Cardiac Troponins T and I in Patients with End-Stage Renal Disease: The Relation with Left Ventricular Mass and Their Prognostic Value

ADNAN ABACI, M.D., FESC, EYUP EKICI, M.D.,† ABDURRAHMAN OGUZHAN, M.D., FESC,* BULENT TOKGOZ, M.D.,† CENGİZ UTAS, M.D.†

Department of Cardiology, Gazi University School of Medicine, Ankara; Departments of *Cardiology and †Nephrology, Erciyes University School of Medicine, Kayseri, Turkey

Summary

Background: Cardiac troponins are frequently elevated in patients with end-stage renal disease (ESRD) in the absence of acute myocardial ischemia. The cause and prognostic value of cardiac troponin elevations in such patients are controversial.

Hypothesis: The aims of this study were (1) to define the incidence of cTnT and cTnI elevations in patients with ESRD, (2) to evaluate the relationship between troponin elevations and left ventricular mass index (LVMI), and (3) to evaluate the prognostic value of elevations in cTnT and cTnI prospectively.

Methods: We included 129 patients with ESRD (71 men, age 44 ± 16 years) with no clinical evidence of coronary artery disease. All patients underwent cardiac examinations, including medical history, physical examination, electrocardiogram, and transthoracic echocardiography. Left ventricular mass index was calculated and all patients were followed for 2 years.

Results: The cTnT concentration was >0.03 – 0.1 ng/ml in 27 (20.9%) and >0.1 ng/ml in 27 (20.9%) of the 129 patients. The cTnI concentration was >0.5 ng/ml in 31 (24%) of 129 patients. Multiple logistic regression analysis identified LVMI ($p < 0.001$), diabetes ($p = 0.001$), and serum albumin level ($p = 0.009$) as a significant independent predictor for elevated cTnT. Left ventricular mass index was the only significant independent predictor for elevated cTnI ($p = 0.002$). There were

25 (19.4%) deaths during follow-up. Multivariable analysis showed that elevation of cTnT and cTnI did not emerge as an independent predictor for death. Serum albumin level ($p < 0.001$) was the strongest predictor of mortality, followed by age ($p = 0.002$) and LVMI ($p = 0.005$).

Conclusions: Cardiac troponin T and I related significantly to the LVMI. The increased serum concentration of cardiac troponins probably originates from the heart; however, they are not independent predictors for prognosis.

Key words: kidney, enzymes, hypertrophy, prognosis

Introduction

It has been shown that cardiac troponins are elevated in up to 70% of patients with end-stage renal disease (ESRD) in the absence of acute myocardial ischemia.^{1–6} The precise source of elevated troponins remains unclear. Some studies suggest that elevation of cTnT may be due to the increased expression of cTnT in myopathic skeletal muscle in patients with renal disease.⁷ The most accepted explanation is that the elevated levels of troponins reflect myocardial cell damage; however, causes of myocardial cell damage are not clear. Some suggest that troponin elevations in patients with ESRD indicate coronary artery disease (CAD).^{8,9} Left ventricular hypertrophy (LVH) is common in patients with ESRD and the increase in troponin levels may be related with LVH.^{10,11}

Several previous studies have also evaluated the prognostic utility of troponins in patients with ESRD.^{3–6,12–15} The majority of these studies demonstrated that troponin elevation is a strong, independent prognostic indicator for short- and long-term adverse outcomes.^{3–5,14,15} However, other studies failed to confirm the association between troponin and death in patients with ESRD.^{4,6,12,13}

The aims of this study were (1) to define the incidence of cTnT and cTnI elevations in patients with ESRD, (2) to evaluate the relationship between troponin elevations and left ven-

---

Address for reprints:

Adnan Abaci, M.D., FESC
Gazi Üniversitesi Tıp Fakültesi
Kardiyoloji Anabilim Dalı
Besevler-06500, Ankara, Turkey
e-mail: abacia@hotmail.com

Received: July 29, 2004

Accepted with revision: September 29, 2004

tricular mass index (LVMI), and (3) to evaluate the prognostic value of elevations in cTnT and cTnI prospectively.

Methods

Patients

We included all patients with ESRD followed in the Nephrology Unit of our institution. Patients with angiographically proven stenosis (>50% of luminal diameter), acute coronary syndromes, history of myocardial infarction (MI), chronic stable angina pectoris, previous coronary revascularization, regional wall motion abnormalities in echocardiography, and significant electrocardiographic (ECG) changes suggestive of myocardial ischemia were excluded from the study. In all, 129 patients met these criteria and were enrolled in the study. Of these, 52 (40.3%) were treated with hemodialysis, 46 (35.7%) with peritoneal dialysis, and 31 (24%) were treated without dialysis. The study was approved by the local ethics committee of our institution, and all patients gave written informed consent.

Measurement of Serum Markers

Blood was collected from the antecubital vein in tubes without additives. Samples were centrifuged, and aliquots were stored at -70°C for subsequent measurements of troponins and C-reactive protein (CRP). Serum creatine kinase (CK) and CK-MB mass were determined immediately. The cTnT was measured using the Elecsys System 2010, an enzyme-linked immunosorbent assay (third generation) from Roche Diagnostics (Mannheim, Germany). We used a level of 0.03 ng/ml as the cTnT positivity. The patients were also grouped according to the standard diagnostic threshold for MI of 0.1 ng/ml. The cTnI was measured using the AxSYM System, a microparticle enzyme immunoassay from Abbott Laboratories (Abbott Park, Ill., USA). The cut-off value chosen for an abnormal cTnI was 0.5 ng/ml.

Echocardiography

Left ventricular (LV) diameters and wall thickness were measured by M-mode echocardiograms derived from two-dimensional (2-D) images in the parasternal long axis. Since LV volume fluctuates in patients on hemodialysis, echocardiography was performed on the day after dialysis to obtain echocardiograms at the patient's dry weight. The LV mass was calculated by the formula described by Devereux,¹⁶

$$\text{LV mass (g)} = 0.8 \times 1.04 [(\text{IVS} + \text{LVEDD} + \text{PWT})^3 - (\text{LVEDD})^3] + 0.6$$

where LVEDD is LV end-diastolic dimension, PWT is posterior wall thickness, and IVS is ventricular septal wall thickness. The LVMI was calculated as LV mass / body surface area; LVH was defined as LVMI > 134 g/m² in men and > 110 g/m² in women.¹⁷

Follow-Up

All patients were followed for 2 years. Hospital records as well as interviews with the patient, attending physician, or family were used for the verification of the cause of death or hospitalization. Cardiovascular mortality was defined as death due to MI, cardiogenic shock, heart failure, arrhythmias, stroke, and pulmonary embolism. Causes of death were categorized as cardiovascular, infectious, and other causes including unknown deaths. Survival was calculated from the time of the study entry until death or the end of the study period.

Statistical Analysis

Continuous variables were expressed as mean values $\pm$ standard deviation (SD), and categorical variables as percentages. Categorical variables were compared by Pearson chi-square statistic. Comparisons of continuous variables between two groups have been performed by Student's *t*- or Mann-Whitney U test. The differences in continuous variables among the three groups were performed by analysis of variance or Kruskal-Wallis test. Univariate and multivariate stepwise logistic regression analysis was used to assess the independent predictors for troponin positivity; the following variables were included in the analysis: age, gender, diabetes mellitus, hypertension, CRP, CK-MB, blood urea nitrogen (BUN), creatinine, serum albumin level, and LVMI.

Survival among patients with elevated or normal troponins was compared with the log-rank test. Univariable and multivariable associations of variables with the endpoints were assessed using the Cox regression analysis. These variables were age, gender, diabetes mellitus, hypertension, hemoglobin, serum albumin level, BUN, CRP, cTnT, cTnI, type of dialysis (hemo, peritoneal, none), LV ejection fraction, and LVMI. We analyzed troponins as a continuous and as a categorical variable.

For all tests, a value of $p < 0.05$ was considered statistically significant. The Statistical Package for Social Sciences (version 10.0) (SPSS, Inc., Chicago, Ill., USA) was used to perform all statistical calculations.

Results

Baseline characteristics of the study patients are summarized in Table I. The cTnT concentration was >0.03 to 0.1 ng/ml in 27 (20.9%) and >0.1 ng/ml in 27 (20.9%) and the cTnI concentration was >0.5 ng/ml in 31 (24%) of the 129 patients. Univariate logistic regression analysis indicated that cTnT positivity was closely associated with age, diabetes, hypertension, CRP, serum albumin level, and LVMI (Table II). Multiple logistic regression analysis identified LVMI, diabetes, and serum albumin level as a significant independent predictor for elevated cTnT. The LVMI is the strongest independent correlate of cTnT positivity. Univariate logistic regression analysis indicated that cTnI positivity was closely as-

TABLE I The clinical baseline characteristics of the study patients

	cTnT ≤ 0.03 ng/ml (n = 75)	cTnT 0.03–0.1 ng/ml (n = 27)	cTnT > 0.1 ng/ml (n = 27)	cTnI < 0.5 ng/ml (n = 98)	cTnI > 0.5 ng/ml (n = 31)
Age (years)	42 ± 15	46 ± 16	50 ± 16	44 ± 15	45 ± 18
Male	36 (48)	16 (59.3)	19 (70)	51 (52)	20 (65)
Diabetes	3 (4) ^b	6 (22.2)	15 (55.6)	20 (20.4)	4 (12.9)
Hypertension	44 (58.7) ^a	21 (77.8)	25 (92.6)	64 (65.3)	26 (83.9)
Albumin (g/dl)	4.07 ± 0.41 ^b	3.82 ± 0.49	3.59 ± 0.54	3.95 ± 0.46	3.81 ± 0.57
BUN (mg/dl)	63 ± 20	61 ± 19	73 ± 27	62 ± 21	74 ± 23 ^a
Creatinine (mg/dl)	8.2 ± 3.7	7.8 ± 3.2	8.8 ± 3.6	8.0 ± 3.6	9.0 ± 3.5
cTnT (ng/ml)	0.005 ± 0.009 ^b	0.066 ± 0.023	0.410 ± 0.588	0.098 ± 0.346	0.115 ± 0.152
cTnI (ng/ml)	0.197 ± 0.488 ^b	0.341 ± 0.437	0.785 ± 1.308	0.059 ± 0.129	1.271 ± 1.121 ^b
CRP (mg/l)	9.0 ± 15.9 ^a	20.8 ± 24.4	21.8 ± 27.1	12.5 ± 20.0	19.1 ± 24.2
CK-MB (U/l)	11.7 ± 6.8	13.9 ± 14.3	17.1 ± 14.3	13.3 ± 10.9	13.3 ± 9.9
LVEF (%)	68.1 ± 7.2 ^b	63.6 ± 12.4	56.6 ± 11.8	66.1 ± 8.6	60.4 ± 14.2 ^a
LVMI g/m ²	124 ± 43 ^b	168 ± 70	170 ± 56	134 ± 49	171 ± 69 ^a
LVH (%)	35 (46.7) ^b	20 (74.1)	23 (85.2)	54 (55.1)	24 (77.4) ^a

Data presented are mean value ± standard deviation or number (%) of patients.

^a p < 0.05.

^b p ≤ 0.001.

Abbreviations: BUN = blood urea nitrogen, LVMI = left ventricular mass index, LVH = left ventricular hypertrophy, CRP = C-reactive protein, CK-MB = creatine kinase-MB, LVEF = left ventricular ejection fraction.

TABLE II Factors associated with elevated troponin levels

	cTnT > 0.03 ng/ml				cTnI > 0.5 ng/ml			
	Univariate		Multivariate		Univariate		Multivariate	
	Wald χ^2	p Value	Wald χ^2 (OR [95% CI])	p Value	Wald χ^2	p Value	Wald χ^2 (OR [95% CI])	p Value
Age	4.671	0.031			0.011	NS		
Diabetes	17.478	<0.001	11.736 (11.124 [2.803–44.141])	0.001	0.860	NS		
Hypertension	9.702	0.002			3.642	NS		
CRP	8.596	0.003			2.135	NS		
BUN	1.061	NS			7.221	0.007		
Albumin	14.744	<0.001	6.848 (0.275 [0.105–0.723])	0.009	1.988	NS		
LVMI	16.489	<0.001	14.452 (1.013 [1.006–1.020])	<0.001	8.861	0.003	9.976 (1.010 [1.004–1016])	0.002

Abbreviations: OR = odds ratio, CI = confidence interval, NS = not significant.

Other abbreviations as in Table I.

sociated with BUN and LVMI. Multiple logistic regression analysis identified LVMI as the only significant independent predictor for elevated cTnI. There is no significant correlation between creatinine and cTnT or cTnI.

Follow-Up and Prognostic Significance of Troponin Measures

There were 25 (19.4%) deaths at follow-up (Table III). The incidence of death was significantly higher in patients with el-

evated cTnT than in patients with normal cTnT. Survival among cTnT-positive patients was significantly lower than that in cTnT-negative patients (log-rank 23.85, p < 0.0001, Fig. 1). The incidence of death was significantly higher in patients with elevated cTnI than in patients with normal cTnI. The Kaplan-Meier survival analysis showed that survival was significantly lower in patients with positive cTnI than that in cTnI-negative patients (log-rank 5.15, p = 0.0232, Fig. 1).

Univariable analysis identified age, diabetes, hypertension, cTnT, cTnI, CRP, serum albumin level, and LVMI as a signif-

TABLE III Outcomes

	cTnT ≤ 0.03 (n = 75)	cTnT 0.031–0.1 (n = 27)	cTnT > 0.1 (n = 27)	cTnI < 0.5 (n = 98)	cTnI > 0.5 (n = 31)	Total (n = 129)
All-causes deaths	6 (8.0) ^b	6 (22)	13 (48.1)	15 (15.3)	10 (32.3) ^a	25 (19.4)
Causes of death						
Cardiovascular	3 (4.0) ^c	4 (14.8)	5 (18.5)	5 (5.1)	7 (22.6) ^a	12 (9.3)
Infection	2 (2.7)	2 (7.4)	3 (11.1)	5 (5.1)	2 (6.5)	7 (5.4)
Other	1 (1.3)	0 (0)	5 (18.5)	5 (5.1)	1 (3.2)	6 (4.7)

Data presented are number (%) of patients.

^a < 0.05, ^b < 0.001, ^c < 0.05 for cTnT ≤ 0.03 vs. > 0.03 ng/ml.

FIG. 1 Kaplan-Meier curves of survival free of death.

TABLE IV Cox regression analysis for all-cause mortality

	Wald χ^2		Wald χ^2		
	Univariate	p Value	Multivariate	Adjusted hazard ratio (95% CI)	p Value
Age	8.730	0.003	9.668	1.047 (1.017–1.077)	0.002
Diabetes	15.576	< 0.001			
Hypertension	5.460	0.019			
cTnT ng/ml	11.503	0.001			
cTnT					
≥ 0.03 ng/ml					
> 0.03–0.1 ng/ml	18.170	< 0.001			
> 0.1 ng/ml					
cTnI (ng/ml)	9.307	0.002			
cTnI					
≤ 0.5 ng/ml	4.783	0.029			
> 0.5 ng/ml					
CRP	4.505	0.034			
BUN	3.732	0.053			
Albumin	20.037	< 0.001	17.779	0.201 (0.095–0.423)	< 0.001
LVMI	5.279	0.022	7.857	1.010 (1.003–1.017)	0.005

Data presented are mean value $\pm$ standard deviation or number (%) of patients.

Abbreviation: CI = confidence interval. Other abbreviations as in Table I.

icant univariate predictors for death (Table IV). However, multivariable analysis showed that elevation of cTnT and cTnI did not emerge as an independent predictor for death. Serum albumin was the strongest predictor of mortality, fol-

lowed by age and LVMI. We further explored the relationship between continuous troponin values and mortality and found that neither cTnT nor cTnI concentration was an independent predictor of death.

Discussion

The present study confirms and extends earlier observations on the high prevalence of increased troponin concentrations in patients with ESRD. However, our study expands on previous studies in several areas of clinical importance. We demonstrated a highly significant association between troponin elevation and LVMI; LVMI, but neither cTnT nor cTnI, was an independent predictor of mortality.

Causes of Troponin Elevations in End-Stage Renal Disease

Uremia itself is unlikely to explain elevated serum cTnT and cTnI levels in patients with ESRD, since it is seen only in some patients. In our study, we observed no correlation between elevated troponins and serum creatinine or BUN, which is in agreement with previous studies.^{2,7,12} Since the kidney is unlikely to be responsible for the troponin clearance, it is impossible that the decreased clearance of troponin is responsible for the elevations.⁹

Re-expression of the cardiac isoform of cTnT in myopathic skeletal muscle of patients with ESRD is controversial.^{7,8,18} Cross reactivity with skeletal muscle is unlikely, since the troponin T assay has been refined; cross reaction with skeletal muscle is not a problem with the second- and third-generation assays.¹⁸

Troponin elevation may be due to repeated episodes of clinically silent, small MIs^{8,9} because CAD is common in these patients. However, increased cTnT is frequently encountered in patients at low risk for CAD,^{2,5,7} and troponin elevations are as frequent in patients without CAD as in those with known CAD.^{2,5,7,13} Our findings were not consistent with a major contribution from CAD since we excluded patients with CAD from the study.

Many patients with ESRD have LV pressure and volume overload, mainly due to hypertension and anemia. Left ventricular hypertrophy is harmful because of myocyte death, decrease in capillary density, and increase in myocardial fibrosis.¹⁹ Two studies examined the factors associated with increased serum levels of cTnT and found that LVMI was independently associated with cTnT;^{10,11} our data are in agreement with these studies. Only one report examined the relation between LVMI and cTnI positivity, and it was found that only age is associated with cTnI positivity. In our study, multiple logistic regression analysis identified LVMI as an independent predictor for elevated cTnT and the only significant independent predictor for elevated cTnI. Therefore, the relationship between cardiac enzyme elevations, both cTnT and cTnI and the presence of LVH allows us to speculate that the cause of troponin elevations in patients with ESRD might be cardiac damage caused by LVH.

Prognostic Utility of Troponins in End-Stage Renal Disease

Several previous studies have evaluated the prognostic utility of cardiac troponins in patients with ESRD.^{3,4,12–15,20} The majority of these studies demonstrated that elevated

cTnT is an important independent predictor for adverse events and death during 1 to 2 years of follow-up;^{3,4,14,15,20} however, some studies have found no increase in mortality with increased cTnT.^{12,13} Although these studies found cTnT to be an independent predictor of survival, they did not determine LVH and/or LVMI. The only study including both LVMI and cTnT in multivariate analysis found that cTnT and LVMI were independent predictors of mortality;¹¹ however, we identified LVMI, but not cTnT, as an independent predictor for mortality. There is an apparent discrepancy between the results of this and our study; that study included patients with CAD, whereas ours did not. Inclusion of patients with CAD may increase the prognostic power of cTnT. Indeed, Lang *et al.* showed that correlation between troponin elevation and mortality was low or absent in patients with ESRD without CAD.¹³

The relationship between cTnI and mortality is more controversial than that between mortality and cTnT.^{4–6,12–15} A majority of these studies demonstrated that elevated cTnI is not an independent predictor for death;^{4,6,12,13,15} again, these studies did not determine LVH and/or LVMI.

Limitations

Exclusion of CAD was mainly based on the history of pre-existing CAD, and on ECG and echocardiography findings. Manifestations of CAD, such as angina pectoris or MI, are not sensitive to the diagnosis of CAD in patients with ESRD. Some patients with CAD may be missed in our study, and it is possible that some patients may have had subclinical CAD.

Conclusion

Our data demonstrate that cardiac troponins relate significantly to LVMI, and most patients with elevated troponins had LVH. The increased serum concentration of cardiac troponins probably originates from the heart and is a marker of LVH; however, cardiac troponin elevations are not an independent predictor for prognosis.

References

1. Frankel WL, Herold DA, Ziegler TW, Fitzgerald RL: Cardiac troponin T is elevated in asymptomatic patients with chronic renal failure. *Am J Clin Pathol* 1996;106:118–123
2. Ooi DS, House AA: Cardiac troponin T in hemodialyzed patients. *Clin Chem* 1998;44:1410–1416
3. Dierkes J, Domröse, Westphal S, Ambrosch A, Bosselmann HP, Neumann KH: Cardiac troponin T predicts mortality in patients with end-stage renal disease. *Circulation* 2000;102:1964–1969
4. Ishii J, Nomura M, Okuma T, Minagawa T, Naruse H, Mori Y, Ishikawa T, Kurokawa H, Hirano T, Kondo T, Nagamura Y, Ezaki K, Hishida H: Risk stratification using serum concentrations of cardiac troponin T in patients with end-stage renal disease on chronic maintenance dialysis. *Clin Chim Acta* 2001;312:69–79
5. Beciani M, Tedesco A, Violante A, Cipriani S, Azzarito M, Sturmiolo A, Spendiani G: Cardiac troponin I (2nd generation assay) in chronic haemodialysis patients: Prevalence and prognostic value. *Nephrol Dial Transplant* 2003;18:942–946

6. Khan IA, Wattanasuwan N, Mehta NJ, Tun A, Singh N, Singh HK, Vasavada BC, Sacchi TJ: Prognostic value of serum cardiac troponin I in ambulatory patients with chronic renal failure undergoing long-term hemodialysis. *J Am Coll Cardiol* 2001;38:991–998
7. McLaurin M.D., Apple FS, Voss EM, Herzog CA, Sharkey CW: Cardiac troponin I, cardiac troponin T and creatine kinase MB in dialysis patients without ischemic heart disease: Evidence of cardiac troponin T expression in skeletal muscle. *Clin Chem* 1997;43:976–982
8. Haller C, Zehelein J, Remppis A, Muller-Bardorff M, Katus HA: Cardiac troponin T in patients with end-stage renal disease. Absence of expression in truncal skeletal muscle. *Clin Chem* 1998;44:930–938
9. Freda BJ, Tang WHW, Van Lente F, Peacock WF, Francis GS: Cardiac troponins in renal insufficiency. *J Am Coll Cardiol* 2002;40:2065–2071
10. Iliou MC, Fumeron C, Benoit MO, Tuppin P, Courvoisier CL, Calonge VM, Moatti N, Buisson C, Jacquot C: Factors associated with increased serum levels of cardiac troponins T and I in chronic hemodialysis patients: Chronic Hemodialysis and New Cardiac markers Evaluation (CHANCE) study. *Nephrol Dial Transplant* 2001;16:1452–1458
11. Mallamaci F, Zoccali C, Parlongo S, Tripepi G, Benedetto FA, Cutrupi S, Bonanno G, Fatuzzo P, Rapisarda F, Seminara G, Stancanelli B, Bellanuova I, Cataliotti A, Malatino LS: Troponin is related to left ventricular mass and predicts all-cause and cardiovascular mortality in hemodialysis patients. *Am J Kidney Dis* 2002;40:68–75
12. Mockel M, Schindler R, Knorr L, Muller C, Heller G Jr, Stork TV, Frei U: Prognostic value of cardiac troponin T and I elevations in renal disease patients without acute coronary syndromes: A 9-month outcome analysis. *Nephrol Dial Transplant* 1999;14:1489–1495
13. Lang K, Schindler S, Forberger C, Stein G, Figulla HR: Cardiac troponins have no prognostic value for acute and chronic cardiac events in asymptomatic patients with end-stage renal failure. *Clin Nephrol* 2001;56:44–51
14. Apple FS, Murakami MM, Pearce LA, Herzog CA: Predictive value of cardiac troponin I and T for subsequent death in end-stage renal disease. *Circulation* 2002;106:2941–2945
15. Löwbeer C, Gutierrez A, Gustafsson SA, Norrman R, Hulting J, Seeberger A: Elevated cardiac troponin in peritoneal dialysis patients is associated with CRP and predicts all-cause mortality and cardiac death. *Nephrol Dial Transplant* 2002;17:2178–2183
16. Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, Reichek N: Echocardiographic assessment of left ventricular hypertrophy: Comparison to necropsy findings. *Am J Cardiol* 1986;57:450–458
17. Devereux RB, Lutas EM, Casale PN, Kligfield P, Eisenberg RR, Hammond IW, Miller DH, Reis G, Alderman MH, Laragh JH: Standardization of M-mode echocardiographic left ventricular anatomic measurements. *J Am Coll Cardiol* 1984;4:1222–1230
18. Ricchiuti V, Voss EM, Ney A, Odland M, Anderson PAW, Apple FS: Cardiac troponin T isoforms expressed in renal diseased skeletal muscle will not cause false-positive results by the second generation cardiac troponin T assay by Boehringer Mannheim. *Clin Chem* 1998;44:1919–1924
19. Parfrey PS, Foley RN: The clinical epidemiology of cardiac disease in chronic renal failure. *J Am Soc Nephrol* 1999;10:1606–1615
20. Ooi DS, Veinot JP, Wells GA, House AA: Increased mortality in hemodialyzed patients with elevated serum troponin T: A one-year outcome study. *Clin Biochem* 1999;32:647–652

Clin. Cardiol. 27, 709 (2004)

Progress in Clinical Trials

INTERHEART (A Global Study of Risk Factors in Acute Myocardial Infarction)

Presenter: Salim Yusuf, M.D., at the European Society of Cardiology 2004 Annual Meeting, Munich, Germany.

Background: Over 80% of the cardiovascular disease (CVD) burden occurs in low and middle income countries from which there are few data on CVD risk factors.

Aims: The aim of INTERHEART was to evaluate the association (odds ratio [OR]) of risk factors for myocardial infarction (MI) globally, and in each region, and among major ethnic groups in the world, and to quantify the impact of each risk factor alone and in combination on each population (population attributable risk [PAR]) overall and in each region, ethnic group, gender, and age group.

Methods: Data from 262 sites in 52 countries were gathered on first MI via blood sample and questionnaire covering demographics, lifestyle, health history, psychosocial factors, height, weight, hip circumference, blood pressure, and heart rate. The cohort included 15,000 patients with first acute MI and 15,000 matched asymptomatic controls.

Results: Nine potentially modifiable independent risk factors (adjusted) easily assessed in clinical practice were identified: ApoB/ApoA-1 (5 vs. 1) (OR 3.87), current smoking (2.95), diabetes (3.08), hypertension (2.48), abdominal obesity (2.22), psychosocial (2.51), daily vegetable/fruit consumption (0.70), exercise (0.72), alcohol intake (0.79). Combined they provided an adjusted OR of 129.2 and represented 90.4% of PAR.

While abdominal obesity assessed by waist-to-hip ratio conferred more than doubled risk, high body mass index without abdominal obesity was not associated with AMI.

The most important risk factors, overall, were abnormal ApoB/ApoA-1 ratio and smoking, conferring >90% of the PAR globally and in most regions. Risk factors were more important in younger individuals.

Conclusions: The vast majority of AMI cases can be explained by the presence of simple and potentially modifiable risk factors.

Discussion (Salim Yusuf): Implementing preventive strategies based on our current knowledge would avert the majority of premature chronic heart disease worldwide.