CHAPTER II

LITERATURE REVIEW

July, 1964. Vakil[13] studied the clinical and electrocardiographic characteristics of the preinfarction or intermediate coronary syndrome, which form a distinct and clinically recognizable pattern in many cases, are summarized in order to facilitate recognition of this important entity in practice. The high incidence (40.6%) of acute myocardial infarction within three months of onset of the intermediate coronary syndrome is stressed to encourage attempts at prophylaxis. He tried to determine whether it is possible, on the basis of ECG findings, to predict an oncoming attack of myocardial infarction, and whether patients with certain types of ischemic patterns are more prone to infarction than others. Another objective was to determine whether any predictable relation exists between the site of the myocardial ischemia in the preinfarction phase and the site or localization of the subsequent infarct. He found that the localization or site of myocardial ischemia in the preinfarction phase as well as that of myocardial infarction in the latter stages (whenever possible) was delineated. A relative preponderance of anterior over posterior wall involvement was obvious in each case.

A clear cut and predictable relationship could not be established between the site of the initial ischemia on the one hand and that of the subsequent myocardial infarction on the other.

May, 1972. Krauss et al.[11] reviewed the clinical courses of 100 patients with acute coronary insufficiency (ACI), ACI was defined as prolonged coronary pain without laboratory evidence of myocardial infarction (MI). Of these 100 patients, there was only a single hospital death. Six cases developed later MI during hospitalization. Over an average follow up period of 20 months after hospital discharge, 26 additional patients died, 8 from complications of MI, 13 suddenly, and 5 from other causes. The one-year survival was 58%. Patients who presented with deterioration of chronic angina had a significantly increased mortality over those with the recent new onset of coronary pain. All six hospital MIs and the single hospital death occurred in patients with recurrent pain after admission to the coronary care unit. But the factors which operated to provide a more favorable immediate prognosis are difficult to identify.

April, 1972. Fulton et al.[50] reported the first eighteen months of a study of the natural history of unstable angina. Of 167 cases, 3 died suddenly and 23 developed acute myocardial infarction within three

months: 17 of these 26 complications occurred within four weeks of the onset of symptoms. During the same period, 79 further cases of sudden death occurred. The majority had no known preceding chest pain, 14% of patients who complain to a physician of unstable angina develop acute myocardial infarction. Sudden death is a relatively infrequent sequel. Furthermore, it is apparent that sudden death is seldom preceded by ischemic symptoms which are reported to a physician.

August, 1973. Gazes et al.[12] followed 140 patients with preinfarctional (unstable) angina for ten years for the purpose of determining the natural history and the prognostic significance of electrocardiographic findings. Twenty one percent (29 of 140) of the patients developed an acute myocardial infarction within eight month after the onset of the diagnosis of preinfarction angina with an associated mortality of 41.4% (12 of 29). A combination of high-risk factors in a patient, e.g., frequent angina in the hospital, prior stable angina, and ischemic ST change during pain, were identifed as a high risk case. Thirty-five percent(19 of 54 patients) of this subgroup developed a myocardial infarction within three months after the onset of preinfarction angina with an associated mortality rate of 63% (12 of 29 patients). At the first year follow-up, 18% (25 of 140) of the patients died ; 74% (140 of 140) had less angina, and 8 % (11 of 140)did not show a change in their anginal pattern.

January, 1974. Russek[44] reported 133 patients with severe angina pectoris due to coronary artery disease. Marked amelioration of pain, increase in exercise tolerance and improvement in ischemic exercise-electrocardiographic patterns were observed in 90.2 percent of the patient in response to titrated does of propanolol and sublingual isosorbide dinitrate administered concominantly. The prospects for five-year survival were found to be excellent in patients with good left ventricular function and no adverse clinical signs. The annual mortality in a group of 102 "good risk" patients was only 1.2 percent. In contrast, the yearly addition rate in subjects with poor left ventricular function approximated 25 percent. A patient was considered a "poor risk" if he had any one of the following unfavorable criteria: congestive heart failure, past or present, significant enlargement of the heart, multiple myocardial infarctions, gallop rhythm, refractory hypertension (blood pressure persisting above 170 mm. Hg. systolic and 100 mm Hg diastolic, despite adequate and vigorous therapy), atrial fibrillation, severe and uncontrolled diabetes, previous "Stroke" or cerebrovascular insufficiency, advance age (over 70 years old).

Cannom et al.[63] Studied the hemodynamic in patients with unstable angina pectoris by monitoring brachial and pulmonary arterial pressures in 26 patients

for 48 hours. The clinical course of these patients could not be predicted from the presence or absence of continued angina at rest or the type of hemodynamic abnormalities associated with resting angina. Three patients had myocardial infarction as demonstrated by serum enzyme changes. None of these patients had subsequent pain in the hospital, possibly because of infarction of the ischemic area. He concluded that the resting and pain associated hemodynamic status was not helpful in distinquishing the high risk patient for early myocardial infarction or operative death in his small group. The abnormal hemodynamic status, particularly changes in left ventricular compliance, may well be an important cause of the unstable nature of the angina or a precipitating factor in myocardial infarction.

April,1976. Duncan et al.[64] studied the natural history of new and worsening angina pectoris in 251 men aged under 70 years, for two and a half year.. Most were ambulant and all were referred by selected general practitioners to a special hospital clinic. Heart attacks developed in 39 patients, nine of them died. Seventy-two percent of the attacks occurred within six weeks of the onset or worsening of angina, Of the 212 patients who did not suffer myocardial infarction and who were clinically reviewed six months after their first attendance, 66 had been pain free for the previous three months and 14 had experienced only infrequent attack of angina. Of the 128

men aged under 65 years who were previously in employment, 81% had returned to full time work six months after their first attendance. A discriminant function analysis using many variables (history of myocardial infarction, cigarette smoking habits, ECG Minesota code 4 (S-T segment depression) or 5 (T-wave items), cardiothoracic ratio, age, exacerbating pattern of pain, ECG minesota code 3 (high amplitude R waves) and 8 (cardiac arrhythmia), systolic blood pressure, heart rate, weight gain over the previous year, height - weight index ($^{W}/_{H^2}$), packed cell volume, and serum cholesterol concentration) was made to develop a predictive index that would allow patients with new or worsening angina who were likely to develop serious cardiac complications to be identified. This did not prove possible, and the only predictive factor of signficance was an increased cardio-thoracic ratio.

August, 1980. Plotnick et al.[67] reviewed the clinical, arteriographic, and hemodynamic findings in 218 consecutive catheterized patients with unstable angina. Unstable angina was defined as ischemic cardiac pain at rest associated with transient ECG changes but no evidence for acute myocardial infarction. Patients were divided into two groups according to the duration of symptoms: 134 patients with cresendo angina (new, or increasing, rest pain with previous ischemic symptoms present for more than three months) and 84 with recent

onset angina (symptoms present for less than three months). Compared with patients with recent onset symptoms, patients with crescendo angina had more extensive coronary disease and lower ejection fraction, which may explain their poor prognosis.

January, 1981. Olson et al[53] evaluated 193 consecutive unstable angina patients by clinical features, hospital course and electrocardiography. All patients were managed medically. Of the 193 patients, 150 (78%) had a technetium 99 m pyrophosphate (Tc-PYP) myocardial scintigram after hospitalization. Of these, 49 (33%) had positive scintigrams. At a follow-up of 24.9 ± 10.8 months after hospitalization, 16 of 49 patients (33%) with positive scintigrams died from cardiac causes, compared with six of 101 patients (6%) with negative scintigrams ($p<0.001$). Of 49 patients with positive scintigrams, 11 (22%) had had nonfatal myocardial infarction at follow-up, compared with seven of 101 patients (7%) with negative scintigrams ($p<0.01$). Age, duration of clinical coronary artery disease, continuing angina during hospitalization, ischemic ECG, cardiomegaly and a history of heart failure also correlated with cardiac death at follow-up. Ischemic ECG and a history of angina with a crescendo pattern also correlated with nonfatal infarction at follow-up. Patients with continuing angina, an ischemic ECG and a positive scintigram constituted a high-risk unstable

angina subgroup with a survival rate of 58% at 6 months, 47% at 12 months and 42% at 24 and 36 months.

January, 1982. Johnson et al.[65] assessed the value of two-channel Holter monitoring during the initial hours of hospitalization in patients with unstable angina pectoris (UAP) to identify those with severe coronary artery disease (CAD), variant angina, and/or poor prognosis over the next 3 months. Accordingly, 116 UAP patients had Holter monitoring for 27 ± 7 (mean ± SD) (range 12 to 50) hours following hospitalization. Of these, 24 evolved myocardial infarction (MI) during monitoring and 92 did not. Transient ST segment alterations occurred in 21 of the 92. Of these 21, 4 had variant angina, and respond well with calcium antagonists. Each of the remaining 17 had severe fixed CAD (left main or three-vessel) (n = 12) and/or poor prognosis over the 3 months after discharge as manifested by death (n = 1), MI (n = 3), and/or severe angina (n = 3). In contrast, 71 patients did not demonstrate transient ST segment alterations: none had variant angina ($p<0.001$), nine had left main or three-vessel CAD ($p<0.001$), and fifty were alive well 3 months after discharge ($p<0.001$), Ventricular tachycardia (VT) was demonstrated by Holter monitor in 5 of the 92 patients: four had three-vessel CAD and the other had severe persistent angina. Thus in patients hospitalized with unstable angina, transient ST segment alterations

and/or VT on Holter monitor are specific predictors of "high-risk" subgroup UAP patients with left main or three-vessel CAD, variant angina, and/or poor 3-month prognosis.

November, 1982. Boucek et al.[61] analyzed the data from the symptoms, ECGs, exercise stress responses, left ventricular perfusion and function, and the topography of obstructive coronary artery disease (⩾ 70% crosssectional stenosis in the left main, left anterior descending, circumflex, and right coronary arteries and their major branches) in 200 patients 65 years of age or older with angina pectoris. Males showed a significantly higher incidence of stenosis of the left main and the left circumflex coronary arteries and poorer left ventricular perfusion than females. One-vessel obstructive disease was found in one-fifth of the aged patients of each sex with angina pectoris.

Febuary, 1983. Graham et al.[54] followed 586 men who survived an initial attack of unstable angina or myocardial infarction for up to 15 years. A policy of early mobilization and sustained risk factor advice was employed. A conservative approach to treatment was adopted during the acute and follow-up stages. Drugs were employed only for symptomatic reasons, and only two patients proceed to coronary artery bypass surgery. Survival at 5, 10, and 15 years were 80%, 61% and 43%

simultaneously. Older patients and those with more severe initial attacks had a higher mortality, but these factors did not relate to combined fatal and nonfatal recurrence of myocardial infarction. Of 22 studies reviewed, 18 report a higher mortality than does our study. Four studies,none strictly comparable, report a similar 5-year mortality. A conservative management does not appear to be harmful and may be beneficial.

July, 1983. Haines et al.[57] studied the significance of the development of new T-wave inversion in 118 consecutive patients with unstable angina. The electrocardiograms during hospitalization in the coronary care unit were analyzed for occurrence of new T-wave inversion $\geq$ 2 mm and correlated with findings at coronary angiography (73 patients) and at follow - up (112 patients). Twenty - nine patients had anterior T-wave inversion. Of these, 25 patients (86%) had $\geq$ 70% diameter reduction of the left anterior descending (LAD) artery, compared with 11 (26%) of 42 patients without anterior T-wave inversion ($p<0.001$). The sensitivity of T-wave inversion for significant LAD stenosis was 69%, specificity 89%, and positive predictive value 86%. Two patients had T-wave inversion in the inferior leads. Both patients had significant right coronary artery disease, compared with 18 of 55 patients without inferior T-wave inversion (difference not significant (p = NS). Seventy - one patients who

were treated medically had 16 ± 9 months' follow-up. Of 26 patients who had T-wave inversion, 10 (38%) had cardiac events, compared with 7 (16%) of the remaining 45 patients without T-wave inversion ($p<0.05$). Forty-one patients who had undergone coronary bypass surgery had 19 ± 9 months' follow-up. Of 22 patients with T-wave inversion, 4 (18%) had cardiac events, compared with 2 (11%) of the remaining 19 patients without T-wave inversion (p = NS).

Thus, development of new T-wave inversion ≥ 2 mm in patients with unstable angina (1) is predictive of significant coronary artery stenosis, and (2) identifies a subgroup with poor prognosis when treated medically.

Febuary, 1984. Narahara et al.[62] studied 30 consecutive patients with unstable angina during pain-free intervals with gated blood pool scintigraphy. The initial study was performed within 18 hours of admission to the coronary care unit. A second study was performed near the time of hospital discharge, after stabilization with medical therapy. Three months thereafter patients were categorized according to their worst anginal status following hospital discharge. Fifteen patients were New York Heart Association functional class I or II (group A); 15 patients were in functional class III or IV (group B). Left ventricular ejection fraction was similar at the time of initial study (55.9 ± 2.18% and 56.0 ± 3.55% for groups A and B respectively). At the time

of hospital discharge the ejection fraction had risen to 60.3 ± 1.85% ($p<0.01$) in group A and in group B it had fallen to 48.1 ± 3.4% ($p<0.005$). End-systolic volume index in group B rose from 37 ml/m² ± 6.1 to 43 ± 6.2 ml/m² ($p<0.005$) at the time of the follow-up study. There were no significant intergroup differences in the amount of nitrates or beta blockers received by the patients during the two scintigraphic examinations. Eleven group B patients subsequently underwent coronary artery bypass surgery. A significant increase in ejection fraction and a significant decrease in and systolic volume index were noted when these patients were restudied an average of 3.2 months after surgery. This study suggests that changes in left ventricular function during the course of unstable angina pectoris are common and may be detected by serial gated blood pool scintigraphy. The direction of the change in ejection fraction was associated with the severity of angina in the follow-up period. A fall in ejection fraction and a rise in end-systolic volume index from admission to the time of the follow-up study were associated with an unfavorable clinical outcome and may represent clinically silent ischemic depression of left ventricular function.

April, 1985. Mulcahy et al.[66] followed 100 patients admitted to coronary care with unstable angina for a period of 1 year. A conservative approach to treatment was adopted. Routine beta blockers, calcium

antagonists, and anticoagulants were not employed. Patients with persistent pain following admission were treated with nitrates only and with symptomatic treatment. One death and nine nonfatal infarctions occurred within the first 28 days after admission. A total of eight deaths, 14 nonfatal infarctions, and three readmissions for unstable angina occurred during the follow-up period of 1 year. Of the various initial factors studied, persistence of pain and the magnitude and extent of ECG ST-T changes were the only predictors of an unfavorable outcome. Non-smokers and those with a previous history of angina on effort had a significantly higher incidence of persistence of pain. The withdrawal of beta blockers on admission and the late administration of beta blockers to those with persistent pain did not appear to influence outcome.

January, 1986. de Servi et al[59] analyzed the clinical, ECG, and angiographic features of a large series of consecutive patients with angina at rest. Transient ST segment elevation during pain was observed in 219 patients (group I), while 220 patients showed ST segment depression during pain (group II). Group II patients were found to have higher incidence of hypertension ($p<0.001$), prior myocardial infarction ($p<0.0005$), history of exertional angina ($p<0.0005$), and a progressive aggravation of symptoms before hospitalization ($p<0.0005$), while group I patients had a

prevalence of recent onset angina ($p<0.05$) and more frequently developed severe ventricular arrhythmias during pain ($p<0.0005$). Furthermore, a larger number of patients showing ST segment depression during chest pain had multivessel disease ($p<0.0005$), left main involvement ($p<0.005$), and lower values of left ventricular ejection fraction ($p<0.001$) than patients with ST segment elevation during pain. Survival curves of medically treated patients showed a significantly better longterm prognosis in patients of group I ($p<0.001$). The direction of the ST segment shift during anginal attacks at rest may therefore allow a classification of patients included into the broad spectrum of unstable angina. This distinction should be taken into consideration in studies aimed at evaluating longterm prognosis or the results of medical and surgical therapy.