Paper PO14

ROLE OF FIBRINOGEN, HDL CHOLESTEROL AND CARDIO RESPIRATORY FITNESS IN PREDICTING MORTALITY DUE TO CARDIO-VASCULAR DISEASE: RESULTS FROM THE AEROBIC CENTER LONGITUDINAL STUDY

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ABSTRACT

Mortality due to Cardio Vascular Disease (CVD) is a leading cause of death. The major aim of the study was to determine the association of plasma Fibrinogen in determining the risk of mortality due to CVD. The secondary aim of the study was to examine the effect of cardio- respiratory fitness (CRF) on this relationship. A cohort of 25673 adults who visited the Cooper Clinic in or after 1990 and are a part of the Aerobic Center Longitudinal Study (ACLS), were followed as part of this study. The main predictor variables were collected at single point in time. SAS 9.2 was used to analyze the data. Survival analysis technique was used to assess the association between the predictors and the outcome. PROC PHREG was used to calculate the survival analysis. HDL cholesterol and Fibrinogen were significant predictors of death due to CVD in univariate models. The association did not reach statistical significance in the multivariate model. CRF has a significant protective relationship with CVD death and may play a role mediating the fibrinogen-CVD death relationship.

Keywords: CVD, Survival analysis
University of South Carolina, University of North Dakota

INTRODUCTION

Cardio Vascular Disease (CVD) is the leading cause of death in the United States, despite the downward trend observed during the past four decades. There are an estimated 61 million people with some form of CVD in the USA. Fibrinogen is a key molecule in the cascades of inflammation and is involved in the pathogenesis of CVD and occurrence of athero-thrombotic complications. The role of Fibrinogen in CVD mortality has not been studied adequately. Increase in physical activity (PA) leads to increase in Cardio Respiratory Fitness (CRF) , which is a very good predictor of CVD.

PURPOSE

The major aim of the study is to determine the association of high density lipoprotein (HDL) cholesterol and plasma Fibrinogen with the risk of death due to CVD. The secondary aim of the study is to look at how cardio-respiratory fitness (CRF) affects this relationship

BACKGROUND

This study was approved by the institutional review boards of the Cooper Institute, Dallas, TX and The University of South Carolina. The data for this study was obtained from the Aerobic Center Longitudinal Study (ACLS). ACLS is an observational study of participants examined at a preventive medicine clinic in Dallas, TX started in 1970. Follow up data for mortality is available through the 31st of December 2003. This study is comprised of people who had visited the clinic in or after 1990, had measurements for HDL, fibrinogen and CRF.

DATA ANALYSES

All data analyses were performed using **SAS** ® statistical software, version 9.2 . PROC UNIVARIATE and FREQ were used to describe the data. PROC PHREG was used to perform cox proportional hazard survival analyses. Univariate model for of all the different covariates were run and subsequently, variables with significant associations were added to the multivariate model.

RESULTS

In the Univariate model, HDL cholesterol was associated with CVD death (HR 0.985 [0.97-0.99] p=0.002).

Similarly, the association between fibrinogen and CVD death was significant in the univariate model, HR 1.007 (1.005-1.010). CRF was significantly associated with CVD death in the univariate analysis (HR = 0.861 p<0.0001) (Table 1). In the Multivariate model, HDL had a protective effect (HR 0.989) on CVD death which was not statistically significant (CI 0.974- 1.004) p= 0.155 and Fibrinogen had an association with CVD death (HR 1.003), which was also not statistically significant (CI 0.999- 1.004) p = 0.101. CRF had a significant protective relationship with CVD death: HR 0.924 (CI 0.879-0.971) (Table 2).

CONCLUSION

This study concludes that fibrinogen plays a role in predicting death due to CVD in adult Caucasian population of higher SES while HDL has a weak association in predicting the mortality due to CVD as it was only marginally significant in the presence of fibrinogen and other covariates. Cardio-respiratory fitness provides a protective effect on death due to CVD. CRF may have a mediating relationship with fibrinogen and CVD death.

REFERENCES

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Univariate Analysis	HR	95% CI	p value
Fitness (Minutes)	**0.861**	0.829- 0.894	<0.0001
HDL (mg/dl)	**0.985**	0.972-0.998	0.0227
Fibrinogen (mg/dl)	**1.007**	1.005-1.010	<0.0001
Age (years)	**1.123**	1.013-1.143	<0.0001
Gender #	**2.238**	1.225-3.990	0.0063
Family H/O CVD	**1.635**	1.106-2.418	0.0137
H/O CVD	**11.689**	6.559-20.831	<0.0001
H/O BP	**2.419**	1.569-3.729	<0.0001
Smoking	**0.611**	0.421-0.884	0.0091
BMI (kg/m^2)	**1.295**	1.005-1.670	0.0450
Cholesterol (mg/dl)	**1.003**	1.001-1.005	0.0076
Glucose (mg/dl)	**1.011**	1.007-1.015	<0.0001
Diastolic BP (mm hg)	**2.096**	1.466-3.038	<0.0001
Systolic BP (mm hg)	**2.383**	1.623-3.497	<0.0001
History of Cancer	1.639	0.856-3.138	0.1360
History of DM	1.946	0.714-5.303	0.1930
Alcohol consumption	0.810	0.620-1.058	0.1220
Stress	0.866	0.668-1.122	0.2762

Table1. Results of Univariate Analysis
Note: Significant HR presented in bold
#- Reference is female
H/O - History of

Full Model (with Fitness)	HR	Parameter Estimate	Standard Error	95% CI	p value
Fitness (Minutes)	**0.924**	-0.0792	0.0255	0.879-0.971	0.0019
HDL (mg/dl)	0.989	-0.0109	0.0077	0.974-1.004	0.1550
Fibrinogen (mg/dl)	1.003	0.0026	0.0016	0.999-1.004	0.1012
Age (years)	**1.101**	0.0967	0.0112	1.078-1.126	<0.0001
Gender	**2.08**	0.7322	0.3603	1.026-4.214	0.0421
Family H/O CVD	1.066	0.0644	0.2029	0.717-1.587	0.7510
H/O CVD	**4.182**	1.4309	0.3052	2.299-7.607	<0.0001
H/O BP	1.142	0.1327	0.2353	0.720-1.811	0.5728
Smoking	0.822	-0.1961	0.1946	0.561-1.204	0.3136
BMI (kg/m^2)	0.944	-0.0581	0.1522	0.700-1.272	0.7027
Cholesterol (mg/dl)	1.002	0.0012	0.0015	0.999-1.004	0.3100
Glucose (mg/dl)	1.003	0.0035	0.0030	0.997-1.009	0.2561
Diastolic BP (mmhg)	1.497	0.4032	0.2100	0.992-2.258	0.0548
Systolic BP (mmhg)	0.944	-0.0576	0.2222	0.611-1.459	0.7950

Table2. Results of Multivariate Analysis
Significant HR presented in bold
#- Reference is female
H/O - History of

REFERENCES

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SAS Syntax:

```
proc univariate data = ACLS.CVD;
var fitness HDL fibrinogen age BMI cholesterol glucose DiastolicBP
SystolicBP ;
run;

proc freq data = ACLS.CVD;
tables FCVD CVD BP Smoking Cancer DM Alcohol Stress;
run;


proc phreg data= ACLS.CVD;
         model yrs*cvd(0)= fitness HDL fibrinogen Age gender FCVD  CVD BP
Smoking BMI glucose cholesterol systolicBP diastolicBP;

run;
```