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Relationship of coronary risk factors to hemodialysis-associated ischemic heart disease

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Relationship of coronary risk factors to hemodialysis-associated ischemic heart disease. The records of 320 hemodialysis patients at risk for developing ischemic heart disease (IHD) were examined to determine the influence of the established risk factors of blood pressure, smoking, serum triglycerides, and age on the incidence of IHD and to develop coronary risk profiles for the hemodialysis population. The role of packed red blood cell volume, race, sex, and cause of renal failure on the development of IHD were also examined. None of these risk factors alone, with the exception of age and chronic pyelonephritis, were found to contribute significantly to the incidence of dialysis-acquired IHD. When the joint contribution of these variables was analyzed using Cox regression analysis, race and diastolic hypertension also were discovered to contribute significantly to IHD. However, smoking and serum triglycerides were not found to be significant risk factors. From these data, it is concluded that older patients are a greater risk than younger patients, that white patients are at a greater risk than black patients, that patients with elevated diastolic blood pressure are at an increased risk and that patients with chronic pyelonephritis as the underlying renal disease are at an increased risk.

Relation entre les facteurs de risque coronarien à cardiopathies ischemiques au cours associé avec hémodialysés. Les dossiers de 320 malades hémodialysés risquant de développer une cardiopathe ischémique (IHD) aient été examiné afin de déterminer l'influence des facteurs de risque connus, pression artérielle, tabagisme, triglycérides sériques et âge sur l'incidence de IHD et de développer des profils de risque coronarien pour la population des hémodialysés. Le rôle du volume des globules rouges, de la race, du sexe, et de la cause de l'insuffisance rénale dans le développement de l'IHD aient été examiné aussi. Aucun de ces facteurs de risque en soi, à l'exception de l'âge et de la pyélonéphrite chronique, aient été trouvé contribuer significativement à l'incidence de l'IHD acquise lors de la dialyse. Lorsque la contribution conjointe de ces variables a été analysée par régression de Cox, la race et l'hypertension diastolique se sont également révélées contribuer significativement à l'IHD. En revanche, le tabagisme et les triglycérides sériques ne sont pas apparus comme étant des facteurs de risque significatifs. De ces données il aie été conclu que les malades plus âgés ont un plus grand risque que les plus jeunes, que les malades blancs ont un plus grand risque que les noirs, que les malades ayant une pression artérielle diastolique élevée ont un risque accru, et que les malades ayant une pyélonéphrite chronique comme néphropathie sous-jacente ont un risque augmenté.

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Patients with endstage renal disease undergoing maintenance hemodialysis have an increased prevalence of conventional coronary risk factors [1–4]. This observation, together with a high cardiovascular mortality, has led to the view that hemodialysis patients have an accelerated rate of atherosclerosis and an increased mortality from coronary artery disease [5]. While the concept of accelerated atherosclerosis and accelerated coronary mortality in this population has been questioned by several investigators including ourselves [6–9], there is agreement that coronary risk factors, especially hypertriglyceridemia, hypertension and left ventricular hypertrophy (LVH), are present with increased frequency. However, few detailed studies have been carried out to examine whether these or other risk factors indeed are associated significantly with the development of dialysis-related ischemic heart disease (IHD). Two studies of the Seattle dialysis population have shown an association between smoking and hypertension and mortality of all causes, including stroke and myocardial infarction [10], and an association between hypertriglyceridemia and cardiovascular events [11]. Since these studies did not exclude patients with preexisting ischemic cardiovascular disease and because of the inordinately high death rates from myocardial infarction when compared to other published reports [9, 12], these demonstrated associations truly may not reflect a relationship between conventional risk factors and presumed increased coronary risk following the initiation of hemodialysis. In another study, Vincenti et al [13] found an association between hypertension and hemodialysis-associated atherosclerosis. However, the importance of this single variable in the development of dialysis-related atherosclerosis may be questioned since no age adjustments were made in this study population in which the most severe atherosclerotic disease was found in patients who were more than a decade older than those with either minimal or moderate disease.

Previously, we examined the incidence of IHD and the prevalence of conventional coronary risk factors in a large hemodialysis population. In this study, we evaluate the association of established coronary risk factors and some additional factors with the development of IHD in a hemodialysis population to investigate the relative influence of these factors on coronary risk and to develop a coronary risk profile for our hemodialysis population.

Table 1. Causes of endstage in hemodialysis population of The University of Alabama Medical Center

Cause	Number	Percent
Unknown	118	31.0
Glomerulonephritis	83	21.7
Malignant hypertension	65	17.0
Polycystic kidney disease	32	8.3
Pyelonephritis	15	4.0
Interstitial nephritis	17	4.4
Diabetic nephropathy	12	3.0
Obstructive nephropathy	16	4.2
Miscellaneous[a]	24	6.2
Total	*382*	*100.0*

[a] These include: myeloma kidney, 5; hereditary nephritis, 5; cortical necrosis, 3; medullary cystic disease, 2; amyloidosis, 5; renal cell carcinoma, 1; renovascular disease, 2; and hypoplasia, 1.

Methods

We reviewed the records of 382 patients who entered the maintenance hemodialysis program at The University of Alabama in Birmingham and at the Birmingham Veterans Administration Medical Center between January 1971 and December 1975. These patients were followed for intervals up to 7 years (January 1971 to January 1978). The mean duration of this follow-up was 29.5 months (median, 28 months; range, 1 to 84 months). The characteristics of this group and the criteria for acceptance into our hemodialysis program have been described previously [9]. Of the 382 patients entering the maintenance hemodialysis program during this time, 320 patients had no evidence for ischemic heart disease prior to the onset of hemodialysis. These patients constituted the population at risk and were the basis for our analysis. The mean age of this study population was 42.2 ± SD 16.1 (age range, 6 to 79 years). There were 165 women and 155 men. The group was divided almost evenly between blacks and whites (164 vs. 156, respectively).

Table 1 shows the distribution of diseases causing endstage renal disease in our population. Glomerulonephritis was diagnosed if it was documented by renal biopsy, if the patient had a systemic disease often associated with glomerulonephritis, or if urinalysis and urinary electrolyte and protein excretion suggested this diagnosis. Malignant hypertension was diagnosed if the patient had diastolic blood pressures greater than 130 mm Hg in association with grades 3 or 4 hypertensive retinopathy but in the absence of any evidence for other causes of renal disease. Polycystic kidney disease was diagnosed by physical examination, family history, and x-ray. Pyelonephritis was said to be present in patients with chronically infected urine in the absence of other causes of renal disease. Interstitial nephritis was said to be present if the patient had a history of analgesic overuse, long-term exposure to lead, usually in the form of moonshine whiskey, or recurrent stone passage. Objective evidence of interstitial nephritis and pyelonephritis included x-ray evidence of papillary necrosis or asymmetrically shrunken kidneys. The presence of hyperchloremic acidosis and urinary concentrating defects were considered as functional parameters for this diagnosis. Diabetic nephropathy was diagnosed as progressive renal failure in a patient with diabetes mellitus and evidence of diabetic retinopathy but in the absence of other causes of renal disease. Obstructive uropathy was diagnosed in patients with a history of obstructive symptoms, stones, and x-ray evidence of reflux or hydronephrosis. If no diagnosis could be established, the patient was placed in the category of unknown disease.

IHD was diagnosed when typical signs and symptoms of angina pectoris or myocardial infarction occurred. The diagnosis of myocardial infarction was confirmed by serial electrocardiographic (ECG) QRST changes, by enzyme changes, or, as in one instance, by autopsy. The clinical, laboratory, and ECG criteria used to make the diagnosis of IHD were reviewed in detail by Logue and Hurst [14]. LVH was diagnosed using the Estes ECG criteria [15]. Fasting plasma triglyceride concentrations were obtained during the first month of hemodialysis and were determined by standard laboratory techniques. Age-related normal values were similar to those described by Frederickson, Levy, and Lees [16]. Initial blood pressure represents that pressure measured prior to the first hemodialysis. Dialysis blood pressure represents the average blood pressure recorded prior to each dialysis treatment during the course of hemodialysis. A patient was considered to have a positive smoking history if ten or more cigarettes were smoked per day. Pipe smoking, cigar smoking, tobacco chewing, and snuff usage occurred infrequently and, therefore, were not included in the consideration of tobacco use.

An investigation was made into the possible joint contributions of the variables recorded for these patients to the probability of acquiring IHD. To do this, we used the method of Cox regression analysis. The Cox regression technique is a method of survival analysis which investigates the simultaneous explanatory power of a number of independent variables in predicting the likelihood of survival or occurrence of an event [17]. One or more such explanatory variables are assumed to be available for each individual in the analysis. The assumption of the Cox model is that the hazard function is a function of a linear combination of the explanatory variables, each weighted by unknown regression coefficients. This function, in turn, may be multiplied by an arbitrary or unknown function of time. Using these assumptions, a partial likelihood function is formed and an estimation of the coefficients is achieved by the method of maximum likelihood. Once the parameters are estimated, the relative risk may be calculated for factors considered in the overall risk or hazard and may be generated for any particular situation with respect to prognosis. The statistical procedure used in the analysis was implemented by Frank E. Harrell, Jr., of Duke University. It is a FORTRAN procedure (PHGLM) written for inclusion in the Statistical Analysis System (SAS) and contains algorithms for straight Cox regression, for forward stepwise Cox regression, and for backward elimination Cox regression. The Breslow modification was used for tied data [18]. The backward elimination method was chosen as best able to handle interactions among the variables when they were present. Because care had to be taken that no higher order interaction was retained with related lower order interactions or with main effects deleted, this backward elimination method was implemented in a "hands on" manner.

Table 2. Coronary risk factors in population at risk for developing ischemic heart disease (IHD) following the onset of hemodialysis[a]

Group[b]	N	Sex, %		Age	Race, %		Initial BP	Dialysis BP	LVH, %	Plasma triglyceride concentration	Smoking
		Male	Female	yrs	Black	White	mm Hg	mm Hg		mg/dl	%
1	31	32.3	67.7	49.1 ± 9.9	41.9	58.1	173.2 ± 26.8 / 99.5 ± 20.2	146.0 ± 20.5 / 82.5 ± 11.4 (N = 29)	41.9	173.1 ± 89.0 (N = 27)	43.3 (N = 30)
2	160	46.9	53.1	42.9 ± 14.5	55.6	44.4	165.7 ± 32.9 / 98.8 ± 22.5 (N = 158)	147.2 ± 18.8 / 84.3 ± 10.6 (N = 138)	46.8 (N = 156)	144.3 ± 65.9 (N = 135)	45.2 (N = 155)
3	8	50.0	50.0	40.4 ± 8.8	25.0	75.0	177.5 ± 41.6 / 113.8 ± 27.8	146.4 ± 11.7 / 84.0 ± 5.5	75.0	154.6 ± 98.5 (N = 7)	75.0
4	123	52.8	47.2	37.7 ± 15.3	50.4	49.6	166.7 ± 33.9 / 100.9 ± 22.7	150.0 ± 21.9 / 85.3 ± 10.3 (N = 49)	38.8 (N = 121)	140.8 ± 71.8 (N = 41)	42.6 (N = 115)

[a] Values are mean ± SD except for sex, race, LVH, and smoking, which are percentages. LVH is left ventricular hypertrophy. Numbers in parentheses represent sample size when data were only available for a subset of the whole group.

[b] Groups: 1, patients who developed IHD in 2 years or less; 2, patients followed for more than 2 years with no IHD; 3, patients who developed IHD after 2 years; 4, patients followed 2 years or less with no IHD.

Table 3. Variables contributing significantly to risk of ischemic heart disease[a]

Variables[b]	Regression coefficient	SEM	P
Age	0.319	0.126	<0.0117
Age squared	−0.003	0.001	<0.0241
Race	0.668	0.380	<0.0786
Initial diastolic blood pressure	0.019	0.008	<0.0185
Chronic pyelonephritis	1.040	0.494	<0.0350

[a] Analysis by Cox regression model.

[b] Variables not included in the final model were: Sex ($P = 0.90$); linear age × race ($P = 0.96$); linear age × sex ($P = 0.97$); race × sex ($P = 0.87$); linear age × race × sex ($P = 0.93$); systolic initial blood pressure ($P = 0.83$); smoking ($P = 0.35$); packed cell volume ($P = 0.59$); malignant hypertension ($P = 0.23$); serum triglycerides ($P = 0.25$).

Results

Coronary risk factors in patients undergoing hemodialysis who were at risk for developing ischemic heart disease. The patients at risk for ischemic heart disease were placed in four groups (Table 2). The first group contains those patients who developed IHD within a 2-year period following the onset of hemodialysis. Group 2 contains those patients who were followed for at least a 2-year period and showed no signs of IHD. Group 3 represents patients who developed IHD anytime after the initial 2-year period. The group 4 patients had follow-up times less than or equal to 2 years but did not have IHD during this follow-up period. For purposes of describing a group developing IHD and a group without symptomatic IHD, groups 1 and 2 are the most comparable. As shown in Table 2, group 1 has more female patients than group 2 (67.7% compared to 53.1%). Group 1 patients were about 6.2 years older than group 2 patients and had a higher percentage of white patients (58.1% compared to 44.4%). No group differences were apparent between groups 1 and 2 with respect to the presence of LVH, history of smoking, or dialysis blood pressure. Group 1 had a mean initial systolic blood pressure that was 7.5 mm Hg greater than in group 2. A higher triglyceride concentration (28.8 mg/dl) was also noted in group 1.

Multivariable analyses. The proportional hazards or Cox regression model was used to investigate the relative contributions of the variables mentioned above to the risk for developing IHD in this set of dialysis patients. For the preliminary analysis a "full" model was used which yielded a likelihood ratio test statistic of 323.3, which was significant at the 0.01% level. This "full" model included the following effects: linear age ($P = 0.0077$), age squared ($P = 0.0120$), race ($P = 0.4000$), sex ($P = 0.3535$), race by sex ($P = 0.3444$), linear age by race ($P = 0.5894$), linear age by sex ($P = 0.4336$), linear age by race and sex ($P = 0.3775$), chronic pyelonephritis ($P = 0.0392$), malignant hypertension ($P = 0.1488$), initial systolic blood pressure ($P = 0.9011$), initial diastolic blood pressure (0.1674), triglycerides ($P = 0.1719$), packed cell volume ($P = 0.2592$), and smoking ($P = 0.2192$). Because of the high correlations which would be expected among such variables as systolic and diastolic blood pressure and the age, race, and sex variables with their interactions, a stepwise procedure was used to eliminate extraneous variables and to expose which of the total variables listed were important for assessing risk for IHD. The reduced model would be expected to be more easily interpretable and more stable. The regression coefficients, their standard errors, and their P-values appear in Table 3. The significant effects were linear age ($P = 0.0117$), squared age ($P = 0.0241$), race ($P = 0.0786$), initial diastolic blood pressure ($P = 0.0185$), and the presence of chronic pyelonephritis ($P = 0.0350$). A summary of relative risks for selected values of these variables is found in Table 4. According to this summary, older patients would be at a greater risk for IHD than younger patients, although there was a slight curvature in the age relationship in the higher end of the age range which would place a 60-year-old

Table 4. Relative risk of acquiring ischemic heart disease in hemodialysis patients as a function of risk factor[a]

Factor	Relative risk		Risk ratio
	Favorable	Unfavorable	
Age	0.5760 (30)	1.7131 (40)	2.9741
		2.7963 (50)	4.8547
		2.5051 (60)	4.3491
Race	0.7235 (B)	1.4111 (W)	1.9504
Chronic pyelonephritis	0.9527 (−)	2.6964 (+)	2.8303
Diastolic			
Initial BP	0.6845 (80)	1.4579 (120)	2.1299
		2.1276 (140)	3.1083

[a] $\text{Log}_e\,(H_i(t)/H_0(t)) = 0.3190\,(\text{Age} - 41.4317) - 0.0030\,(\text{Age}^2 - 1931.6739) + 0.6680\,(\text{Race} - 0.4845) + 1.0404\,(\text{Chronic pyelonephritis} - 0.0466) + 0.0189\,(\text{Diastolic initial BP} - 100.0531)$

where $H_i(t)/H_0(t)$ is the relative risk for the ith observation by the Cox regression model. Coding used in these models are: race (black, 0; white, 1); male, 0; female, 1; specific disease (absent, 0; present, 1).

Symbols: Numbers in parentheses represent age or diastolic pressure; letters in parentheses represent race; (−), absent; (+), present.

patient at a little less risk than a 50-year-old patient even though both would be at much greater risk than a 30-year-old patient. White patients were at greater risk than black patients for IHD. Patients who had chronic pyelonephritis as the underlying renal disease were at increased risk compared to those with other diseases. Lastly, patients with higher levels of initial diastolic blood pressure were at greater risk than those with lower levels. The relative risk for a patient with any given profile can be estimated using the function provided at the bottom of Table 4.

Discussion

This study demonstrates that, by using the method of Cox regression analysis, we were able to define a group of factors which was associated significantly with an increased risk for developing IHD during hemodialysis therapy. These factors were linear age, age squared, race, and initial diastolic blood pressure. Surprisingly, we also found that the presence of chronic pyelonephritis as the underlying renal disease appeared as a risk factor for the development of IHD. Older patients in general were at a greater risk for IHD than younger patients. The risk ratio was 2.97 for a 40-year-old patient compared to a 30-year-old patient and 4.85 for a 50-year-old patient compared to a 30-year-old patient. The relative risk for a white patient compared to a black patient was almost twice as great (1.95). If chronic pyelonephritis was the precipitating cause of renal failure, the relative risk, holding other factors constant, was 2.83. Patients with initial diastolic blood pressures around 120 mm Hg had a relative risk of 2.13 compared with patients whose diastolic blood pressures were around 80 mm Hg. If the initial diastolic blood pressures were as high as 140 mm Hg, the risk for IHD was three times as great as it would have been with diastolic blood pressures of 80 mm Hg. Because the number of men and women developing IHD were about the same, this analytic method could not distinguish sex as a statistically significant risk factor. Nevertheless, sex must be considered a clinically important risk factor because rates of IHD in women have not been found generally to equal or exceed those of men until age 68 years [19].

Our findings underscore the importance of hypertension in the development of IHD in the hemodialysis population and are in agreement with those of Haire et al [10]. We also concur with Vincenti et al [13] that rigorous control of hypertension in the incipient stages of renal failure may significantly reduce the frequency of IHD developing after the onset of hemodialysis. Our rather surprising finding that the average blood pressure on dialysis which was significantly lower than the initial (predialysis) blood pressure (Table 1) appeared not to influence coronary risk either favorably or unfavorably also supports observations of Vincenti et al [13] who found an equal percentage of hypertensive dialysis patients among those with the mildest and most severe degrees of atherosclerosis.

The positive association between serum triglyceride concentration and coronary artery disease which has been noted in nondialysis patients [20] and also reported for Seattle dialysis patients [11] was not found in our population. This observation is in accord with the analysis of Somer et al [21] which suggested that the lipid disorders found in chronic renal failure may not be important factors in the atherogenic process. The lack of association between serum triglyceride concentration and risk for IHD in our patient population, however, should not be construed to mean that all abnormalities of lipid metabolism, found with high prevalence in patients undergoing hemodialysis, are unimportant since we did not measure other indices of altered lipid metabolism such as increased levels of low density lipoprotein (LDL) or reduced levels of high density lipoprotein (HDL). In this regard also, we have reported previously that women had the highest elevations of serum triglyceride which may have contributed to their accelerated rate of IHD [9]. This concept is strengthened by the studies of Heyden et al [22] who found serum triglyceride concentrations to be predictive of IHD in women but not in men.

Smoking did not contribute significantly to coronary risk in our population unlike the Seattle study [10]. While smokers have been noted to have more intense changes of coronary atherosclerosis in the nondialysis patient population than nonsmokers, there is no agreement regarding the association of smoking in either myocardial infarction or angina pectoris [23].

The conflicting data regarding the relative importance of coronary risk factors in the Seattle dialysis population and in our own group of patients may be explained in several ways. First, differences in the racial composition of our population may be important for there were more blacks in our study population than in the Seattle group. Second, the two Seattle studies did not exclude patients with pre-existent IHD. Third, the endpoints examined were different for each study population. In the Seattle studies, death from myocardial infarction and stroke or the development of any cardiovascular event was used whereas in our studies the development of symptomatic IHD (myocardial infarction or angina pectrois) was used as the endpoint. We recognize that the endpoint we have chosen may represent a small overestimate of the incidence of atherosclerotic heart disease since symptomatic IHD can occur in the absence of all evidence of coronary atherosclerosis [24]. Thus,

the absence of standardized endpoints and differences in the composition of the study populations underscore some of the difficulties in interpreting data from different epidemiologic studies.

An important implication of this study is that many of the factors which we have shown to be associated strongly with coronary risk do not appear to be readily controllable by the physician. Of these factors, race, age, sex, and the underlying cause of renal failure and hypertension, only hypertension that exists prior to the onset of dialysis therapy seems amenable to correction since the level of blood pressure on dialysis did not affect coronary risk favorably or unfavorably. These observations, coupled with the finding that most new IHD events occurred in older patients within the first year of treatment [9], suggest that variables present prior to the onset of hemodialysis may contribute significantly to coronary risk and that the atherosclerotic process may be well into its course when dialysis is initiated. In this regard, there may be other factors not considered in this study, such as the duration of renal disease prior to the onset of dialysis [25] and factors which are associated with this variable that may contribute to dialysis coronary risk.

In conclusion, the data from these studies show that irrespective of whether or not one believes that the rates of IHD are accelerated in the hemodialysis population, several important risk factors for the development of IHD in this population have been defined. These include diastolic hypertension existing prior to the onset of dialysis, race, age, and sex. The presence of chronic pyelonephritis as a cause of endstage renal disease also appeared as a significant risk factor for unexplained reasons. In our population, smoking and triglycercide concentrations were not significantly associated with risk for IHD despite their increased prevalence in the dialysis population.

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References

1. Roodvoets AP, Neerbos BR, van Hooghwinkel GJM, Hulsman HAM, Buekers H: Hyperlipidemia in patients on regular dialysis. *Proc Eur Dial Transplant Assoc* 4:257–263, 1967
2. Bagdade J, Casaretto A, Albers J: Effects of chronic uremia hemodialysis and renal transplantation on plasma lipids and lipoproteins in man. *J Lab Clin Med* 87:37–48, 1976
3. Pierides AM, Weightman D, Goldfinch M, Aljama P, Kerr DNS: Hyperlipidemia of regular hemodialysis and successful transplantation. *Cardiovasc Med* 3:185–206, 1978
4. Bagdade JD, Porte D, Bierman EL: Hypertriglyceridemia: A metabolic consequence of chronic renal failure. *N Engl J Med* 279:181–185, 1968
5. Lindner A, Charra B, Sherrard DJ, Scribner BH: Accelerated atherosclerosis in prolonged maintenance hemodialysis. *N Engl J Med* 290:697–701, 1974
6. Lundin AP, Friedman EA: Vascular consequences of maintenance hemodialysis—an unproven case. *Nephron* 21:177–180, 1978
7. Burke JR Jr, Francos GC, Moore LL, Cho SY, Lasker N: Accelerated atherosclerosis in chronic-dialysis patients—another look. *Nephron* 21:181–185, 1978
8. Blagg CR, Scribner BH: Long-term dialysis: Current problems and future prospects. *Am J Med* 68:633–635, 1980
9. Rostand SG, Gretes JC, Kirk KA, Rutsky EA, Andreoli TE: Ischemic heart disease in patients with uremia undergoing maintenance hemodialysis. *Kidney Int* 16:600–611, 1979
10. Haire HM, Sherrard DJ, Scardapane D, Curtis FK, Brunzell JD: Smoking, hypertension and mortality in a maintenance dialysis population. *Cardiovasc Med* 3:1163–1168, 1978
11. Haas LB, Brunzell JD, Sherrard DJ: Atherosclerotic risk factors in a chronic dialysis population *(abstract). Kidney Int* 16:888, 1979
12. Roguska J, Simon NM, delGreco F, Krumlovsky FA: Ten year experience with maintenance hemodialysis for chronic uremia. *Trans Am Soc Artif Intern Organs* 20:579–582, 1974
13. Vincenti F, Amend WJ, Abele J, Feduska NJ, Salvatierra O Jr: The role of hypertension in hemodialysis—associated atherosclerosis. *Am J Med* 68:363–369, 1980
14. Logue RB, Hurst JW: Clinical recognition of coronary atherosclerotic heart disease and its complications, in *The Heart,* edited by Hurst JW, Logue RB, New York, McGraw-Hill, 1970, pp. 946–984
15. Estes EH Jr: Electrocardiography and vectorcardiography, in *The Heart,* edited by Hurst JW, Logue RB, New York, McGraw-Hill, 1970, pp. 305–308
16. Fredrickson DS, Levy RI, Lees RS: Fat transport in lipoproteins—An integrated approach to mechanisms and disorders. *N Engl J Med* 276:148–156, 1967
17. Cox DR: Regression models and life tables. *J Ro Sta B* 34:187–220, 1972
18. Breslow NE: Covariance analysis of censored survival data. *Biometrics* 30:89–99, 1974
19. The Framingham Study, Sections 6–8, Washington, D.C., United States Department of Health, Education, and Welfare, 1968
20. Carlson LA, Bottiger LE: Ischemic heart disease in relation to fasting values of triglyceride and cholesterol. *Lancet* 1:865–868, 1972
21. Somer JB, Aijken JM, Abbott LK, Charlesworth JA, MacDonald G, Blacket RB: Lipoprotein lipids in chronic renal failure and hemodialysis: The influence of etiology and implications for atherogenesis. *Atherosclerosis* 34:353–364, 1979
22. Heyden S, Heiss G, Hames CG, Bartel AG: Fasting triglycerides as predictors of total and CHD mortality in Evans County, Georgia. *J Chronic Dis* 33:275–282, 1980
23. Seltzer CC: Smoking and coronary heart disease: What are we to believe? *Am Heart J* 100:275–280, 1980
24. Ockene IS, Shay MJ, Alpert JS, Weiner BH, Dalen JE: Unexplained chest pain in patients with normal coronary arteriograms. *New Engl J Med* 303:1249–1252, 1980
25. Bonomini V, Feletti C, Scolari MP, Stefoni S, Vangelista A: Atherosclerosis in uremia: A longitudinal study. *Am J Clin Nutr* 33:1493–1500, 1980