

13638 COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

TABLE I
Criteria for Congestive Heart Failure*

Major criteria
Paroxysmal nocturnal dyspnea or orthopnea
Neck vein distension
Rales
Cardiomegaly
Acute pulmonary edema
S ₃ gallop
Increased venous pressure ≥ 16 cm H ₂ O
Circulation time ≥ 25 second
Hepatjugular reflux
Minor criteria
Ankle edema
Night cough
Dyspnea on exertion
Hepatomegaly
Pleural effusion
Vital capacity decreased 1/3 from maximum
Tachycardia (rate ≥ 120 /min)
Major or minor criterion,
Weight loss ≥ 4.5 kg in 5 days in response to treatment

* Patients were considered to have congestive heart failure if two major or one major and two minor criteria were present concurrently.

TABLE II
Annual Incidence of Congestive Heart Failure by Age, Sex and Presence of Prior Coronary or Rheumatic Heart Disease: 18 Year Follow-Up Study

Age (yr)	Total Population			Subjects with Prior CHD or RHD		
	Person Years at Risk	New CHF Events	Incidence per 10,000	Person Years at Risk	New CHF Events	Incidence per 10,000
Men						
45-54	14,109	28	20	1,074	17	158
55-64	10,414	43	41	1,564	28	179
65-74	3,700	26	70	762	14	184
Women						
45-54	17,598	11	6	678	5	74
55-64	13,688	41	30	1,202	24	200
65-74	5,232	34	65	766	20	261

CHD = coronary heart disease; CHF = congestive heart failure; RHD = rheumatic heart disease.

Criteria

At each biennial examination a diagnosis of congestive heart failure was entertained on clinical grounds and the opinion of a second examiner obtained. All suspected cases thus uncovered from biennial clinic examinations or from interim information obtained from hospital records and physician's office reports were reviewed by a panel of investigators using uniform criteria. The diagnosis of congestive heart failure was accepted only in persons with at least two major or one major and two minor criteria present concur-

rently as indicated in Table I. Minor criteria that could be attributed to some other medical condition were rejected. Only about half the persons diagnosed as having congestive heart failure at the time of the clinical examination on the basis of the examination or interim hospital or physician's office information were included in this study.

Persons who had congestive failure at the time of the initial examination were excluded, leaving a population of 5,192 men and women aged 30 to 62 years at risk. Follow-up study during the ensuing 18 years was reasonably complete, with 80 percent of subjects receiving every possible biennial examination. The remaining 20 percent were seen at less frequent intervals, and admissions to the only general hospital in town were monitored daily. Only 2 percent of the sample were completely lost to follow-up study.

Glucose intolerance was assessed from casual blood sugar determinations, urinary sugar values, or a history of clinical "diabetes." Blood sugar levels were determined by the Somogy-Nelson method. A diagnosis of diabetes was made in subjects who (1) had an abnormal glucose tolerance test during hospitalization or their physician's laboratory evaluation, (2) were taking insulin or oral hypoglycemic agents, or (3) had casual blood sugar values > 160 mg/100 ml.

Statistical Techniques

Incidence rates for congestive failure were ascertained according to diabetic status, age, sex and coronary (or rheumatic) heart disease status. Subjects were reclassified by age at each examination; a case was defined as a subject free of congestive heart failure at a given examination but having failure at the time of the next biennial examination. The method of Mantel-Haenszel³ was used to construct summary chi squares to assess differences in the frequency of congestive heart failure in diabetic and nondiabetic subjects and to estimate the risk of heart failure in the presence of diabetes. To assess the joint and net effect of diabetes taking into account other related atherogenic variables, multivariate coefficients were computed and compared with bivariate coefficients taking only age into account. Analysis was confined to subjects aged 45 to 74 years since too few cases occurred before age 45 for meaningful analysis. The bivariate function to assess the regression of incidence of congestive heart failure on diabetic status and age was estimated by the method of Walker and Duncan.⁴ The multivariate function was estimated by the Walker and Duncan maximal likelihood method using, in addition to the variables of age and diabetic status, systolic blood pressure, serum cholesterol and relative weight.

Results

Frequency of congestive heart failure: During the 18 year follow-up period, congestive heart failure, as defined by the specific criteria, developed in 97 men and 86 women aged 45 to 74 years. The incidence of heart failure increased sharply with age. As expected, the incidence was considerably greater in the subjects with prior coronary or rheumatic heart disease. There was a male predominance at all ages (Table II), but this predominance appeared to wane with advancing age. Among subjects with prior coronary or rheumatic heart disease, there was a male predominance only under age 55 years. About half of the subjects with a diagnosis of congestive heart failure had coronary disease; more than three-fourths had hypertension. About 16 percent had antecedent diabetes, an apparent excess over the expected rate.¹