preop.	–	10^{-6}	0.005	NS			NS
Systolic blood pressure							
Mean	146	117	130	138	147	–	139
SD	19	13	16	20	17	–	17
Significance							
WRT preop.	–	10^{-6}	10^{-5}	NS	NS	–	NS
Diastolic blood pressure							
Mean	88	71	85	91	93	–	89
SD	12	9	10	11	12	–	9
Significance							
WRT preop.	–	10^{-6}	NS	NS	NS	–	NS
Shortening fraction, %							
All bypasses							
Mean	–	9.8	12.8	13.3	13.7	14.5	14.2
SEE	–	0.42	0.52	0.48	0.50	0.52	0.53
Control regions							
Mean	–	11.5	12.0	13.1	13.7	13.7	13.9
SEE	–	0.97	1.06	0.98	0.89	0.93	0.80

NS = Not statistically significant at the 0.05 level (paired Student's t test); SD = standard deviation; SEE = standard error of the estimate; WRT = 'with respect to'.
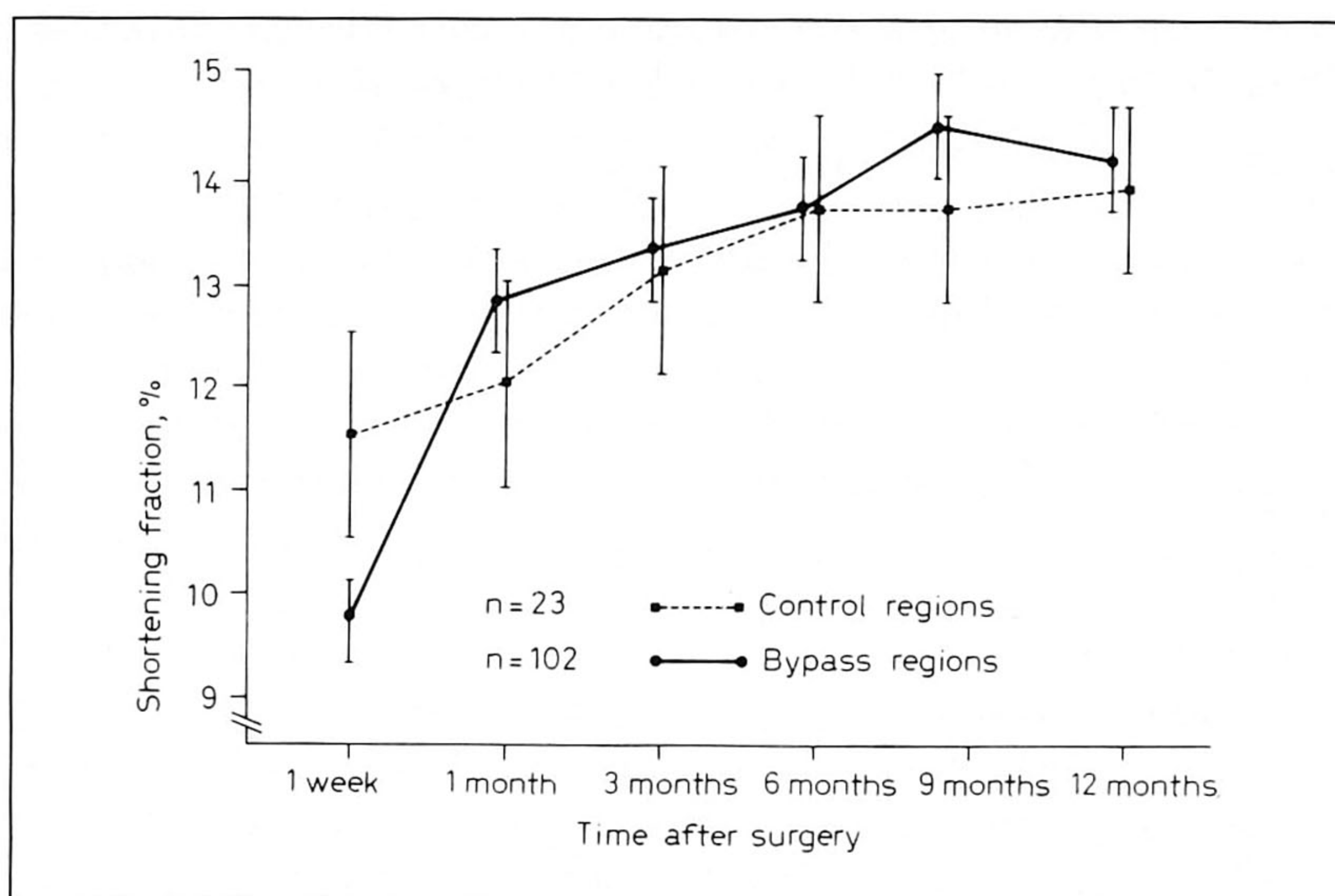
Fig. 2. Regional shortening fraction (mean ± SE) from control and bypass regions over the follow-up period.

ranged from 31 to 194 min (mean 121 ± SD 35 min). The total aortic cross-clamping time ranged from 12 to 68 min (mean 40 ± SD 10 min). These results are presented in greater detail in table III, where patient subgroups are formed on the basis of the regional function in the 1 week after surgery: group 1 (4 patients) showed paradoxical systolic expansion in one or more regions; group 2 (35 patients) had a shortening fraction of less than or equal to 10 % in one or more regions, and group 3 (10 patients) had a shortening fraction greater than 10% in all regions. 7 patients were excluded because of either insufficient or ambiguous data. There were no significant differences in aortic cross-clamping duration or mean revascularization flow between these three groups, which represent respectively poor regional function (group 1) moderate function (group 2), and very good regional function (group 3). There is an apparent trend in the cardiopulmonary bypass duration dropping from 148 min (group 1) to 125 min (group 2) and 109 min (group 3), but this difference fails to achieve statistical significance at the 0.05 level. In summary, for the range of cardiopulmonary bypass, aortic cross-clamping, and mean revascularization flow, as recorded in the clinical setting, no connection was found between regional shortening and surgical technique.

Table III. Regional shortening at 1 week in relation to some aspects of surgical technique (means ± SD)

	Cardiopulmonary bypass duration, min	Aortic cross-clamping duration, min	Mean revascularization flow, ml/min
Group 1 Paradoxical systolic expansion in one or more regions (n = 4)	148 ± 32	46 ± 14	170 ± 65
Group 2 0–10% shortening fraction in one or more regions (excluding paradoxical systolic expansion; n = 35)	125 ± 37	41 ± 12	146 ± 113
Group 3 More than 10% shortening fraction in all regions (n = 10)	109 ± 44	42 ± 18	143 ± 110

n= Number of patients.

Discussion

Ischemic injury to the myocardium during bypass surgery has been repeatedly demonstrated from a spectrum of clinical evidence (*Sung* et al., 1977; *Boudoulas* et al., 1976). A significant incidence of perioperative myocardial infarction (*Dixon* et al., 1973; *Oldham* et al., 1973; *Righetti* et al., 1977a), and abnormal septal movement (*Righetti* et al., 1977b) is frequently observed. Thus, myocardial trauma resulting in depression of left ventricular function should be expected in the postoperative period in spite of renewed perfusion via the graft(s). This work was undertaken to document the magnitude of this depression, the time course of its recovery, and the major contributing factors.

The vast majority of patients had stable angina pectoris and were electively operated. *Hagl* et al. (1978) have shown that patients with stable angina are not able to demonstrate an acute effect of myocardial revascularization either on segmental or total left ventricular function when compared to the pronounced effect seen in unstable angina. While the results of *Hagl* et al. (1978) are not directly comparable with ours, their results being confined to the perioperative period, the findings do appear consistent.

A superficial summary of the results in table I would suggest that, in spite of an improvement in NYHA class and symptomatology 1 year after surgery, there is little improvement in left ventricular function and a nearly universal impairment in regional shortening up to 3 months after surgery. Others have also shown little improvement in ejection fraction. Indeed, because ejection fraction was largely in the normal range for the majority of patients before surgery, this is to be expected. However, significant changes did occur in left ventricular loading conditions (end-diastolic volume and pressure, and aortic pressure), and these must be considered in the evaluation of left ventricular functional changes.

V_{max} has been shown to be much less influenced by loading conditions than ejection fraction. Therefore, the relative constancy of V_{max} (49 vs. 48 s^{-1}) from preoperatively to 1 year postoperatively suggests that there was no essential change in contractility. As ejection fraction also showed no change over the same period, we must presume that changes in the loading of the left ventricle largely canceled each other with respect to ejection fraction: the increase in preload (end-diastolic volume from 74 to 89 ml/m^2 and end-diastolic pressure from 14 to 18 mm Hg) should cause an increase in ejection fraction, while the increase in afterload (mean aortic pressure from 106 to 115 mm Hg and peripheral resistance from 1,430 to 1,700 dyn · s · cm^{-5}) should cause a decrease in ejection fraction. The increased peripheral resistance can be largely attributed to less frequent use of β-adrenergic blockade and diuretics in these patients after surgery as a result of improvement in symptomatology and complaints. The changes in end-diastolic volume and pressure are less easy to explain. Certainly, the opening of the pericardium and the development of adhesions must affect compliance (*Glantz and Parmley,* 1978), but also a redistribution of blood volume as a result of the increased peripheral resistance is likely. Whatever the explanation of the loading changes, it is clear the ejection fraction was not changed from the preoperative study to 1 year after surgery. Since the shortening fraction must behave similarly to the ejection fraction in this regard, it might be supposed that the average regional shortening fraction also did not change, although regional compensation is possible and clearly needs further study in this context. That is, before surgery regional shortening in the bypassed regions may well have been less than that found 1 year after surgery, in spite of the invariance in ejection fraction, because normally perfused tissue could compensate for insufficient shortening in ischemic regions. With this provision in mind, the best available estimate for the preoperative epicardial shortening fraction would be 14% on average, the

value found between 9 and 12 months after surgery. In the presence of regional compensation it would be less.

The more frequent measurements made in the postoperative phase (table II) provide some insight into the time course of the left ventricular functional changes. The measurements made before and 1 week after surgery show an increase in the chest X-ray heart size, a decrease in systolic and diastolic cuff blood pressure, and an increased heart rate. Measurements from the chest photo are liable to errors from several sources in spite of careful checking for artifacts. Nevertheless, we find the magnitude of these changes in cardiothoracic ratio (from 46.5% preoperatively to 52.8% at 1 week) to be well beyond the measurement error. The pattern of recovery is also consistent with that found for blood pressure and regional shortening. It thus represents an important increase in the left ventricular dimensions in the early postoperative period which returns to preoperative levels at about 3 months. The increase in resting heart rate may represent a compensatory mechanism to preserve cardiac output in patients with a depression of ventricular function after surgery. This may be the result of baroreceptor reflexes because of the decreased blood pressure. Also, a high sympathetic drive after surgical stress probably occurs during the first week (*Boudoulas* et al., 1976), but this factor is less likely after this period. The explanation for the lower postoperative systolic and diastolic blood pressures is not known, but this may be due to hypovolemia in the early postoperative period while fluid balance is being adjusted.

In comparison with the preoperative state, the early postoperative evaluation shows an increase in preload reflected by increased heart size and a decrease in afterload. These combined changes in loading conditions are known to enhance ejection fraction and therefore the shortening fraction. As the shortening fraction probably falls (see above discussion on preoperative shortening fraction), contrary to the expectation from the loading changes, we take this as further evidence for a myocardial depressive effect present up to 3 months after surgery. The increase in heart rate (from 74 to 96 beats/min) would be expected to reduce the shortening fraction, however, previous studies of the shortening fraction during pacing in our laboratory have shown a sensitivity of -0.041%/beat/min. An increase of 22 beats/min would account for an absolute change in the shortening fraction of -0.9%, much less than the change in the shortening fraction over the entire follow-up period.

The pattern of change in shortening fraction in the postoperative period also suggests recovery from myocardial depression. Between the 1st week

and the 1st month the decrease in preload and the increase in afterload demonstrated by the rise in diastolic arterial pressure would decrease ejection fraction and shortening fraction, everything else held constant. Thus, the increase in shortening fraction in the early postoperative period is not directionally related to changes in loading conditions, and the decrease in heart rate is quite insufficient to explain the change in shortening fraction. The slow rise in regional shortening must be attributed to recovery of the myocardium from perioperative injury.

The major quantifiable factors relating to surgical technique include the cardiopulmonary bypass duration, aortic cross-clamping time, and total myocardial revascularization flow. While a trend is apparent in cardiopulmonary bypass time (from 148 min in 4 patients with paradoxical systolic expansion to 109 min in 10 patients with shortening fractions of more than 10% in all regions), we were unable to show any statistically significant relation between these factors and the regional performance. The explanation possibly is that the use of cardiopulmonary bypass, rather than its duration as seen in clinical practice, is the more important factor. Similarly, the duration of aortic cross-clamping was not judged to be excessive in any patient, and in no case could an inadequate shortening fraction be traced back to prolonged aortic cross-clamping time. Also, the deleterious effect of anoxic arrest during multiple grafting is possibly counterbalanced by the benefit of more complete revascularization. The literature on this subject is somewhat conflicting. Copeland et al. (1968) reported that ischemia or infarction correlated with total perfusion time, but not with aortic cross-clamping and that a causal relationship could not be assumed. Lee et al. (1973) and Brewer et al. (1973) demonstrated that patients developing perioperative myocardial infarction had a prolonged pump time, and aortic cross-clamping, and a larger number of multiple grafts. In contrast, Morton et al. (1975) demonstrated no difference in duration of cardiopulmonary bypass, total duration of anoxic arrest, or number of grafts performed between the groups with and without myocardial infarction.

Recent studies on cardioplegic agents have clearly implicated the duration of anoxic arrest as the cause of depression in myocardial function in dogs (Behrend and Jochim, 1978; Serruys et al., in press). Anesthesia and cardiopulmonary bypass were shown not to be a major contributing factor in the loss of left ventricular function. However, a single period of anoxic arrest in dogs, lasting from 1 to 1.30 h cannot be compared to current surgical practice where intermittent cross-clamping, of less than 15 min per graft, is employed.

In summary, the recovery from circulatory depression following coronary artery bypass grafting is completed between 3 and 6 months. The fact that both control and bypass myocardial regions are affected suggests that some aspect of the surgical procedure not directly related to bypass grafting is involved. The mechanism of depression is not entirely clear, but either the duration of anoxic arrest or cardiopulmonary bypass is suggested. The evaluation of left ventricular function after coronary artery bypass grafting should be performed at least 3 months after surgery to avoid this transient period of depressed myocardial performance.

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