Coronary Heart Disease and Life Insurance

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Coronary heart disease morbidity and mortality are dynamic issues. Outcomes from medical and surgical treatments are having dramatic effects. For the life insurer it is vital to follow closely the changing history of the disease.

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Coronary artery disease accounts for 930,000 deaths each year in the United States.[1] The life insurer must be aware of the advances in the understanding of the pathogenesis of the disease and the risk factors. Further modifications in risk factors are beginning to affect the natural history of the disease. At last, the sophistication and comprehensiveness of the clinical studies are increasing as they are performed on large, often multicultural populations across national boundaries.

EPIDEMIOLOGY AND PATHOGENESIS

Magnitude of the Threat

As we enter the new millennium, cardiovascular disease accounts for more than 930,000 deaths in the United States annually (43% of deaths from all causes). This includes approximately 500,000 deaths due to coronary disease, a majority of which are sudden deaths.[1] More than 156,000 cardiovascular deaths occur annually before the age of 65 years, and more than half of all deaths from cardiovascular disease occur in women.[2] Coronary heart disease (CHD) is a major cause of morbidity and mortality in women beyond their middle to late 50s.[3] It has been estimated that almost 5 million years of potential life in people who are younger than 75 years old are lost annually in the United States because of cardiovascular disease.

Death rates from cardiovascular diseases have been declining over the past several decades.[4] From 1980 to 1990, the age-adjusted death rate from CHD fell 32.6%, and from stroke, 32.4%. The decline in incidence is consistent with dramatic improvements in CHD risk-factor profiles particularly smoking, hyperlipidemia and hypertension. Improvements in short-term survival among patients hospitalized for myocardial infarction (MI) probably resulted from the greater use of

beneficial therapies, including aspirin, anticoagulants, and thrombolytic agents. However, there remains much room for progress.

In 1990, 5.2 million people were hospitalized with a first-listed discharge diagnosis of cardiovascular disease, 2 million with a discharge diagnosis of CHD, and approximately 675,000 with a diagnosis of acute MI.[1]

According to 1990 statistics, an estimated 6.2 million Americans have significant CHD. Many of these people are at increased risk for sudden death or MI. Approximately two thirds of sudden deaths due to coronary disease (about 350,000 annually)—representing the most prominent medical emergency in the United States today—take place outside the hospital and usually occur within 2 hours after onset of symptoms.

Pathogenesis of Coronary Atherosclerosis

Atherosclerosis (ICD 440) is the cause with the largest number of deaths as a single disease category. Its development and pathogenesis may be divided into 3 major phases. The first stage is the early development of atherosclerotic plaque in asymptomatic persons. The second stage is the progression to a more advanced plaque that usually narrows the lumen and may cause chest pain especially with strenuous activity or stress. The third stage is the occurrence of acute disruptive changes with rupture of the plaque that lead to sudden arterial occlusion and such accompanying tertiary clinical end points of ischemic heart disease as intractable angina pectoris, MI, congestive heart failure, myocardial revascularization, malignant cardiac arrhythmias, sudden death with resuscitation, and death.[5]

PATTERNS OF SURVIVAL AND EXCESS MORTALITY

General Patterns of Survival and Excess Mortality

Intractable angina, MI, congestive heart failure, myocardial revascularization, malignant cardiac arrhythmias, and death are simultaneously tertiary end points of ischemic CHD and biostatistically dependent variables in a regression caused by or significantly affected by a number of independent variables. These independent variables include anatomic extent and severity of obstructive CHD; left ventricular function; comorbidities such as severity of angina, MI, congestive heart failure, diabetes mellitus, malignant cardiac arrhythmias, and peripheral and cerebral vascular disease; composite risk estimation (Framingham Study, accelerated-failure model); and treatment-related survival differences.

Underwriting Focus

The following should be the focuses for underwriters:

- Determine CHD class on the basis of anatomic extent and severity.
- Determine CHD stage on the basis of left ventricular function.
- Determine the patient's basic risk rating on the basis of CHD class and stage, as well as the patient's age and treatment mode.
- Modify the basic rating, taking into account comorbidities, composite risk, and disease progression.
- Factor in the predictive power of noninvasive testing and prognostic markers.

Subjects Studied and Follow-up

In the Duke University Medical Center Study (CASS Study) by Jones and colleagues,[6] 9263 patients with coronary artery disease were confirmed by cardiac catheterization between 1984 and 1990; 2449 patients were prospectively treated medically; 2924 patients were prospectively treated with percutaneous transluminal coronary angioplasty (PTCA); and 3890 patients were prospectively treated with coronary artery bypass grafting (CABG) surgery.

Patients were divided into 9 anatomic subgroups with prognostic implications, including single-vessel, double-vessel, and triple-vessel coronary artery disease with or with-

Table 1. 6-Year Survival by Treatment in Each Anatomic Subgroup[6]

Grade	Vessel Disease*	95% Proximal Stenosis	Left Anterior Descending	Bypass Surgery (%)	Angioplasty (%)	Medicine (%)
				Treatment		
1	1	No	—	0.92	0.96	0.93
2	1	Yes	—	0.91	0.94	0.91
3	2	No	—	0.90	0.92	0.88
4	2	Yes	—	0.90	0.90	0.86
5	1	Yes	95% Proximal	0.89	0.88	0.83
—	2	Yes	95%	—	—	—
6	2	Yes	95% Proximal	0.89	0.85	0.79
—	3	No	Yes	—	—	—
7	3	Yes	Yes	0.88	0.80	0.73
8	3	Yes	Proximal	0.86	0.75	0.67
9	3	Yes	95% Proximal	0.85	0.68	0.59
10	Left main	≥50%	—	0.74/8 year[7]	—	—

* 1 indicates single-vessel coronary artery disease; 2, double-vessel coronary artery disease; and 3, triple-vessel coronary artery disease.

out 95% proximal left anterior descending lesions.

Table 1 indicates the percentage of survival over 6 years related to coronary anatomical subgroups 1–9 treated with CABG, PTCA, and medical therapy. The 10th anatomic subgroup was derived from the study by Adler and colleagues,[7] indicating the post-CABG 8-year survival time for left main coronary artery disease.

Conclusions

- CABG surgery, PTCA, or both offered superior long-term survival over medical intervention in all groups.
- PTCA provided the greatest survival in patients with single-vessel disease unless that single vessel was the left anterior descending coronary artery with a 95% proximal stenosis.
- CABG offered greatest survival for all patients with proximal 95% left anterior descending coronary artery lesions.
- CABG is superior in all patients with more extensive disease and with left main coronary artery disease.

SURVIVAL IMPACT: LEFT VENTRICLE FUNCTION AND EXTENT AND SEVERITY OF CHD

An ejection fraction (EF) of 45% or greater is the acceptable norm when assessing left ventricular function. Table 2 summarizes the 8-year survival of patients who were initially treated with surgery.[8] The results and conclusions were made on the basis of 6922 men and 1291 women. On average, survival of up to 15 years was not significantly different for both men and women initially treated with bypass surgery for single- and double-vessel disease (excluding the higher operative mortality in women).

The survival rates and annual mortality were as follows:

- For single-vessel disease, the average 15-year survival rate between men and women was 68% and the annual mortality was 2.1%.
- For double-vessel disease, the average 15-year survival rate between men and women was 54% and the annual mortality was 3.1%.
- For triple-vessel disease, the 15-year sur-

Table 2. 8-Year Survival for Men and Women With Initial Surgical Management*[8]

Variable	Single-Vessel CAD (%)	Double-Vessel CAD (%)	Triple-Vessel CAD (%)
LV function ejection fraction >45%, patients aged >65 years			
Men	0.92	0.89	0.83
Women	0.92	0.82	0.77
Average	0.92	0.86	0.80
LV function ejection fraction ≥45%, patients aged ≥65 years			
Men	0.76	0.82	0.72
Women	0.80	0.73	0.73
Average	0.78	0.78	0.73
LV function ejection fraction <45%, patients aged <65 years			
Men	0.82	0.76	0.69
Women	0.62	0.72	0.58
Average	0.75	0.74	0.64
LV function ejection fraction <45%, patients aged ≥65 years			
Men	0.69	0.59	0.52
Women	0.50	0.66	0.54
Average	0.60	0.63	0.54

* CAD indicates coronary artery disease; LV, left ventricle.

vival rate was significantly different: in men, the survival rate was 45% and the annual mortality was 3.7%; and in women, the survival rate was 32% and the annual mortality was 4.5%.

The 15-year survival *benefit,* however, was similar for men and women.

Between 8 and 10 years after surgery, the slope of the surgical survival curves describing truncated mean survival time become steeper as a result of increased mortality due to saphenous vein graft occlusion. For long-term outcome projections—15 years and longer—the Kaplan-Meier survival averaged 3% mortality per artery per year and the shape of the survival curves never flattened with any treatment mode, resulting in increasing age-specific mortality. The decreasing left EF (below 45%) was correlated with increasing age-specific mortality for all treatment modalities.

ALTERNATIVE INDICATORS OF LEFT VENTRICULAR FUNCTION

Alternative indicators of left ventricular function include heart-wall motion studies performed via techniques such as echocardiography and radionuclide angiography.[9–12] To assess EF, use attending physician statement-reported EFs of ≤45% as normal when given, or should go to the following:

- If there are no resting abnormalities, an EF of >45% should be used.
- If hypokinesis is localized in a single segment, an EF of >45% should be used.
- If multiple-segment hypokinesis is found, if akinesis is present, or both, an EF of <45% should be used.
- If hypokinesis of several large segments or if global hypokinesis is present, an EF of <45% should be used.

Another measure left ventricular function is left ventricular end-diastolic volume, made

Table 3. Bruce Protocol of Multiples of Resting Oxygen Consumption and the Equivalent Ejection Fraction

Completed Stage	Multiple of Resting Oxygen Consumption	Ejection Fraction (%)
0.5	4	—
1	5	—
2	7	<45
3	10	>45
4	13	>45
5	16	>45

by catheter measurement. For an end-diastolic volume of 14–18 mm Hg, an EF of >45% should be used. For an end-diastolic volume of 19–24 mm Hg, an EF of <45% should be used. For an end-diastolic volume of >24 mm Hg, results are not available.

Finally, treadmill exercise capacity[13,14] may be used to assess left ventricular function. Table 3 summarizes the Bruce protocol of multiples of resting oxygen consumption and the equivalent EF.

ALTERNATIVE INDICATORS THE EXTENT AND SEVERITY OF CHD

Alternative indicators of the extent and severity of CHD include the following: angiography results; single-photon emission computerized tomography (SPECT); heart-wall motion; myocardial imaging; electrocardiogram (ECG); exercise stress test; and ECG by default.

Angiography Results

Angiography results, when available, may be used. Ultrafast computed tomography is not equivalent to angiography. The 4 major coronary arteries to be analyzed are left main, left anterior descending, circumflex, and right coronary arteries. The APS-reported ≤75% greater stenosis in a major vessel should be used if given.

SPECT Imaging

SPECT tomographic myocardial imaging consists of thallium or sestamibi scintigraphy performed with single-photon emission.[15–17] SPECT imaging is a more powerful test of prognosis than is the exercise ECG because it is a more sensitive and specific marker of ischemia. It reflects both the extent (proportion of myocardium at risk or number of diseased vessels) and severity (magnitude of ischemia within a given zone or severity of an individual stenosis) of coronary artery disease.

If SPECT imaging finds CHD to be small to medium or inferior or posterior, and if it finds no exercise-induced abnormalities, use class I, stage A. If it finds an anterior medium defect, use class II, stage A. If it finds a large defect in many regions, use class III, stage B.

Heart-Wall Motion

Heart-wall motion may be assessed via radionuclide angiography or echocardiography.[9–12] If hypokinesis is found localized in a single segment, or if no exercise-induced abnormalities are found, use class I, stage A. If hypokinesis is found in multiple segments, if akinesis is found, or if single-segment dyskinesis is found, use class II, stage B. If hypokinesis is found in several large segments or if global hypokinesis is found, and if there is a τ5% drop in EF, use class III, stage B.

Myocardial Imaging

Planar myocardial imaging[18] involves thallium or sestamibi scintigraphy. If a small to medium defect is found, use class I, stage A. If a medium defect is found, use class II, stage A. If a large defect is found in several regions, use class III, stage B.

ECG Stress Test

The ECG exercise stress test[13,14] should only be used if better anatomical information cannot be obtained. If equivocal changes are found, the patient should be referred to a

doctor. If no ischemia is found, use class I, stage A. If the ECG wave segment (ST) is depressed by 1.0–1.9 mm, use class II, stage A. If the ECG ST is depressed by 2.0–2.9 mm, use class III, stage B. The patient should be referred to a doctor if the ECG ST is ∊3.0 mm, if the patient has angina symptoms, if significant arrhythmia is present, if the patient has a drop in blood pressure, or if early or persistent changes are present.

ECG by Default

Current ECG should be used only when more reliable information is not present. The ECG ST, T-wave changes, or both should be assessed. If there are no changes, use class I, stage A. If there are minor changes or if the waves are nonspecific, use class II, stage A. The patient should be referred to a doctor or postponed if there are major changes, if changes are diffuse, if T-waves are inverted, or if the ECG wave segment depression is ≥1.0 mm.

SURVIVAL IMPACT: COMORBIDITIES WITH KNOWN CHD

Comorbidities with known CHD include the following: severity of angina[19]; MI[20–23]; congestive heart failure[24,25]; malignant cardiac arrhythmias[26]; diabetes mellitus[27]; and peripheral vascular disease and central vascular disease.[28]

Severity of Angina

The relative risk, described based on angina characteristics,[19] is described in Table 4. The relative risk increases with the increasing severity of angina are as follows: for stable angina, the relative risk is 1.3 and the additional debits are +25. For progressive angina, the relative risk is 1.5 and the additional debits are +50. For unstable angina, the relative risk is 1.7 and the additional debits are +75.

Myocardial Infarction

Several researchers have assessed the role of MI as a comorbidity with CHD. In the

Table 4. Relative Risk and Angina Characteristics

Characteristic	1-Year Mortality Rate (%)*
Nonanginal chest pain	0.4
Atypical angina	0.8
Stable angina	1.3
Progressive angina	1.5
Unstable angina	1.7

* The mortality rate is for a 60-year-old patient with no comorbid conditions.

Reykjavik Study, Sigurdsson and colleagues[20] evaluated the incidence, prevalence, characteristics, and prognosis associated with clinically unrecognized MI as diagnosed by ECG changes in 9141 men born between 1907 and 1934. The late survival and relative risk for death in patients with different categories of MI are as follows. For unrecognized MI, the 10-year survival is 49%; the 15-year survival is 45%; the relative risk without angina is 4.6; and the relative risk with angina is 16.9. For recognized MI, the percentage of 10-year survival is 62%; the percentage of 15-year survival is 48%; the relative risk without angina is 6.3; and the relative risk without angina is 8.5.

The Reykjavik Study[20] found 10-year survival to be 62% in patients with recognized MI, and they found the annual mortality to be 3.8%. This study found that mortality ratios at age 55 years are not dissimilar to the outcomes noted for double-vessel disease with a left ventricle score of >10 (EF < 45%) treated with CABG in the CASS Registry Study.[8]

Lieu et al[21] found that for single-vessel occlusion, the 3-year survival was 90% and the annual mortality was 3.3%. For double- or triple-vessel occlusion, the 3-year survival was 77% and the annual mortality was 6.0%.

McGovern et al[22] found that for patients who experienced their first MI, the 3-year survival time was 88% for men, with an annual mortality of 4.0%, and 82% for women,

Table 5. Findings of 12-Year Survival by the CASS Study[25]

Heart Failure	Survival (%)	Annual Mortality (%)
No heart failure	81	1.6
Functional class I	71	2.4
Functional class II	54	3.8
Functional class III	25	6.3
Functional class IV	11	7.5*

* Five-year mortality was >50%.

with an annual mortality of 6.0%. They found that in patients with recurrent MI, the 3-year survival time was 73% for men, with an annual mortality of 9.0%, and 64% for women, with an annual mortality of 12.0%.

Finally, the study of Behar et al[23] noted that there was no prognostic difference in late mortality by multivariate analysis between first Q-wave anterior wall versus first Q-wave inferior wall MI (odds ratio, 1.12). For anterior MI, the 5-year survival was 75% and the annual mortality was 5.0%. For inferior MI, the 5-year survival was 81% and the annual mortality was 3.8%.

Congestive Heart Failure

The Framingham Study[24] found that the 10-year mortality rate in patients who experienced heart failure (including both systolic and diastolic dysfunction) was 79% for women and 89% for men. Heart failure mortality increased markedly with age and sex by 27% per decade for men and 61% per decade for women.

The CASS Study[25] found that 12-year survival was dramatically affected by the presence of heart failure at baseline. Table 5 summarizes the findings of the CASS Study.

Congestive heart failure was the clinical variable most strongly associated with the risk of cardiovascular death. In general, the effect of medical therapy on mortality in heart failure is modest at best when treated with angiotensin-converting enzyme inhibi-

tors; digitalis appears to reduce hospitalizations, but it does not appear to reduce mortality. People with heart failure should be referred to a medical director.

Malignant Arrhythmias

O'Rourke[26] discusses second- (Mobitz II) and third-degree heart block, tachyarrhythmia, and bradyarrhythmias. Arrhythmias are only rarely independently associated with cardiac death because the prognosis of most serious arrhythmias is closely related to left ventricular abnormalities and ischemia.

Diabetes Mellitus

The BARI Investigators[27] studied diabetes mellitus patients (type I or type II) who were in treatment; they made up 19% of a randomized cohort of 1829 patients. The researchers found that diabetes patients treated with PTCA had a 5-year survival of 65.5%, and diabetes patients treated with CABG had a 5-year survival of 80.6%. For patients without diabetes mellitus who were treated with PTCA, the 5-year survival was 86.3%; and for patients without diabetes mellitus who were treated with CABG, the 5-year survival was 89.3%.

The age-specific mortality ratios of the BARI Investigators' diabetes mellitus CABG-treated group[27] generally followed the very large magnitude mortality ratios of nondiabetic class III, stage A, CHD treated by CABG in the CASS Study,[6] as summarized in Table 6. Patients with diabetes who were treated with PTCA experienced far worse mortality outcomes; a difference of 15 percentage points in 5-year survival was found in favor of CABG. The overall annual mortality in patients with CHD who had diabetes compared with those who did not have diabetes was as follows: mortality of nondiabetic patients averaged 2% per year for multivessel disease treated with CABG and 2.7% per year for PTCA. Mortality of diabetic patients averaged 4% per year for multivessel disease treated with CABG and 7% per year for PTCA.

Table 6. Comparison of CASS[6] and BARI[27] Studies' Mortality Outcomes for Patients With and Without Diabetes*

CASS Study: 8-Year Survival of Patients Without Diabetes		BARI Study: 5-Year Survival of Patients With Diabetes	
Age (y)	Mortality Ratio	Age (y)	Mortality Ratio
Class III, stage A, treated with CABG (survival ratio, 80%)		Class II, treated with CABG (survival ratio, 80.6%)	
45	1348	45	1970
55	544	55	896
65	104	65	231
Class III, stage B, treated with CABG (survival ratio, 73%)		Class III, treated with PTCA (survival ratio, 65.5%)	
45	1981	45	4000
55	866	55	2000
65	438	65	727

* CABG indicates coronary artery bypass grafting; PTCA, percutaneous transluminal coronary angioplasty.

Peripheral and Cerebral Vascular Disease

Eagle et al[28] compared 2296 patients with known stable coronary artery disease and peripheral vascular disease to 13,953 patients without peripheral vascular disease. Peripheral vascular disease had a highly significant correlation with mortality (chi-square = 25.83; hazard ratio = 1.25). There was a 25% increased risk of dying compared with those without peripheral vascular disease. Cerebrovascular disease correlated with an even worse prognosis (hazard ratio = 1.43, indicating a 43% greater risk of death at any time) than noncerebral peripheral vascular disease.

SURVIVAL IMPACT

Composite Risk Estimation

Califf et al[29] found that fundamentally, selected clinical research groups, exemplified by the Framingham Study and by making use of mathematical modeling, have synthesized multiple causative risk factors into a single composite estimate of probability (relative risk) of future morbid cardiovascular events and mortality for afflicted individuals (the accelerated-failure model). Eight causative risk factors are included: sex, age, high-density lipoprotein levels, total serum cholesterol, systolic blood pressure while at rest, cigarette smoking (yes or no), diagnosis of diabetes (yes or no), and the presence or absence of left ventricular hypertrophy obtained from ECG (yes or no). Depending on the values, categories, and points assigned to these risk factors, 5- and 10-year predictions of the probability (relative risk) of developing a clinical manifestation of coronary artery disease, including death, can be calculated.

Treatment-Related Survival Differences

Bittl[30] and Cameron et al[31] (the latter a CASS Study), in clinical trial results, compared the survival benefits of medicine, surgery, and PTCA. Their findings suggest that the long-range clinical benefit of a specific intervention depends on the anatomic extent, severity, and left ventricular function associated with CHD as well as certain comorbidities such as diabetes mellitus. The indications for a specific category of intervention are clearly illustrated by the differences in long-term survival noted by a number of researchers[6–8,25] comparing the late outcomes of medicine, surgery, and PTCA by CHD class, stage (left ventricle function), and the presence or absence of diabetes.

Bittl[30] compares the long-term survival benefits of new therapies. The efficacy of therapies such as balloon PTCA, coronary stents, directed atherectomy, rotational atherectomy, excimer-laser PTCA, and extraction atherectomy have yet to be demonstrated. These new treatments—except possibly for coronary stents—have not reduced the rates of acute complications or restenosis after coronary PTCA.

The CASS Study[31] compared survival for graft closure of the saphenous vein and the internal thoracic artery. This study found that internal thoracic artery graft was an indepen-

dent predictor of improved survival and was associated with a relative risk of dying of 0.73. An internal thoracic artery graft improved survival; this was also observed in subgroups including patients ≥65 years of age, both men and women, and patients with impaired ventricular function. The internal thoracic artery graft survival advantage increased with time, suggesting that the initial selection of the conduit was a more important factor in survival than problems appearing long after surgery, such as the progression of coronary disease. There is an increased likelihood of saphenous vein graft closure 8–10 years after CABG.

PREDICTION OF RISK WITH NONINVASIVE TESTING

A fundamental principle of probabilistic decision-making is that the probability of a bad outcome depends partly on the prior probability of that outcome in the group as a whole (Bayes Theorem). Prior probability is then modified by additional information obtained from diagnostic tests or risk scores. Therefore, testing is not expected to be of much value in patients who have a low pretest risk; pretest probability begins only in patients with a moderate to high likelihood of coronary artery disease.

Pharmacologic Stress Perfusion Imaging (Scintigraphy)

In patients unable to perform maximal stress tests, pharmacologic stressors may be used, including dipyridamole, adenosine, and dobutamine. Younis et al[9] used dipyridamole-thallium-201 perfusion imaging and found the sensitivity to be 89%–100% and the specificity to be 53%–80%. This method was apparently superior to stress testing and is a useful test for patients who cannot exercise. Shaw et al[10] used dobutamine stress echocardiography. They found that in patients undergoing vascular surgery, the presence of new or worsening dys-synergy was associated with a 5- to 14-fold increase in risk of subsequent death or reinfarction.

Exercise Radionuclide Angiography

Jones et al[11] used exercise radionuclide angiography and found that regardless of the radionuclide technique (first-pass or gated), exercise EF is the best univariate and multivariate predictor of a cardiac event. The summary odds of a cardiac event are fourfold higher for patients with an abnormal peak radionuclide angiogram versus those with a normal examination. They also found that patients who had a normal EF but who experienced ventricular wall motion or functional abnormalities during exercise were associated with worsening 4-year survival.

Exercise Echocardiography

Poldermans et al[12] found that adverse outcomes are more likely in patients in whom new or increased heart-wall motion abnormalities can be induced by exercise or pharmacologic agents such as dipyridamole, dobutamine, or dobutamine with atropine. Patients without clinical risk factors rarely had positive tests or postoperative events. The researchers used the following to assign class and stage to patients: in patients with local single-segment hypokinesis or no exercise-induced abnormality, they assigned class I, stage A. In patients with multiple-segment hypokinesis, akinesis, or single-segment dyskinesis, they assigned class II. In patients with hypokinesis of many large segments or patients with global hypokinesis and a τ5% drop in EF, they assigned class III, stage B.

Exercise ECG

Mark et al[13] and Singer and Bruce[14] studied and followed up on 7872 men in 3 diagnostic cohorts between 1971 and 1981. A total of 4105 men were healthy (mean age, 44.6 years), and 1396 men were hypertensive (mean age, 50.0 years). Hypertensive men were so classified if there was a prior diagnosis of hypertension, either treated or untreated. A total of 2371 men in their studies had chronic heart disease (mean age, 53.6 years).

Table 7. Prediction of Risk by Exercise Electrocardiogram Responses in Healthy Men, Men With Hypertension, and Men With Chronic Heart Disease, All Ages Combined

Risk Group	Healthy Men Mortality Ratio (%)	Men With Hypertension Mortality Ratio (%)	Men With Chronic Heart Disease Mortality Ratio (%)
Low	58	156	436
Moderate	91	190	595
High	550	305	1340

For an exercise response in healthy men and men with hypertension to be considered abnormal, the following criteria had to be met:

- Exercise-induced angina or an exercise duration of <6 minutes.
- A maximal heart rate of <90% of the age-predicted value.
- An ECG ST depression of 1 mm or more.

Men with or without hypertension were classified as low risk if none of these symptoms were present. Moderate-risk men with or without hypertension had risk factors present but did not experience abnormal responses to exercise. High-risk men without hypertension met 2 or more of the above criteria and had at least 1 additional risk factor; and high-risk men with hypertension had at least 1 abnormal exercise response and 1 or more risk factors.

The abnormal exercise responses for men with chronic heart disease are defined as follows:

- Low-risk group: Absence of exertional myocardial ischemia and absence of left ventricular dysfunction (multiples of resting oxygen consumption achieved).
- Moderate-risk group: ECG ST depression of 1 mm or more and chest pain with exercise.
- High-risk group: Cardiac enlargement at rest; a duration of exercise <3 minutes (less than stage II), and peak exercise systolic pressure of <130 mm Hg.

Table 7 summarizes the prediction of risk by exercise ECG response.

Planar Thallium-201 Stress Myocardial Perfusion Imaging

Wackers et al[18] found that positive planar thallium-201 stress myocardial perfusion imaging tests indicating "transient perfusion defects" that fill in the delayed images are consistent with exercise-induced myocardial ischemia. A high-risk scan may be defined as the presence of several perfusion defects, increased lung uptake, or left ventricular dilatation. Multiple-perfusion defects indicate multivessel disease. Scarred or fixed defects reflect infarcted tissue. Unfortunately, planar imaging is suboptimal (higher false-negative and false-positive results compared with SPECT) for assessing myocardial perfusion because frequent overlap of normally and abnormally perfused myocardial regions limits its ability to detect, localize, and size myocardial perfusion defects.

SPECT Tomography Myocardial Perfusion Imaging

SPECT tomography is superior to planar thallium imaging[15–17] in its sensitivity and specificity, including its enhancement of the overall detection of exercise-induced ischemia, especially in the circumflex artery distribution; in its better prediction of extent of disease; and in its more accurate localization of stenosed branches of coronary vessels re-

sponsible for a given perfusion defect. Most important is its quantitative (digital) analysis ability for image interpretation, which significantly improves visual analysis of the tomographic slices.

TRENDS IN MORTALITY BY AGE AND TIME

Age-specific mortality analyses provide a smoothly graded progression of excess mortality by CHD class, stage, treatment mode, and pertinent comorbidity that is useful for risk classification. A Framingham Study composite risk calculation model is available from me upon request.

Mortality ratios decreased with increasing age, but within a very high range, for example, in the CASS Registry study by Davis and colleagues.[8] Mortality ratios decreased from 733% to 190% in the low-risk (class I, stage A) group. They decreased from 3394% to 1172% in the moderate-risk (class III, stage A) group. And they decreased from 4883% to 1354% in the high-risk (class III, stage B) group.

Excess death rate progression is largely due to the increase in mean expected annual mortality, q', with advancing age. Excess death rate, however, is relatively constant and decreased only moderately with increasing age. For low-risk groups, the excess death rate was 3 to 5 per 1000 (ages 45 to 65 years). For moderate-risk groups, the rate was 33 per 1000 to 11 per 1000 (ages 45 to 65 years). For high-risk groups, the excess death rate remained constant, from about 49 per 1000 at age 45 years to 46 per 1000 at age 65 years.

Interestingly, the constancy in excess death rate with advancing age represents a characteristic pattern of the late mortality experience in most series of chronic heart disease and post-MI patients in which mean survival—although truncated—is extended, but the steep slope of Kaplan-Meier CHD survival curves never flattens with any treatment mode.

The relative risk of death between patients with angina pectoris and MI is summarized in Table 8. Table 9 provides comparative survival and mortality information about patients who were initially treated with surgery. Table 10 summarizes the 15-year survival of patients who were initially managed with surgery.

UNDERWRITING CONSIDERATIONS AND REQUIREMENTS

Accurate CHD underwriting presumes pertinent current information (obtained within 1 year) on which to assess coronary artery disease status:

- Extent and severity of coronary class.
- Stage (left ventricular function).
- Comorbidities.
- Treatment modes.
- Risk factors (for composite relative risk estimation) and disease progression (recurrence of clinical signs and symptoms in those with treated chronic heart disease).
- Exercise prognostic markers.

Alternative indicators of CHD class and stage are provided above; these should only be used when first-priority, pertinent clinical information is unavailable. First-priority information includes APS (indicating direct measurement of CHD class and stage), history of systems, blood profile, ECG (both current and past), invasive (coronary catheterizations), and noninvasive tests (for example, exercise stress tests and echocardiograms). However, a comprehensive angiogram followed by annual imaging stress tests can be used for underwriting even several years later.

Steps in Underwriting CHD

Consideration for life insurance should be postponed for at least 6 months after successful therapy has ended if the CHD was acute and recent (within 6 months) and if the patient has tertiary end outcomes including angina, MI, congestive failure, PTCA, CABG, or malignant dysrhythmias.

For chronic CHD that has been in evidence

Table 8. Comparison of Late Survival, Mortality, and Relative Risk of Death Between Patients With Angina Pectoris and Patients With Myocardial Infarction

| | Survival | | Annual Mortality | | Relative Risk of Death |
Variable and Reference	%	Time Survival Was Assessed	%	Average (%)	
Angina pectoris					
Medical treatment[6]	80	6 years	3.3	—	—
Percutaneous transluminal coronary angioplasty[6]	85	6 years	2.5	—	—
Coronary artery bypass grafting[6]	89	6 years	1.8	2.5	—
Myocardial infarction*					
Unrecognized myocardial infarction[20]	49	10 years	(5.1)	—	—
Recognized myocardial infarction[20]	62	10 years	3.8	—	1.52
Single-vessel occlusion[21]	90	3 years	3.3	—	1.32
Double- or triple-vessel occlusion[21]	77	3 years	7.7	5.5	3.08
First myocardial infarction, men[22]	88	3 years	4.0	—	—
First myocardial infarction, women[22]	82	3 years	6.0	5.0	2.0
Anterior myocardial infarction[23]	75	5 years	5.0	—	—
Inferior myocardial infarction[23]	81	5 years	3.8	4.4	1.76
Recurrent myocardial infarction, men[22]	73	3 years	9.0	—	—
Recurrent myocardial infarction, women[22]	64	3 years	12.0	10.5	4.2

* The average percentage of annual mortality for all myocardial infarctions is 4.8%, with a relative risk of death of 1.87.

6 months or longer, follow the underwriting steps below, and use the defaults as necessary.

- Assign coronary class on the basis of anatomic extent (number of diseased major vessels) and severity (75% or greater stenosis).
- Assign a coronary stage, which is made on the basis of left ventricular function. Stage A comprises a left ventricular EF of 45% or more; stage B comprises a left ventricular EF of <45%.
- Review comorbidities, risk factors, treatment modes, and test results.
- Review APS to determine chronic CHD stability or progression.
- Determine the age-specific basic rating.
- Modify the basic rating as follows. Additional debits are appropriate for comorbidities, composite risk factors (relative risk), question of medical versus surgical therapies (see a medical director for this), ad-

verse test results indicating CHD progression, ischemia, or arrhythmias. No credits are given if the patient is within 1 year of diagnosis of CHD or has a history of coronary event; credits are not to exceed −50 overall for CHD cases; and −25 to −50 credits are given for complete and negative noninvasive testing.

- Refer any questions to the medical director.

ANGINA PECTORIS

Angina pectoris is a clinical syndrome typically characterized by exertion-induced substernal chest pain indicating myocardial ischemia. It usually has a slow onset and offset, and it is frequently associated with transient ST-segment depression on ECG. It is relieved by rest and by nitroglycerine. It may be induced by excitement, cold weather, and eating heavy meals.

Table 9. Comparative Survival and Mortality of Patients Initially Managed With Surgery*[8]

Left Ventricle Function†	Entrant, Sex (n)	8 Years			15 Years		
		Cumulative Survival (%)	Select Mortality Ratio (Q)	Mean Annual Excess Death Rate	Cumulative Survival (%)	Select Mortality Ratio (Q)	Mean Annual Excess Death Rate
Single-vessel CAD‡							
Age <65 years	Male (854)	92	(3)	(0.0062)	66	135	0.0041
	Female (242)	92	87	(0.0006)	69	110	0.0012
	Average	92	42	(0.0030)	67.5	160	0.0059
Age ≥65 years	Male (54)	76	71	(0.0042)	—	—	—
	Female (30)	80	219	0.0080	—	—	—
	Average	78	129	0.0030	—	—	—
Double-vessel CAD							
Age <65 years	Male (1367)	89	65	(0.0021)	56	225	0.0147
	Female (259)	82	409	0.0136	51	462	0.0286
	Average	85.5	215	0.0060	53.5	326	0.0223
Age ≥65 years	Male (141)	82	8	(0.0134)	—	—	—
	Female (60)	73	384	0.0191	—	—	—
	Average	77.5	136	0.0038	—	—	—
Triple-vessel CAD							
Age <65 years	Male (1836)	83	207	0.0065	45	344	0.0286
	Female (259)	77	584	0.0212	32	832	0.0579
	Average	80	371	0.0141	38.5	537	0.0432
Age ≥65 years	Male (315)	72	116	0.0023	—	—	—
	Female (99)	73	384	0.0191	—	—	—
	Average	73	204	0.0110	—	—	—
Normal left ventricle function, all ages	Male (60)	—	—	—	—	187	0.0102
	Female (52)	—	—	—	—	581	0.0308
	Average	—	—	—	—	297	0.0194
Abnormal left ventricle function, all ages	Male (36)	—	—	—	—	463	0.0426
	Female (32)	—	—	—	—	832	0.0579
	Average (34)	—	—	—	—	616	0.0509

* The mean age of the entrants into the CASS Study[8] averaged 56.1 years; 54.6% ± 8.5% of the patients were men and 57.5% ± 8.7% were women ($P <$ .0001). The basis for expected mortality was 1975–1980 Select and Ultimate tables. Numbers in parentheses have a negative value (zero debits). There was a total of 8213 entrants, 6922 men and 1291 women.

† Left ventricle function had an ejection fraction of ≥45%.

‡ CAD indicates coronary artery disease.

Table 10. 15-Year Survival With Initial Surgical Management*

Variable	Men (%)	Operative Mortality of Men (%)	Women (%)	Operative Mortality of Women (%)	P Value for Sex	P Value for Operative Mortality
Single-vessel CAD†	66	1.1	69	3.3	=.89	=.006
Double-vessel CAD	56	1.9	51	5.1	=.04	=.0001
Triple-vessel CAD	45	3.2	32	6.7	<.0001	<.0001
Left ventricular score <10	60	1.6	52	4.7	=.0009	<.0001
Left ventricular score ≥10	36	4.2	32	7.8	=.002	=.005

* Mortality rates of patients treated with coronary artery bypass grafting increased after 8 years, probably as a result of saphenous vein graft closure, so that at 15 years, survival rates were similar for surgically and medically managed patients. On average, the 15-year survival for men and women differed only by their differences in operative mortality. The survival benefit of bypass surgery was similar for both men and women.

† CAD indicates coronary artery disease.

Stable Angina Pectoris

Stable angina pectoris is generally characterized by the unchanging character of the frequency, severity, and duration of pain and ECG changes and by response to treatment. It is frequently associated with single- or double-vessel coronary artery disease with normal EF of >45% (class I or II, stage A CHD). It usually does not include the following:

- 95% stenosis of the left anterior descending coronary artery.
- >75% proximal stenosis of the left anterior descending coronary artery.
- Triple-vessel or left main disease.

The 6-year survival[6] for stable angina pectoris is 90% with medical treatment (annual mortality, 1.7%); 93% with PTCA treatment (annual mortality, 1.2%); and 91% with CABG treatment (annual mortality, 1.5%).

The mortality risk classification for stable angina pectoris should be postponed 6 months from diagnosis or successful completion of therapy. The CHD basic risk classification should be used if adequate information is available concerning CHD class and stage and should be used for the best-case scenario. Otherwise, proceed to the default below: with inadequate information, consider rating as class II, stage A, if the ECG is stable and has normal or minor T-wave changes or poor R-wave progression only in precordial leads, if the patient has a stable clinical pattern, or if the patient has only received medical treatment. The basic rating should be modified as appropriate.

Progressive Angina Pectoris

Progressive angina pectoris is characterized by progressive increases in the frequency of pain within a 2–8 week period; in the severity of pain; in the duration of pain; or if the pain has a crescendo-decrescendo quality. It may occur with only minimal exertion or even at rest. Patients may possibly experience resistance to the usual pain medications. Patients with progressive angina pectoris have stable ECG with ST-segment depression, major T-wave changes, major conduction defects, and left anterior hemiblock or complete right bundle branch block. Progressive angina pectoris is frequently associated with single-, double-, or triple-vessel disease, including 95% stenosis of proximal left anterior descending coronary artery and a normal EF.

The 6-year survival[6] of patients with progressive angina pectoris is as follows: the survival is 72% for patients who receive medical treatment (annual mortality, 4.7%); 79% for patients who receive PTCA (annual mortality, 3.5%); and 87% for patients who receive CABG (annual mortality, 2.2%).

The mortality risk classification should be postponed 6 months from the successful completion of therapy. Then, the CHD basic rating classification should be used if adequate treatment and follow-up information concerning CHD class and stage is available. It should also be used for the best-case scenario if information on CHD class and stage is given. Otherwise, proceed to these defaults. With inadequate information, consider the CHD to be class III, stage A, if the patient has stable ECG readings but the findings are above the clinical characteristics and if the patient has a clinical history of continuing progressive pattern additional debits may be applied. Modify the basic ratings as appropriate.

Unstable Angina Pectoris

Unstable angina pectoris[32] is characterized by prolonged coronary pain that is clinically suggestive of acute MI without enzymatic or ECG evidence of infarction. In high-risk individuals, at least one of the following features must be present:

- Prolonged ($\geq$20 minutes), ongoing pain while at rest.
- Pulmonary edema that is ischemic in origin.
- Angina while at rest with dynamic ST-segment changes on ECG ($>$1 mm).
- Angina with new or worsening mitral reflux murmur.
- Angina with S3 murmur or new or worsening rales.
- Angina with hypotension.

The 8-year survival of patients treated with CABG[7] is 74% (annual mortality, 3.3%); the 12-year survival of patients treated medically only[33] is 40% (annual mortality, 5.0%).

The mortality risk classification should be postponed for 6 months from the successful completion of therapy. Then, the CHD basic rating classification should be used. The CHD basic rating classification should be used if adequate treatment and follow-up information concerning CHD class and stage is available. It should also use for the best-case scenario if information on CHD class and stage is given. Otherwise, proceed to the defaults outlined below if only scanty information is given.

Class III, stage A, should be considered if information about whether the patient has received PTCA or CABG is known, but no information about class or stage is known; and consider this if APS definitively indicates close follow-up and successful resolution of clinical and ECG instability. Determination should be postponed if inadequate information for accurate risk assessment exists. The basic rating should be modified as appropriate.

Variant (Prinzmetal) Angina

Variant angina[34,35] is diagnosed by documenting ST segment elevation (as opposed to the ST segment depression normally associated with angina) during anginal pain and returning to baseline on resolution of pain. It may be associated with MI, life-threatening ventricular arrhythmias, and heart block. Survival[35] is as follows:

- 85% of patients have proximal fixed obstructive lesions in any of the 4 major coronary arteries noted by angiography with spasm occurring at these sites.
- Survival equates with the class, stage, treatment modality, and comorbidities associated with obstructive CHD.
- 15% of patients have no significant coronary artery lesions at angiography and should be treated medically with nitrates and calcium channel blockers.

Mortality risk classification should be postponed for 6 months from successful completion of therapy. For patients with obstructive CHD, the CHD basic rating classification should be used if information about the CHD class and stage is available. Patients with no obstructive CHD and who have had successful medical treatment should receive a modified rating as appropriate.

SILENT ISCHEMIA

Silent ischemia[36–38] is ischemia without angina, and it is common.[36] It can be detected by exercise testing, which shows ischemic ST depression, thallium defects with reperfusion, or new chest-wall motion abnormalities that were discovered by use of radionuclide imaging or echocardiography.

Mortality from MI[37] in patients with silent ischemia is at least as high as that in patients with angina. For these patients, PTCA or CABG is more effective than medical treatment.[38]

Mortality risk classification for silent ischemia is as follows. The CHD basic rating classification should be used if the treatment regiment is known.

SYNDROME X

Syndrome X is discussed by Chauhan et al[39] and Egashira et al.[40] It is angina that is documented by ECG or physiologic studies but nonetheless has normal or minimally diseased coronary arteries (as found by angiography) and has no evidence of spasm or valvular heart disease or any detectable left ventricular myocardial abnormality.[39] It occurs in men and women and has an excellent overall prognosis. Despite various plausible etiologic explanations,[40] the cause remains obscure. The mortality risk classification for Syndrome X is usually standard.

MYOCARDIAL INFARCTION

Acute MI[41] is the classic, sudden tertiary end-point syndrome of ischemic CHD. It is characterized by the full thickness death of myocardial tissue in the specific ventricular regions supplied by one or more totally occluded coronary arteries, and it is accompanied by serial ECG changes and the transient rise in the serum levels of enzymes released from the myocardium. The term may also be used to describe myocardial fibrosis (silent infarction) that develops during a period of months or years in patients with silent coronary artery disease.

In the United States, MI occurs in approximately 1,500,000 people annually; 800,000 are hospitalized and 500,000 die suddenly outside of the hospital. It is the leading cause of death in the United States and in most other developed countries. The disease is much more prevalent in men than in women up to age 74 years, and the occurrences increase steeply with age in both sexes.

Determinants of Survival and Late Mortality

Late risk of death (6 months and beyond) is directly related to the specific mortality burden of the following:

- Class and stage of obstructive CHD.
- Continued ischemia and angina.
- Disease progression.
- Electrical instabilities (arrhythmias).
- Treatment-related differences.
- Comorbidities and risk factors.

The mortality risk classification should be postponed for 6 months from successful completion of therapy. Then, for best-case scenario, use the CHD basic rating classification if information concerning coronary artery disease class and stage is available. Otherwise, default to class II, stage A, if information is available concerning stable ECG (moderate Q-wave and ST- and T-wave residuals only); if the patient has had a negative exercise stress test within 2 years; if the patient has no recurrent clinical signs and symptoms of CHD; and if the patient's exercise echocardiogram has 1 moderate or 2 small areas hypokinesis only additional debits should be applied. With minimal information and ''what if'' scenarios, refer the patient to a doctor and consider no offer. Modify the basic rating as appropriate. Patients with recurrent MI should be referred to a doctor and consider no offer.

CONGESTIVE HEART FAILURE

Congestive heart failure[24,25,32] is not a specific disease but a syndrome composed of signs and symptoms of pulmonary venous

congestion, systemic venous congestion, low cardiac output, or a combination of these symptoms. It is the clinical comorbidity most strongly associated with the risk of cardiovascular death. In the Framingham study,[24] over 75% of those who developed heart failure had hypertension, and nearly 50% of men and 25% of women had CHD. In the SOLVD registry study[42] (EF of 35% or less), CHD accounted for about 50% of patients, hypertension 15%, idiopathic cardiomyopathy 18%, and valve disease 7%.

The risk factors for heart failure include age, systemic hypertension including systolic hypertension, diabetes, obesity, smoking, and possibly hypercholesterolemia. The determinants of survival and late mortality are as follows:

- Left ventricular EF. This is the single most powerful predictor of survival in many studies.
- Higher left ventricle filling pressure. This is a predictor of lower survival rates.
- Low cardiac index (cardiac output).
- Ventricular arrhythmias, such as frequent premature ventricular contractions and nonsustained ventricular tachycardia.
- Hypertension and ECG findings of left ventricular hypertrophy with strain.

The 10-year survival[24] for congestive heart failure is 16%; the annual mortality is 8.4%.

The mortality risk classification for congestive heart failure is as follows. The patient should be declined if congestive heart failure is present on examination; if the patient has a history of CHD, diabetes, hypertension, valve disorders, and congenital and other forms of primary heart disease; or if the patient has idiopathic congestive (dilated) cardiomyopathy.

For patients with transient secondary congestive cardiomyopathy, which may be the result of alcohol or drugs, toxins, peripartum, infections (bacterial, viral, or parasitic), sarcoidosis, connective tissue disorders, severe anemia, vitamin deficiency (beriberi), or paroxysmal atrial fibrillation unrelated to structural heart disease, if they are recovered and their heart size has returned to normal, the patient should be postponed for 6 months.

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