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Is immobilization associated with an abnormal lipoprotein profile? Observations from a diverse cohort

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Objective: The potential effects of ethnicity, gender, and adiposity on the serum lipid profile in persons with spinal cord injury (SCI) were determined.

Subjects: Subjects with SCI were recruited during their annual physical examination from Rancho Los Amigos Medical Center, Downey, California. Sedentary able-bodied controls were Bridge and Tunnel Officers of the Triboro Bridge and Tunnel Authority of the New York City metropolitan area.

Methods: Serum lipid profiles were investigated in 320 subjects with SCI and compared to those obtained from 303 relatively sedentary able-bodied controls. Serum lipid studies were obtained in the fasting state. Data were collected between 1993 and 1996. All lipid determinations were performed by the same commercial laboratory.

Main outcome measures: The dependent variables were the values from the lipid profile analysis. The independent variables consisted of study group, gender, ethnic group, age, duration of injury, and anthropometric measurements.

Results: The serum high-density lipoprotein cholesterol (HDL-c) level was reduced in the SCI compared with the control group (mean $\pm$ SEM) (42 ± 0.79 *vs* 47 ± 0.67 mg/dl, $P < 0.0005$). The serum HDL-c level was significantly lower in males with SCI than males in the control group (39 ± 0.83 *vs* 45 ± 0.70 mg/dl, $P < 0.0001$), but not for females (51 ± 1.54 *vs* 54 ± 1.52 mg/dl, n.s.). Within the subgroups for whites and Latinos, HDL-c values were also lower in subjects with SCI than in controls (whites: 41 ± 1.02 *vs* 46 ± 0.86 mg/dl, $P < 0.0001$; Latinos: 37 ± 1.53 *vs* 42 ± 1.59 mg/dl, $P < 0.05$), but not for African Americans (49 ± 1.56 *vs* 51 ± 1.27 mg/dl, n.s.). African Americans had higher HDL-c values than whites or Latinos (SCI: 49 ± 1.56 *vs* 41 ± 1.02 or 37 ± 1.53 mg/dl, $P < 0.0001$; controls: 51 ± 1.27 *vs* 46 ± 0.86 mg/dl, $P < 0.01$ or 42 ± 1.59 mg/dl, $P < 0.0005$). In persons with SCI, the serum HDL-c values were inversely related to body mass index and estimated per cent body fat ($r = 0.27$, $P < 0.0001$).

Conclusion: In white and Latino males, but not in females or African Americans, immobilization from SCI appears to be associated with lower HDL-c values than in controls.

Keywords: high density lipoprotein cholesterol; spinal cord injury; coronary heart disease; ethnicity; gender

Introduction

Chronic spinal cord injury (SCI) is an excellent model of immobilization that may permit the study of associated changes in the serum lipid profile. Persons with SCI have been reported to have premature cardiovascular disease,[1–4] as may be the case with other conditions which restrict mobility. In the general population, a depressed serum high-density lipoprotein cholesterol (HDL-c) level is associated with increased risk for coronary heart disease (CHD).[5–9] Several reports have demonstrated that the primary lipid

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abnormality in the population with SCI is a depressed serum HDL cholesterol value.[10–16] Generally, however, previous studies have not compared lipid values in a cohort with SCI to that of an able-bodied population, and none published to date have assessed possible gender or ethnic differences. The aim of this study was to compare components of the serum lipid profile, using the same commercial laboratory between two relatively large cohorts: those with SCI and a comparable age-, gender- and ethnic-matched able-bodied control population.

Subjects and methods

From May 1994–May 1996, out-patients with SCI being seen for routine annual physical examination at the Comarr Spinal Injury Clinic at Rancho Los Amigos Medical Center, Downey, California, were entered into this study ($n=656$). The able-bodied group consisted of the Bridge and Tunnel Officers (controls) of the New York Metropolitan Transportation Authority, employed from 1993–1995, and those who had retired since 1985 ($n=526$). The two cohorts were compared and subdivided into two categorical groups for gender and ethnicity [white (non-Latino), African American, and Latino]. Subjects in both groups with missing data or serum triglycerides greater than three standard deviations from the mean were excluded (ten in the group with SCI and 31 in the control group). In order to assure a comparable age, gender and ethnic distribution between the SCI and control groups, a random iterative process was used to produce similar histogram distributions of gender and ethnicity. Following this procedure, 320 subjects with SCI and 303 subjects in the control group were included for comparison.

In general, the group with SCI was extremely sedentary. All subjects had some degree of immobilization: 65.6% were motor complete and 34.4% were motor incomplete. Approximately 13% of the subjects were able to ambulate with assistive devices (various types of long leg braces), but less than 1% of the subjects were motor incomplete enough to actually bear weight. Eighty-seven per cent of the subjects required a wheelchair for mobility.

Subjects in the control group completed a physical activity questionnaire obtained from The Lipids Research Clinics Program Prevalence Study.[16] The majority of controls were also sedentary. A toll collection officer typically sits or stands in place for most of the work shift with the exception of breaks; 81.9% of controls reported no strenuous physical activity on the work site. The majority (72.4%) of controls also reported no participation in any form of exercise during their leisure time. Only a small per cent (17.6%) of the control subjects reported participating in some form of strenuous physical activity three or more times per week.[17] Thus, both study groups were relatively inactive, but those in the control group were able to weight bear and ambulate for activities of daily living.

All laboratory analyses from California (subjects with SCI) and New York (controls) were performed by the same clinical laboratory facility (Quest Diagnostics, Inc., Teterboro, NJ, USA). During the time of data collection from this study (1993–1996), Quest Diagnostics, Inc. participated in the National Institutes of Health, Heart, Lung, and Blood Institute lipid testing certification program, which was administered by the Center for Disease Control. In addition, this facility has been consistently within the grading guidelines for lipid values for state and federal proficiency testing. Serum lipid profiles were performed on subjects with SCI after an overnight fast and after a minimum of 4 h fasting in controls. Serum total cholesterol (TC) and triglycerides (TG) were assayed on an automated blood analyzer (Hitachi, model 736). Serum HDL cholesterol (HDL-c) was determined by phosphotungsten precipitation with enzymatic quantification by spectrophotometry. Serum low density lipoprotein cholesterol (LDL-c) was calculated by the equation of Friedwald.[18]

Serum lipid risk factors for CHD were determined using criteria established by the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults.[19] The ratio of serum total cholesterol to HDL cholesterol (TC/HDL-c) has been reported as a potent predictor of risk for CHD[20,21] and, as such, was computed.

Body mass index (BMI) was calculated [body weight/height squared (kg/m^2)] for all subjects studied. An estimate of per cent body fat (%fat) in controls and subjects with SCI was performed using regression equations to predict %fat; these regression equations (unpublished) were developed from previous BMI determinations and dual X-ray absorptiometry measurements of body fat.

Subjects with SCI
%Fat (all ethnicities) $= 3.929 + 1.246$(BMI); ($n=60$, $r=0.58$, $P<0.0001$)
Controls
%Fat (white) $= 2.06$(BMI) $- 30.4$; ($n=60$, $r=0.77$, $P<0.0001$)
%Fat (African American) $= 1.56$(BMI) $- 18.2$; ($n=105$, $r=0.76$, $P<0.0001$)
%Fat (Latino) $= 1.33$(BMI) $- 1.78$; ($n=119$, $r=0.76$, $P<0.0001$)

All analyses were performed on a Power Macintosh computer using the Statview 4.5 and/or SuperANOVA 1.11 software programs (Abacus Concepts Inc., Berkeley, CA, USA). The results were reported as mean plus or minus standard error of the mean (mean $\pm$ SEM). The dependent variables included the values from the lipid profile analysis (TC, TG, HDL-c, LDL-c, and TC/HDL-c) and HDL-c <35 mg/dl (the HDL-c risk factor for CHD). The independent variables consisted of: study group (SCI, control), gender (male, female), ethnic group (white, African

American, Latino), age, duration of injury (SCI only), estimated per cent body fat, body mass index (BMI), and BMI obesity group (males: BMI 27.8 kg/m^2, females: BMI 27.3 kg/m^2).[22]

An unpaired *t*-test was used for comparisons between the SCI and control groups for age and BMI, and on the dependent variables of TC, TG, HDL-c, LDL-c, and TC/HDL-c. This same comparison was also used between the SCI and control groups when stratified by gender or ethnicity. Comparisons between the males and females within the SCI and control groups for age, BMI, TC, TG, HDL-c, LDL-c, and TC/HDL-c were also performed by an unpaired *t*-test. The distribution of TG values were skewed to the right, therefore, a natural log transformation was performed. Analysis of variance (ANOVA) was used for the comparisons among the subgroups factored by ethnicity (white *vs* African American *vs* Latino) within the SCI or control groups on age, BMI, TC, TG, HDL-c, LDL-c, and TC/HDL-c. A Scheffe' *post hoc* F ratio was applied to the ANOVA models to determine if significant pairwise differences existed among the ethnic groups. Statistical power calculations were determined for serum HDL-c for the groups and each of the subgroup (ethnicity and gender) comparisons.[23] A stepwise regression model, using 12 continuous variables of interest to determine the most important predictors of HDL-c, was applied. Because the length of fasting among the subjects varied from at least 4 h to an overnight fast, a multiple regression model was applied to determine group differences for serum HDL-c, controlling for TG levels.

Chi-squared analyses were performed to determine distribution differences between the SCI and control groups for gender and ethnicity. The SCI and control groups were stratified by gender and ethnicity, using a chi-squared analysis compared for distribution and per cent occurrence of differences on the variables of BMI obesity and HDL-c risk for CHD. Simple regression analyses were used to determine the associations between HDL-c and TG; BMI and estimated per cent fat. Two analysis of covariance (ANCOVA) models were used to determine the covariance of the two groups on either BMI or estimated per cent body fat with HDL-c.

Results

The characteristics of the study populations (SCI *vs* controls) and the subgroups stratified by gender and ethnicity are presented (Table 1). As expected because of the subject selection process, no differences were found for age, proportion of males to females, or distribution by ethnicity (Table 1). Of the total group studied, 477 were men (233 SCI and 244 controls) and 146 were women (87 SCI and 59 controls). The per cent of males and females in the SCI compared with the control groups were 73% ($n=233$) and 27% ($n=87$) *versus* 81% ($n=244$) and 19% ($n=59$), respectively. The distribution by ethnicity for the total group was 51% ($n=318$) white, 28.1% ($n=175$) African American and 20.9% ($n=130$) Latino. There was a similar distribution between the SCI and control groups, for ethnicity (SCI: 47, 28, 26% *vs* control: 56, 29, 15% for the white, African American or Latino subgroups, respectively). All subjects with SCI were injured for at least 1 year, range of 1.4–56.7, with the average duration of injury (DOI) of 15.0 ± 0.52 years. The BMI was significantly greater in the control group than the SCI group (Table 1), as well as in each of the subgroups for gender and ethnicity (Table 2). Approximately twice as many controls had BMI values greater than the cut-off for obesity (males 27.8 kg/m^2 and females 27.3 kg/m^2)[22] than those in the group with SCI; this was also noted in the subgroups for gender and ethnicity (Table 2). Despite significantly higher mean BMIs in the control group

Table 1 Characteristics of the study populations

	SCI (n = *320*)		*Control* (n = *303*)		
	Mean ± SEM	*(range)*	*Mean ± SEM*	*(range)*	P
Age (years)	41 ± 0.62	(20–77)	42 ± 0.57	(21–75)	
DOI (years)	15 ± 0.52	(1–57)	–	–	
BMI (kg/m^2)	25 ± 0.31	(13.8–54.8)	29.9 ± 0.31	(19.7–49.9)	<0.0001
% Body Fat (est.)	36 ± 0.39	(21.1–72.3)	31 ± 0.62	(10.2–72.5)	<0.0001
	%	n	%	n	
BMI ⩾ 27.8*	28	88	64	189	<0.0001
White	47	149	56	169	
African American	28	88	29	87	
Latino	26	83	16	47	
Male	73	233	81	244	
Female	27	87	20	59	

SCI = spinal cord injury; DOI = duration of injury; BMI = body mass index; and for % Body Fat (est. = estimated; refer to the methods section). *BMI ⩾ 27.8 for males and ⩾ 27.3 for females[22]. No significant differences were found for age, nor for distributions for ethnicity or gender

Table 2 Characteristics of the study populations statified by gender and ethnic subgroups

	SCI	*Control*	P
Gender			
Males	(*n* = 233)	(*n* = 244)	
Age (years)	41.4 ± 0.69	42.3 ± 0.65	
DOI (years)	15.3 ± 0.52	n/a	
BMI (kg/m^2)	25.0 ± 0.37	30.1 ± 0.34	<0.0001
% Body Fat (est.)	35.1 ± 0.46	31.2 ± 0.68	<0.0001
BMI ⩾ 27.8*	29% (*n* = 67)	66% (*n* = 161)	<0.0001
Females	(*n* = 87)	(*n* = 59)	
Age (years)	41.5 ± 1.33	39.7 ± 1.10	
DOI (years)	14.6 ± 0.52	n/a	
BMI (kg/m^2)	24.9 ± 0.59	29.1 ± 0.79	<0.0001
% Body Fat (est.)	34.9 ± 0.74	28.3 ± 1.41	<0.0001
BMI ⩾ 27.8*	24% (*n* = 21)	47% (*n* = 28)	<0.005
Ethnicity			
White	(*n* = 149)	(*n* = 169)	
Age (years)	41.2 ± 0.92	42.3 ± 0.78	
DOI (years)	17.3 ± 0.78	–	
BMI (kg/m^2)	24.7 ± 0.52	30.0 ± 0.41	<0.0001
% Body Fat (est.)	34.7 ± 0.65	31.4 ± 0.85	<0.005
BMI ⩾ 27.8*	27% (*n* = 40)	61% (*n* = 103)	<0.0001
African American	(*n* = 88)	(*n* = 87)	
Age (years)	42.0 ± 1.22	41.2 ± 1.07	
DOI (years)	13.3 ± 0.97	–	
BMI (kg/m^2)	25.0 ± 0.55	29.9 ± 0.66	<0.0001
% Body Fat (est.)	35.1 ± 0.69	30.5 ± 1.27	<0.005
BMI ⩾ 27.8*	28% (*n* = 25)	61% (*n* = 53)	<0.0001
Latino	(*n* = 83)	(*n* = 47)	
Age (years)	41.2 ± 1.14	40.9 ± 1.29	
DOI (years)	13.2 ± 0.92	–	
BMI (kg/m^2)	25.4 ± 0.46	29.8 ± 0.62	<0.0001
% Body Fat (est.)	35.5 ± 0.57	27.9 ± 0.82	<0.0001
BMI ⩾ 27.8*	28% (*n* = 23)	70% (*n* = 33)	<0.0001

SCI = spinal cord injury; DOI = duration of injury; BMI = body mass index; and for % Body Fat (est. = estimated; refer to the methods section). *BMI ⩾ 27.8 for males and ⩾ 27.3 for females[22]

than in the SCI group (29.9 ± 0.31 *vs* 25.0 ± 0.31 kg/m^2, $P < 0.0001$), the estimated per cent body fat was significantly greater in those with SCI than in the control group (35.5 ± 0.39% *vs* 31 ± 0.62%, $P < 0.0001$), and in the subgroups for gender and ethnicity.

Comparison of the serum lipid profiles between the two groups revealed that the mean serum lipid values for TC, TG, HDL-c, and LDL-c were significantly lower, and the TC/HDL-c ratio was significantly higher, in the SCI group than in the control group (Table 3). Most importantly, the mean serum HDL-c value was 11% lower in the group

Table 3 Comparison of serum lipid results between the study groups

	SCI (n = *320*)	*Control* (n = *303*)	P
TC	190 ± 2.27	207 ± 2.34	<0.0001
TG	108 ± 3.08	118 ± 3.25	<0.05
HDL-c	42 ± 0.79	47 ± 0.67	<0.0005
LDL-c	126 ± 2.13	137 ± 2.16	<0.0001
TC/HDL-c	5.0 ± 0.11	4.6 ± 0.08	<0.01

SCI = spinal cord injury; TC = total cholesterol in mg/dl; TG = triglycerides in mg/dl; HDL-c = serum high density cholesterol in mg/dl; LDL-c = serum low density cholesterol in mg/dl; and TC/HDL-c = the ratio of total to HDL-c. Significant differences were found between the SCI and control groups for all serum lipid variables

with SCI than in the control group. The serum HDL-c comparison was found to have very high statistical power (>0.99, $P < 0.05$). Similarly, a greater proportion of subjects in the SCI compared with the control group had serum HDL-c levels less than 35 mg/dl, an independent risk factor for CHD (34% *vs* 12%, $X^2_{(1)} = 45.4$, $P < 0.0001$). Controlling for TG values, subjects in the SCI group had significantly lower serum HDL-c values than in the control group (multiple $r = 0.46$, $P < 0.0001$, partial r for the group = 0.35, $P < 0.0001$).

Stratifying the groups by gender revealed that the significant differences found for the serum lipid values between the SCI and control groups existed in males only, not in females (Table 4). Forty-four per cent of the males with SCI had a low serum HDL-c (<35 mg/dl) compared with 13% of those in the control group ($X^2_{(1)} = 57.2$, $P < 0.0001$). In contrast, a significant difference was not found in females between the SCI and control groups for the proportion of those with the HDL-c risk factor for CHD (9% *vs* 7%, n.s.). However, using a serum HDL-c value of 45 mg/dl, which represents an approximate 10 mg/dl reduction from the expected mean level in women (a reduction that is similar to a cutoff level of 35 mg/dl in men), significantly more females with SCI had lower values than in the control group (33% *vs* 17%, ($X^2_{(1)} = 4.8$, $P < 0.05$).

In both groups, serum HDL-c levels were significantly higher in females than in males (SCI: 51 ± 1.54 *vs* 39 ± 0.83, $P < 0.0001$; controls: 54 ± 1.52 *vs* 45 ± 0.70, $P < 0.0001$). Females had lower serum TG values than males in both groups (SCI: 94 ± 4.76 *vs* 114 ± 3.79 mg/dl, $P < 0.005$; controls: 82 ± 5.00 *vs* 126 ± 3.64 mg/dl, $P < 0.0001$). Serum LDL-c values for females were lower than for males (SCI: 118 ± 3.45 *vs* 129 ± 2.60 mg/dl, $P < 0.05$; controls: 129 ± 5.29 *vs* 139 ± 2.35 mg/dl, $P < 0.05$). The TC/HDL-c ratios were higher for males in both groups than those of females (SCI: 5.4 ± 0.14 *vs* 4.0 ± 0.16, $P < 0.0001$; controls: 4.8 ± 0.08 *vs* 3.9 ± 0.18, $P < 0.0001$).

Stratifying the groups by ethnicity, revealed the following for serum lipids. Within the white and Latino subgroups, serum TC, TG, HDL-c, and LDL-c values remained significantly lower in subjects with SCI compared with controls; none of the lipid parameters were significantly different between SCI and controls for African Americans (Table 5). The power ($P<0.05$) for serum HDL-c was 0.96 for whites, 0.17 for African Americans, and 0.56 for Latinos. No significant differences were found between the SCI and control groups for TC/HDL when factored by ethnicity, although these ratios were consistently higher in all ethnic subgroups with SCI (Table 5). For each of the subgroups factored by ethnicity, those in the SCI subgroups had a significantly greater percentage of low HDL-c values (<35 mg/dl) than those in the control subgroups (whites: 34% *vs* 12%, $X^2_{(1)}=21.8$, $P<0.0001$; African Americans: 17% *vs* 6%, $X^2_{(1)}=5.5$, $P<0.05$; and Latinos: 54% *vs* 21%, $X^2_{(1)}=13.3$, $P<0.0005$).

Table 4 Comparison of serum lipid results between the study groups by gender

Gender	*SCI*	*Control*	P
Males	($n=233$)	($n=244$)	
TC	191±2.27	209±2.62	<0.0001
TG	114±3.79	126±3.64	<0.05
HDL-c	39±0.83	45±0.70	<0.0001
LDL-c	129±2.60	139±2.35	<0.01
TC/HDL-c	5.4±0.14	4.8±0.08	<0.0005
Females	($n=87$)	($n=59$)	
TC	188±3.76	199±5.11	
TG	94±4.76	82±4.99	
HDL-c	51±1.54	54±1.52	
LDL-c	118±3.45	129±5.29	
TC/HDL-c	4.0±0.16	3.9±0.18	

SCI = spinal cord injury; TC = total cholesterol in mg/dl; TG = triglycerides in mg/dl; HDL-c = high density cholesterol in mg/dl; LDL-c = low density cholesterol in mg/dl; and TC/HDL-c = the ratio of total to HDL-c. Significant differences were found between the SCI and control groups for all serum lipid variables in males, but none were found in females

Table 5 Comparison of serum lipid results between the study groups by ethnicity

Ethnicity	*SCI*	*Control*	P
White	($n=149$)	($n=169$)	
TC	187±3.32	209±2.95	<0.0001
TG	105±4.20	119±4.00	<0.01
HDL-c	41±1.02	46±0.86	<0.0001
LDL-c	125±3.01	138±2.82	<0.005
TC/HDL-c	5.0±0.16	4.7±0.10	
African American	($n=88$)	($n=87$)	
TC	195±4.55	204±4.86	
TG	91±4.79	101±5.65	
HDL-c	49±1.56	51±1.27	
LDL-c	128±4.46	133±4.51	
TC/HDL-c	4.4±0.18	4.2±0.14	
Latino	($n=83$)	($n=47$)	
TC	190±4.24	209±5.85	<0.01
TG	132±6.95	143±10.01	
HDL-c	37±1.53	42±1.59	<0.05
LDL-c	126±3.78	138±4.75	<0.05
TC/HDL-c	5.7±0.24	5.2±0.19	

SCI = spinal cord injury; TC = total cholesterol in mg/dl; TG = triglycerides in mg/dl; HDL-c = high density cholesterol in mg/dl; LDL-c = low density cholesterol in mg/dl; and TC/HDL-c = the ratio of total to HDL-c. Significant differences were found between the SCI and controls for various serum lipid variables in the White and Latino ethnic subgroups, but not in the African American subgroup

Comparisons among the ethnic categories within the SCI and the control groups showed that African Americans had higher HDL-c values than whites or Latinos (SCI: 49±1.56 *vs* 41±1.02 mg/dl, $P<0.0001$ or 37±1.53 mg/dl, $P<0.0001$, respectively; controls: 51±1.27 *vs* 46±0.86 mg/dl, $P<0.01$ or 42±1.59 mg/dl, $P<0.0005$, respectively) (Figure 1A). Differences in serum TG values were also evident based on ethnicity. Within the SCI and control groups, African Americans had significantly lower serum TG than Latinos (SCI: 91±4.80 *vs* 132±6.95 mg/dl, $P<0.0001$; controls: 101±5.65 *vs* 143±10.01 mg/dl, $P<0.0005$); within the control group, African Americans had significantly lower serum TG levels than whites (101±5.65 *vs* 119±4.00 mg/dl, $P<0.05$) (Figure 1B). For both groups, whites also had significantly lower serum TG than Latinos (SCI: 105±4.20 *vs* 132±6.95 mg/dl, $P<0.001$; controls: 119±4.00 *vs* 143±10.01 mg/dl, $P<0.05$) (Figure 1B). Lower serum TC/HDL cholesterol ratios were also demonstrated in the African Americans compared with the whites or Latinos within the SCI or control groups (SCI: 4.4±0.18 *vs* 5.0±0.16 mg/dl, $P<0.06$ or 5.7±0.24 mg/dl, $P<0.0001$, respectively; controls: 4.2±0.14 *vs* 4.7±0.10, $P=0.05$ or 5.2±0.19, $P<0.0005$).

In both groups, the serum HDL-c was inversely related to BMI and estimated per cent body fat (SCI: $r=0.27$, $P<0.0001$; control: $r=0.22$, $P<0.0001$). Serum HDL-c values were approximately 8 mg/dl lower for any given BMI in those with SCI. The slope of HDL-c with estimated per cent fat in those with SCI was found to be significantly steeper than in the control group (−0.546±111 *vs* −0.246±0.062, $F=5.9$, $P=0.015$).

The serum HDL-c values were found to be inversely correlated with serum triglycerides in both groups (SCI: $r=0.42$, $P<0.0001$; controls: $r=0.43$, $P<0.0001$). Factoring for gender or ethnicity, all subgroups demonstrated a significant inverse relationship between serum HDL-c and serum TG values (SCI males: $r=0.40$, $P<0.0001$; control males: $r=0.36$, $P<0.0001$; SCI females: $r=0.39$, $P<0.005$; control females: $r=0.47$, $P<0.0005$; SCI African Americans: $r=0.29$, $P<0.01$; SCI Latinos: $r=0.48$, $P<0.0001$; SCI whites: $r=0.36$, $P<0.0001$; control African

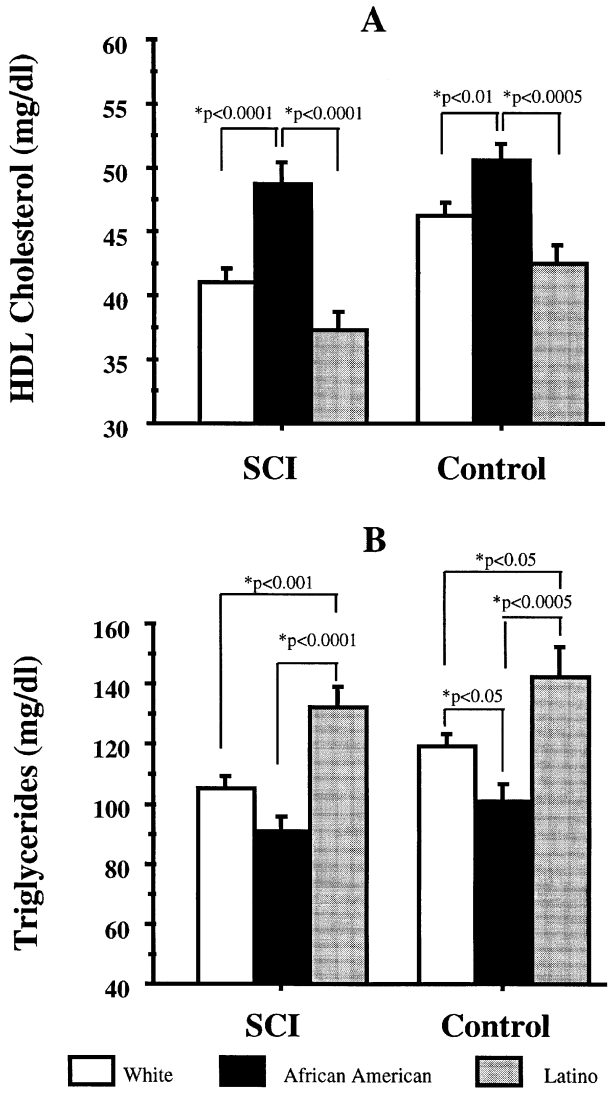

Figure 1 Comparison of Serum HDL Cholesterol and Triglycerides Among the Ethnic Subgroups. In the groups with spinal cord injury (SCI) and controls categorized by ethnicity, shown are bar graphs of (**A**) serum HDL cholesterol levels and (**B**) serum triglyceride levels

Americans: $r=0.38$, $P<0.0005$; control Latinos: $r=0.40$, $P<0.01$; and control whites: $r=0.42$, $P<0.0001$).

The significant predictors of serum HDL-c determined from stepwise regression analysis in order of importance include: serum TG, SCI/control group membership, gender, BMI, TC, and age ($P<0.05$ for all variables).

Discussion

Cardiovascular disease is a leading cause of mortality in individuals with chronic SCI,[1,2] appearing prematurely and being the most frequent cause of death among persons surviving more than 30 years after injury, accounting for 46% of all deaths.[1] An inverse relationship exists between serum HDL cholesterol level and CHD.[5–9] Serum HDL cholesterol has been reported to be depressed in individuals with SCI.[10–16] To date, the effect of gender or ethnicity on serum HDL cholesterol levels in subjects with SCI has not been addressed. In prior studies, cohorts with SCI were relatively small, most lacked a control population, all lacked women, and none published to date have addressed or controlled for possible differences in ethnicity.

Using a criterion established by the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, a serum HDL-c value less than 35 mg/dl is recognized as an independent risk factor for coronary heart disease.[19] Approximately 10% of the population in the United States has a serum HDL-c level less than 35 mg/dl.[24] In our study herein, approximately one-third of the subjects with SCI had serum HDL-c as a risk factor for CHD, whereas, the per cent of subjects in the control group with this risk factor (12%) was similar to that reported for the general population.

Subjects were studied for serum lipid determinations from 4–12 h post-prandially. Serum TG may be increased in a non-fasted state, and be associated with changes in serum HDL-c. To determine the effect of group membership (SCI *vs* control), controlling for serum TG, a multiple regression analysis was performed, which demonstrated that the difference between the groups was even stronger than those of the simple regression, strengthening the findings of a reduced serum HDL-c in subjects with SCI.

Cigarette smoking is well appreciated to influence the serum lipid profile. Serum HDL-c values have been reported to be lower in smokers than nonsmokers.[25,26] In a prior report, Spungen *et al*[27] noted that 31% of veterans with SCI were current smokers, a percentage which is comparable to that found in the general population.[28] In the study herein, the number of current male cigarette smokers appears to be evenly distributed for SCI and controls (27.9 *vs* 25%, respectively).[17,29] The females in the SCI groups had a lower prevalence of smokers than those in the control group (12.9 *vs* 40%, respectively).[17,29] Thus, cigarette smoking appears not to be the etiology of the lower serum HDL-c values in the SCI compared with the control group.

Moderate alcohol consumption has been recognized to raise the serum HDL-c level.[30,31] In the study herein, there was no rigorous attempt to screen patients in either group for alcohol consumption. However, an elevation of a serum liver function test, gamma-glutamyl transpeptidase (GGT), has been employed as a sensitive indicator of liver enzyme induction and may be associated with alcohol consumption,[32,33] as well as other pharmacological agents,[34] or viral hepatitis, was available for analysis in both groups. With the limitations of such an analysis appreciated, one may extrapolate using

serum GGT levels in a population to ascertain the prevalence of alcohol usage. The mean serum GGT was in the normal range for both groups, but was significantly higher for the SCI than the control group; 73 of those with SCI and 38 of the controls had levels above the normal range (unpublished observation by the authors). An elevation in serum GGT is a nonspecific finding and may certainly have represented a higher frequency of prescribed medications in persons with SCI than in the able-bodied population. However, since moderate alcohol consumption is associated with an increase in serum HDL-c, and subjects with SCI had a serum marker for alcohol intake that was within the normal range or modestly elevated compared with the control group, the finding herein of a lower mean serum HDL-c level in those with SCI does not appear to be explained on the basis of alcohol intake.

Diet may influence the serum lipid values, however the effect is usually relatively minor in the absence of stringent dietary prescriptions. All of our subjects, able-bodied and those with SCI, were living freely in the community and eating *ad lib*. In our report herein, there was no attempt to obtain a detailed dietary history. A prior study of veterans with paraplegia compared with age-matched ambulatory veteran controls found a significantly lower mean serum HDL cholesterol level in the group with SCI compared with able-bodied persons despite no significant differences noted for total caloric, saturated fat, or cholesterol intake between the groups.[35]

A provocative finding in this study was the absence of a significant difference in mean serum HDL-c in female controls compared with those in the SCI group. Of note, a higher percentage of women in the control group were current smokers than in the SCI group, which may have depressed mean serum HDL-c values in the controls and contributed to the lack of difference observed between the groups. The average age of the women in both groups was about 40 years, which is expected to be pre-menopausal in approximately 95% of females. Since estrogen is associated with a more favorable lipid profile (i.e., elevation in serum HDL-c and reduction in serum LDL-c),[36] a future study of a sufficient sample size, in post-menopausal (estrogen-deficient) women with SCI should be compared with post-menopausal able-bodied women to determine if a possible difference in serum lipid values exists between the groups. However, it should be appreciated that significantly more women with SCI than those in the control group had serum HDL-c values that were relatively depressed (i.e. less than 45 mg/dl), suggesting that a subgroup of women with SCI are at increased risk for CHD.

The serum HDL-c level has been found in several population-based studies to be higher in African Americans than in other ethnic backgrounds.[37–39] In the study herein, our findings demonstrated that in individuals with SCI, as well as in the controls, African Americans had higher serum HDL-c values than whites or Latinos. Of note, African Americans in the SCI group did not have significantly lower mean serum HDL-c levels compared with those in the control group. There was no significant difference in BMI values across ethnic subgroups within the SCI or control groups which would possibly explain the absence of a difference in serum HDL-c levels in African Americans. However, a greater percentage of African Americans with SCI compared with controls had serum HDL-c levels less than 35 mg/dl. Serum triglycerides were lower and HDL-c levels, higher in the African American group compared with white or Latino group. The higher serum TG levels noted in the Latinos compared with whites in our SCI subjects and controls had previously been reported by other investigators in the able-bodied population.[40]

The ratio of serum total to HDL cholesterol has been reported by Stampfer *et al* to be a particularly strong discriminator for risk of myocardial infarction.[21] A one unit increase in this ratio was associated with a mean increase of 53% in the risk of myocardial infarction. Despite significantly higher serum LDL-c values in the control group, the ratio of serum total cholesterol to HDL cholesterol was significantly higher by about half of one per cent in the SCI group, demonstrating the predominant effect on the lipid profile of the depressed serum HDL-c values in those with SCI. Approximately 43% of those with SCI had a ratio of serum total cholesterol to HDL cholesterol greater than 5.0. Recent studies have clearly demonstrated that a reduction in serum LDL-c level, as well as the ratio of serum total to HDL cholesterol, is associated with reduction in events of CHD.[41–44] African Americans, whether immobilized or not, had mean serum total to HDL cholesterol ratios that were lower than in the other ethnic subgroups studied.

Any immobilizing condition is associated with muscle loss, and persons with SCI have marked muscle atrophy below the level of lesion. In both SCI and control groups, the measures of adiposity, BMI and estimated per cent fat, were inversely correlated with serum HDL-c levels. The finding that serum HDL-c was 8 mg/dl on average lower for any given BMI in the SCI group than in the controls might be explained by the increased adiposity in those with SCI. The absolute BMI value has recognized limitations when applied across study groups with dramatic differences in body composition, as was apparent in this study. Inverse associations were evident between measures of adiposity and serum HDL-c levels in both groups. In the SCI and control groups, and in all the subgroups categorized by ethnicity, a significant inverse relationship was demonstrated between serum HDL-c and triglycerides, which may be a consequence of an insulin resistant state related to the degree of adiposity with associated metabolic sequelae.[45–47]

Our findings suggest that paralysis and immobilization had an effect on the serum HDL-c concentration

only in men, whites and Latinos. A subgroup of women with SCI had relatively lower serum HDL-c values. As has been demonstrated previously in the able-bodied population, African Americans within the control and SCI groups had higher levels of HDL-c than whites or Latinos, without any difference appreciated for African Americans in mean levels between the SCI and control groups. Associations were demonstrated among body adiposity and serum lipid values in specific subgroups of individuals with SCI.[11,48,49] Individuals with SCI who have lower serum HDL-c values and higher ratios of total cholesterol to HDL-c would be expected to have increased risk for CHD.

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References

1 Whiteneck G. Learning from Recent Empirical Investigations. In: Menter R, Whiteneck G (eds). *Aging with Spinal Cord Injury*. Demos Publications: New York, NY, 1992, pp 23–37.
2 Yekutiel M *et al*. The prevalence of hypertension, ischemic heart disease and diabetes in traumatic spinal cord injured patients and amputees. *Paraplegia* 1989; **27:** 58–62.
3 Geisler WO, Joussy AT, Wynne-Jones M, Breithaupt D. Survival in traumatic spinal cord injury. *Paraplegia* 1983; **21:** 364–373.
4 Samsa P, Patrick C, Feussner JR. Long term survival of veterans with traumatic spinal cord injury. *Arch Neurol* 1993; **50:** 909–914.
5 Castelli WP *et al*. HDL-cholesterol and other lipids in coronary heart disease: the cooperative lipoprotein phenotyping study. *Circulation* 1977; **55:** 767–777.
6 Goldbour U, Medalie JH. High density lipoprotein cholesterol and incidence of coronary heart disease: The Israeli ischemic heart disease study. *Am J Epidemiol* 1979; **109:** 296–308.
7 Castelli WP. Epidemiology of coronary heart disease: The Framingham Study. *Am J Med* 1984; **76 (2A):** 4–12.
8 Castelli WP, Leaf A. Identification and assessment of cardiac risk – an overview. *Cardiol Clin*. 1985; **3:** 171–178.
9 Gordon T, Castelli WP. High density lipoprotein as a protective factor against CHD: The Framingham Study. *Am J Med* 1977; **62:** 707–709.
10 Bauman WA *et al*. Depressed serum high density lipoprotein cholesterol levels in veterans with spinal cord injury. *Paraplegia* 1992; **30:** 697–703.
11 LaPorte RE *et al*. HDL-cholesterol across a spectrum of physical activity from quadriplegia to marathon running. *Lancet* 1983; **1:** 1212–1213.
12 Brenes G *et al*. High density lipoprotein cholesterol concentrations in physically active and sedentary spinal cord injured patients. *Arch Phys Med Rehabil* 1986; **67:** 445–450.
13 Dearwater SR *et al*. Activity in the spinal cord-injured patient: An epidemiologic analysis of metabolic parameters. *Med Sci Sports Exerc* 1986; **18:** 541–544.
14 Hooker SP, Wells CL. Effects of low- and moderate-intensity training in spinal cord-injured persons. *Med Sci Sports Exerc* 1989; **21:** 18–22.
15 Bauman WA *et al*. The effect of residual neurological deficit on serum lipoprotein profiles in persons with chronic spinal cord injury. *Spinal Cord* 1998; **36:** 13–17.
16 Bauman WA *et al*. Ethnicity effect on the serum lipid profile in persons with spinal cord injury. *Arch Phy Med Rehabil* 1998; **79:** 176–180.
17 Herbert R *et al*. Occupational Coronary Heart Disease among Bridge and Tunnel Officers. (in press).
18 Friedwald WT, Levy RJ, Fredrickson DS. Estimation of the concentration of low density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. *Clin Chem* 1972; **18:** 499–502.
19 Summary of the second report of the national Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel II). American Medical Association. *JAMA* 1993; **269:** 3015–3023.
20 Kannel WB, Wilson PWF. Efficacy of lipid profiles in prediction of coronary disease. *Amer Heart J* 1992; **124:** 768–774.
21 Stampfer MJ *et al*. A prospective study of cholesterol, apolipoprotein values and the risk of myocardial infarction. *N Engl J Med* 1991; **325:** 373–381.
22 National Institutes of Health Consensus Development Panel Conference Statement: Health implications of obesity. *Ann Intern Med* 1976; **60:** 80–88.
23 Cohen J. In: *Statistical Power Analysis for the Behavioral Sciences*. 2nd Edn. Lawrence Erlbaum Associates: Hillsdale, New Jersey 1988, pp 211–214.
24 Grundy SM *et al*. The place of HDL in cholesterol management. A perspective from the national cholesterol education program. *Arch Intern Med* 1989; **149:** 505–510.
25 Criqui MH *et al*. Cigarette smoking and plasma high-density lipoprotein cholesterol. Ther lipid research clinics program prevalence study. *Circulation* 1980; **62(suppl IV):** 70–76.
26 Facchini FS *et al*. Insulin resistance and cigarette smoking. *Lancet* 1992; **339:** 1128–1130.
27 Spungen AM, Bauman WA, Almenoff PL, Lesser M. Prevalence of cigarette smoking in a group of male veterans with chronic spinal cord injury. *Military Med* 1992; **160:** 308–311.
28 Centers for Disease Control: Cigarette smoking among adults – United States. *MMWR* 1992; **41:** 354–355.
29 Spungen AM, Bauman WA, Adkins RH, Waters RL. Smoking prevalence in a diverse California-based out-patient population with spinal cord injury. *J Spinal Cord Med* 1998; **21:** 176.
30 Haskell WL *et al*. The effect of cessation and resumption of moderate alcohol intake on serum high-density-lipoprotein subfractions. A controlled study. *N Engl J Med* 1984; **310:** 805–810.
31 Bertiere MC, Betoulle D, Apfelbaum M, Girard-Globa A. Time-course, magnitude and nature of the changes induced in HDL by moderate alcohol intake in young non-drinking males. *Atherosclerosis* 1986; **61:** 7–14.
32 Rosman AS. Utility and evaluation of biochemical markers of alcohol consumption. *J Substance Abuse* 1992; **4:** 277–297.
33 Rosman AS, Leiber CS. Biological Markers of Alcoholism. In: Leiber CS (ed). *Medical and Nutritional Complications of Alcoholism*. Plenum Press. New York, NY 1992, pp 534–536.
34 Salaspuro M. Conventional and coming laboratory markers of alcoholism and heavy drinking. *Alcoh Clin Exp Res* 1986; **10:** 5S–12S.
35 Zlotolow SP, Levy E, Bauman WA. The serum lipoprotein profile in veterans with paraplegia: the relationship to nutritional factors and body mass index. *J Amer Paraplegia Soc* 1992; **15:** 158–162.
36 Tikkanen MJ. Estrogens, progestins and lipid metabolism. *Maturitas* 1996; S51–S55.
37 Rubins HB *et al*. Distribution of lipids in 8,500 men with coronary artery disease. Department of Veterans Affairs HDL Intervention Trial Study Group. *Am J Cardiol* 1995; **75:** 1196–1201.
38 Sprafka JM *et al*. Life-style factors do not explain racial differences in high-density lipoprotein cholesterol: the Minnesota Heart Survey. *Epidemiology* 1992; **3:** 156–163.
39 Anderson RA *et al*. Genetic markers associated with high density lipoprotein cholesterol levels in a biracial population study. *Genet Epidemiol* 1992; **9:** 109–121.

40 Srinivasan SR, Powers CR, Webber LS, Berenson GS. Serum lipid and lipoprotein profiles of military personnel and their families: Fort Polk Heart Smart Program. *Mil Med* 1993; **158:** 323–326.
41 The Lipid Research Clinics Coronary Primary Prevention Trial Results, II: The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. *JAMA* 1984; **251:** 365–374.
42 Randomized trial of cholesterol lowering in 444 patients with coronary heart disease: The Scandinavian Simvastatin Survival Study (4S): *Lancet* 1994: **344:** 1383–1389.
43 Shepherd J *et al*. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. *N Engl J Med* 1995; **333:** 1301–1307.
44 Frisk MH *et al*. Helsinki Heart Study: Primary-prevention trial with gemfibrozil in middle-aged men with dyslipidemia: safety of treatment, changes in risk factors, and incidence of coronary heart disease. *N Engl J Med* 1987; **317:** 1237–1245.
45 Yalow RS, Rose HG, Bauman WA. Hyperinsulinemia. *Am J Med* 1988; **85:** 22–30.
46 Reaven GM, Greenfield MS. Diabetic hypertriglyceridemia: Evidence for three clinical syndromes. *Diabetes* 1981; **30:** 66–75.
47 Golay A *et al*. High density lipoprotein (HDL) metabolism in noninsulin-dependent diabetes mellitus: Measurement of fHDL turnover using tritiated HDL. *J Clin Endocrinol Metab* 1987; **65:** 512–518.
48 Reaven GM. Syndrome X. *Clin Diabetes* 1994; March-April 32–36.
49 DeFronzo RA, Ferrannini E. Insulin resistance: A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diabetes Care* 1991; **14:** 173–194.