MEDICAL VERSUS SURGICAL INTERVENTION AND THE NATURAL HISTORY OF SEVERE ANGINA PECTORIS

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It is common belief that severe and refractory forms of angina pectoris generally portend catastrophic complications and early demise. This concept has been strengthened recently by Kannel and Feinleib[1] in the Framingham study which has shown a formidable mortality even among patients with "uncomplicated" angina pectoris. It is from such conviction, that surgeons today often justify the dangers of myocardial revascularization even in patients with mild to moderate symptoms whether previously treated appropriately by medical means or not. Careful examination of the data, however, suggests that this aggressive attitude may not be warranted on the basis of the natural hazards of the disease alone. Thus, while the Framingham group have reported a mortality rate of approximately 4 per cent per year in anginal patients without prior myocardial infarction, the natural hisotry of the disease for their series, unclassified by risk factors and untreated by any specific regimen, may not at all be applicable today to categories at varied risk under modern comprehensive medical management.

The treatment of angina pectoris does not begin and end with nitroglycerin as some physicians appear to believe. Proper management entails dietary control, weight reduction when indicated, hypocholesterolemic drugs, therapy for hypertension and diabetes, curtailment of stress and tobacco, exercise training, and in refractory cases the use of propranolol and isosorbide dinitrate.[2-5]

It is also well known that a number of factors influence the prognosis in angina pectoris. Among those contributing to risk are congestive heart failure, cardiac enlargement, multiple myocardial infarctions, hypertension, atrial fibrillation, valvular heart disease, diabetes mellitus and other complicating vascular and non-vascular disease states.

From these considerations it seemed that it might be possible to identify a group of patients who, despite even severe initial symptoms, have excellent prospects under optimal medical therapy for both dramatic clinical improvement and relatively long survival.

We have previously shown the feasibility of dividing patients with acute myocardial infarction, on the basis of clinical prognostic signs, into "good risk" and "poor risk" categories as a means of determining the need for anticoagulant therapy.[6] With such calssification, the low morbidity and mortality rates found in "good risk" patients did not appear to justify even the small hazard attending the use of anticoagulant drugs. It seemed possible therefore, that similar classification of anginal patients might also provide data which could prove helpful in weighing the risks of surgery against the natural hazards of the disease.

A prospective study was therefore begun in November 1967 of all patients presenting with severe forms of angina pectoris who had failed to respond satisfactorily to both prescribed alterations in life style and the customary use of nitroglycerin, long-acting nitrates, sedatives and tranquilizers.

MATERIAL

A total of 133 consecutive patients with ages ranging from 29 to 80 years form the basis of the present report. Of this number 102 were men and 31 women. In each instance slight to moderate physical or emotional stress regularly evoked classical episodes of angina pectoris which could not be adequately controlled or prevented despite careful use of the nitrates. As a consequence, the activities of daily living, occupational performance and even sleep were frequently disturbed. The diagnosis was confirmed in each patient by an unequivocal history of the classic symptoms, present for one year or more, and typical ischemic ECG patterns after exercise, previous episodes of myocardial infarction, or cine-coronary angiographic evidence of advanced disease. Thirty-two patients in the series had been studied by angiography and 26 of this number were found to have severe triple coronary artery disease. A history of one or more myocardial infarctions requiring hospitalization was elicited in 55 of the 133 patients and confirmed by electrocardiogrphy. Seventeen in the series were on digitalis therapy prescribed for previous congestive heart failure. Eight suffered from other complications such as cerebrovascular insufficiency, previous stroke or severe and uncontrolled diabetes. Twelve patients were over the age of seventy years.

Classification of Patients

Although all patients suffered from severe and refractory forms of angina pectoris, they were classified as "good risk" or "poor risk" at the time of their initial examinations on the basis of certain clinically recognized poor prognostic signs. Thus a patient was considered to be a poor risk for relatively long survival if he presented *any one* of the following unfavorable criteria:

1. Congestive heart failure, past or present
2. Significant enlargement of the heart
3. Multiple myocardial infarctions
4. Gallop rhythm
5. Severe hypertension
6. Atrial fibrillation
7. Severe and uncontrolled diabetes
8. Previous "stroke" or cerebrovascular insufficiency
9. Advanced age

Of the 133 patients in the series, 102 qualified as "good risk" by manifesting none of the pre-designated unfavourable indices while 31 were identified as "poor risk" on the basis of these criteria (Table I).

When judged by functional status (New York Heart Association) 87 of the patients were found to be in class III and 46 in class IV.

Therapeutic Management

All patients were placed on a regimen designed to achieve or maintain optimum weight. Serum lipid abnormalities were treated by means of diet and often by hypocholesterolemic agents. Hypertension and diabetes were managed with appropriate drugs with the aim of careful control. Tobacco and stimulants were proscribed. Alterations in life style to minimize stress were adopted where feasible. When left ventricular function was not impaired graduated exercise on a daily basis, always preceded by prophylactic medication, was encouraged.

Medicinal treatment in all cases consisted of the combined administration of propranolol and isosorbide dinitrate (ISDN). The dosage of propranolol was determined in each patient by careful titration to discover the amount needed to reduce resting heart rate to a frequency of 55 to 60 beats per minute. Isosorbide dinitrate was administered

TABLE I

CLASSIFICATION AND CHARACTERISTICS OF PATIENTS WITH SEVERE ANGINA PECTORIS

Type	No.	Av. Age	Over 70 Yrs.	C.H.F.	Prev. M.I.	Other Complic.
"Good risk"	102	58·8	0	0	28	0
"Poor risk"	31	65·2	12	17	27	8

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sublingually in a dosage carrying between 2·5 and 10 mg. according to individual tolerance and response. The dose of propranolol was taken orally *before* each meal and that of ISDN sublingually *after* each meal in order to obtain the longest possible period of synergistic activity during expected times of physical stress.[2-5] When congestive heart failure was detected or even suspected digitalis and an oral diuretic were prescribed prior to the use (or continuation) of propranolol.

RESULTS

Clinical Manifestations

The striking clinical response to propranolol and isosorbide dinitrate observed among subjects in this series has been previously reported.[2-5] In 90·2 percent of the 133 patients marked amelioration of angina pectoris associated with significant increments in exercise tolerance have been documented by controlled observations. These favorable responses correlate closely with improvement in ischemic electrocardiographic patterns evoked by standard exercise. In 50 percent of 62 patients so tested, there has been complete reversal of exercise-electrocardiographic abnormalities when evaluations were performed during periods of combined pharmacologic activity of these agents. Furthermore, follow-up studies have disclosed no tendency for an attenuation of effect with the passage of time.

Improvement in functional class following the administration of propranolol-isosorbide dinitrate therapy has been most significant (Table II). Twenty of the 87 patients originally in class III showed sufficient improvement to be grouped in class I while 63 shifted to class II. Of the 46 patients in class IV at commencement of study, 18 were judged to be in class II and 19 in class III after the institution of therapy.

Myocardial Infarction

Over the five year period, 22 of the 102 "good risk" patients suffered attacks of acute myocardial infarction and of these 18 recovered and 4 succumbed. In the "poor risk" group myocardial infarction occurred in 24 and accounted for death in 17 of the 31 patients during the same period.

Mortality

Only 4 of the 102 "good risk" patients followed from two to five years have died. None of 102 died during the first year, two of 102 died during the second year, one of 83 died during the third year and one of 57 died during the fourth year. Only 18 have been followed through the fifth year during which there were no deaths. From the mortality experience in this study, the probability of death in "good risk" and "poor risk" patients has been plotted. It can be seen that 5 percent of "good risk" patients may be expected to die by the end of the fourth year of follow-up, indicating an average annual mortality of 1·25 percent for this group. In sharp contrast, the average yearly fatality rate for "poor risk" patients may be anticipated to exceed 16 percent with only about one-third of the patients surviving to the end of the fourth year. These data make it clear that over-all mortality rates in any reported series will depend on the composition of the sample with respect to the numbers of "good risk" and "poor risk" patients.

TABLE II

COMPARISON OF NEW YORK HEART ASSOCIATION FUNCTIONAL CLASS BEFORE AND AFTER PROPRANOLOL-ISDN THERAPY

Functional Class	No. of Patients	
	Pre-Treat.	Post-Treat.
I		20
II		81
III	87	23
IV	46	9

DISCUSSION

Knowledge of the natural history of disease enables the physician to estimate its relative severity, probable course, residual effects, and ultimate outcome in the individual case. Moreover, it is only with a background of such knowledge that the physician can hope to weigh the possible benefits and hazards of any form of therapy, old or new, against the risk attending the natural course of the disease in a given patient. This is particularly true in coronary heart disease in which the clinical course is remarkably variable and the indications for any therapeutic intervention can only be considered on an individual basis.

In the present era of "coronary bypass" surgery for angina pectoris, justification for operative intervention if often based on little more than the contention that there is an appalling mortality rate with any form of medical management. Thus, it has been claimed that 50 percent of patients on conservative therapy die within five years, a decimation rate averaging 10 percent per year.[7] In sharp contradiction to this alleged threat to life even under optimal medical care, are the more favorable results reported by other investigators. Thus, Zukel and Mattingly[8] in a 15 year follow-up have shown that about 3 percent of patients angina pectoris die each year while Kannel and associates[7] in the Framingham study have indicated an annual mortality of approximately 4 percent in this disease, Moreover, since these more favorable results have been reported in large series of patients at varied risk and under no specific program of therapy, an even better prognosis seemed likely for carefully selected "good risk" patients participating in a modern comprehensive medical regimen. This was actually the finding in the present study which has shown that in such patients the probability of death over a period of four years is only 5 percent or approximately 1·25 percent per year. The significance of this observation is perhaps more meaningful when it is realized that it has been made in patients who, at the time of entry into this study, were suffering from severe and refractory forms of angina pectoris often associated with triple coronary artery disease but with relatively *normal left ventricular function.* Inasmuch as coronary bypass surgery in similar patients is associated with an immediate operative mortality in the neighborhood of 10 percent as well as with a formidable incidence of non-fatal complications and graft failure, early and late, these data make it difficult to justify surgical intervention unless disabling symptoms persist despite optimal medical care.

The relatively favorable outlook for "good risk" patients in this study despite presenting symptoms of severe angina pectoris is undoubtedly related to comparatively normal left ventricular function in all cases. In this regard, the use of non-invasive measures may prove valuable to identify or confirm those believed to be at minimal risk. Nevertheless, the total medical regimen directed at the removal of coronary risk factors and the utilization of propranolol in combination with isosorbide dinitrate to prevent recurrent bouts of coronary insufficiency may have played an important, although presently undefined, role in determining prognosis in these patients.

In any event, the identification of patients at relatively lower risk and the utilization of comprehensive therapy with specific objectives for the individual case appear adequate to explain the far better survival experience in our "good risk" patients than in the undifferentiated series of the Framingham group!

When refarctory angina pectoris is associated with impairment of left ventricular performance as observed in "poor risk" patients of this series, the prognosis appears grave whether medical or surgical therapy is adopted. In spite of excellent symptomatic response to medical treatment in most cases, 25 percent of these "poor risk" subjects died within the first year and 67 percent failed to survive to the end of the fourth year. Equally dismal, however, are the results of surgical therapy in which the immediate mortality has been reported to be as high as 40 percent or more with the chances of salvage relatively poor. In this

category too, therefore, operative intervention should be considered only after the most careful circumspection.

Although saphenous vein bypass surgery is a potentially useful procedure in some cases of angina pectoris, it should be recognized that coronary disease is not necessarily ominous without heroic interventions. Indeed, it is possible to identify the large segment of patients who are not only responsive to antianginal therapy but in whom the prognosis for life and prolonged survival is often reasonably good. Certainly more harm than benefit is likely to ensue when surgery is undertaken without prior consideration of the natural history of the disease and without meticulous selection of patients in whom the risks appear warranted and technical success seems reasonably assured. More frequent and better utilization of available drugs and medical procedures would undoubtedly reduce the incidence of refractoriness and disability and thereby diminish the haste for often unattainable surgical solutions.

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