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An appraisal of symptom relief after coronary bypass grafting

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Summary

Subjective symptomatic improvement is experienced by 90% of patients after coronary bypass surgery. Objective exercise testing reduces this incidence to 70%. An analysis of the multifactorial genesis of pain relief based on data of non-randomized trials reveals that graft patency plays a dominant but not unique role in causing improved symptomatology. In a number of cases, intra-operative myocardial infarctions seem to explain the pain relief but may also have opposite effects. Changes in left ventricular function operate bi-directionally but data on this variable in relation to changes in symptomatology are not amenable for detailed analysis. Progression in native vessel lesions apparently opposes pain relief and has its greatest impact in connection with graft closure. Residual post-operative angina is evidently related also to incomplete revascularization.

Introduction

Aortocoronary bypass surgery in ischaemic heart disease (Favaloro, 1969; Effler, Favaloro and Groves, 1970; Johnson, Flemma and Lepley, 1970) is mainly practised with two objectives, the relief of disabling angina, and the improvement of the prognosis. The final proof for the latter alternative must await the results of current randomized multicentre trials, although similar medical and surgical groups have been compared (McNeer *et al.*, 1974). Pain relief, on the other hand, has been reported as being impressive in the majority of patients (Mitchel *et al.*, 1970; Sabiston, 1971; Spencer *et al.*, 1971; Morris *et al.*, 1972).

The following are proposed to explain this improvement in symptomatology: (1) flow via patent grafts to the ischaemic areas; (2) the psychogenic impact of surgery; (3) intra-operative myocardial infarctions making pain-triggering ischaemic areas painless; (4) destruction of the peri-coronary nerve plexus by surgical manipulation; (5) reduced myocardial oxygen demand due to a reduction in wall stress as a result of better left ventricular function and a reduction in left ventricular cavity size. Factors opposing the pain relief are: (1) occlusion of bypass grafts; (2) enhancement by the bypass graft of the progression in the native vessel lesions; (3) deterioration of left ventricular function leading to decreased epi-endocardial perfusion gradient and increase in left ventricular cavity size.

The aim of this report is to scrutinize the evidence available on the role of the various variables in the genesis of pain relief.

Incidence of subjective improvement

Table 1 gives some series with more than one hundred patients. The follow-up times have been variable and post-operative graft angiographies have not been systematically performed or the graft patency related to the functional status of the patients. The incidence of improvement is uniformly high. It was somewhat lower (83%) in the series of ninety-three patients of Alderman *et al.* (1973) who compared the state of grafts of their sixty-three patients with the subjective improvement. This comparison did not yield entirely satisfactory agreement. The same applies to the appraisal of Kouchoukos, Kirklin and Oberman (1974), who found post-operative angina in 37% of patients with all grafts patent and no angina in 39% of patients with all grafts occluded.

TABLE 1. Incidence of subjective improvement in some illustrative series

Reports	No. of patients	Percentage improved
Mitchel *et al.* (1970)	112	96
Spencer *et al.* (1971)	166	95
Anderson *et al.* (1972)	128	89
Morris *et al.* (1972)	471	92
Cannom *et al.* (1974)	375	88

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TABLE 2. Selection of studies comparing subjective improvement with objective exercise testing

Reports	Objective testing		Subjective evaluation	
	No. of patients*	Percentage improved	No. of patients	Percentage improved
Ross *et al.* (1972)	12	75	48	89
Bartel *et al.* (1973)	68	56	123	68 (symptom-free)
Griffith *et al.* (1973)	65	86	71	86
Guiney *et al.* (1973)	40	75	40	92
Lapin *et al.* (1973)	46	59	46	85
Balcon *et al.* (1974)	31	65	50	96
Hammermeister *et al.* (1974)	40	50	40	80
Frick (1974)	52	79	52	92

* Not necessarily the exact size of the series but the amount of patients amenable for analysis.

Comparison of objective and subjective improvement

A number of studies have compared subjective improvement with objective exercise testing. Table 2 shows a selection of these studies and represents 354 patients tested objectively with a 68% mean incidence of improvement. With one exception (Griffith *et al.*, 1973) the studies reveal an approximately 20% lower incidence of improvement in exercise testing than the rate based on the patient's own testimony. This difference cannot be taken as the full 'placebo effect' since this variable is also involved in objective exercise testing. It is especially evident when maximal exercise testing is performed, including the patient's own subjective symptoms to decide the end-point.

Graft patency, intra-operative myocardial infarction and objective improvement

Ross *et al.* (1972) found exercise tolerance clearly improved in six patients with patent grafts and unchanged or only moderately improved in another six patients with graft occlusions. Bartel *et al.* (1973) studied this aspect in a series of twenty-seven patients with a pre-operatively positive treadmill test. Post-operatively twelve of eighteen patients with at least one patent graft had a negative exercise response (67%) while three of nine patients with all grafts closed exhibited a negative treadmill test (33%). Thirty-three patients were similarly tested by Lapin *et al.* (1973) who demonstrated a significant improvement in a sub-group of seventeen with all grafts patent; the sub-group, with occluded grafts but at least one patent, showed no improvement. The same was true of a group of nine patients with all grafts occluded. In a series of thirty-three patients, Balcon *et al.* (1974) found increased exercise tolerance or a better atrial pacing result in seventeen of twenty-four patients with all grafts patent (71%); in the sub-group of nine patients, with one or more occluded grafts, five exhibited improvement (56%). Di Luzio, Roy and Sowton (1974) specifically studied fifteen patients with occluded grafts and concluded that occluded grafts to the left coronary artery had more influence on the post-operative exercise tolerance than occluded grafts to the right coronary artery. Frick, Harjola and Valle (1975a) objectively tested a series of fifty-two patients and found considerable improvement in a sub-group of thirty-six patients with all grafts patent whereas sixteen patients with one or more occluded grafts remained at the pre-operative level.

The incidence of intra-myocardial infarction has been variable depending on whether Q wave criteria have been used or the more unspecific changes in the repolarization have been taken into account in the electrocardiographic analysis. In affecting post-operative exercise tolerance this variable seems to operate bidirectionally. Four of seventeen patients with patent grafts in the series of Lapin *et al.* (1973) had intra-operative infarction and showed no objective improvement in post-operative testing. On the other hand, one patient with occluded grafts and infarction was significantly improved. Bartel *et al.* (1973) disclosed three patients, with all grafts occluded and intra-operative infarctions, who improved their exercise tolerance. Achuff *et al.* (1972) found a high incidence of intra-operative infarctions and arrived at the conclusion that clinical improvement may be partly related to infarction of the ischaemic myocardium. In the study of Frick *et al.* (1975a) intra-operative infarctions were equally distributed into the groups of patent and occluded grafts but only the sub-group with patent grafts improved exercise tolerance.

Pain relief, left ventricular function and progression of native vessel lesions

Improved left ventricular function after bypass surgery may be related to pain relief via reduction in the size of the left ventricular cavity and by decrease of the left ventricular end-diastolic pressure thus increasing the epi-endocardial perfusion gradient. On the other hand, improved contractility is paralleled by increased myocardial oxygen uptake. Deteriora-

tion of left ventricular function would oppose pain relief having opposite effects on left ventricular size and pressure. Furthermore, a decline in stroke volume would evoke tachycardia increasing the myocardial oxygen consumption. Data on left ventricular function after bypass surgery differ (Ross *et al.*, 1972; Achuff *et al.*, 1972; Bourassa *et al.*, 1972; Kline *et al.*, 1972; Lapin *et al.*, 1973; Griffith *et al.*, 1973; Hammermeister *et al.*, 1974). An improvement has been observed in some series early after surgery but repeated studies later in follow-up have not consistently displayed improvement. There is some evidence that bypass surgery may prevent further deterioration of left ventricular function contrary to the situation in medially managed patients (Gaarder, Corzo and Sanmarco, 1974). Changes in left ventricular function have not been systematically included in the analyses of factors evoking pain relief after surgery. Heart volumes were monitored by Frick *et al.* (1975a) who found no difference between the subgroups of graft patency and occlusion.

In addition to a certain attrition rate of the inserted grafts, emphasis has recently been attached to the changes in the native coronary arteries following bypass grafting (Aldridge and Trimble, 1971; Bousvaros *et al.*, 1972; Rösch *et al.*, 1972; Alderman *et al.*, 1973; Griffith *et al.*, 1973; Malinow *et al.*, 1973; Maurer *et al.*, 1974; Glassman *et al.*, 1974). The greatest incidence of progression takes place proximal to graft anastomosis and is not related to serum lipids or the presence of hypertension (Frick *et al.*, 1975b). This phenomenon is clearly a factor opposing pain relief since it causes myocardial infarction if it occurs in connection with graft occlusion.

The native vessel progression has not been systematically taken into account in the studies on post-operative exercise tolerance. Some data suggest that the beneficial effect of graft patency is superior to the opposing effect of native vessel progression (Frick *et al.*, 1975a).

Studies with random design

Schwade *et al.* (1973) reported on the fate of twenty-four patients on medical management and twenty patients after bypass surgery. At 12 months' follow-up the surgical patients had an overall better functional status than the medical cases, but this difference was not attainable at 18 months' follow-up. No data on graft patency or other relevant variables related to the genesis of angina were included. Tilkian *et al.* (1974) found exercise tolerance improved in thirty-two surgically treated patients in contrast to no change observed in twenty-nine medically managed patients at 1-year follow-up. The prevalence of exercise-induced ventricular arrhythmias was somewhat higher in the surgical patients. The data were not related to the state of the grafts. Mathur and Guinn (1973) found the angina frequency and objective functional state of twenty-six surgically managed patients superior to that in the same number of medically treated patients at 9 months' follow-up. The extended series of the same centre was recently reported (Mathur *et al.*, 1975). Thirty-five surgically treated patients increased their exercise tolerance more than the sub-group of thirty-five medically managed patients. The progression of native vessel lesions was roughly of the same frequency in both groups. Data on graft patency in relation to the functional state of the surgical patients was not analysed.

Discussion

Of the various mechanisms capable of relieving pain after coronary bypass surgery, flow via patent grafts to the ischaemic myocardium is the chief example. Accordingly, graft patency has been in the focus in most of the studies. The rate of subjective improvement (Tables 1 and 2) is 10–20% higher than after sham operations (Cobb *et al.*, 1959; Dimond, Kittle and Crockett, 1960) and corresponds roughly to the anticipated graft patency rate at 1 year in these studies. There is highly suggestive but not decisive evidence that graft patency is the principal factor in improved symptoms. The deviation from ideal fit is exemplified by clear improvement in some patients with occluded grafts and failure to improve with patent grafts. Lack of simultaneously recorded data favouring and opposing the disappearance of angina makes it impossible to analyse in detail the role of other relevant variables evoking a change in the anginal pattern. Intra-operative myocardial infarctions (Achuff *et al.*, 1972; Bartel *et al.*, 1973; Lapin *et al.*, 1973) seem to play an independent role since they are not related to graft patency or occlusion (Fruehan *et al.*, 1974; Frick *et al.*, 1975a). Pericoronary denervation is an interesting theoretical possibility (Soloff, 1973) but it tends to occur equally in patients with patent and occluded grafts.

The finding that patients with only one occluded graft do not as a group exhibit improvement (Lapin *et al.*, 1973; Frick *et al.*, 1975a) focuses attention on the consequences of incomplete revascularization. It is likely that there is no difference in the subjective threshold for angina triggered by a small or large amount of ischaemic myocardium or by a single area as opposed to multiple areas of ischaemia. An obstructed artery left ungrafted because of poor peripheral run-off has the same post-operative consequences. Some surgeons (Semb, personal communication) leave coronary arteries ungrafted, especially the left circumflex coronary artery, if these are well supplied by collaterals. There is some evidence that collaterals and their enhancement by ischaemia are not sufficient to prevent clinical symptomatology

(Frick *et al.*, 1975c). It seems likely, therefore, that the achievement of a symptom-free state post-operatively demands a complete revascularization. There is evidence that improved results can be reached by more complete revascularization (Anderson *et al.*, 1974; Siegel *et al.*, 1974), and that patients with all significant lesions bypassed and all grafts open exhibit a normal myocardial flow response to stress combined with normal treadmill test contrary to patients with occluded grafts or non-bypassed significant lesions (Knoebel *et al.*, 1974).

The desired improvement in left ventricular function after bypass surgery has not been found systematically. This may be due to the real ineffectiveness of bypass grafting or to a near normal pre-operative function as a prerequisite for accepting patients for surgery. At present, no conclusions can be drawn from the effect of post-operative left ventricular function on symptom relief. Deterioration of left ventricular function after bypass surgery was found by Shepherd *et al.* (1974) in the group with occluded grafts which nevertheless exhibited symptomatic improvement.

A comparison of randomized medical and surgical groups evidently reveals the overall effect of myocardial revascularization. While this approach is essential in studying the effect of bypass surgery on longevity, it falls short in disentangling the various mechanisms of pain relief unless the surgically treated patients are divided into sub-groups characterizing the changes in the relevant variables related to improved symptomatology. While the similarity of the entry characteristics with the medical group must simultaneously be ascertained, it follows that the size of the series must be considerable. It is to be hoped that the multicentre trials currently in progress fulfil the necessary requirements.

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