THE PROBABILITY OF A MAJOR CARDIOVASCULAR EVENT AND ASSOCIATED RISK FACTORS IN THE CORONARY CARE UNIT PATIENT WITH MYOCARDIAL INFARCTION RULED OUT

by

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Chapter 1

INTRODUCTION

Coronary artery disease is the major cause of illness and death in the United States and in most of the industrialized world today. In the United States it is the cause of one-third to one-half of all deaths. Myocardial infarction (MI), one of the symptomatic presentations, often strikes without warning and is a catastrophic consequence of this disease. Men in the prime of life are affected; women are spared for 10 years relative to men. Recognition of coronary heart disease in any of its clinical forms raises the possibility of sudden death, and even minimal symptoms may portend more serious disease (Sokolow, 1979).

Primary prevention of the disease is most desirable, since there is no curative therapy. Progress is being made in this area with the identification of risk factors associated with the development of coronary artery disease and with the introduction of related health education. However, attempts at tertiary prevention in the United States have been frustrated by the high incidence rate of out-of-hospital sudden deaths and their seeming unpredictability (Schroeder, 1977). It is imperative to attempt to identify patients at high risk for a major cardiovascular event (myocardial infarction or sudden cardiac death). With such identification,

preventive measures can be initiated and the individual educated.

One risk factor related to a major cardiovascular event suggested by recent studies is the development of severe ischemic chest pain requiring hospital admission (Schroeder, 1977; Nordlander, 1979). The purpose of this study is to further explore the probability of occurrence of a subsequent major cardiovascular event or cardiac morbidity in the form of unstable angina in those patients admitted to the hospital with severe ischemic chest pain, particularly those patients in whom myocardial infarction has been ruled out (MI R/O). In addition, those characteristics which are present at the time of admission and during the hospital stay which are related to a major cardiovascular event or to cardiac morbidity will be identified.

Review of the Literature

In the sections to follow, the probability of a major cardiovascular event will be considered for the following populations: the general population, those suffering from angina, those who have suffered a myocardial infarction, and those suffering from unstable angina. In addition, those risk factors which are related to the probability of a major cardiovascular event in each of the populations will be discussed.

Risk and Risk Factors in General Population

The Framingham study (Gordon & Kannel, 1972) is a well known prospective study conducted with a sample of 5,127 persons drawn from the general population. The study identified the probability of a major cardiovascular event and the risk factors associated with coronary artery disease. It was reported that the probability of a cardiovascular event occurring within 8 years of the study's onset increased from 2% in patients with no risk factors to 49% when 5 risk factors were present. The probability was an intermediate one when fewer risk factors were present (Kannel, 1976). The average American male child presently has one chance in three of a cardiovascular catastrophe before reaching age 60 (Kannel, 1978). Brand (1976) found that the probability of a middle-aged male (age 40 to 60) developing symptoms of coronary heart disease, either angina, myocardial infarction, or sudden death due to myocardial infarction, was slightly less than 1% per year.

Risk factors related to the development of coronary disease identified by the Framingham study are: hypertension, hyperlipidemia, diabetes, family history of early atherosclerosis, age, male sex, and cigarette smoking. Other factors of lesser importance are: behavior patterns, sociocultural factors, decreased physical activity, and emotional stress of life.

Dick and Stone (1978) studied a random sample of 283 men

and 250 women between the ages of 20 and 69 and found that young men have a greater prevalence of three coronary risk factors (smoking, hypercholesterolemia, and hypertension) than women. The investigators suggested that smoking added to either of the other two factors is of great importance in men. The final report of the National Cooperative Pooling Project (Cook, 1978) reported that measurements of serum cholesterol, blood pressure and cigarette use made at a single examination of adult American men, were shown to be highly indicative of risk of first heart attack over the next decade.

Electrocardiogram (ECG) findings may be of value in predicting a major cardiovascular event according to some reseachers. Reunanen (1978), in his prospective study of 5,738 Finnish men, found that in a group of seemingly healthy men with no typical chest pain symptoms, no history of myocardial infarction, and no congestive heart failure, only those with ST segment depressions and small T-waves on a resting ECG had significantly greater risk of death by coronary heart disease in the follow-up period as compared with men without these ECG findings. Humphries (1977) suggested that an abnormal resting ECG in the absence of other conditions such as valvular or congenital heart disease should be added to the standard risk factors.

These studies are summarized on Table 1, page 15 and Table 2, page 16, according to a framework offered by Dimsdale (1979). He developed a useful classification system of risk

factors; part of the classification system was employed in the present study. Dimsdale studied four risk factor orientations: clinical, epidemiological, psychosomatic, and combined. The clinical orientation used only such data obtainable from an examination of the patient. The epidemiological orientation took cognizance of the patient's past exposure to deleterious substances or experiences. The psychosomatic orientation relied on in-depth interviews and psychometric tests in an effort to explore possible psychosocial antecedents for coronary artery disease. Only the clinical and epidemiological orientations were employed in the present study.

Risk and Risk Factors in Population with Angina

Angina pectoris is a common clinical expression of coronary heart disease and is associated with an increased risk of myocardial infarction or cardiac death. Varying degrees of risk were reported by different investigators. Humphries (1977) reported an overall expected mortality rate of patients with angina pectoris of 5 to 10% a year. However, some patients may have only a 1% chance of dying in the next one to five years while others may have an expected mortality of greater than 50% depending on the severity of the coronary artery disease and the severity of left ventricular damage. Weinblatt (1968), reporting on a male population with recent onset of angina found that the probability of dying within 30 months was 10.5% and the probability of dying a cardiac

death was 7.5% which is four times the expected mortality of a matched group free of coronary disease. Oberman (1978) also reported a high mortality rate for persons with angina, finding it to be approximately five times that of the general population. Additionally, the risk of a myocardial infarction was about 4 to 5% a year for angina pectoris patients. A highly variable mortality rate, from 2 to 11%, was reported by Reeves (1974). This was based on studies indicating that with only one of the three major coronary arterial branches significantly stenosed, the rate was approximately 2% of the cohort while with all three stenosed it was approximately 11%. Kannel and Feinleib (1972) reported the mortality rate to be close to 4% a year for angina patients.

Various risk factors for myocardial infarction and for death have been identified in the population with angina. An abnormal ECG and hypertension as predictors of a poor prognosis were reported by investigators (Weinblatt, 1968; Oberman, 1974). Weinblatt found in a study of 98 men between the ages of 25 and 64 suffering from angina that a specified abnormality, usually a horizontal depression of the ST segment was associated with a 30 month mortality rate of 20.8% as contrasted with 5% in men with a normal ECG. In men with both hypertension and ECG abnormalities, the mortality rate was 31.8% as contrasted to 3.5% for a 30 month period in men with normal blood pressure and normal ECG. Oberman (1974) found changes in the ST segment of the ECG to be the most

significant risk indicator for prediction of death. Other indicators were a history of myocardial infarction, heart size, ventricular conduction defects, and anti-hypertensive therapy.

Duncan (1976) in a study of 251 men with angina pectoris found the only significant predictive factor for serious cardiac complications to be an increased cardiothoracic ratio. Age and sex were found to be risk factors for those persons who developed angina in the Framingham study (Kannel, 1972). Chances of surviving an extended period are better at younger than older ages and in women the chances are better than in men.

Risk and Risk Factors in Population with Myocardial Infarction

Survivors of an acute myocardial infarction are at great risk of dying of a major cardiovascular event within the first several months following discharge from the hospital. The immediate mortality is about 33%. Of the survivors, 50% will develop significant angina pectoris and will face a tenfold increase in risk of left ventricular failure, a fourfold increase in risk of sudden death, a 6% annual recurrence rate and a 4% annual mortality (Borow, 1978; Kannel, 1976). Humphries (1977) reported that although the probability of death is relatively high in the first several months or first year following an acute infarction, the probability during subsequent years returns to an estimated 4 to 5% a year, similar to the overall mortality for patients with

chronic angina pectoris.

It is possible to identify patients with an especially high probability of death. ECG indications of increased risk of dying have been reported by investigators (Vismara, 1977; Moss, 1976; Coronary Drug Project Research Group, 1974). Vismara (1977) carried out a series of studies on the problem of ventricular ectopy as it relates to the entire spectrum of sudden death in coronary disease. In a study of 64 patients with acute myocardial infarction, 20 patients died over a period of 25.8 months. Twelve of these died suddenly and all 12 had ventricular ectopy late in their hospitalization. This finding differentiated them from the survivors. ECG indications of increased probability of dying were also reported by Moss (1976) who cited a ventricular beat frequency of more than 20 per hour on a 6 hour ECG tape recording as an indication of high probability of death.

The Coronary Drug Research Group (1974) found 10 parameters to identify the high risk group and listed them in decreasing order of importance: ST segment depression, cardiomegaly on chest X-ray, New York Heart Association functional class, ventricular conduction defects, use of diuretics, history of intermittent claudication, serum cholesterol, frequent ventricular ectopic beats, physical inactivity during leisure time, and Q or QS pattern on the ECG. Kostis (1979) cited factors associated with a poor

prognosis in patients who have had a myocardial infarction to be age, hypercholesterolemia, hypertension, and cigarette smoking.

Long term survival of patients following myocardial infarction was studied by Norris (1974) who found in a 6 year follow-up of 349 patients that chances of survival between 3 and 6 years after recovery were associated with age and factors dependent on the severity of the myocardial infarct such as pulmonary congestion, pulmonary edema, and cardiac enlargement. A five-year follow-up study was conducted by Mulcahy (1977). He examined the effect of age, weight, severity of infarction, diastolic blood pressure, serum cholesterol, and cigarette smoking at the time of the initial attack on postinfarction morbidity and death. Only severity of infarction adversely influenced the long-term mortality rate. Also, there was an increased death rate among those who continued to smoke.

More detailed invasive studies (Humphries, 1977) have suggested that extent of coronary artery disease and left ventricular function correlate with post infarct mortality. Sokolow (1978) stated that over a five year period a person with three vessel disease and poor left ventricular function has 10 times the mortality rate of a person with single vessel disease and good left ventricular function.

Risk and Risk Factors in Population with Unstable Angina

Unstable angina has been called by many terms: rest

angina, acute coronary insufficiency, intermediate syndrome, and pre-infarction angina. Unstable angina represents a syndrome midway between angina and myocardial infarction and patients with this syndrome have an increased incidence of acute myocardial infarction, sudden death, and ventricular arrhythmias in the 1 to 2 years after onset (Sokolow, 1978). Gazes and coworkers reported in a follow-up study of 140 patients that 18% had died in the year following the diagnosis (Gazes, 1973). Krauss (1972) conducted a retrospective review of 100 patients hospitalized with unstable angina. In the year following hospital discharge the rate of myocardial infarction was 20% and the mortality rate 15%. Cairns (1976) in his review reported that in recent studies acute infarction occurs in under 15.5% and death in under 2%.

Pain persisting with bed rest, prior angina pectoris or prior myocardial infarction were among the high risk factors identified by investigators (Gazes, 1973; Cairns, 1976; Krauss, 1972). Gazes (1973) reported on a combination of factors contributing to increased mortality: frequent angina in the hospital, prior stable angina, and ischemic ST change during pain. Cairns (1976) reported that pain persisting with bed rest and a prior stable angina or myocardial infarction increases risk. Krauss (1972) reported that patients with deterioration of angina had increased mortality over those with a recent onset of angina.

Patients with unstable angina are often admitted to

coronary care units with an admission diagnosis of rule/out (R/O) myocardial infarction. Dussia (1976) in a retrospective study of 466 coronary care unit (CCU) patients reported that patients admitted with a history typical for a myocardial infarction appeared to have a comparable in-hospital mortality rate after 48 hours, a comparable one-year mortality rate, and a comparable incidence of recurrent myocardial infarction during the first year whether or not they developed confirmatory ECG or serum enzyme changes.

Two additional retrospective studies have been conducted on this population. The first by Schroeder, et al. in 1977 found that patients with suspected myocardial infarction who do not have an infarction in the hospital are at high risk for cardiovascular death after hospital discharge. They found the one-year mortality rate to be 10% and the two-year mortality rate to be 20% in the 170 patients studied. Similar results were obtained by Nordlander and Nyquist in their retrospective study of 193 patients followed for one year (Nordlander, 1979). The one-year mortality rate was 9% and when non-coronary cases in the study were excluded a one-year mortality rate of 11% was found.

Schroeder (1977) was unable to identify risk factors when he compared serial ST wave changes, frequency of PVCs, and conduction defects of patients who died with those who survived. However, Nordlander (1979) was able to select a high risk group by the identification of transient ST-T

changes in serial ECGs.

Schroeder (1980) conducted a prospective study on 211 CCU patients and found a rate of myocardial infarction or death of 8% at 6 months and 21.6% at a mean of 27.8 months for patients who had infarction ruled out as compared with 7.7% at 6 months and 21.8% at a mean of 27.8 months for those who had suffered a myocardial infarction. Cardiomegaly, congestive heart failure, and angina after discharge from the hospital increased the risk of morbidity and mortality in both groups.

Some investigators reported that the most important prognostic indicator was the extent of vessel disease and the number of vessels involved (Sokolow, 1978; Humphries, 1977; Oberman, 1978). However, the angiographic studies required to assess the extent of vessel disease are expensive and are not without risk. Sokolow (1978) stated that the presence of a small acute myocardial infarction in a patient considered to have unstable angina increased the danger of performing coronary angiography. Cairns (1976) reported that a potential source of morbidity and death which must be considered is that occurring during coronary angiography.

A noninvasive method of predicting the extent of vessel disease and subsequent risk of death was attempted by Oberman (1978). He found that some clinical indicators could be used to gauge the extent of coronary disease:

previous myocardial infarction, congestive heart failure, cardiomegaly, and ECG abnormalities. Dimsdale (1979) examined the ability of four risk factor orientations to predict the presence of anatomical narrowing of the coronary arteries as demonstrated by angiography. The orientations studied were clinical, epidemiological, psychosomatic, and combined; each orientation utilized a different data base. He found that the clinical orientation was the most successful in predicting vessel disease followed by the epidemiological model which was also successful. Psychosomatic factors were not accurate predictors of vessel disease. Combining the clinical and epidemiological orientations yielded even more accurate results.

The data from the literature can be summarized as follows: First, risk factors for the development of coronary artery disease have been identified most frequently as age, sex, history of diabetes, hyperlipidemia, family history of atherosclerosis, hypertension, and cigarette smoking. Second, the probability of death has been variously calculated at 4 to 10% for the population with angina. Third, the probability of death for the population with myocardial infarction has been reported to be from 4 to 20% in the first year after discharge. Fourth, there is no consensus on risk factors for the previous two groups; however, many researchers reported risk factors to be: ST segment depression on the ECG, hypertension, history of myocardial infarction, cardio-

megaly, ventricular conduction defects, use of diuretics, history of angina, and worsening of angina. Invasive studies indicated that left ventricular function and the extent of coronary artery disease were associated with high risk. Fifth, the probability of death for those patients with unstable angina has been variously estimated to be from 2 to 20%. The risk factors reported most frequently were deterioration or worsening of angina, ST segment depression, and cardiomegaly. The extent and nature of the disease is the most important factor according to recent studies. The tables on the following two pages summarize the data from the studies.

It may be noted that there are relatively few studies which focus on the patient with MI R/O and there is a lack of comparative data regarding MI R/O patients and MI patients. Knowledge of the probability of a major cardiovascular event and associated risk factors for the patient with MI R/O is essential for the practice of nursing. Such knowledge will enable the nurse to make intelligent patient assessments and to plan, implement and evaluate effective nursing interventions.

One area that will be improved by knowledge gained by this study is that of education for the patient and family At the present time, in many centers the patient with MI R/O is not included in rehabilitation programs or in special education programs. If this study demonstrates an increased

Table 1

Probability of Major Cardiovascular Event and Epidemiological Risk Factors

STUDY & POPULATION	AGE	HYPER-TENSION	HISTORY OF DIABETES	FAMILY HISTORY ATHEROSCLEROSIS	HYPERLIPIDEMIA	SMOKING	SEX
FRAMINGHAM NORMAL, N=5, 127	S	S	S	S	S	MS	S
		(High probability when five factors present)					
DICK & STONE NORMAL, N=283M 250F	-	S	-	-	S (cholesterol)	S	S
		(Probability of event with combination of three factors)					
POOLING PROJECT (1974)	-	S	-	-	S (cholesterol)	S	-
WEINBLATT ANGINA, N=98	-	S	-	-	-	-	-
OBERMAN ANGINA, N=417	-	S	-	-	-	-	-
DUNCAN ANGINA, N=251	NS	NS	-	-	-	NS	-
CORONARY DRUG PROJECT GROUP MI, N=8, 341	-	-	-	-	S (cholesterol)	-	-
NORRIS MI, N=349	S	MS	-	-	-	-	-
MULCAHY MI, N=213	NS	NS	-	-	NS	MS	-

S = SIGNIFICANT
NS = NO SIGNIFICANCE
MS = MODERATE SIGNIFICANCE

Table 2

Probability of Major Cardiovascular Event and Clinical Risk Factors

STUDY & POPULATION	HISTORY OF ANGINA	HISTORY OF MYOCARDIAL INFARCTION	NEW YORK HEART ASS'N FUNCTIONAL CLASS	ST SEGMENT ABNORMALITY	CARDIO-MEGALY	VENTR. CONDUCTION DEFECT	DIUR-ETICS	PVCs
REUNANEN NORMAL, N=5, 738	-	-	-	S (with small T waves)	-	-	-	-
HUMPHRIES NORMAL, N=102	-	-	-	S	-	-	-	-
WEINBLATT ANGINA, N=98	-	-	-	S	-	-	-	-
OBERMAN ANGINA, N=417	-	S	-	S	S	S	-	-
DUNCAN ANGINA, N=251	-	NS	-	NS	S	-	-	-
VISMARA MI, N=64	NS	NS	-	-	-	-	-	S
CORONARY DRUG RESEARCH GROUP MI, N=8, 341	-	-	S	S	S	S	S	S
MORRIS, N=349	-	-	-	-	S	-	-	-
GAZES UNSTABLE ANGINA, N=140	S	-	S	S	-	-	-	-
KRAUSS UNSTABLE ANGINA, N=100	-	-	S	-	-	-	-	-
NORDLANDER R/O MI, N=193	-	-	-	S	-	-	-	-
SCHROEDER R/O MI, N=211	-	-	-	-	S	-	-	-

probability for a major cardiovascular event for the patient with MI R/O, such programs should be provided for the patient and family. These people should be given information about heart disease, cardiac drugs, the importance of prompt treatment of cardiac symptoms and instruction in resuscitation. Any knowledge about risk factors gained from the study can be added to current knowledge and used in patient education regarding avoidance of risk factors.

The advent of coronary care units in this country has made an impact on the number of deaths from myocardial infarction by initiating prompt treatment and careful surveillance. Therapeutic and increased intervention may make an impact on the number of deaths from unstable angina. A noninvasive method of identifying those patients with one or more coronary vessels affected by obstructive lesions and thus at high risk according to recent studies would be an important advance.

Purpose of the Study

The purpose of this investigation is to add to current knowledge regarding the magnitude of the probability of a major cardiovascular event and to further identify the risk factors for those patients in whom myocardial infarction has been ruled out. The frequency of subsequent major cardiovascular events will be noted as well as those characteristics of the patient which are related to the occurrence of major cardiovascular events.

Hypotheses

Hypothesis 1: The probability of a major cardiovascular event resulting in death within one year in a CCU patient with the final diagnosis of MI R/O does not differ from the risk of a CCU patient who has suffered an MI.

Hypothesis 2: The probability of a major cardiovascular event which does not result in death in one year in a CCU patient with the final diagnosis of myocardial infarction ruled out does not differ from the risk of a CCU patient who has suffered a myocardial infarction.

Hypothesis 3: The frequency of unstable angina during the year following admission of CCU patients with a final diagnosis of MI R/O does not differ from that of patients who have suffered MIs.

Hypothesis 4: There is a positive relationship between the incidence of a major cardiovascular event or unstable angina and the presence of the following epidemiological risk factors: increasing age, hypertension, history of diabetes, family history of atherosclerosis, hypercholesterolemia, and smoking history.

Hypothesis 5: There is a positive relationship between the incidence of a major cardiovascular event or unstable angina and the presence of the following clinical risk factors: history of angina, history of myocardial infarction, New York Heart Association functional class, ST segment depression on the ECG, cardiomegaly, ventricular conduction defect,

premature ventricular contractions, and use of diuretics.

Hypothesis 6: There is a positive relationship between the incidence of a major cardiovascular event or unstable angina and the number of clinical and epidemiological risk factors.

Chapter II

METHODS

In the sections to follow, the method of selection of subjects and the setting in which the study took place will be described. In addition, the method of data collection, the design and procedure of the study and the data analysis will be described.

Subjects and Setting

The population from which the sample for this retrospective investigation was selected was that group of male patients admitted to a hospital coronary care unit with the initial diagnosis of suspected myocardial infarction. The names and hospital numbers of such patients were drawn from the daily census book of the coronary care unit (CCU) at the Veteran's Administration Hospital in Portland, Oregon. The admission criteria for the CCU at Veteran's Hospital are as follows: 1) central chest pain lasting for more than 15 minutes, beginning within the last 48 hours, 2) frank pulmonary edema without previously known valvular lesion, uremia or intoxication, 3) syncope with electrocardiogram (ECG) suspicion of acute myocardial infarction, 4) shock without suspicion of acute hypovolemia or intoxication, 5) intractable angina pectoris, 6) pacemaker failure,

7) heart block, 8) post code, 9) rhythm disturbance, or 10) hemodynamic therapy/evaluation.

Two groups of patients were included in the study. The criteria for inclusion in the present study for the first group was: admission to CCU with chest pain due to suspected myocardial infarction with infarction ruled out. Myocardial infarction ruled out was identified when there were no new Q waves, there were no evolutionary changes in the creatine phosphokinase (CPK) level, and the patient had either ST segment depression, history of myocardial infarction, or history of angina. Charts of patients consecutively admitted to the CCU from June, 1978 were examined until 100 persons meeting the above criteria were obtained. In those cases in which the patient was admitted more than once, only the first admission was included.

The criteria for inclusion in the present study for the second group were: admission to the CCU with chest pain due to suspected myocardial infarction and a final diagnosis of myocardial infarction. The diagnosis of myocardial infarction as defined by the World Health Organization depends on the presence of at least two of the following triad: (a) a history of typical chest pain; (b) evolutionary changes in the ECG, with development of Q waves; and (c) elevated serum enzymes: serum glutamic oxaloacetic transaminase (SGOT), lactic dehydrogenase (LDH), and creatine phoshokinase (CPK).

Charts of patients consecutively admitted to the CCU from June, 1978 were examined until the first group, the group with myocardial infarction ruled out was complete. Only the first admission was included in the group when a patient had been admitted more than once in the year. Those patients who died within 48 hours of admission were not included.

Data Collection

Data for this study were obtained from patient records, both inpatient and outpatient. Data were gathered about major cardiovascular events occurring in the year following the CCU admission and about risk factors related to major cardiovascular events.

Measurement of a major cardiovascular event. A major cardiovascular event was either a myocardial infarction or cardiac death. Information regarding the occurrence of these events was extracted from either the inpatient or outpatient records of the patients' charts.

Measurement of cardiac morbidity. Cardiac morbidity was unstable angina and information regarding this event was extracted from either the inpatient or outpatient records.

Measurement of risk factors. Data were gathered on 14 risk factors, 6 epidemiological and 8 clinical. The 6 epidemiological factors measured were: age, hypertension, history of diabetes mellitus, family history of atherosclerosis, hypercholesterolemia, and smoking history. The 8

clinical factors measured were: history of angina, history of myocardial infarction, New York Heart Association functional class, ST segment depression on the ECG, cardiomegaly, ventricular conduction defect, premature ventricular contractions, and use of diuretics.

Hypertension was scored as present if the patient had been treated with antihypertensive medication or if he had been informed by a physician that he was hypertensive. This information was obtained from the admission history.

A history of diabetes mellitus was scored as present if the patient had been treated with any anti-diabetic agent or if he had been informed by a physician that he was diabetic and needed to be on an anti-diabetic diet. This information was obtained from the admission history.

A family history of atherosclerosis was scored as positive if a parent or sibling had an onset of heart disease before the age of 50. This information was obtained from the admission history.

Hypercholesterolemia was measured by laboratory examination of blood samples taken during the hospital admission. Elevation of cholesterol levels over 250 mg% was identified as a positive finding.

Smoking history was scored as positive if the patient had a history of smoking until less than two years prior to admission. This information was obtained from the admission history. A history of angina was obtained from the admission

history as was a history of previous myocardial infarction.

The extent of angina during hospitalization was estimated by guidelines developed by the New York Heart Association. These guidelines are:

Class I Asymptomatic with ordinary physical exertion.

Class II Symptomatic with ordinary physical exertion.

Class III Symptomatic with less than ordinary physical exertion.

Class IV Symptomatic at rest.

A positive functional class was scored if the patient was classified as Class III or Class IV in the progress notes by the attending physician or if notations in the progress records revealed the status of the patient to be at these levels on at least two occasions during hospitalization.

The ECG abnormality of ST segment depression was measured by examination of the ECG record on the chart. A standard 12-lead ECG is obtained on admission and each morning during the following three days. Leads I, II, III, aVR, aVL, aVF, CR4R, CR1, CR2, CR4, CR5, and CR7 are used and the electrode positions are indicated on the chest wall by a marker pen to secure the same electrode positions in succeeding ECGs. The ECGs are recorded with a paper speed of 25mm per second and with an amplification of a mV per 10mm. An ST segment depression is a depression of the ST segment of 1.0 mm or more. The ST depression should occur in at least two of the twelve ECG leads during the first 3 days to be scored as positive. Those patients who were on digitalis during

the hospitalization were noted in the study as digitalis can cause ST segment depression.

Cardiomegaly was measured by X-ray examination of the chest. Increased cardiothoracic ratio was noted by the radiologist and recorded on the chart. Ventricular conduction defect was measured by the ECG and was identified when the QRS interval was prolonged, exceeding 0.10 seconds. Premature ventricular contractions were also measured by the daily ECGs and were scored as present when there were more than 5 per minute or when there were 2 or more in a row.

The use of diuretics was identified when such drugs were recorded in the patient's hospitalization record. Any drugs from the following classifications were classified as diuretics: the benzothiazides, spironolactones, ethacrynic acid, and furosemids.

Design and Procedure

The design of this study was that of a retrospective investigation. An attempt was made to add to current knowledge by linking the manifestation of a phenomenon existing in the present (presence of a major cardiovascular event) to other phenomena existing in the past (risk factors). This type of research lacks the control advantage of true experimental research, both in terms of inability to manipulate the independent variable and inability to randomize. Because of this lack of control there is a risk of erroneous interpretation of results. However, experimental research would

not be feasible for this problem and the retrospective investigation was an appropriate approach.

Data collection was accomplished by means of extraction from the patients' records. The records were requested, examined, and returned in such a way that the privacy of the records was maintained. The records were transported from the record room by the investigator, examined in a section of an office set aside for this purpose and returned immediately after examination to the record room by the investigator. Code numbers were assigned to each case to insure anonymity.

Analysis of Data

In order to calculate the frequency of subsequent major cardiovascular events, the first purpose of the study, the occurrence of two major events: cardiac death and major cardiovascular event without death were recorded separately for the 100 patients in the first group (myocardial infarction R/O). The same method of recording was used for the second group (myocardial infarction) and the frequencies of each event were compared to the first group. In this way, the hypothesis would either be supported or refuted that the probability of a major cardiovascular event with death or without death is the same for the patient with a final diagnosis of myocardial infarction ruled out as for the patient who has indeed suffered a myocardial infarction.

In order to calculate the frequency of subsequent cardiac

morbidity, the occurrence of such morbidity was recorded for each of the two groups and the frequencies compared. The hypothesis that the frequency of cardiac morbidity in the CCU patient with myocardial infarction R/O does not differ from that of a patient who has suffered a myocardial infarction would be either supported or refuted.

In order to identify those characteristics which may be related to a major cardiovascular event for the myocardial infarction R/O patient the data were analyzed as follows: each characteristic identified as a possible risk factor was placed in a contingency table for examination of a possible relationship with a subsequent cardiovascular event. The chi-square statistic was then computed to test the significance of the findings. The characteristics examined in this way were: history of hypertension, history of diabetes, family history of atherosclerosis, hypercholesterolemia, smoking, history of angina, history of myocardial infarction, New York Heart Association functional class, SI segment depression, cardiomegaly, ventricular conduction defects, premature ventricular contractions, and use of diuretics.

Contingency tables were constructed for each characteristic: each table demonstrated the relationship between the characteristic and a subsequent event for a myocardial infarction R/O patient.

The rank point-biserial correlation coefficient was used

as a measure of the relationship between age and a subsequent major cardiovascular event for those patients with myocardial infarction ruled out. The same correlation coefficient was used to measure the relationship between the number of risk factors and a subsequent major cardiovascular event.

Chapter III

RESULTS

Between June 1978 and April 1979, 436 patients were admitted to the Coronary Care Unit (CCU) of the Veteran's Administration Hospital in Portland, Oregon. The admission diagnosis of possible myocardial infarction was made on 263 (60.3%) of those admissions. Twenty of the possible myocardial infarction admissions were repeat admissions in the same year. The charts of all 243 patients were requested from the medical records department; 208 charts were available for examination. Sixty-two patients did not fulfill the criteria for admission to either of the two study groups and were not included in the study.

Characteristics of the Subjects

One hundred subjects were admitted to the first group, that having a common final diagnosis of MI R/O. The mean age of the sample was 61.6 years with ages ranging from 32 to 98. Fifteen of the patients had had a coronary artery bypass graft (CABG) one to eight years prior to admission, and 12 had a CABG after admission. Twenty-one charts of patients with the final diagnosis of MI R/O were not available, bringing the total possible number of the group to 121.

There were 12 patients in the examined group with no follow-up after discharge from the hospital. Six of these

patients were from the Portland area, and six were either from elsewhere in Oregon or from out of state. Characteristics of these patients can be compared with those of patients with follow-up in Table 3.

Table 3

Comparison of Patients with Follow-up to Those with None

	Follow-up	No Follow-up
Number	88	12
Mean Age	61.6	60.16
Mean Number Risk Factors	4.79	4.33
ST Depression	47%	25%
Cardiomegaly	25%	25%
History of Angina	68%	50%
History of MI	61%	83%
Hypercholesterolemia	28%	25%
Conduction Defects	35%	33%
Diuretics	39%	25%

Forty-seven patients were admitted to the second group, that group having the final diagnosis of myocardial infarction. The mean age of this group was 62.6 with a range of age 42 to 91. Six charts were not available for the group, bringing the total possible number to 53. There were 6 patients in this group with no follow-up after discharge. A summary of cardiovascular events for the two groups is included in the Appendix (See Table B-1).

Sixty-two patients with the admission diagnosis of possible myocardial infarction did not fulfill the criteria for admission to either of the two groups. In addition, 7 patients whose charts were not available had a discharge diagnosis in the CCU other than myocardial infarction or myocardial infarction ruled out. Among the diagnoses of those not admitted to the study were such diagnoses as pulmonary embolism, aortic valve replacement, atrial-ventricular block, chronic obstructive pulmonary disease, pericarditis, and sacral spasm. One woman was not admitted to the study because the sample was to be all male. Those patients who died within 48 hours of admission were not admitted to the study.

Probability of Death

It was hypothesized that the probability of a major cardiovascular event resulting in death within one year in a CCU patient with the final diagnosis of MI R/O does not differ from that risk of a CCU patient who has suffered an MI. In the present study, a total of 9 cardiac deaths occurred in the first group, those with MI R/O within the first year. This was 10% of the population of 88 available charts. Ten deaths (24%) occurred in the MI group in the same time period. However, when those deaths which occurred in the hospital were excluded, there was a total of 5 deaths or 12% in the MI group. This is not a significant difference ($X^2 = .2$, $p > .05$) (See Appendix, Table A-1.)

The mean age of those who died in the MI R/O group was

67 and of those in the MI group 69.8. The mean age of those MI patients who died in the hospital was 71.8 and of those who died out of hospital 67.8. Three patients who died in the MI R/O group had had CABG surgery 4-7 years prior to admission. Three patients in the MI R/O group, although dying of cardiac causes, also had conditions other than cardiac disease. One had cancer of the pancreas, one had chronic renal failure and one had newly diagnosed lung cancer. Only one patient in the MI group had a condition other than cardiac disease. This patient had pneumonia at the time of death. The mean length of time after hospitalization until death for the MI R/O group was 15 weeks; for the MI group 17 weeks. There were 3 additional deaths in the MI R/O group which were not counted, one patient died at 13 months; one died of chronic obstructive pulmonary disease, and one died of bronchogenic cancer.

Probability of a Myocardial Infarction

It was hypothesized that the probability of a major cardiovascular event which does not result in death in one year in a CCU patient with the final diagnosis of myocardial infarction ruled out does not differ from the probability of a CCU patient who has suffered an MI. Six patients (or 6.8%) in the MI R/O group suffered an MI within the first year after discharge. Eleven MIs occurred in the MI group (26.8%). This was a significant difference ($X^2 = 14.3$, $p < .001$). See Table 4. The mean age of those suffering

MIs in the MI R/O group was 70.7; the mean age in the MI group was 65.09. One patient in the MI R/O group had had a CABG 3 years previously.

Table 4

Percentage of MIs in MI R/O Compared with MI in the Year Following Discharge

	MI	No MI
MI R/O Group	6.8	93.2
MI Group	26.8	73.2

$X^2 = 14.3$, $p < .001$

Probability of Cardiac Morbidity (Unstable Angina)

It was hypothesized that the frequency of unstable angina during the year following admission of CCU patients with a final diagnosis of MI R/O does not differ from that of patients who have suffered MIs. In the present study, 28 patients, or 31.8%, in the MI R/O group suffered unstable angina in the first year after discharge compared with 11 patients, or 26.8%, of the MI group. This was not a significant difference ($X^2 = .58$, df1, $p > .05$). See Appendix, Table A-3. Eight patients in the MI R/O group had had CABG surgery 1-5 years prior to admission to the CCU.

Epidemiological Risk Factors

It was hypothesized that there is a positive relationship between the incidence of a major cardiovascular event or unstable angina and the presence of the following epidemiological risk factors: increasing age, hypertension, history of diabetes, family history of atherosclerosis, hypercholesterolemia, and smoking history.

In the present study, the point biserial correlation coefficient was used to assess the relationship between the age of the MI R/O patients and a subsequent cardiovascular event. This statistic has the formula

$$r_{pbi} = \frac{M_p - M_q}{\sigma t} \sqrt{pq}$$

where M_p = mean of X values (age) for the higher group in a dichotomous variable

M_q = mean of the lower group

p = proportion of cases in higher group

q = proportion of cases in lower group

σt = standard deviation of the total sample

Since r_{pbi} depends directly upon the difference between the means a significant departure from a mean difference of zero also indicates a significant correlation. A t-test of the difference between means can be used to test the significance of the departure of the correlation coefficient from zero (Guilford, 1956). As indicated in Table 5 there was no significant relationship between age and a subsequent cardio-

vascular event.

Table 5

Relationship of Age/Cardiovascular Event for MI/RO

	Mean Age	r_{pbi}
Whole Sample	61.6	
Any Major Event	70.7	.39*
No Event	61.5	
Death	67	.17
MI	70.8	.18
Unstable Angina	61.07	.12

* t-test = 3.38, $p > .05$

Four additional epidemiological risk factors also failed to demonstrate a significant relationship with a subsequent major cardiovascular event or unstable angina. Those factors were hypertension, history of diabetes, family history of atherosclerosis and smoking history and the results are depicted in the Appendix, Tables A-4 through A-13, and A-30 through A-34. Only hypercholesterolemia demonstrated a significant relationship with the occurrence of unstable angina in the following year, as depicted in Table 6.

Clinical Risk Factors

It was hypothesized that there is a positive relationship between the incidence of a major cardiovascular event or unstable angina and the presence of the following clinical risk factors: history of angina, history of myocardial

Table 6

Relationship of Hypercholesterolemia/Unstable Angina*

	Unstable Angina	No Unstable Angina
Hypercholesterolemia	12	13
No Hypercholesterolemia	12	38

X^2 = 4.4117, df 1 Contingency Coefficient = .2357

Probability is .03368

*Information on cholesterol not available for 4 patients

infarction, New York Heart Association functional class, ST segment depression on the ECG, cardiomegaly, ventricular conduction defect, premature ventricular contractions, and use of diuretics.

Two of these clinical risk factors were found to be significantly related to a higher incidence of death in the MI R/O group: ST segment depression on the ECG and cardiomegaly. The results are demonstrated in Tables 7 and 8. The nonsignificant relationships between clinical risk factors and death are depicted in the Appendix, Tables A-14, 16, 18, 24 26 and 28.

No clinical risk factors were significantly related to the occurrence of an MI in the MI R/O group. See Tables A15, 17, 19, 21, 23, 25, 27, 29. However, four clinical risk factors were significantly related to the occurrence of an unstable angina in the following year for the MI R/O

group: history of angina, history of MI, conduction defects and use of diuretics. These findings are summarized in Tables 9 through 12.

Table 7

Relationship of ST Depression/Death in MI R/O

	Cardiac Death	No Death
ST Depression	8	34
No Depression	1	45

X^2 = 6.8083, df 1 Contingency coefficient = .2679

Probability is .00905

(Note: Only one patient with cardiac death in this group was on Digoxin)

Table 8

Relationship of Cardiomegaly/Death in MI R/O

	Cardiac Death	No Death
Cardiomegaly	6	16
No Cardiomegaly	3	63

X^2 = 9.2827, df 1 Contingency coefficient = .3089

Probability is .00277

Table 9

Relationship of History of Angina/Unstable Angina

	Unstable Angina	No Unstable Angina
History of Angina	23	37
No History	5	25

X^2 = 4.3807, df 1 Contingency coefficient = .2154

Probability is .03430

Table 10

Relationship of History of MI/Unstable Angina

	Unstable Angina	No Unstable Angina
History of MI	23	33
No History	5	29

X^2 = 6.8617, df 1 Contingency coefficient = .2661

Probability is .00880

Table 11

Relationship of Conduction Defect/Unstable Angina

	Unstable Angina	No Unstable Angina
Conduction Defect	15	16
No Defect	13	46

X^2 = 6.58526, df 1 Contingency coefficient = .2611

Probability is .01015

Table 12

Relationship of Diuretics/Unstable Angina

	Unstable Angina	No Unstable Angina
Diuretics	15	20
No Diuretics	13	42

X^2 = 3.6869, df 1 Contingency coefficient = .1983

Probability is .05195

Four clinical risk factors were found not to be related significantly to the occurrence of unstable angina: functional class, ST depression, cardiomegaly, and PVCs. These findings are depicted in the Appendix, Tables A-37, 38, 39 and 41.

Number of Epidemiological and Clinical Risk Factors

The final hypothesis stated that there is a positive relationship between the probability of a major cardiovascular event or unstable angina and the number of clinical and epidemiological risk factors. In this study the point biserial correlation coefficient was used. A significant relationship was demonstrated between the number of risk factors and the occurrence of a cardiovascular event with or without resulting death in the following year for the MI R/O group (See Table 13). However, there was no significant relationship found between the number of risk factors and death, MI, or unstable angina when these were considered separately. The

mean number of risk factors for the entire group was 4.79 (total number of possible risk factors was 13). The number of risk factors per patient ranged from a low of 2 to a high of 8.

Table 13

Relationship of Number of Risk Factors/Cardiovascular Event

	Mean Number Risk Factors	r_{pbi}
Any Major Event	6.08	.48*
Death	5.1	.06
MI	5	.02
Unstable Angina	5.73	.3417

*t-test = 5, $p < .01$

Chapter IV

DISCUSSION

In beginning discussion of the findings of this study, some observations are in order. First of all, as mentioned in Chapter II, a retrospective investigation lacks the control advantage of true experimental research, both in terms of inability to manipulate the independent variable and of inability to randomize. Because of this lack of control there is a risk of erroneous interpretation of results.

A second point to note is the absence of some data due either to the lack of availability of some charts or to a lack of follow-up. Although an attempt was made to identify pertinent information about these missing patients, no conclusions can be drawn. The only apparent major differences were a greater percentage of patients with ST depression, history of angina and using diuretics in the follow-up group, while the group with no follow-up contained a greater percentage with a history of MI (see Table 3, Chapter III). Inclusion of these charts and missing data could have made a significant difference in the results.

A further limitation in the present study is the finding of a history of MI in 61% of the MI R/O group, prohibiting a distinct division between purely MI R/O patients and MI patients. Although criteria were followed in placing the

patients into two groups, 61% of the MI R/O group shared one characteristic with the MI group raising the possibility that the two groups may have been more similar than dissimilar. A history of MI was not found to be significantly related to a subsequent major cardiovascular event. However, the common characteristic may have affected the findings.

In addition, as the study progressed, it became apparent that the addition of data regarding risk factors for the MI group would have provided much valuable information, both for assessment of that group and for comparison with the MI R/O group. Further refinement of the measurement of risk factors may have made a difference as well.

Finally, it must be noted that the sample in this study was selected from patients at the Veteran's Administration Hospital and possibly the sample was somewhat older, more indigent and in possession of a higher number of risk factors than may be found in patients of other CCUs. Thus the findings of this study may not be generalizable to all CCU patients.

With these limitations in mind the problems addressed by this study will be reviewed and conclusions drawn from statistical analysis of the findings.

Frequency of Major Cardiovascular Event

The findings in this study can be compared with previous studies done in this area (Schroeder, 1977; Nordlander, 1979; Schroeder, 1980). The frequencies of major cardiovascular events resulting in death and of major cardiovascular events

not resulting in death are demonstrated in Table 14.

Table 14

Percentage of Major Cardiovascular Events

	MI R/O		MI	
	Cardiac Death	MI	Cardiac Death	MI
Schroeder, 1977 N=170	10.1% N = 17	10% N = 17	not recorded	
Nordlander, 1979 N=193 (MI R/O) N = 187 (MI)	9% N = 17	7% N = 14	11% N = 20	14% N = 27
Present Study, 1980 N=88 (MI R/O) N=41 (MI)	10% N = 9	6.8% N = 6	12% N = 5	26.8% N = 11

In this study patients who are admitted to the CCU with chest pain and who have a myocardial infarction ruled out appear to be at high risk for cardiovascular death. As indicated in Table 14 the percentages of cardiac death are similar in the three studies and the probability of a major cardiovascular event resulting in death does not differ significantly from the group which has suffered a myocardial infarction.

However, the number of myocardial infarctions in the year following discharge from the CCU differs both in the two groups in each study and in the two studies. The reason for this discrepancy is not readily apparent.

The frequency of cardiac morbidity was evaluated for

both groups in the present study in the form of unstable angina. This aspect was not discussed in the studies by Schroeder, 1977; Nordlander, 1979; or Schroeder, 1980. In the present study 31.8% of the MI R/O group suffered unstable angina in the following year while 26.8% of the MI group suffered unstable angina. This is not a significant difference when tested with chi square ($X^2 = .58$, $p > .05$).

In an attempt to identify a high risk subgroup in those patients in the MI R/O group, several epidemiological and clinical risk factors were examined.

Epidemiological Factors

The first of the epidemiological risk factors, age, did not show statistical significance in its relationship with any cardiovascular events, either alone or combined. Age was found to be a factor in one of the studies drawn from normal populations for the development of coronary heart disease (Framingham, 1972). Only Norris (1974) in his follow-up study of MI patients found age to be a factor. The ages reported by Nordlander are compared with the ages in the present study in Table 15.

Table 15

Age Range and Mean Age for

Cardiovascular Events in MI R/O

	Death		MI	
Nordlander, 1979	Range:	47-85	Range:	45-75
	Mean:	68	Mean:	60
Present Study 1980	Range:	48-90	Range:	47-83
	Mean:	67	Mean:	70

Although the lower ages are similar in all four categories, it is apparent that the upper ages are higher in the present study and the mean age for having an MI in the year after hospitalization is 10 years more than in the Nordlander study.

The patients in Schroeder's study of 1980 had a mean age of 57.3 in the MI R/O group compared with a mean age of 61.6 in the present study's same group. Similarly the mean age in Schroeder's MI group was 56.3 compared to the present study's MI group mean of 62.6. The older sample in the present study, although not significantly affecting the incidence of cardiovascular events may have had an effect on certain of the risk factors such as history of angina or hypertension.

The next three epidemiological risk factors, hypertension, history of diabetes, and family history of atherosclerosis did not relate significantly to any of the subsequent cardiovascular events. All three were found to be related to the development of coronary artery disease in the Framingham study. Only hypertension was found to be a significant factor in later studies such as Dick and Stone, 1978; the Pooling Project, 1978; Weinblatt, 1968; Oberman, 1974; and Norris, 1974. However, Weinblatt and Oberman paired hypertension with an abnormal ECG as a risk factor for a poor prognosis while Norris (1974) found hypertension to be of lesser importance than factors related to the degree of myocardial damage. It appears that hypertension in itself is not always a significant factor for cardiovascular events

but may gain significance when linked with other risk factors. It is interesting to note that 35 patients had a history of hypertension. This was 39% of the sample, and it supports the finding of the Framingham study that hypertension is a factor in the development of coronary disease. Similarly, 15 of the patients in the MI R/O group had diabetes, a percentage of 17% of the sample, and 26 patients (29.5%), had a family history of atherosclerosis.

Hypercholesterolemia was not significantly related to either death or a myocardial infarction in the year following discharge. However, it was found to be related to a higher incidence of unstable angina in the following year ($X^2 = 4.4$, $p = .03$). Framingham (1972); Dick and Stone (1978); and the Pooling Project (1978) all found hypercholesterolemia to be a factor in the development of coronary artery disease, particularly when linked with other risk factors such as hypertension and smoking. The Coronary Drug Project (1974) found cholesterol to be a risk factor in a group of MI patients.

The lack of significant findings other than the relationship with unstable angina in the present study may be due to the fact that interactions with other risk factors were not considered. Table 16 demonstrates the increasing importance of hypercholesterolemia when added to other risk factors for the MI R/O patient.

Table 16

Hypercholesterolemia Plus Other Risk Factors/Unstable Angina

	Unstable Angina	No Unstable Angina
Total with Hypercholesterolemia	12	13
Hypercholesterolemia Only	3 (25%)	5 (38%)
Hypercholesterolemia and Smoking	4 (33%)	5 (38%)
Hypercholesterolemia, Smoking and Hypertension	5 (41%)	3 (23%)

One problem with the measurement of the risk factor hypercholesterolemia was the lack of information on every patient for this factor. The blood cholesterol is not routinely measured on every patient; only 75 out of the sample of 88 had a record of blood cholesterol. However, 25 of this number or 33% had an elevation above 250 mg%.

The last epidemiological risk factor, smoking had no statistical significance in the occurrence of a major cardiovascular event or unstable angina. This was a surprising finding, as Framingham (1972); Dick and Stone (1978); and the Pooling Project (1978) found smoking to be a significant factor in the development of coronary artery disease, Weinblatt (1968) found it to be of significance for angina patients and Mulcahy (1977) found it to be of moderate significance for MI patients.

There are a few possible explanations for this failure to find smoking a significant factor. First, 54 patients or 61% of the sample of MI R/O patients were smokers, thus supporting findings that cigarette smoking may be a risk factor in the development of coronary artery disease. However, this large percentage of smokers was a skewed distribution and may have affected the findings. In the second place, the measurement of smoking itself was not sensitive, being limited to smoking as opposed to non-smoking. Information was not kept on the number of pack years per patient. A later spot check revealed the number of pack years to vary from 20 to 120 years. A more detailed measurement may have revealed some differences. Finally, the interactions between smoking and other risk factors were not studied. Table 16 demonstrates the importance of smoking when added to other risk factors such as hypercholesterolemia and hypertension in the occurrence of subsequent unstable angina. Doyle (1979) in his workshop presentation on carbon monoxide and cardiovascular disease stated that arterial hypertension and heavy cigarette smoking powerfully increase the risk of coronary heart disease in the presence of hypercholesterolemia. He stated that the mechanism by which cigarette smoking aggravates and accelerates atheropoiesis is unknown, but carbon monoxide and mobilization of catecholamines are probably implicated.

Clinical Factors

A history of angina in the MI R/O patient was not found to be significantly related to either death or an MI in the following year. However, there was a significant relationship with occurrence of unstable angina in that year ($X^2 = 4.38$, $p = .037$.) Weinblatt found that a history of angina increased the probability of death or an MI, as did many other investigators (Humphries, 1977; Oberman, 1978; Reeves, 1974; Kannel and Feinleib, 1972). None of the literature reviewed addressed the problem of the relationship between a history of angina and subsequent unstable angina. The fact that 60 patients or 68% of the sample of MI R/O patients had a history of angina and 23 patients or 38% went on to suffer unstable angina in the following year reflects the increased cardiac morbidity in this sample. This is no surprise considering that coronary artery disease is a progressive condition.

Similarly, a history of MI as it relates to subsequent unstable angina in the MI R/O patient is not addressed in the literature reviewed. Schroeder (1980) in his prospective study did find that the MI R/O group included more patients with a history of previous infarction and stable angina before hospitalization than the MI group. In the present study, data regarding history of MI were not gathered in the MI group so it was not possible to make a comparison. Fifty-four patients or 61% of the MI R/O group had a history of MI, and experienced high cardiac morbidity as 23 of them or 42% went on to suffer unstable angina.

The third clinical risk factor, New York Heart Association functional class was not significantly related to any cardiovascular event in the following year for the MI R/O patient. It was a significant risk factor for a poor prognosis in MI patients in the Coronary Drug Research Project. In addition, Krauss (1972) and Gazes (1973) found deterioration of angina in the hospital to be a high risk factor for increased mortality in the unstable angina patient. Only 15 patients in the present study were classified as Class III or IV during the hospital stay or suffered continuing pain at rest or with minimal exertion according to the progress notes. Perhaps if the criteria had been changed to include use of nitroglycerin more patients would have been in this category. Krauss (1972) found that 36 of 100 patients continued to experience prolonged ischemic chest pain after 12 hours of bed rest. Gazes (1973) found 54 patients out of 140 at this level.

ST segment depression was found to be a significant risk factor for death in the present study, supporting many previous studies which have found this one factor to be ominous (Reunanen, 1978; Humphries, 1977; Weinblatt, 1968; Oberman, 1978; Coronary Drug Research Group, 1974; Gazes, 1973; Nordlander, 1979). According to the literature, this one sign in an ECG can be a risk factor in a sample drawn from a normal population, patients with angina, MI patients, patients with unstable angina, and patients with MI R/O.

Forty-two of the present sample had ST segment depression in at least two leads in the first three hospital days. Of the 9 patients who died in the MI R/O group 8 had ST segment depression. No other information was sought at the time of data collection regarding the onset or persistence of ST depression. At a later date an attempt was made to get this information, particularly for those patients who had died, but unfortunately many of the charts were unavailable. Three records of patients who had died showed that ST depression was new for two of the patients and it persisted throughout the hospital stay and after discharge. One patient had ST depression before admission, during the stay and after discharge. Any future studies should include the onset, timing and persistence of ST depression to further refine this important risk factor. Nordlander (1979) used an ST depression of 1.5 mm for his criteria. Perhaps a further study could categorize patients into groups with different measurements.

Cardiomegaly was also found to be an important risk factor for death in this sample, but unrelated to morbidity or subsequent cardiovascular event. In fact, this factor showed the greatest level of significance in the study ($X^2 = 9.2$, $p = .002$). This finding supports the findings of many previous studies (Oberman, 1978; Duncan, 1976; Coronary Drug Research Group, 1974; Norris, 1974; Schroeder, 1980). Duncan (1976) found an increased cardiothoracic

ratio to be the only significant predictive factor for serious cardiac complications in a population with angina. Schroeder (1980) stated that cardiomegaly tended to increase the risk of morbidity and mortality in both MI R/O and MI patients. In the present study, 6 out of 9 patients who died had cardiomegaly. This lends further support to the identification of cardiomegaly as a potent risk factor for cardiac death.

Ventricular conduction defect, measured as a prolonged QRS interval was found to be a significant factor in the occurrence of unstable angina in the following year. Oberman (1978) and the Coronary Drug Research Group (1974) found a ventricular conduction defect to be a significant risk factor for populations of MI patients. Nordlander (1979) defined a QRS duration over 0.12 s as a bundlebranch block and found 13 of 193 patients with this sign. Three patients died and none had an MI. These patients were significantly older than the rest of the patients. Thirty-one patients in this study were found to have a conduction defect (a QRS duration > 0.10 s); their average age was 63.4, only slightly older than the sample mean.

Premature ventricular contractions (PVCs) were not found to be a significant factor in any subsequent cardiovascular event. In the literature reviewed, Vismara (1977) found these arrhythmias to be a significant factor in MI patients. Moss (1976) and the Coronary Drug Research Group also cited PVCs as a factor increasing the risk of death for MI patients.

None of the research reviewed cited PVCs as a risk factor for MI R/O patients and this indeed, may be the case; this finding may also be related to the low incidence of PVCs in the MI R/O group.

The final clinical risk factor, use of diuretics was found to be significantly related to the occurrence of unstable angina in the following year. Thirty-five patients or 39.7% of the sample were on diuretics. The use of diuretics was cited by only one group, the Coronary Drug Research Group (1974) as a risk factor for a population of MI patients. The reason for this finding in the present study is not clear at this time. An attempt to link use of diuretics with hypertension as a joint risk factor did not reveal a relationship; similarly an attempt to do the same with cardiomegaly was fruitless. Only 5 patients with cardiomegaly suffered unstable angina in the subsequent year.

When the relationship between the number of risk factors and a subsequent event was assessed by the point biserial correlation coefficient an r_{pbi} of .48 was found. This finding supports that of Kannel (1972) reporting that in a general population the probability of a cardiovascular event increased when more risk factors were involved.

Chapter V

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

This study has attempted to add to the current knowledge regarding the probability of a subsequent major cardiovascular event or unstable angina and to further identify the related risk factors for those Coronary Care Unit patients in whom myocardial infarction has been ruled out. A review of the literature revealed that there was an increased probability of a major cardiovascular event for these patients and indicated there were many possible risk factors.

A retrospective investigation was undertaken; 147 charts from the same time period were examined, 100 from the MI R/O group and 47 from the MI group. Data concerning subsequent cardiovascular events and certain epidemiological and clinical risk factors were extracted from the charts and placed in contingency tables. The data were then analyzed by the chi-square statistic and in two instances by the point biserial correlation coefficient.

It was found that the MI R/O group did have an increased risk of a major cardiovascular event in the following year. The percentage of cardiac deaths (10%) was comparable to that of the MI group (12%). There was not as great a probability of a myocardial infarction in the MI R/O group but this group had a greater probability of cardiac morbidity

in the form of unstable angina in the following year.

Two risk factors were found to be significantly related to cardiac mortality in the year following discharge for the MI R/O group: ST segment depression and cardiomegaly. Five risk factors were found to be significantly related to the occurrence of unstable angina in the following year: history of angina, history of MI, ventricular conduction defect, use of diuretics and hypercholesterolemia.

Conclusions

The following is a summary of the findings of this study and others in relation to each of the hypotheses. Because of the limitations of the study described in Chapter IV, the following are tentative conclusions, each needing further investigation.

The first hypothesis that the probability of a major cardiovascular event resulting in death within one year in a CCU patient with the final diagnosis of MI R/O does not differ from the risk of a CCU patient who has suffered a myocardial infarction was supported in this study, adding to similar findings by Schroeder (1977); Nordlander (1979); and Schroeder (1980).

The second hypothesis that the probability of a major cardiovascular event which does not result in death in one year in the CCU patient with the final diagnosis of MI R/O does not differ from the risk of a CCU patient who has suffered

an MI was not supported in this study, in contrast to previous studies done by Schroeder (1977) and Nordlander (1979).

The third hypothesis that the frequency of unstable angina during the year following admission of CCU patients with a final diagnosis of MI R/O does not differ from that of patients who have suffered MIs was supported in this study. The comparison of cardiac morbidity was not done in any of the studies covered in the review of the literature.

The fourth hypothesis that there is a positive relationship between the incidence of a major cardiovascular event or unstable angina and the presence of the following epidemiological risk factors: increasing age, hypertension, history of diabetes, family history of atherosclerosis, hypercholesterolemia, and smoking history was partially supported. Only one factor, hypercholesterolemia, was found to be significantly related to an increased incidence of unstable angina. This relationship was not cited in the studies covered in the review of the literature.

The fifth hypothesis that there is a positive relationship between the incidence of a major cardiovascular event or unstable angina and the following clinical risk factors: history of angina, history of myocardial infarction, New York Association functional class, ST segment depression on the ECG, cardiomegaly, ventricular conduction defect, premature ventricular contractions, and use of diuretics was only partially supported. ST segment depression was significantly

related with death supporting findings reported by many investigators. Cardiomegaly was also significantly related with death supporting a recent finding by Schroeder in the MI R/O group (1980). Significant relationships with unstable angina were found with the following clinical risk factors: history of angina, history of MI, conduction defect, and the use of diuretics. These latter findings for an MI R/O group were not reported in the studies covered in the review of the literature.

The sixth hypothesis that there is a positive relationship between a major cardiovascular event or unstable angina and the number of clinical and epidemiological risk factors was supported in this study. This relationship for an MI R/O group was not cited in studies covered in the review of the literature.

Recommendations

It is recommended that further studies be carried out as a result of this study. There is a lack of information at present regarding the patient with MI R/O which can only be remedied by further studies. Such studies should explore the risk factors for this group, perhaps refining them further by breaking them into categories such as types of anti-diabetic therapy, number of pack years of cigarettes, and size of ST depression. Further examination is also needed of the interaction of risk factors such as hypercholesterolemia

and smoking, smoking and hypertension, and hypercholesterolemia, smoking plus hypertension.

More research is needed regarding unstable angina and other forms of cardiac morbidity for the MI R/O patient. Also needed are prospective studies, comparing risk factors and the occurrence of cardiovascular events in an MI R/O group with those of an MI group. A limitation of this study was the lack of data on risk factors for the MI group and a consequent lack of opportunity to compare the incidence of risk factors in two groups. This could be done in future studies and much valuable information would be gained. Such studies could also further differentiate the sample into an MI R/O group with no history of MI, an MI R/O group with a history of MI, and an MI group, thus eliminating any possible similarities in the groups due to one common characteristic.

In the present study, the MI R/O group was found not to differ significantly from the MI group in the occurrence of death and cardiac morbidity in the form of unstable angina in the year following discharge from the CCU. Therefore, the patient should be included in rehabilitation and patient education classes and the family should be taught resuscitation techniques. Patients with those epidemiological or clinical findings which were found to be significantly related to a subsequent event in this study should especially be included in classes.

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APPENDIX A

Tables of Chi Square Analysis

Table A-1

Percentage of Deaths in MI R/O Group Compared with Deaths in MI Group in Year Following Discharge

	Death	No Death
MI R/O	10	90
MI	12	88

X^2 = .2, df 1

Probability > .05

Table A-2

Percentage of MIs in MI R/O Group Compared With MIs in MI Group in Year Following Discharge

	MI	No MI
MI R/O	6.8	93.2
MI	26.8	73.2

X^2 = 14.3, df 1

Probability is < .001

Table A-3

Percentage of Unstable Angina in MI R/O Group Compared With MI Group in Year Following Discharge

	Unstable Angina	No Unstable Angina
MI R/O	31.8	68.2
MI	26.8	73.2

X^2 = .58, df 1

Probability > .05

Table A-4

Relationship of Hypertension/Death for MI R/O

	Death	No Death
Hypertension	2	33
No Hypertension	7	46

X^2 = 1.29, df 1 Contingency coefficient = .1201

Probability is .25517

Table A-5

Relationship of Hypertension/Myocardial Infarction (MI) for MI R/O

	Myocardial Infarction	No MI
Hypertension	3	32
No Hypertension	3	50

X^2 = .28, df 1 Contingency coefficient = .0564

Probability is .60276

Table A-6

Relationship of Diabetes/Death for MI R/O

	Death	No Death
Diabetes	2	13
No Diabetes	6	66

X^2 = .37, df 1 Contingency coefficient = .0652

Probability is .54951

Table A-7

Relationship of Diabetes/Mocardial Infarction for MI R/O

	MI	No MI
Diabetes	1	14
No Diabetes	5	68

X^2 = .0006, df 1 Contingency coefficient = .0027

Probability is .97782

Table A-8

Relationship of Family History of Atherosclerosis/Death for MI R/O

	Death	No Death
Family History	3	23
No Family History	6	54

X^2 = .045, df 1 Contingency coefficient = .023

Probability is .82513

Table A-9

Relationship of Family History of Atherosclerosis/MI for MI R/O

	MI	No MI
Family History	2	24
No Family History	4	56

X^2 = .029, df 1 Contingency coefficient = .0184

Probability .85822

Table A-10

Relationship of Hypercholesterolemia/Death

	Death	No Death
Hypercholesterolemia	0	25
No Hypercholesterolemia	5	42

X^2 = 2.85, df 1 Contingency coefficient = .1953

Probability is .08721

Table A-11

Relationship of Hypercholesterolemia/MI

	MI	No MI
Hypercholesterolemia	1	24
No Hypercholesterolemia	2	56

X^2 = .015, df 1 Contingency coefficient = .0135

Probability is .89730

Table A-12

Relationship of Smoking/Death for MI R/O

	Death	No Death
Smoking	3	50
No Smoking	6	29

X^2 = 3.03, df 1 Contingency coefficient = .1823

Probability is .07830

Table A-13

Relationship of Smoking/MI for MI R/O

	MI	No MI
Smoking	4	50
No Smoking	2	33

X^2 = .09, df 1 Contingency coefficient = .0329

Probability is .75412

Table A-14

Relationship of History of Angina/Death for MI R/O

	Death	No Death
History of Angina	4	55
No History of Angina	5	24

X^2 = 2.31, df 1 Contingency coefficient = .1601

Probability is .12409

Table A-15

Relationship of History of Angina/MI for MI R/O

	MI	No MI
History of Angina	4	55
No History of Angina	2	27

X^2 = .0004, df 1 Contingency coefficient = .0021

Probability is .98144

Table A-16

Relationship of History of MI/Death for MI R/O

	Death	No Death
History of MI	6	48
No History of MI	3	31

X^2 = .11, df 1 Contingency coefficient = .0367

Probability is .73039

Table A-17

Relationship of History of MI/MI for MI R/O

	MI	No MI
History of MI	4	50
No History of MI	2	32

X^2 = .07, df 1 Contingency coefficient = .0294

Probability is .77903

Table A-18

Relationship of Functional Class/Death for MI R/O

	Death	No Death
Functional Class	1	14
No Functional Class	8	65

X^2 = .25, df 1 Contingency coefficient = .0531

Probability is .62355

Table A-19

Relationship of Functional Class/MI for MI R/O

	MI	No MI
Functional Class	0	15
No Functional Class	6	67

X^2 = 1.32, df 1 Contingency coefficient = .1217

Probability is .24879

Table A-20

Relationship of ST Depression/Death for MI R/O

	Death	No Death
ST Depression	8	34
No ST Depression	1	45

X^2 = 6.80, df 1 Contingency coefficient = .2679

Probability is .00905

Table A-21

Relationship of ST Depression/MI for MI R/O

	MI	No MI
ST Depression	3	39
No ST Depression	3	43

X^2 = .013, df 1 Contingency coefficient = .0123

Probability is .90408

Table A-22

Relationship of Cardiomegaly/Death for MI R/O

	Death	No Death
Cardiomegaly	6	16
No Cardiomegaly	3	63

X^2 = 9.28, df 1 Contingency coefficient .3089

Probability is .00277

Table A-23

Relationship of Cardiomegaly/MI for MI R/O

	MI	No MI
Cardiomegaly	1	21
No Cardiomegaly	5	61

X^2 = .23, df 1 Contingency coefficient = .0519

Probability is .63129

Table A-24

Relationship of Conduction Defect/Death for MI R/O

	Death	No Death
Conduction Defect	5	22
No Conduction Defect	4	57

X^2 = 2.91, df 1 Contingency coefficient = .1791

Probability is .08401

Table A-25

Relationship of Conduction Defect/MI

	MI	No MI
Conduction Defect	3	24
No Conduction Defect	3	58

X^2 = 1.1, df 1 Contingency coefficient = .1125

Probability is .2879

Table A-26

Relationship of PVCs/Death for MI R/O

	Death	No Death
PVCs	1	7
No PVCs	8	72

X^2 = .05, df 1 Contingency coefficient = .0237

Probability is .81874

Table A-27

Relationship of PVCs/MI for MI R/O

	MI	No MI
PVCs	1	7
No PVCs	5	75

X^2 = .48, df 1 Contingency coefficient = .0711

Probability is .51109

Table A-28

Relationship of Use of Diuretics/Death for MI R/O

	Death	No Death
Use of Diuretics	5	30
No Use of Diuretics	4	49

X^2 = 1.04, df 1 Contingency coefficient = .1082

Probability is .30819

Table A-29

Relationship of Use of Diuretics/MI for MI R/O

	MI	No MI
Use of Diuretics	3	32
No Use of Diuretics	3	50

X^2 = .28, df 1 Contingency coefficient = .0564

Probability is .60276

Table A-30

Relationship of Hypertension/Unstable Angina for MI R/O

	Unstable Angina	No Unstable Angina
Hypertension	10	25
No Hypertension	18	37

X^2 = .17, df 1 Contingency coefficient = .0437

Probability is .68154

Table A-31

Relationship of Diabetes/Unstable Angina for MI R/O

	Unstable Angina	No Unstable Angina
Diabetes	6	9
No Diabetes	22	53

X^2 = .66, df 1 Contingency coefficient = .0855

Probability is .57909

Table A-32

Relationship of Family History of Atherosclerosis/Unstable Angina for MI R/O

	Unstable Angina	No Unstable Angina
Family History	10	16
No Family History	17	45

X^2 = 1.05, df 1 Contingency coefficient = .1085

Probability is .30634

Table A-33

Relationship of Hypercholesterolemia/Unstable Angina

	Unstable Angina	No Unstable Angina
Hypercholesterolemia	12	13
No Hypercholesterolemia	12	38

X^2 = 4.41, df 1 Contingency coefficient = .2357

Probability is .03368

Table A-34

Relationship of Smoking/Unstable Angina for MI R/O

	Unstable Angina	No Unstable Angina
Smoking	18	37
No Smoking	10	25

X^2 = .17, df 1 Contingency coefficient = .0437

Probability is .68154

Table A-35

Relationship of History of Angina/Unstable Angina for MI R/O

	Unstable Angina	No Unstable Angina
History of Angina	23	37
No History of Angina	5	25

X^2 = 4.38, df 1 Contingency coefficient = .2154

Probability is .03430

Table A-36

Relationship of History of MI/Unstable Angina for MI R/O

	Unstable Angina	No Unstable Angina
History of MI	23	33
No History of MI	5	29

X^2 = 6.86, df 1 Contingency coefficient = .2661

Probability is .00880

Table A-37

Relationship of Functional Class/Unstable Angina for MI R/O

	Unstable Angina	No Unstable Angina
Functional Class	7	10
No Functional Class	21	52

X^2 = .99, df 1 Contingency coefficient = .1043

Probability is .67957

Table A-38

Relationship of ST Depression/Unstable Angina for MI R/O

	Unstable Angina	No Unstable Angina
ST Depression	13	29
No Unstable Angina	15	33

X^2 = .0009, df 1 Contingency coefficient = .0032

Probability is .97426

Table A-39

Relationship of Cardiomegaly/Unstable Angina for MI R/O

	Unstable Angina	No Unstable Angina
Cardiomegaly	5	18
No Cardiomegaly	23	44

X^2 = 1.26, df 1 Contingency coefficient = .1177

Probability is .25960

Table A-40

Relationship of Conduction Defect/Unstable Angina

	Unstable Angina	No Unstable Angina
Conduction Defect	15	16
No Conduction Defect	13	46

X^2 = 6.58, df 1 Contingency coefficient = .2611

Probability is .01015

Table A-41

Relationship of PVCs/Unstable Angina for MI R/O

	Unstable Angina	No Unstable Angina
PVCs	4	4
No PVCs	24	58

X^2 = 1.46, df 1 Contingency coefficient = .1264

Probability is .22466

Table A-42

Relationship of Use of Diuretics/Unstable Angina for MI R/O

	Unstable Angina	No Unstable Angina
Use of Diuretics	15	20
No Use of Diuretics	13	42

X^2 = 3.68, df 1 Contingency coefficient = .1983

Probability is .05195

APPENDIX B

Table B-1

Incidence of Cardiovascular Event in MI R/O and MI Groups

	MI R/O (n = 88)	MI (n = 41)
In-Hospital Death	0	5
Death After Discharge	9 (CABG in 3 patients)	5
Non-cardiac Death	3	1
Myocardial Infarction	6 (CABG in 1 patient)	11
Unstable Angina	28 (CABG in 8 patients)	11

AN ABSTRACT OF THE THESIS OF

ELEANOR SMITH

For the MASTER OF NURSING

Date of Receiving this Degree: June 12, 1981

Title: THE PROBABILITY OF A MAJOR CARDIOVASCULAR EVENT AND ASSOCIATED RISK FACTORS IN THE CORONARY CARE UNIT PATIENT WITH MYOCARDIAL INFARCTION RULED OUT

Approved: [redacted]
Christine A. Tanner, Ph.D., Thesis Advisor

The purpose of this study was to add to current knowledge regarding the probability of a subsequent major cardiovascular event or unstable angina and to further identify the related risk factors for those Coronary Care Unit patients in whom myocardial infarction has been ruled out. A review of the literature revealed that there was an increased probability of a major cardiovascular event for these patients and indicated there were many possible risk factors.

A retrospective investigation was undertaken: 147 charts from the same time period were examined, 100 from the MI R/O group and 47 from the MI group. Data concerning subsequent cardiovascular events and certain epidemiological and clinical risk factors were extracted from the charts and placed in contingency tables. The data were then analyzed

by the chi square statistic and in two instances by the point biserial correlation coefficient.

It was found that the probability of death for the patient with MI R/O does not differ significantly from the patient who has suffered a myocardial infarction in the year after discharge. The probability of a myocardial infarction was significantly less for the patient with myocardial infarction ruled out, while the probability of unstable angina in the following year did not differ significantly between the two groups.

Two clinical risk factors were found to be significantly related to cardiac mortality in the year following discharge in the MI R/O group: ST segment depression and cardiomegaly. Five risk factors were found to be significantly related to the occurrence of unstable angina in the following year: the clinical factors being history of angina, history of myocardial infarction, ventricular conduction defect, and use of diuretics, and one epidemiological factor being hypercholesterolemia.