Prediction of Cardiovascular Mortality in Coronary Angiogram Patients

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Introduction

- Cardiovascular disease (CVD) continues to be a leading cause of morbidity and mortality among adults in developed, as well as, in developing countries.

- There is strong evidence indicating serum lipids, smoking, hypertension, and diabetes to be CVD risk factors.

- More recent studies have implicated other attributes, including haemostatic, inflammatory and genetic factors, possibly increasing risk for CVD.

Introduction

- Prospective studies assessing the influence of various risk factors on CVD mortality have utilized community-dwelling populations.

- There are fewer studies examining risk factors, new and old, among patients with coronary artery disease (CAD) symptoms.

- The present study has attempted to examine predictive influences of the risk factors, markers, and therapeutic strategies on CVD mortality in patients with CAD symptoms.

Methods: Study Population

- The present study was designed as a mortality follow-up of the initial research, the Oklahoma Marker Study.

- The study cohort consisted of a consecutive series of patients with CAD symptoms who underwent coronary angiography from November 1992 through March 1994 at the Veterans Administration (VA) Medical Center, Oklahoma City,Oklahoma.

- The cohort was followed for a period of 8 years.

Methods: Medical Records and Blood Samples

- The present study used information on prognostic factors collected at the time of the coronary angiography (index catheterization) and during the follow-up period.

- The predictor variables were defined according to the standard clinical definitions at the time. Laboratory reference values were used to define normal and abnormal levels of the factors that were measured in blood samples of the patients.

Methods: Data

- Predictor variables :
- ➤ Age at the time of index catheterization, gender, race, smoking status
- ➤ Baseline measurements of serum lipids and lipoproteins, haemostatic factors, genetic marker, serum ferritin, inflammatory factors, and body mass index
- ➤ Presence of CAD at baseline, hypertension, and diabetes
- ➤ Occurrence of coronary events over the follow-up
- ➤ Prescription of cardiovascular medications and revascularization procedures performed during follow-up

- Abstracted from the medical and pharmacy records of the patients, coronary catheterization reports, or measured from blood samples.

Methods: ICD Codes and Survival Status

- The primary outcomes examined were: vital status and cause-specific mortality (underlying cause of death).

- Survival duration was defined as the time from the date of the index catheterization to death or till December 31, 2000 (for those who survived till the end of the study).

- The cause-specific mortality due to CVD was defined by the International Classification of Disease, Ninth Revision (ICD-9) codes 401-405, 410-414, 420-429 and 430-438.

Methods: ICD Codes and Survival Status

- ICD-9 titles and codes defining CVD are: hypertensive disease (401-405), ischemic heart disease (410-414), other forms of heart disease (420-429), and cerebro-vascular disease (430-438).

- Information on vital status was obtained in 2001-2002 from the official mortality records of the Vital Statistics Office of the Oklahoma State Department of Health and VA hospital records.

- Information on causes of death was obtained from the death certificates provided by the Oklahoma State Department of Health.

Statistical Methods

- Survival data analysis techniques (e.g., Cox Proportional Hazards modeling technique) and other appropriate statistical techniques were used for data analyses.

- A statistical significance level of 5% ($\alpha = 0.05$), for two-tailed hypothesis tests, was used for all analyses.

Sample Sizes and Exclusions

- A cohort of 528 patients with CAD symptoms and complex clinical and risk factor profiles was followed over a period of 8 years.

- 137 subjects were excluded: females (n = 4), racial groups other than white and black (n = 6), cardiac transplantations during follow-up period (n = 4), occurrence of myocardial infarction (MI) within 30 days prior to the index catheterization (n = 51), and missing baseline and follow-up information (n = 72).

- Thus, data for 391 subjects were analyzed further (239 subjects survived and 152 died). Out of these 152 subjects, 101 subjects died due to CVD.

Results

- The final analysis was conducted on a sample of 340 subjects with complete data.

- Out of these 340 subjects, 239 (70.2%) survived till the end of the study and 101 (29.7%) died from CVD.

- Mean age of patients at the time of the index catheterization was 61.2 years.

- Mean age for those who survived was 60.1 years and for those who died was 64.1 years.

Characteristics of the Study Cohort (N = 340)

Characteristic	Frequency (%)
Age at the time of the Index Catheterization	
≤55 years	84 (24.7)
>55 - ≤65 years	124 (36.5)
>65 - ≤75 years	117 (34.4)
>75 years	15 (4.4)
Race	
Whites	319 (93.8)
Blacks	21 (6.2)
Smoking Status	
Never smokers	29 (8.5)
Current smokers	137 (40.3)
Former smokers	174 (51.2)

Genetic Attribute of the Study Cohort
(N = 340)

Characteristic	Frequency (%)
Apo E Genotype	
ε2ε2	6 (1.8)
ε3ε2	39 (11.5)
ε3ε3	197 (57.9)
ε4ε2	5 (1.5)
ε4ε3	83 (24.4)
ε4ε4	10 (2.9)

Laboratory Measures at Baseline

Laboratory Measures	N	Mean	Median	SD
Serum total cholesterol (mg/dl)	340	222.5	214.0	56.2
LDLc (mg/dl)	329	154.3	148.0	49.7
HDLc (mg/dl)	340	32.1	30.0	8.6
Triglycerides (mg/dl)	340	189.9	162.5	132.7
Lp(a) (mg/dl)	340	36.8	21.5	38.6
Fibrinogen (mg/dl)	340	354.4	326.5	124.0
Factor VIIa (ng/dl)	338	2.5	2.3	1.3
WBC count ($10^3/\mu L$)	340	8.2	8.0	2.3
Platelet count ($10^3/\mu L$)	340	245.2	231.5	85.2
Ferritin ($\mu g/L$)	272	184.2	141.5	150.6

Clinical Characteristics of the Study Cohort
(N=340)

Characteristic	Frequency (%)
Obesity (BMI ≥ 30 kg/m^2)	
Present	112 (32.9)
Absent	228 (67.1)
Hypertension	
Present	217 (63.8)
Absent	123 (36.2)
Diabetes	
Present	107 (31.5)
Absent	233 (68.5)

Clinical Characteristics of the Study Cohort (N=340)

Characteristic	Frequency (%)
CAD with Obstructive Lesion	
Present	269 (79.1)
Absent	71 (20.9)
MI during the Follow-up Period	
Occurred	81 (23.8)
Not occurred	259 (76.2)

Treatment during the Follow-up Period
(N=340)

Treatment	Frequency (%)
Prescription of lipid-lowering drugs	
Ever Prescribed	181 (53.2)
Never Prescribed	159 (46.8)
Prescription of beta blockers	
Ever Prescribed	257 (75.6)
Never Prescribed	83 (24.4)
Performance of PTCA	
Performed	111 (32.7)
Not Performed	229 (67.3)

Statistical Analysis

- Cox Proportional Hazards modeling technique was used to evaluate predictive ability of various markers.

- Initially, univariate models were tested.

- Variables that showed statistically significant relationships with CVD mortality with univariate models were examined in the multivariate models.

- Other covariates were also included in these multivariate models.

Interactions

- Index age was seen to be interacting with different variables, therefore, further analyses were conducted in two groups of index age:

- ➤ ≤ 65 years of age at the time of the index catheterization (total = 208 subjects, 160 survived (77%) and 48 (23%) died).

- ➤ > 65 years of age at the time of the index catheterization (total = 132 subjects, 79 survived (59.9%) and 53 (40.1%) died).

- The variables that showed statistically significant relationships with CVD mortality when adjusted for other markers and covariates were tested further.

Hazard Ratios and 95% Confidence Limits
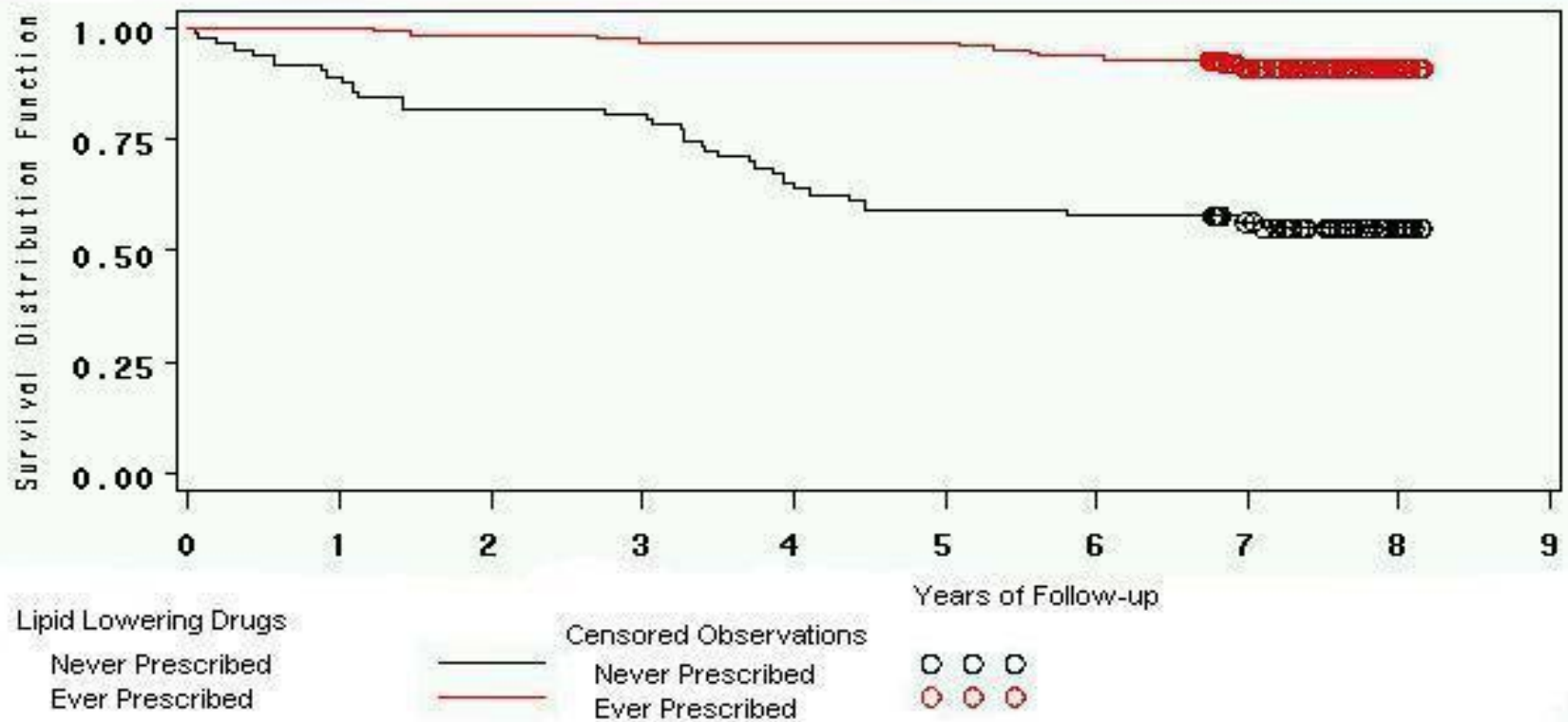## (Men <= 65 Years Old)

Variable	Hazard Ratio	95% C.I.
Baseline CAD with obstructive lesion	5.28	2.13, 13.10
MI occurrence	3.06	1.63, 5.72
Smoking Status		
Former vs. current	0.45	0.23, 0.89
Never vs. current	0.63	0.19, 2.09
Prescription of lipid lowering drugs	0.24	0.11, 0.50
Prescription of beta-blockers	0.39	0.20, 0.77
Performance of PTCA	0.24	0.10, 0.56

# Hazard Ratios and 95% Confidence Limits
(Men > 65 Years Old)

Variable	Hazard Ratio	95% C.I.
Baseline plasma fibrinogen	3.15	1.72, 5.77
Baseline CAD with obstructive lesion	2.84	1.10, 7.33
Prescription of lipid lowering drugs	0.18	0.07, 0.41
Prescription of beta-blockers	0.44	0.24, 0.79

Survival Curves for Two Strata of Prescription of Lipid Lowering Drugs in Men <= 65 Years at the Time of the Index Catheterization

Survival Curves for Two Strata of Prescription of Lipid Lowering Drugs in Men > 65 Years of Age at the Time of the Index Catheterization
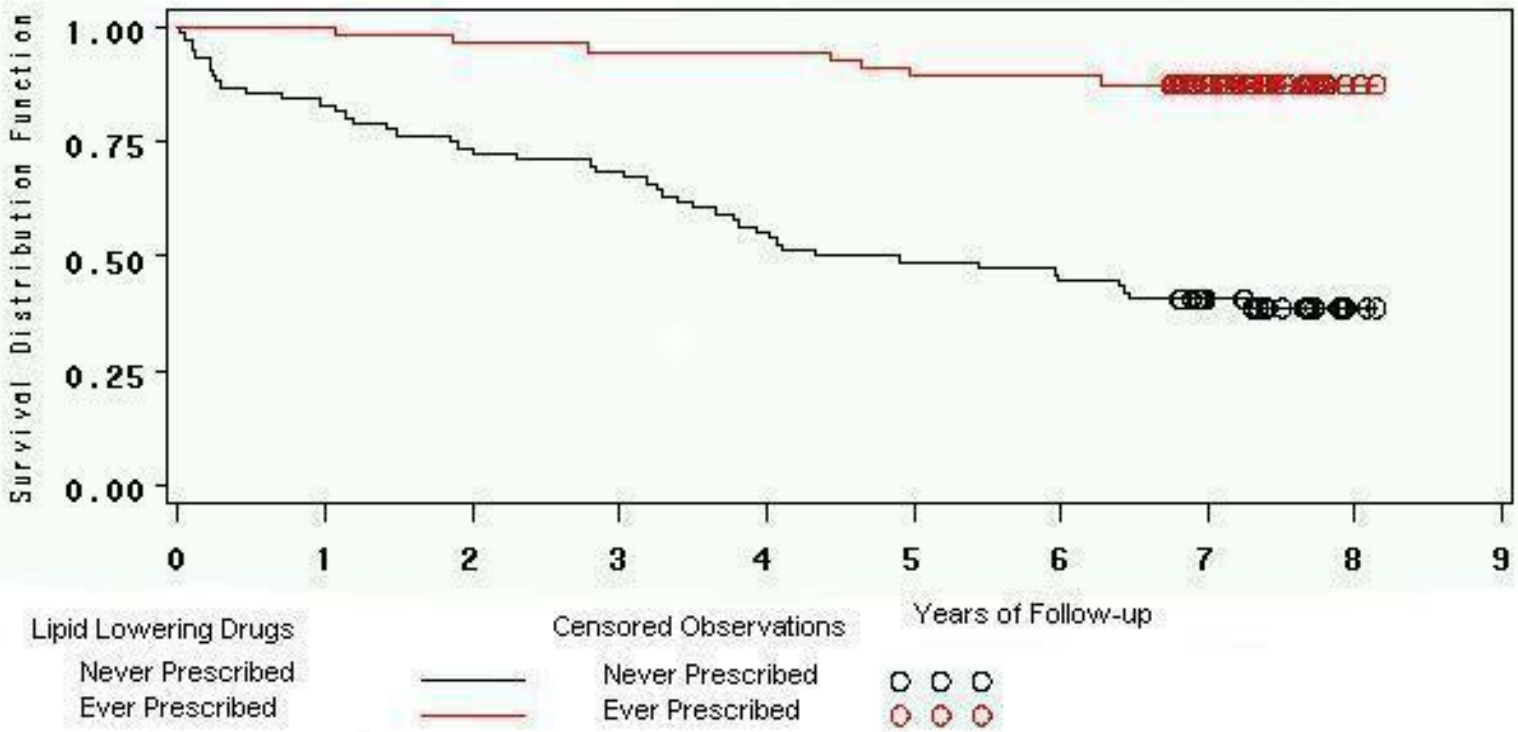
Conclusions

- This study has identified a small set of prognostic factors that can help VA physicians to determine the patients with heart disease who may be at higher CVD mortality risk.

- Also, certain medical and invasive interventions are seen to be effective in reducing mortality in this high risk, unselected patient population.

- A combination of preventive, medical and surgical strategies may reduce the risk of CVD mortality and may improve overall survival of male military veterans who are suffering from a variety of co-morbidities along with CAD symptoms.