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SURVEY OF SERUM LIPID LEVELS IN CHILDREN FROM PARENTS WITH PREMATURE CORONARY ARTERY DISEASE

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ABSTRACT

BACKGROUND- **LIPID FACTORS ARE CURRENTLY CONSIDERED TO BE THE MAIN AGENT RESPONSIBLE FOR CARDIOVASCULAR RISK IN YOUNG INDIVIDUALS. SEVERAL EPIDEMIOLOGICAL STUDIES HAVE SHOWN THAT ATHEROSCLEROSIS BEGINS IN CHILDHOOD. THEREFORE, THERE IS A GENERAL CONSENSUS THAT THE EARLIER THE CONTROL BEGINS, THE BETTER THE RESULTS WILL BE. NOW THERE ARE MANY CONTROVERSIES REGARDING THE EARLY DIAGNOSIS OF HYPERLIPIDEMIA IN CHILDREN. THE AIM OF THIS STUDY WAS TO EVALUATE SERUM LIPID LEVELS IN CHILDREN WHOSE PARENTS SUFFER FROM PREMATURE CORONARY ARTERY DISEASE (CAD).**

METHODS- **IN THIS CROSS SECTIONAL STUDY, 76 CHILDREN BETWEEN 2-10 YEARS OLD (38 CHILDREN, WHOSE PARENTS HAD PREMATURE CAD, AND 38 HEALTHY, AGE AND SEX-MATCHED CONTROLS, WHOSE PARENTS DID NOT HAVE PREMATURE CAD) WERE STUDIED. THE HEIGHT, WEIGHT AND BODY MASS INDICES WERE SIMILAR IN BOTH GROUPS. SERUM LIPID LEVELS [TOTAL CHOLESTEROL, TRIGLYCERIDE, HIGH DENSITY LIPOPROTEIN (HDL) AND LOW DENSITY LIPOPROTEIN (LDL)] WERE MEASURED AFTER 10 HOURS FASTING FOR 2 TIMES, ONE WEEK APART, AND THE MEAN OF THE TWO VALUES WAS CONSIDERED AS THE AMOUNT OF EACH VARIABLE. DATA WERE ANALYZED WITH EPI 6, AND $P<0.05$ WAS CONSIDERED AS SIGNIFICANT.**

RESULTS- **RESULTS SHOWED THAT MEAN TOTAL CHOLESTEROL AND LDL WERE 167±20 AND 135±30MG/DL IN THE CASE GROUP AND 121±20MG/DL AND 101±20MG/DL IN THE CONTROL GROUP AND THAT THESE DIFFERENCES WERE SIGNIFICANT STATISTICALLY. THERE WERE NO DIFFERENCES BETWEEN THE TWO GROUPS FOR**

TRIGLYCERIDES AND HDL. IN THE CASE GROUP, SIX CASES HAD LDL LEVELS GREATER THAN 160MG/DL, WHILE THERE WERE NO SUCH CASES IN THE CONTROL GROUP.

Conclusion- We Therefore Concluded That Total Cholesterol And LDL Levels Were Higher In Children Of Parents With Premature CAD. This Necessitates Evaluation Of Serum Lipid Levels In Children Of Parents With Premature CAD ***(Iranian Heart Journal 2005; 6 (1,2): 6-10).***

KEY WORDS**: LIPID LEVEL ■ CHILDREN ■ PREMATURE CORONARY ARTERY DISEASE**

SEVERAL EPIDEMIOLOGIC STUDIES AND CLINICAL AND PATHOLOGICAL REPORTS HAVE SHOWN THAT ATHEROSCLEROSIS BEGINS IN CHILDHOOD. IN SEVERAL STUDIES, THE FATTY STREAK HAS BEEN SEEN IN THE AORTA OF MOST CHILDREN UNDER 10 YEARS AND ALSO FIBROUS PLAQUES IN TEENAGERS.[11] ATHEROSCLEROSIS IS THE MAIN CAUSE OF CAD IN ADULTS. SYMPTOMATIC CAD IN MEN UNDER 55 AND WOMEN UNDER 65 IS CALLED PREMATURE CAD.

THE KNOWN RISK FACTORS OF THIS DISEASE INCLUDE LIPID DISORDERS, DIABETES, SMOKING, HYPERTENSION AND GENETIC FACTORS.

SEVERAL STUDIES HAVE SHOWN THAT THERE IS A RELATION BETWEEN THE SERUM CHOLESTEROL LEVEL OF YOUNG ADULTS AND PREMATURE CAD.[3,9,13]

Measuring Serum Lipids Of Children Is Therefore Quite Important In Predicting The Level Of Serum Lipids In The Future.

Several studies have shown that serum lipid profile in children, after some years, may have a trend to average level.[4,5,9] National Cholestrol Education Program (NCEP) recommendations for detection and treatment of lipid disorders in children include a combined strategy of both population and individualized approaches. The population approach is aimed to affect lipid levels by population-wide changes in nutrient intake and eating patterns. The purpose of the individualized approach is to identify children who are at greatest risk by selective screening on the basis of family history of CAD or dyslipidemia. Universal serum lipid screening measures are not recommended in children, because the predictiveness of serum lipid values in children with respect to adult values is not considered adequate enough. Several authors have suggested some serious methods for primary prevention of CAD and evaluation of childrens' serum lipid values.[6,8,12] This study was carried out both to evaluate the importance of the relationship between lipid disorders in the children and CAD in adults and to screen high risk children. Its purpose was to find the incidence of lipid disorders in children of parents with premature CAD.

Methods

In this cross-sectional study, 76 children (38 children aged 2-10 years old, whose parents suffered from premature coronary artery disease, and 38 healthy children as controls with the same age and sex as the first group) were studied.

They were selected from patients with acute myocardial infarction (men under 55 and women under 65) hospitalized in CCU ward of Ali-ibn Abitaleb Hospital.

The patients were asked to fill out questionnaires, and their 2-10 year-old children, if any, were selected voluntarily for lipid tests.

The control group were selected from the children after 10 hours' fasting.

Serum lipids, including total cholesterol, triglycerides and HDL levels of all the samples were measured by one trained technician, and LDL was obtained by the calculation method.

The serum lipids of all the samples were measured twice at a one- week interval. When the difference

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between the two samples was more than 30 mg/dL, sampling was repeated at a one- week interval.

The average level of two or three samples was considered as that person's lipid level.

The independent T-test was used to analyze the data for comparing individualized values between the two groups.

The two-tailed test was used to compare the averages of the two groups, and chi-square test was utilized for sex comparison between the two groups.

Results

In this cross-sectional study, 76 children between 2 and10 years of age (38 children of parents with premature CAD and 38 healthy children of healthy families) were studied.

The mean age of the case group was 5.7±2.1years, and that of the control group was 5.4±2.4 years. In each group, there were 16 females (42.1%) and 22 males (57.9%).

In the case group, there were 25 children of fathers with CAD and 10 children of mothers with CAD, and 3 children had both parents with premature CAD.

The average of total cholesterol, triglycerides, LDL and HDL levels is shown in Table I.

Table. I. The mean and standard deviation of serum lipid levels in case and control groups

Variables	*groups*	No	Mean+ standard deviation	Std. Error *Mean*
Triglycerides	Case	38	177.8+ 35.3	5.8
	Control	38	176.1+ 35.7	6.06
Cholesterol	Case	38	167.2+ 30.1	5.74
	Control	38	121.6+ 30.7	5.72
HDL	Case	38	44.3+ 11.6	1.85
	Control	38	46.5+ 19.4	3.16
LDL	Case	38	135.8+ 23.1	5.88
	Control	38	101.1+ 20.3	5.69

Table II. Statistical analysis of the mean of variables in two groups

Variables	T	df	Sig 2- Tail	Mean difference
Triglycerides	2.253	74	0.10	10.9
	8.831	74	0.000	45.6
HDL	2.253	74	0.07	1.2
LDL	3.188	74	0.02	34.7

The mean total cholesterol and LDL in the case group was 167.2±30.1 and 135.8±23.1 mg/dL, and in the control group (121.6±30.7 and 101.1±20.3 mg/dL, respectively). There was a meaningful difference between the levels in the two groups. In the case group, 6 subjects (15.7%) had LDL levels higher than 160 mg/dL, but in the control group, none of them had LDL higher than 160 mg/dL. In the case group, 12 (31.5%) persons had cholesterol higher than 170 mg/dL, and 6 subjects (15.7%) had levels higher than 200 mg/dL. In the control group, 6 cases (15.7%) had cholesterol higher than 170, and 2 persons (5.2%) had levels higher than 200mg/dL.

The total cholesterol in the case group was higher than that in the control group in both females and males; that is, in the males, the levels were 158.8 and 102.5mg/dL, and in the females, 171.2 and 121.8 mg/dL, respectively (p=0.001). This difference was statistically meaningful, but there were no gender-related differences between the means of triglycerides, LDL and HDL in the two groups.

Discussion

The results of this study showed that the level of total cholesterol and LDL in the children of parents with premature CAD was higher

than levels in the children of parents without CAD, such that 15.7% of the children from parents with CAD had LDL levels higher than 160 mg/dL; 31.4% had cholesterol levels higher than 170; and 15.7% had cholesterol more than 200 mg/dL, which required treatment measures.

In one study on 250 children (6-12 years) of parents with premature CAD, the mean total cholesterol, LDL and TG in these children was considerably higher than that in the control group, but the absolute total cholesterol level and LDL in the children of parents with CAD was in the normal range. There was increased TG levels in 22.5% of the children of parents with premature CAD.[15] Also in the study of Azizi et al. in Tehran, 23% of the children (3-19 years old) had cholesterol levels of 170-179mg/dL, and 16% had cholesterol levels higher than 200mg/dL. However, in their study, a more extensive range of age had been considered (compared to our study), and the level of LDL had not been evaluated.[1]

Nevertheless, in a study by Sarrafzadegan et al., 23% of the children (2-6 years old) had cholesterol levels more than the 95th percentile, and in this study, 31% had high cholesterol.[2]

The difference may be due to the selection of high risk children in our study.

In the Prieto-Albino et al. study on 2150 children (2-6years) in the province of Caceres, Spain, 27.9% of the children had cholesterol higher than 200 mg/dL, and this incidence was higher in females before maturity.[7]

In the Yamata et al. study on 2626 children (7-15 years old) in Japan, there was an increase in the mean cholesterol of the boys (7-10 years old), and after schools encouraged physical exercise, the levels of cholesterol and triglycerides were lower and HDL was higher.[14]

The results of Resinco and colleagues' study on 6568 children showed that 28.2% of them had LDL levels qualified for treatment, and these results were similar to those of our study, in which 31.4% of the children had cholesterol levels higher than 170 mg/dL.[10] But in our study, the lipid levels in the children who were at greatest risk (from parents with premature CAD) were compared to this level in the children with less risk, and we showed that the cholesterol levels higher than 170mg/dL and LDL higher than 160mg/dL in the children with the greatest risk were much higher than those in the control group.

A study on 165 children (15-18years) of parents with hypercholesterolemia or premature CAD showed that 57.3% of them had cholesterol levels higher than 200 mg/dL and that 66.7% had LDL higher than 130 and 12% HDL less than 35mg/dl. The authors concluded that there was a high incidence of lipid disorders in this group.[16] Although in this study the incidence of lipid disorders was higher than that in our study, the results of both studies showed a high incidence of lipid disorders in the children of parents having premature CAD, which emphasized the necessity of evaluating the serum lipids in these children. The higher incidence of lipid disorders in the above study can be due to the subjects' different nutritional habits and different daily activities.

In a study by Dennison et al. on 331 children (4-17 years) of parents with CAD, the incidence of high cholesterol was 1.4 times, and high LDL level was twice that of the control group. Also 40% of the white children and 21% of black children with high LDL had parents with CAD. The results showed that the screening of

children for high LDL, only on the basis of the presence of CAD in their parents, was questionable.[17]

The results of this study conforms to the results of our study; that is, their level of total cholesterol was considerably higher than that in the control group, which emphasizes the high incidence of lipid disorders in the children of parents with premature CAD.

Another study on 806 Israeili children (6-14 years) showed that 49% of the children with hypercholesterolemia had parents with hypercholesterolemia and that 13% of them had history of premature CAD in their family. The results, therefore, showed that population screening was the most effective method in specifying the children having hypercholesterolemia.[18]

This study suggests a population screening for identifing lipid disorders in children with the purpose of knowing that children having hyperlipidemia implicates the presence of CAD and lipid disorders in their parents. It is different from our results, which advocate screening for lipid disorders in children with high-risk parents. Since the former method involves heavy expenses, it seems that the results of our study, recommending screening for hyperlipidemia based on high-risk parents, is more suitable.

Conclusions

In respect to higher cholesterol and LDL levels in the children of parents with premature CAD, it is necessary to study the serum lipids in these children and treat them, if they are qualified for treatment, so that this primary prevention strategy for CAD can be useful from childhood.

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Linseed Trial in Hyperlipidemic Patients

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Abstract

Background - Hyperlipidemia is an important cause of coronary artery diseases. Linseed contains large amounts of omega-3 fatty acids, and it has a major role in lowering serum lipid levels. This study evaluated the effect of linseed powder in patients who did not respond to regular diet regimens.

Methods - We conducted an interventional study (before and after) of 56 patients with hyperlipidemia that had not responded to a 3-month regular diet and had serum levels of total cholesterol >240 or TG>300 or LDL>160 or HDL<30 (mg/dl). We prepared the dose of 6 gr/day of linseed powder in the form of a biscuit and gave it to the patients for 3 months plus their regular diet regimen. The serum levels of lipids were measured before and after the 3-month intervention program. The data were analyzed using SPSS software with paired t-test.

Results - The mean (±SD) of serum level of total cholesterol before treatment was 258 (±55.59) mg/dl and afterwards was 232.05 (±41.47) mg/dl (P=0.0001). The mean serum triglyceride level before and after treatment was 289.92 (±126.57) mg/dl, and 225.07 (±82.58), respectively (P=0.0001). Also, the mean serum LDL decreased from 173.82 (±52.87) to 141.12 (±39.94) mg/dl (P=0.0001). However, no significant difference on HDL levels was found before and after intervention (43.89 (±25.66) vs. 43.53 (±13.84), P=0.85). Overall, the linseed powder regimen for 3 months decreased the total cholesterol by 10.2%, serum triglyceride by 22.33% and LDL cholesterol level by 18.8%. HDL level increased by 1.45%.

Conclusion - Linseed powder plus regular diet decreased the lipoprotein levels significantly. Thus, we recommend roughly 6 gr. daily consumption of linseed as a compliment of regular diet regimen in lowering the level of serum lipids ***(Iranian Heart Journal 2005; 6 (1,2): 37-42).***

Key words: hyperlipidemia ■ linseed ■ cholesterol ■ triglyceride■ LDL■ HDL■ diet

Cardiovascular diseases are a common cause of mortality and morbidity in the world, and hyperlipidemia is the major risk factor of these diseases. Primary and secondary cares showed that with interventional programs which result in decreasing serum lipid levels, the risk of coronary events will be decreased and also lead to regression of atherosclerotic plagues in coronary arteries.

Thus, the National Center of cholesterol in United States recommended interventional program in the general population.

This recommendation first emphasizes on diet and physical activities.

Due to the genetic susceptibility, many subjects with hyperlipidemia may not respond to regular diet regimens alone.

In this case, drug therapy for lowering lipid levels is recommended.

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step for controlling lipid levels.

The presence of fat in the diet is necessary for health status, and it provides the required energy, fatty acids and vitamins for bodily activities.[1]

Published studies confirm that cholesterol and triglyceride (TG) of serum has a direct relationship with the type and amount of daily fat consumption. Saturated fatty acids elevate the level of total cholesterol, and polyunsaturated and monounsaturated fatty acids decrease the cholesterol level.[2-4] The required fatty acids include omega-6 linoleic acid (LA) and omega-3 alpha linolenic acid (LNA). These fatty acids with polyunsaturated fatty acids (PUFA) must be provided through daily diet consumption.[5] WHO and FAO recommend that at least 15% of the daily-received energy be provided from fatty acids. Also, the ratio of LA to LNA must be between 5:1 and 10:1, and linoleic acid must provide 10 to 40% of daily energy supply.[1]

Linseed, or *Linum usitatissimum*, is a plant cultivated for extracting oil from its seed or using its fiber. Linseed oil is supplied from linolenic acid (LNA), and its combination is different in relation to type, size, seed and climatic conditions. In a study, 35g linseed oil (20.7g omega-3 LNA and 4.9g omega-6 LA) was extracted from each 100 grams of linseed.[6] In another study, it was shown that 52% fatty acid supplied in linseed was made from LNA and 17% from LA, and that also the ratio of PUFA to saturated fat was 6/9.[7] Linseed is the only plant oil which contains more than 50% LNA[8-10], and the rate of omega-3 fat of linseed is three times greater than that of fish oil.[6]

Published studies on the effect of omega 3 fat on serum lipids have almost always used fatty acid extracted from seafood (fish). There are a few studies of the effect of linseed on lipids of serum, and their results also are somewhat contradictory. Since linseed is the main source of omega 3 fatty acid, this interventional study was conducted to determine the effect of linseed powder on decreasing lipid levels in patients who did not respond to regular diet regimen.

Methods

We conducted an interventional study (before and after) in patients with hyperlipidemia who did not respond to the recommended 3-months regular diet regimens alone without drug therapy; i.e. their lipid levels (TG, Chol, LDL, HDL) did not change toward the normal level. In our formal definition, regular diet was defined as formal diet without animal oil, plant oil, red meat and any other internal components of sheep such as liver, kidney, etc., and the maximum consumption of yolk (of egg) allowed was 1 egg per week. We recruited 75

patients consecutively with convenience sampling method. All these patients gave informed consent before undergoing our linseed intervention program plus regular diet. We included subjects into the study whose cholesterol was >240 or TG>300 or HDL <30 and LDL>160. Subjects who did not give an informed consent, those who did not tolerate drug therapy due to any side effects and also patients with diagnosis of coronary artery diseases or cerebrovascular diseases or any other systematic diseases were excluded from our study.

The preparation of linseed oil is difficult and problematic and should be done in conditions without light. The lin fiber invokes bile acids and results in modifying the cholesterol level. In addition, consumption of linseed powder alone has an unpleasant taste. Thus, the linseed powder was converted to biscuit form for convenience and compliance of the subjects under study. Our laboratory analysis for determining the oil combination of linseed and preparation of biscuit package was conducted by The Iranian Agricultural and Industrial Company, Ghoncheh.

The laboratory analysis showed that linseed contained 39.3% oil, which was combined with linolenic acid (56.49%) and linoleic acid (10.08%). In the north of Iran, Ghoncheh Company is responsible for preparing linseed and the process of its disinfection. First, linseed is changed to powder and then converted to biscuits in formats of 12 gr. Each biscuit contains white wheat flour (2.008g), sugar powder (3.05g), vitamin C (0.24g), baking powder (0.001g), vanillin (0.001g) and water (0.7mL). Each package of biscuits contains 33 pieces for consumption, which was handed to the subjects. The daily dose of consumption for each subject was 6g linseed powder, prepared as 12g biscuits. These biscuits in addition to regular diet were used for 3 months in our intervention program.

The serum lipid level of each subject was measured before and after the 3-month regimens. LDL and HDL were measured by calorimetric end point, and TG and CHOL were measured by the end-point method. Out of the 75 subjects under study, 19 patients were excluded: 9 due to a lack of tolerating the taste of the biscuits and 10 patients were lost to follow up. The data of 56 subjects, whose compliance was confirmed by the accompanying person in our follow-up, were analyzed using SPSS software, and we used the paired t-test to determine the significant effect of our intervention program in decreasing the lipid levels.

Results

The mean age (±SD) of the participants was 56.2 (±6.9) years, with the range of 30-79 years, and 19 cases were male and 37 cases were female. The results showed that the mean cholesterol was 258.44 before and 232 after 3-months' intervention (P=0.0001). The mean difference was 26.39 mg/dl, and the decreasing rate was 10.2% (Table I). The mean difference in TG level was 64.85mg/dl, a decrease of 35%. The mean difference in LDL level was 32.7 mg/dl (P=0.0001), a decrease of 18.8%. The mean difference in HDL was 0.64 mg/dl, a 1.45% decrease (P>0.05).

Table I. The mean (SD) of serum lipids before and after intervention with linseed powder.

Serum lipid	Before treatment Mean ± SD (g/dl)	After treatment Mean± SD (g/dl)	P value
Total Cholesterol	258.44±55.95	232.05±41.47	0.0001
TG	289.92±126.57	225.07±82.54	0.0001

LDL	**173.82±52.87**	**141.12±39.94**	**0.0001**
HDL	**43.89±25.66**	**44.53±13.89**	**0.85**

Discussion

Our findings indicate that the consumption of linseed powder plus regular diet regimens significantly decreased the mean cholesterol, TG and LDL in both male and female subjects, but HDL level increased significantly only in females. These results are consistent with those reported that the consumption of polyunsaturated fatty acid leads to a decreased total cholesterol level.[2,4,11,12] In particular, the consumption of omega-3 fatty acid decreases the total cholesterol level.[13] However, Alekseeva et al.[14] and Eristland et al.[15] did not find any significant effect of linseed and omega 3 fatty acid on cholesterol level. These differences might be due to the difference in social factors, genotype with respect to the hyperlipidemia, background diet, dose, method of prescription and the duration of follow-up. Moreover, Kim et al. reported that the consumption of linseed in patients with hyperlipidemia caused a decrease in total cholesterol level up to 25%.[6] This figure is much more than those we estimated in our study (10.2%).We used the least possible dose of linseed in order to prevent any side effect. Thus, the differences essentially might be due to the prescribed dose of linseed which we used. Although the consumption of omega 6 fatty acid induces a relative increase in serum cholesterol level,[16] linseed mostly contains omega 3 fatty acids.[9,10] According to many clinical researchers, this type of fatty acid is expected to decrease the plasma level of triglyceride. Our findings showed that the mean difference of TG was 64.8 mg/dl, a decrease of 22.3%. These results also corresponded to those reported about the effect of omega 3 fatty acid and linseed on TG plasma level.[7,9,10,17,18,19] Our findings did not correspond with those reported by Alekseeva et al., who showed that the consumption of linseed did not change TG level of plasma.[14] Kim et al. also reported that the daily consumption of linseed led to a 65% decrease in serum TG level.[6] We found that this figure was 22.3%. This difference might be due to the dose of linseed prescribed in our study (we used the least dose).

Our findings also revealed that LDL level significantly decreased by a mean of 32.7mg/dl, or 18.8%. This result is also consistent with those reported in the literature.[16,17,20-22] In contrast, Alekseeva et al. and Eristland et al. did not find any significant effect of omega 3 fatty acid on LDL levels.[15,16] The reasons we discussed already can explain these different results.

Published studies reveal that the consumption of omega 6 fatty acid leads to lowering in HDL level[23, 24] and that omega 3 fatty acid increases HDL level or does not change it at all. We also did not find any significant difference on overall HDL level. These findings also corresponded with those reported by Eristland et al,[15] while other published data in the literature have reported a significant increase in HDL level using omega 3 fatty acids.[17, 22]

In addition, when we conducted stratified analysis with respect to the gender, the findings revealed that our intervention program was effective in decreasing the total cholesterol, TG and LDL level in both males and females; however, HDL level tended to decrease in men. This might be due to the small number of men in the study, and also it did not achieve statistical significance. On the other hand, HDL levels increased significantly in females.

A limitation of using linseed oil is that it must be kept in a closed space and packed in dark houses since it is extremely susceptible for oxidation. Also, some kinds of linseed might contain unflavored combinations which could be toxic, such as glucose cyanogen. In

particular, linseed used for cultivation of linen has greater risk than linseed oil, and oil linseed is much less susceptible for such toxigenic activity. The risk of this toxin is greater in premature seed than mature seed, and it can lead to cyanotoxin through hybridization.
According to the report of the Industrial Nutrition Institute of Iran, the major oil consumption in Iranian families is hydrogenous vegetable oil, which accounts for 22% of the total required daily energy. In addition, PUFA comprises only 1.5% of total energy, and its rate of consumption is much lower than recommended levels.[1,2] Taking into account that roughly 40% of mortality is due to cardiovascular diseases,[1] the pattern of consumption of nutrients, especially oil has an important role on overall health. Thus, a community-based intervention program and changing diet behavior, particularly in urban areas is required to modify the present pattern of oil consumption. In this regard, we recommend roughly 6g daily consumption of linseed powder as a compliment of the regular diet regimen for lowering lipid levels.

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The Effect of Aspirin on Converting Enzyme Inhibitors-Induced Coughs: A Double -Blind Clinical Trial

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Abstract

BACKGROUND- **DRY COUGHS ARE THE MOST COMMON ADVERSE EFFECT AND LIMITING FACTOR OF ALL ANGIOTENSIN CONVERTING-ENZYME INHIBITORS (ACEI). PROSTAGLANDINS HAVE BEEN PINPOINTED AS PLAYING AN IMPORTANT ROLE IN THE GENESIS OF THIS PROBLEM.**

THIS DOUBLE BLIND CLINICAL TRIAL WAS DESINGED TO COMPARE THE EFFICACY OF 500 MILIGRAM(MG) ASPIRIN VERSUS PLACEBO IN CONTROLLING ACEI-INDUCED COUGHS.

METHODS-**THE SUBJECTS WERE 32 PATIENTS, WHO HAD DEVELOPED ACEI-INDUCED COUGHS.THEY WERE RANDOMIZED TO A DAILY DOSE OF 500 MG ASPIRIN OR PLACEBO FOR A TREATMENT PERIOD OF 4 WEEKS.THE MEANS OF COUGH SEVERITY BEFORE AND EACH WEEK FOR 4 WEEKS WERE COMPARED IN THE TWO GROUPS.**

RESULTS- **MEANS OF COUGH SEVERITY IN THE ASPIRIN AND PLACEBO GROUPS BEFORE AND AT THE END OF THE FIRST WEEK OF TREATMENT DID NOT SHOW ANY SIGNIFICANT DIFFERENCE. AFTER THE SECOND, THIRD AND FOURTH WEEKS, THE COUGH SEVERITY SCORE WAS SIGNIFICANTLY REDUCED IN THE ASPIRIN GROUP (P<0.001).**

Conclusion-500mg aspirin once daily can suppress or abolish ACEI-induced coughs, and this finding proposes alternative therapeutic approaches for ACEI-related coughs ***(Iranian Heart Journal 2005; 6 (1,2): 17-19).***

Key words: aspirin ■ coughs ■ angiotensin-converting enzyme ihibitor

The angiotensin-converting enzyme inhibitors (ACEI) are the most widely used drugs in the field of cardiovascular medicine.[1]

ACEI may be the first line drugs for diabetics patients with hypertension, in valvular regurgitations, systolic left ventricular dysfunction, diabetic nephropathy and among post-infarction patients.[2]

Dry bothersome coughs are the most common adverse effect of all ACEIs. This side effect has been reported to occur in 5% to 39% of patients treated with ACEI; in most cases, the drug has to be discontinued.[3]

Coughs occur substantially more frequently in women than in men.[4]

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Non steroidal anti-inflamatory drugs (NSAIDs) and thromboxane antagonists resulted in the attenuation or disappearance of ACEI coughs.[7-8] The role of different doses of aspirin in ACEI-induced coughs was not elucidated. The present double-blinded clinical trial was aimed at determining whether 500mg aspirin daily can control ACEI-induced coughs.

Methods

The subjects were 32 patients, who had developed dry coughs while taking ACEI. They were comprised of 8 men and 24 women, whose mean age was 59.1±8.4 years. Evidence of organic pulmonary diseases was ruled out by physical examination and chest x-rays in each of the patients. There was no significant difference in the clinical characteristics between the treatment and placebo groups. After an informed consent had been obtained, the cough severity scoring according to the following scale was done: 0=no coughs; 1, only a tickling sensation on the throat; 2=mild coughs, isolated coughs; 3=moderate coughs, tolerated but severe enough to interrupt daily activities for some time; and 4=severe coughs, persisting and interferring with most of the daily activities or disturbing sleep at night.

They were randomized to either the aspirin group, which received 500mg once daily as a tablet or a placebo group. Randomization was arranged, and neither the patient who took the drug nor the physician who prescribed it was aware of which group he or she belonged to. Over the 4 weeks' treatment period, the patients were asked to mark a self-administered questionnaire; at the end of each week, the patients were visited by physician. The mean of cough severity score for each week in the two groups was calculated and compared. Data were expressed as mean±SD. For comparing and analyzing cough severity in the two groups, independent T-test was used.

Severity of coughs in each group before and after treatment was analyzed by paired T test. A value of $p<0.05$ was considered significant.

Results

In this study, 32 subjects were divided into two groups; in each group, 12 males and 4 females were evaluated. Mean age of the aspirin group subjects was 57.5±8.5, and in the placebo group it was 60.6±8.4 years (Table I).

Table I: baseline characteristics of patients

VARIABLES	ASPIRIN GROUP	PLACEBO GROUP
Age(Mean±SD)	57.5±8.5	60.6±8.4
Male	4	4
Female	12	12

The mean cough severity score before the treatment period in the aspirin group and placebo group was 2.44±0.22 and 2.5±0.16, respectively, showing insignificant difference (P<0.821). At the end of the first week after treatment, the cough severity score remained insignificant between the two groups (p<0.542). After the second, third and fourth weeks after treatment, cough severity in the aspirin group was 1.31±0.12, 0.75±0.14 and 0.63±0.13; in the placebo group, however, it was 25±0.11, 2.38±0.18 and 2.31±0.20, which showed reduction in the cough score throughout the treatment period in the aspirin group. A comparison between these findings and those of the placebo group showed a statistically significant difference between the two groups in all the three measurements (p=0.0015, Table II).

Table II: mean of cough severity before and during treatment period (sg=significance).

Treatment Period	Cough Score (Mean±Sd)		p-value
	ASPIRIN GROUP	PLACEBO GROUP	
Before treatment	2.44±0.22	2.50±0.16	0.821
First week	1.94±0.11	2.06±0.17	0.542
Second week	1.31±0.12	2.25±0.11	0.0015 sg
Third week	0.75±0.14	2.38±0.18	0.0015 sg
Fourth week	0.63±0.13	2.31±0.20	0.0015 sg
Total after treatment	1.03±0.11	2.21±0.13	0.0015 sg

Discussion

Although dry coughs are the most often reported and annoying complication associated with ACEI use, their mechanism remains to be clarified. The incidence of ACEI-induced coughs ranges from 5% to 39%, but it is evident that the coughs are a major limitation of continuing the medication.[3]

The main finding of our study was that aspirin in a dose of 500mg once daily reduced or completely abolished coughing. Although several mechanisms have been proposed, none completely explain how ACEI produce coughs. Bradykinin and prostaglandins are the most frequently proposed causes of coughs[5,6] and many studies using nonsteroidal anti-inflamatory drugs (NSAID), such as sulindac and indomethacin, have been undertaken to attempt to abolish this side effect and thus continue medication.[9,10] Aspirin can inhibit the production of both prostacyclin (vasodilator and antithrombotic) and thromboxanes.[2] There are few clinical reports regarding the role of different doses of aspirin in cough modification. Low doses of

aspirin were ineffective to suppress ACEI-induced coughs; like our study, 500mg aspirin favorably modified the cough severity score in the case group.[2]

In conclusion, 500mg aspirin daily successfuly diminishes ACEI-induced coughs, and this fact supports the hypothesis that ACEI-induced coughs may be associated with excessive generation of bradykinin and PGs. We suggest that patients who have to take ACEI and suffer from dry coughs should be prescribed 500mg aspirin once daily.

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Relationship between Microalbuminuria and Extent of Coronary Atherosclerotic Lesions

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Abstract

Background- Microalbuminuria is a diagnostic tool for screening patients at risk of developing nephropathy. It is also known that patients with microalbuminuria have a greater incidence of cardiovascular events and early mortality. In this study, reliability of the microalbuminuria as an indicator of a risk of progressive cardiovascular disorders was tested by detection of the relationship between microalbuminuria and extension of atherosclerotic coronary lesions.

Methods- The subjects for this study were 228 patients with angiographically confirmed coronary atherosclerotic lesions and mean of age 60 years; they were referred to Madani Hospital Tabriz, Iran. Age and sex-matched apparently healthy individuals (n=114) were used as the control group for a comparative study. The levels of glucose and creatinine and that of post-prandial glucose were determined in venous blood samples by standard methods. The immunoturbidimetric method was employed in the measurement of microalbuminuria.

Results- A direct relationship between microalbuminuria and extension of atherosclerotic coronary lesions was noticed (P = 0.009). The increased albumin / creatinine ratio was markedly correlated with fasting blood sugar, systolic and diastolic blood pressure (P<0.05).

Conclusion- The presented results indicate the existence of significant correlation between extent of atherosclerotic lesions and microalbuminuria. The relationship between diabetes and microalbuminuria was meaningful. These facts may contribute to the higher cardiovascular risk in diabetic patients. An association between hypertension and microalbuminuria was noticed. The result suggests that although risk factors such as hypertension and diabetes are known to cause cardiovascular disease, microalbuminuria may in fact be a contributor indicator of cardiovascular events ***(Iranian Heart Journal 2005; 6 (1,2): 20-25).***

Key words: microalbuminuria atherosclerosis

Atherosclerotic vascular disease is a major cause of death and morbidity in industrialized countries. Recently, attention has been paid to the risk factor of cardiovascular disease as a recognized symptom of atherosclerosis.[1,2] Availability of methods to quantitate small amounts of urinary albumin excretion (microalbuminuria) has allowed early recognition of renal disease in such pathological conditions as diabetes mellitus and essential hypertension. Microalbuminuria has been found to be associated with cardiovascular risk factors, cardiovascular events and mortality even in nondiabetic subjects.[3-5]

Microalbuminuria is traditionally defined as an increase in urinary albumin too subtle to be measured by chemistry sticks for total protein.

With improved methodology, these low levels of albumin (20-200Mg/min, 30-300mg/24h or 20-200 mg/L) can now be measured.[6-8]

Increase in urinary albumin excretion beyond the lower limit of microalbuminuria is the most significant single predictor of progressive

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microvascular disease and macrovasicular disease, nephropathy, atherosclerosis, coronary disease and retinopathy. [9]

The exact mechanisms responsible for these associations have been elucidated to some extent, but many remain to be characterized. Relationship between extension and severity of cardiac heart disease has been reported.[10] the purpose of this study was to investigate the value of microalbuminuria as an indicator of progressive cardiovascular disorders by detection of relationship between the rate of microalbuminuria and extent of atherosclerotic coronary artery lesions already confirmed by angiography.

Methods

We studied 228 patients with angiographically confirmed coronary atherosclerotic lesions and mean ± SE age of 60±0.5 years; they were referred to Madani Hospital, Tabriz, Iran. According to the number of diseased vessels, the patients were divided into two groups: 114 patients with two diseased vessels and 114 patients with three diseased vessels. Because of the low number of patients with one diseased vessel, they were excluded from the study. The level of albumin in all the studied patients was <300mg/24h.Exclusion criteria were: Secondary or malignant hypertension heart failure; cerebrovascular disease and renal insufficiency (Serum creatinine> 1.5 mg/dl in men and > 1.4 mg/dl in women); major noncardiovascular diseases; dislipidaemia requiring pharmacological treatment; uncontrolled diabetes (HbA1c>7.0%); and urinary tract infections. For a comparative study, age and sex-matched apparently healthy subjects (n=114) were chosen as the control group. The mean age of the control group was (mean ± SE) 59±0.5 years. Simple blood samples (5ml) were collected in the fasting state from the patients and the control group. Fasting serum glucose, 2 hours post prandial glucose, serum creatinine and urine creatinine were measured using standard methods in the Cobas mira auto-analyser.

Random urine samples (midstream) were collected in the morning, and the immunoturbidimetric method was employed to determine microalbuminuria. The results were reported as albumin / creatinine ratio. The albumin / creatinine ratio of more than 0.03 was defined as microalbuminuria. Using a special questionnaire, we collected systolic and diastolic blood pressures, smoking, sex, age and other necessary information about the patients.

SPSS 11 for the window computer program was used to perform statistical analysis. Paired students t- test and one-way ANOVA test as appropriate were used to determine the significance of differences between the measured parameters. The relationship between the diseased vessels and albumin / creatinine ratio was evaluated by independent simple test. Results are expressed as mean ± SE, and the statistical significance was set at $P<0.05$.

Results

CLINICAL CHARACTERISTICS OF THE PATIENTS WITH TWO AND THREE VESSELS DISEASE AND THOSE OF THE CONTROL GROUP ARE COMPARED IN TABLE I. NO SIGNIFICANT INTER GROUP DIFFERENCES IN THE CHARACTERISTICS OF THE GROUPS WERE OBSERVED ($P>0.05$).

AS SHOWN IN TABLE II, THE URINARY ALBUMIN /CREATININE RATIO IN BOTH GROUPS OF THE PATIENTS WAS HIGHER THAN THAT OF THE CONTROL ($P=0$). THE RATIO IN THE CONTROL GROUP WAS MARKEDLY LOWER THAN THAT IN THE PATIENT GROUPS.

MEANINGFUL CORRELATION BETWEEN THE NUMBER OF DISEASED VESSELS AND THE URINARY ALBUMIN/ CREATININE RATIO WAS NOTICED (P=0.0009, CI=95%, TABLE III).

Table I. Comparison of clinical characteristics of the two groups of patients and controls.

Variable	Patients with 2 vessels disease (n=114) Mean ± SE	Patients with 3 vessels disease (n=114) Mean ± SE	Control group (n=114) Mean ± SE	P value
Age(years)	59±0.7	60±0.7	59±0.9	0.4
Sex distribution (M/F)	85/29	91/23	90/24	0.2
Smokers (n)	35	30	31	0.14
Weight (kg)	79±4.3	69.9±2	72±1.4	0.10
Height (m)	162±1.2	160.9±0.9	164±1.8	0.5
F.B.S (mg/dl)	100±2.8	102±4	95±6	0.15
Post prandial glucose (mg/dl)	133±5.3	136±6.3	130±2	0.10
Systolic blood pressure (mmHg)	136.2±2	137±1.8	131±1.6	0.10
Diastolic blood pressure (mmHg)	85.2±1.2	83±1.3	80.1±1.5	0.2

SE = *Standard Error*

Table II. Comparison of mean ± SE of urinary albumin / creatinine ratio in control and patients groups

Variable	Control group (n=114) Mean ± SE	Two disease vessels patients (n=114) Mean ± SE	Three disease vessels patients (n=114) Mean ± SE	P value
Albumin/creatinine	0.0038±0.0008	0.015±0.002	0.029±0.004	zero

SE = *Standard Error*

Table III. Correlation between microalbuminuria and extension of atherosclerotic lesions.

Variable	Two disease vessels patients (n=114) Mean ± SE	Three disease vessels patients (n=114) Mean ± SE	P value
Albumin/creatinine	0.015±0.002	0.029±0.004	0.009

SE = *Standard Error*

THE CORRELATION BETWEEN THE MEAN ± SE OF URINARY ALBUMIN / CREATININE RATIO AND BLOOD PRESSURE WAS EXAMINED. A POSITIVE AND MEANINGFUL RELATIONSHIP BETWEEN THE RATIO AND BOTH SYSTOLIC AND DIASTOLIC WAS NOTICED (P=0.002 AND P=0.011, RESPECTIVELY), AND URINARY ALBUMIN EXCRETION WAS HIGH IN THE PATIENTS WITH INCREASED SYSTOLIC AND DIASTOLIC PRESSURE. DIVIDING THE SUBJECTS UNDER STUDY INTO MICROALBUMINURIA AND NORMOALBUMINURIA SUBGROUPS, WE FOUND THAT THE NUMBER OF SUBJECTS WITH INCREASED SYSTOLIC AND DIASTOLIC PRESSURE WITH MICROALBUMINURIA WAS MUCH HIGHER THAN THAT WITH NORMOALBUMINURIA (P<0.0005). SIGNIFICANT CORRELATION WAS ALSO DETECTED BETWEEN THE URINARY ALBUMIN / CREATININE RATIO AND FASTING SERUM GLUCOSE LEVEL (P=0.003), BUT IT WAS NOT MARKED IN THE CASE OF 2 HOURS POST-PRANDIAL SERUM GLUCOSE (P=0.07).

AS PRESENTED IN FIGURE 1A AND 1B, THE PERCENTAGE OF DIABETIC PATIENTS WITH TWO AND THREE DISEASE VESSELS IN THE MICROALBUMINURIA SUBGROUP WAS MORE THAN THAT IN THE NORMOALBUMINURIA SUBGROUP (P<0.0005 IN THE BOTH CASES). NO RELATIONSHIP BETWEEN THE URINARY ALBUMIN / CREATININE RATIO AND AGE, SEX AND SMOKING WAS OBSERVED (P>0.05).

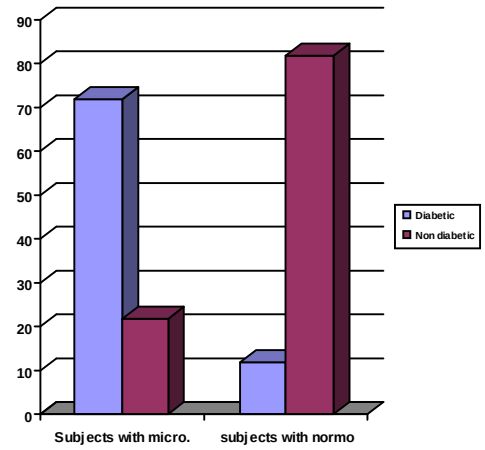

Fig.1a: The percentage of diabetic patients with 2 vessels disease in microalbuminuria (micro) and normoalbuminuria (normo) subgroups (p<0.0005)

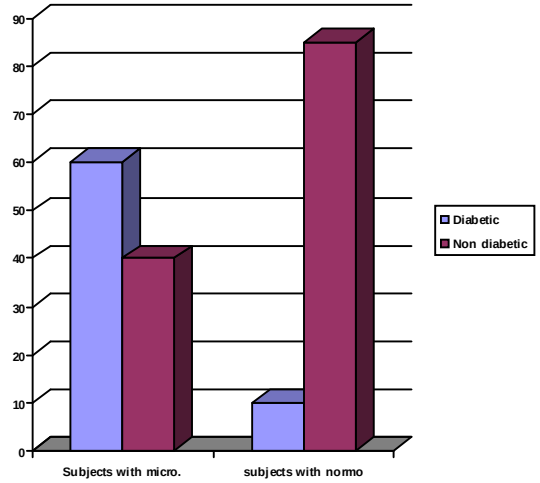

Fig.1b: The percentage of diabetic patients with 3 vessels disease with microalbuminuria (micro) and normoalbuminuria (Normo) subgroups (p<0.0005)

Discussion

Microalbuminuria is an important clinical symptom of deterioration of renal function in diabetic and hypertensive patients and one of the strong predictors of atherosclerotic disease and cardiovascular mortality.[11-15]

The association of microalbuminuria with cardiovascular disease might be explained by endothelial dysfunction and hypertension,

abnormalities in lipid metabolism, insulin resistance and protein glycosylation.[9]

Results of this study indicate the existence of significant correlation between the extension of atherosclerotic lesions and the ratio of albumin/ creatinine in urine. The results agree with those reported by Tuttle et al. They showed that urinary albumin excretion was directly related to angiographic evidence of coronary artery disease.[16] Similarly, Lekatsas et al. also mentioned that there was a close relationship between endothelial dysfunction, as expressed by the presence of microalbuminuria, and the extent and severity of coronary atherosclerosis.[10] Tests for microalbuminuria may be considered some of the most practical, effective and inexpensive tools for diagnosing and monitoring atherosclerotic disease.[13] The pathogenetic mechanisms underlying the development of microalbuminuria are currently poorly known. The severity of the blood pressure load and the increased systemic permeability to albumin, possibly due to early endothelial dysfunction, seem to play a major role in microalbuminuria.[12] On the other hand, several data suggest interplay with a number of additional factors, such as lipids abnormalities, prothrombotic factors, increased activity of the rennin – angiotensin system (RAS) and systemic inflammation. Finally, a functional hemodynamic abnormality and / or the presence of structural changes within the kidney cannot be ruled out as causes of microalbuminuria.[14, 17]

According to our data, the increased urinary albumin / creatinine ratio was markedly correlated with fasting blood sugar and systolic and diastolic blood pressures. Several studies have shown that systolic blood pressure is a risk factor for the development of microalbuminuria in non – diabetic hypertensive subjects.[18] Hypertensive individuals with microalbuminuria manifest a variety of biochemical and hormonal derangements with pathogenic potential, which results in hypertensive patients having a greater incidence of cardiovascular events and a greater decline in renal function than patients with normal urinary albumin excretion.[19] A recent epidemiological study shows a high prevalence of microalbuminuria in vasculopathic diabetic patients compared the vosculopathic nondiabetics.[20] Microalbuminuria may be a prognostic marker for increased cardiovascular morbidity and mortality in patients with type I or type II diabetes.[21]

In the present study, no relationship between microalbuminuria and smoking, sex and age was noticed; it seems that the detection of the relationship between the parameters requires a big sample size.

OUR RESULTS SUGGEST THAT ALTHOUGH RISK FACTORS SUCH AS DIABETES, HYPERTENSION AND HYPERCHOLESTEROLEMIA ARE KNOWN TO CAUSE CARDIOVASCULAR DISEASE, MICROALBUMINURIA MAY IN FACT REPRESENTS THE EARLY RENAL MANIFESTATION OF A GENERALIZED VASCULAR DYSFUNCTION, AND THEREFORE IT IS AN INTEGRATED MARKER OF CARDIOVASCULAR RISK.

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Effects of Coronary Bypass Surgery on Myocardial Performance Index (MPI or Tei index)

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Abstract

Background- Coronary artery bypass grafting (CABG) is a common surgical procedure performed in the world. Coronary artery disease (CAD) has become prevalent in Iran, and the aim of this study is to assess the effects of CABG on LV systolic and diastolic function indices. We also attempted to disclose the CABG effect on the myocardial performance (Tei) index.

Methods- 50 patients were enrolled in this study, all of whom were given instructions about the research program. They were admitted to our center electively for CABG; the first echocardiography was taken just prior to surgery, and the second TTE was performed between 1 and 43 weeks after surgery (mean=11 weeks).

Results- CABG had dramatic effects on the patients, as their mean left ventricular ejection fraction (LVEF) rose from 48.88% to 52.54% (P<0.001). It was more obvious in patients with preoperative LVEF less than 40%, Tei index<0.49, male gender and those with complete revascularization. LVEF had no change in the case of incomplete revascularization. MPI (Tei) decreased significantly after CABG from 0.4992 to 0.4462 (P=0.001), which was more pronounced in those whose preoperative Tei index was equal or more than 0.49 and in patients with triple vessel or left main CAD. Diastolic function recovery had a time-dependent manner with no change or even deterioration during the first few days after CABG, but after 4 weeks nearly half of the patients had normal diastolic function. History of systemic hypertension and old age (>60 years old) are both associated with more preoperative diastolic dysfunction and are negative predictors for diastolic function recovery after CABG. Isovolumetric relaxation time (IVRT), E-wave deceleration time (EDT), peak E-wave velocity (PEV) and peak A-wave velocity (PA) all show significant improvement after CABG. There was no mortality in our series.

Conclusion- CABG has important positive and significant effects on many LV systolic and diastolic indices including LVEF, LVESV, IVRT, PEV, PAV and EDT as well as on the myocardial performance (Tei) index ***(Iranian Heart Journal 2005; 6 (1,2): 26-30).***

Key words: coronary artery bypass surgery Ë myocardial function Ë ejection fraction

Abbreviations: CABG: coronary artery bypass grafting. CAD: coronary artery disease, LVEF: left ventricular ejection fraction, MPI: myocardial performance index (Tei), LVEDD: left ventricular end diastolic dimension, LVESD: left ventricular end systolic dimension, LVEDV: left ventricular end diastolic volume, IVRT: isovolumetric relaxation time, BEF: basal ejection fraction, FS: fractional shortening , EDT:E-wave deceleration time, TTE: transthoracic echocardiography

An essential subject in managing CAD patients is to improve LV function, so one is j sup over irreversibly by CAD.

CABG has dramatic effects on most left ventricular (LV) systolic and diastolic function indices, and numerous studies carried out in different centers consistently show significant improvement in the above-mentioned indices.

Also, there is a recently described index (MPI or (IVRT) and isovolumetric contraction time (IVCT), divided by ejection time (ET). Any pathologic event which may compromise LV systolic or diastolic function prolongs IVCD and IVRT, and shortens ET; consequently, MPI increases. There is

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some controversy among authors for the normal range of MPI, but most agree that values between 0.32 and 0.42 are normal.

This index has some correlation with LVEF, and LVEF can be calculated roughly using MPI: LVEF = 0.60–(0.34 X MPI), although this formula mildly underestimates EF, when assessed by radionuclide ventriculography.[1]

There are several studies suggesting a close relation between MPI and BNP level in heart failure, with 86% sensitivity and 82% specificity by considering 0.47 cut-off point. This research is one of the few studies on the effects of CABG on MPI.

Methods

In this study, we compared pre-CABG LV function with indices such as LVEF, left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD), basal ejection fraction (BEF), fractional shortening (FS) and also peak E-wave velocity (PEV), peak A-wave velocity (PAV), E-wave deceleration time (EDT), isovolumetric relaxation time (IVRT) and mitral inflow pattern (MPI) pre-CABG with postoperative values by echocardiography. Fifty patients were enrolled in this study, all of whom were examined 1 or 2 days before CABG, and the second TTE was performed 1 to 43 weeks after CABG (mean =11 weeks, median=7 weeks).There was no mortality in our study group.

Results

Of the 50 patients, 21 (42%) were female, and 29 (58%) were male. Twenty-two (44%) had systemic arterial hypertension, and 18 (36%) had diabetes mellitus. From the angiographic point of view, 40 patients (80%) had three-vessel or left main coronary artery disease, 8 patients (16%) had two-vessel disease and 2 patients (4%) had single-vessel disease. LVEF was 44.69%, but echocardiographic LVEF calculated by the Simpson method was 48.88%, mean (P=0.001). All angiographic LVEF reports were based on eye-ball estimation.

Table I. Effect of CABG on LV function indices

Variable	Pre-CABG	Post-CABG	change	P-value
EF	48.88%	52.54%	↑3.51%	<0.001
MPI(Tei index)	0.4992	0.4462	↓0.053)	0.001
IVRT	113.56	96.78	↓16.78	<0.001
PEV	0.71	0.80	↑0.09	0.002
PAV	0.84	0.0.74	↓0.1	<0.001
EDT	232.84	200	↓32.84	0.001
LVESD	3.48	3.57	↑0.09	0.241(n)
BEF	57.68%	53.72%	↓ 3.96%	0.041
FS	31.22%	28.24%	↓2.98%	0.019
LVEDV	98.04	96.46	↓1.58	0.595(n)
LVESV	50.68	46.20	↓4.48	0.02
LVEDD	5.03	4.96	↓ 0.07	0.331(n)

variable	Pre-CABG		post-CABG		change	P-value		
	male	female	male	female	male	female	male	female
EF	47.096	51.738	51.379	54.143	↑4.310	↑2.405	0.001	0.019
MPI(Tei)	0.5045	0.4919	0.4595	0.4286	↓0.0455	↓0.0633	0.050	0.005
IVRT	115.41	111.00	100.07	92.24	↓15.34	↓18.76	0.002	0.020
PEV	0.6534	0.7895	0.7672	0.8471	↑0.1138	↑0.0576(n)	0.003	0.216(n)
PAV	0.7786	0.9152	0.7234	0.7695	↓0.0552	↓0.1457(n)	0.50	<0.001
EDT	230.07	236.67	204.14	193.19	↓25.93	↓43.48	0.038	0.015

n= non-significant

As evident from the data of Table I, LVEF and PEV both significantly increased (3.51% and 0.09m/s, respectively), and LVESV, PAV, IVRT, EDT, BEF and FS all significantly decreased (4.48ml, 0.1m/s, 16.78msec, 32.84msec, 3.96%, 2.98%) after CABG. In addition, CABG significantly reduced MPI from a mean preoperative level of 0.4992 to 0.4462, which was more pronounced in patients whose preoperative MPI was equal to or more than 0.49 and in patients with triple-vessel or left main CAD.

LVEF rose from 48.88% to 52.54%, and the increment was more obvious in patients with preoperative LVEF less than 40%, MPI < 0.49; 3 male gender and finally those with complete revascularization; LVEF did not increase in patients with incomplete revascularization.

In some subgroups, LV function indices changed differently; for example males had lower preoperative LVEF and enjoyed more LVEF rise after CABG than females. MPI, however, decreased in both, which was more significant in females.

Table II. Gender difference on CABG results

n= non-significant

Hypertensive patients had a significant rise in their LVEF (3.477%, P<0001) and PEV (0.1105$_{m/s}$, P=0.026) and also significant decrease in MPI (0.06, P=0.012), IVRT (24.27$_{msec,}$ P=0.003), PAV (0.16$_{m/s,}$ P<0.001) and EDT (30.68$_{msec}$, P=0.045). In contrast, normotensives had an insignificant decrease of PAV (0.038$_{m/s}$, P=0.15), but all other indices showed significant improvement.
Diabetic patients had a significant improvement in most indices, including MPI (0.057, P=0.11), LVEF (3.47%, P=0.004), IVRT (21.72$_{msec}$, P=0.009) and PAV (0.16$_{m/s}$, P=0.001), but PEV and EDT both decreased insignificantly. In patients without diabetes, all the indices improved significantly after CABG, LVEF ↑3.531%, P=0.003; MPI ↓0.0506, P=0.024; IVRT ↓14.00$_{msec}$, P=0.006; PEV ↑0.1319$_{m/s}$,

P=0.001; PAV ↓0.0559, P=0.032; EDT ↓37.69, P=0.003].
Patients with preoperative LVEF less than 40% had a greatest increase in their LVEF (↑4.750%, P=0.001) and showed a significant improvement in IVRT (↓34.63, P=0.003), PEV (↑0.22$_{m/s}$, P=0.024) and PAV (↓0.095$_{m/s}$, P=0.047) after CABG. MPI and EDT both improved insignificantly. Those with preoperative LVEF more than 40% showed a significant improvement in all the indices (LVEF ↑3.274%. P=0.001; MPI ↓0.0502, P=0.002; IVRT ↓13.38$_{msec}$, P=0.004; PEV ↑0.0655$_{m/s}$, P=0.025; PAV ↓0.0929$_{m/s}$, P=0.001; EDT ↓34.93$_{msec}$, P=0.002).
In patients with preoperative MPI equal or greater than 0.49, all the indices improved significantly after CABG, (LVEF ↑2.769%, P=0.003; MPI ↓0.0965, P=< 0.001; IVRT ↓22.54$_{msec}$, P=0.001; PEV ↑0.1062$_{m/s}$, P=0.001; PAV ↓0.1081$_{m/s}$, P=< 0.001; EDT ↓45.38$_{msec}$, P=0.009). This subgroup had the greatest improvement in MPI postoperatively. In contrast, patients with preoperative MPI less than 0.49, had a significant improvement only in LVEF (↑4.313%, P=0.004) and PAV (↓0.0771$_{m/s}$, P=0.046). The rise in LVEF in the latter subgroup is more prominent than that in the former, so MPI may have some correlation with myocardial viability, and this issue should be addressed in future studies.

Discussion

This study compares the effects of CABG on systolic and diastolic functions before and after surgery.
Most echocardiographic LV systolic indices such as LVEF, LVESV and MPI improve significantly after CABG, although BEF and FS both significantly decrease after CABG, which translates into the inability of the LV posterior wall's exaggerated excursion to compensate for the interventricular septum's (IVS) abnormal anterior motion, appearing after pericardiotomy. LVEDD also decreases significantly during the first few days after surgery but returns to preoperative values thereafter. LVEF had no change when revascularization was incomplete. MPI significantly improves after CABG, especially in patients with triple-vessel or left main lesions and those with preoperative MPI equal to or more than 0.49. Similarly, LVEF improves more significantly when preoperative MPI is less than 0.49, and this finding may relate to some degree between MPI and myocardial viability.
Diastolic function recovery has a time- dependent manner with no change or even deterioration during the first few days after CABG, but after 4 weeks, nearly half of the patients will recover normal diastolic function. Past history of systemic hypertension and old age (>60 years old) are both associated with more preoperative diastolic dysfunction, and they are negative predictors for diastolic function recovery after CABG.
Diabetes mellitus in itself has no major influence on the early results of CABG and LV function recovery, unless associated with systemic arterial hypertension, which may have detrimental effects on LV diastolic function recovery.
MPI is greater in patients with triple-vessel or left main disease and is reduced more after CABG compared to patients with two or single-vessel disease. Furthermore, improvement of IVRT, PAV, EDT and PEV is more prominent in the former group.
Those with preoperative LVEF less than 40% and male gender have a larger LVEF and PEV increase after CABG; all the patients of the former group had diastolic dysfunction preoperatively, but 17% of the patients with preoperative LVEF equal to or more than 40% had normal diastolic function before CABG.
Old age (>60 years) is associated with a greater improvement in MPI, EDT and PAV in comparison to younger patients, but both have a significant LVEF improvement following complete revascularization.
This study shows MPI to be a safe, noninvasive, reproducible and reliable index in evaluating the effects of CABG on LV function.

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Association between Angiographically-Defined Coronary Artery Disease and Periodontal Diseases

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Abstract

Background- Results of studies seeking for the association between periodontal diseases and coronary artery disease (CAD) are significantly inconsistent. Such inconsistency has been attributed to the varying definitions for CAD and whether or not adjustment for common risk factors has been performed. The main objective of this study was to investigate the association between angiographically- defined CAD and periodontal diseases.

Methods- Fifty-eight patients, who referred to Shaheed Rajaie Cardiovascular Medical Center, were recruited into a case-control design study. They were examined for periodontal indices such as the papillary bleeding index (PBI), probing depth (PD), plaque index (PI) and clinical periodontal attachment level (AL). The subjects were classified as having CAD (CAD+) if they had at least 50% stenosis in at least one major epicardial artery.

Results- Thirty-nine patients (67.2%) were CAD+ and 19(32.8%) were CAD- .CAD+ patients were more likely to be male than female (90.3% versus 40.7%, p=0.000) and of older ages (55±2.7 versus 40.6±4.8, p=0.000). Among periodontal parameters, no significant association was found between the mean of PBI, PD and CAD. On the other hand, there was a significant association between the amount of AL, PI, number of missing teeth and CAD. There was also correlation between the amount of AL and the number of vessels involved (r=0.428). The results of this study remained unchanged after adjustment for CAD risk factors, performing multilogistic regression analysis.

Conclusion- The observation showed a significant relationship between angiographically-defined CAD and periodontal diseases, which can emphasize the importance of early diagnosis and complete treatment of periodontal infections, particularly in CAD susceptible individuals ***(Iranian Heart Journal 2005; 6 (1,2): 31-36).***

Key words: periodontal diseases■ coronary artery disease

Coronary artery disease (CAD) is a major cause of morbidity and mortality[a]. For example, 50% of mortalities occurring in the United States are due to atherosclerosis[b].

The etiology of CAD is multi-factorial. Recent evidence suggests a role for infectious agents in the pathogenesis of CAD; viral and bacterial infections may contribute to both initiation and progression of CAD.

Animal studies have shown that atherum plaque formation can be enhanced by exposure to periodontal pathogens[c].

Some believe that pathogenic bacteria inoculated from the oral environment into the bloodstream may translocate to atherosclerotic lesions or may induce platelet aggregation

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common risk factors such as diabetes mellitus, smoking and dietary habits are the reason of association between CAD and periodontal diseases.

According to the literature, 5-60% of the population in different communities is affected by periodontal diseases[d].

In our country, 27% and 34% of 15-69 year-old people have gingivitis and periodontitis, respectively. Seventy percent of them are in the range of 40-69 years old[4,8,9]. Accordingly, if any association exists between periodontal diseases and CAD, the prevalence of CAD and its consequences can be reduced by oral hygiene education, early diagnosis and effective treatment of periodontal diseases. The results obtained from research conducted in other countries (societies) are not necessarily useful for our population because of differences in race, dietary habits, health situation and prevalence of various risk factors. The criteria for choosing CAD patients in previous research in our country were not based on angiography.

Therefore, this research was conducted based upon angiography as the gold standard for the diagnosis of CAD and routine periodontal examinations.

Methods

This study was an observational- analytic study. Between April and October 2004, fifty-eight individuals were randomly selected from patients having presented for angiography at Shaheed Rajaie Cardiovascular Medical Center. The exclusion criteria were: edentulousness, existence of artificial heart valve and non- compliance of the patients to participate in the study.

Records were assessed and reviewed for cardiovascular risk factors, including hypertension, low- density lipoprotein (LDL), high-density lipoprotein (HDL), cholesterol and triglyceride levels and fasting blood sugar (FBS). The values of blood pressure and blood biochemistry were obtained from each patient's hospital medical records. The patients were asked about family history of heart diseases and smoking.

A periodontal examination was performed to measure the following clinical parameters per 6 teeth: **(**Ramfjord teeth) Maxillary right first molar, left central incisor and first premolar, mandibular left first molar, right central incisor and first premolar. Distal neighboring tooth was selected in the absence of Ramfjord teeth (due to extraction)

(Ramfjord teeth): Plaque Index (PI), Papillary Bleeding Index (PBI), Probing Depth (PD), clinical Attachment level (AL) and number of missing teeth (not considering third molars). PI was determined by moving a periodontal probe along the margin the gingiva and scored by Silness and Loe [12] (score 0: no plaque in gingival area; score 1: a film of plaque adhering to the free gingival margin; score 2: moderate accumulation of plaque

that can be seen with the naked eye; score 3: abundance of soft matter at the gingival margin).

PBI was determined as described by Muhlemann after probing the gingiva at interproximal areas [12](from score 0: no bleeding to score 4: sever bleeding).

PD is measured from the margin the gingiva to the base the gingival sulcus (or periodontal pocket) with a millimeter- calibrated probe.

AL is measured from the cementoenamel junction of the tooth to the base of gingival sulcus (or periodontal pocket) with a millimeter-calibrated probe.

All the experiments were performed by the same examiner, the day before the angiography appointment. The subjects were classified based on the results of diagnostic angiography as: Cases CAD+ or Controls, CAD- (by) a cardiologist

according to the following criteria:

CAD+ was defined as greater than 50% diameter reduction in at least one major epicardial artery .Severity of CAD was also measured by the number of vessels affected.
Data were analyzed by using t-student test to compare group means and chi-square test for the comparison of categorical variables. Logistic regression analysis was used to analyze the association between periodontal diseases and CAD, after adjusting for common risk factors. SPSS (version 11.0) software was used for these data analyses.

Results

Fifty-eight patients, who were candidates for diagnostic angiography, were examined. Among them, 39 (67.2%) were CAD+ and 19 (32.8%) were CAD-. There were 31 (53.4%) males and 27 (46.6%) females.
The prevalence of CAD+ was significantly different between the male and female patients (p=0/000). Twenty-eight males (90.3%) and 11 females (40.7%) had coronary artery involvement (Table I).

Table I. Prevalence of coronary heart disease in the study population according to sex.

CAD / Sex	CAD+		CAD -		SUM	
	prevalence	%	prevalence	%	prevalence	%
Male	28	90.3	3	9.7	31	100
Female	11	40.7	16	59.3	27	100
Sum	39	67.2	19	32.8	58	100

CAD: Coronary Artery Disease.

From the viewpoint of age prevalence, 1 patient (1.7%) of less than 40 years old, 30 (51.7%) of 40-60 years old and 8 patients (13.8%) of greater than 60 years were CAD+.

The mean ages of the patients in total, in male and female individuals, were 50.3±11.4, 54.1±8.9 and 45.9±12.6, respectively.

The mean ages of CAD+ and CAD- individuals were significantly different from each other (p=0.000). They were 55±8.6 and 40.6±10.6 years in CAD+ and CAD- patients, respectively.

One, two and three- vessel involvements were observed in 41%, 33.3% and 25.6% of CAD patients, respectively.

Twelve patients (30.8%) of the CAD+ group were smokers or had a history of smoking, and 27 (69.2%) of them were non-smokers. There were significant differences between CAD+ and CAD- patients in the mean of diastolic and systolic blood pressure. On the other hand, they did not have significant difference in the mean of LDL, HDL, CHOL, TG and FBS (Table II).

Table II. Mean and standard deviation of CAD risk factors in the study population.

Risk Factors	CAD	Mean	Standard deviation	Confidence interval	P value
TG	**CAD+** **CAD -**	220.3 182.1	227.9 89.9	220.3 ± 73 182.1 ± 41.2	0.485 0.366
LDL	**CAD +** **CAD -**	116 113.2	37.3 39.9	116 ± 12 113.2 ± 18.3	0.797 0.802
HDL	**CAD +** **CAD –**	74.2 49.7	9.8 12	47.2 ± 3.1 49.7 ± 5	0.369 0.391
CHOL	**CAD +** **CAD -**	212.3 194.1	68.6 43.8	212.3 ± 22 194.1 ± 20.1	0.294 0.225
FBS	**CAD +** **CAD _**	112.3 110.2	43.9 52.3	112.3 ± 14.1 110.2 ± 24	0.873 0.881
BP (systolic)	**CAD +** **CAD –**	124.7 111.3	19.2 12.5	124.7 ± 6.2 111.3 ± 5.7	0.008 0.002
BP (diastolic)	**CAD +** **CAD -**	74.4 65.6	15.7 12.1	74.4 ± 5 65.6 ± 5.6	0.036 0.024

CAD: Coronary Artery Disease / TG: Triglyceride / LDL: Low Density Lipoprotein / HDL: High Density Lipoprotein / CHOL: Cholesterol / FBS: Fast Blood Sugar / BP: Blood Pressure.

The mean of PBL was 1.9±0.9 in CAD+ and 1.6±0.8 in CAD- patients. There was no significant difference between these two groups (p=0.296). The mean of PD was 3.3±1.1 min and 2.9±0.7 min in CAD+ and CAD- patients, respectively. Again they had no significant difference (p=0.16).

The mean of PI was 2.3±0.97 and 1.7± 0.8 in CAD+ and CAD-patients, respectively, which was significantly different from each other.

The mean of AL was 3.97±1.09 mm in CAD+ and 3.3±l.08 in CAD- patients. They were significantly different from each other (p= 0.035).

According to the results, with increasing amounts of AL in CAD+ patients, the number of the affected coronary vessels increased. So, there was significant relationship between these two parameters (r= 0.428 and P= 0.007, Table III).

Table III. Prevalence of the number of vessels involved according to the level of periodontal clinical attachment level.

Number of Vessel / Clinical attachment	One vessel		Two vessel		Three vessel		Sum	
	prevalence	%	prevalence	%	prevalence	%	prevalence	%
less than 3 mm	5	71.4	2	28.6	0	0	7	100

The mean number of extracted teeth was 7.5±4 and 4.4±3.8 in CAD+ and CAD- patients, respectively. The difference was statistically significant (P= 0.007).
Considering the risk factors of CAD and performing multi-logistic regression analysis, all the mentioned results remained unchanged.

Discussion

This research is the first evaluation of association between periodontal diseases and CAD in our country in which angiographic data have been used for determination of CAD+ and CAD- individuals.
The mean age of CAD+ patients was significantly more than that of CAD- patients, which was the same as that reported by Bazile et al[5].
The prevalence of affected people with CAD was the same as that reported by Malthaner et al[1].There was also a significant difference in the prevalence of CAD between the two sexes (P<0.05).
In this research, among the risk factors of heart diseases like cholesterol, LDL, HDL triglyceride, FBS, familial history of heart diseases and diastolic and systolic blood pressure, there was only a significant association between the mean diastolic and systolic blood pressure with coronary artery disease.
However, Malthaner et al. reported that mean HDL and cholesterol levels were the only relevant variables with coronary artery disease.[1] The mentioned study also emphasized that all the smokers were in the CAD+ group.
The present study showed a significant relationship between coronary artery disease and the mean of AL (attachment level), which was similar to the results of Mattilla et al.,[6] Destefano et al.,[7] Beck et al.,[2] Khorsand et al.,[8] and Moghaddas et al.,[9] There was also an association between the amount of AL and the number of affected coronary vessels (r=0.428).
There was a significant relationship between CAD+ and the number of extracted teeth, which is in accordance with the studies of Joshipura et al,[10] Loesche et al,[11] Khorsand et al.[8] and Moghaddas et al[9]. Bazile et al., however, did not find any relationship between these two variables[5]. Differences in the socioeconomic status of patients in various studies could explain such inconsistent results.
Mean of the plaque index was significantly different between the CAD+ and CAD- groups, which was the same as the results of Joshipura et al. and Loesche et al. It was the same, however, in the control and case groups in the study of Bazile et al. (0.7 versus 1.3), and it

was attributed to the socioeconomic conditions of the selected population.
Bazile et al. and Malthaner et al. did not find any significant relationship between the mean of probing depth and having CAD, which was the same as the finding in our study.
According to the results of this research, there was no significant relationship between the papillary bleeding index and CAD+, but Khorsand et al. reported opposite results. This inconsistency can be related to the method of the research. In both studies, the Muhlman index was used for evaluating PBI. In our study, first, all the surfaces of the tooth were probed with a calibrated probe and then, a maximum amount of PBI was selected as the tooth index. Khorsand et al., on the other hand, measured it in the lingual and facial surfaces in randomly selected quadrants of the mouth. It should be mentioned that the results of this study did not change after adjusting the risk factors of CAD and analyzing by multi-logistic regression. The results of previous studies on the association between periodontal and heart diseases were inconsistent. According to Genco et al,[3] possible reasons for these inconsistent findings could include:
1) Differences in the age of the subjects participating in different studies (It seems that the association between periodontal diseases and coronary heart disease is stronger in younger individuals.).
2) Lack of control of confounding factors like smoking status, which is a common risk factor for both diseases. In this study, adjustment was done for all confounders.
3) Type of heart disease that is considered (CHD, stable angina, unstable angina ,.....) and the way they are measured. While several studies have utilized angiographic data for the assessment of CAD[1,5,6], some others have relied upon data such as patient histories and hospital records to establish the CAD status[2,10] . In the present study, patients with >50 % stenosis in one or more epicardial arteries were considered positive for CAD. This definition defines the patient with hemodynamically significant stenosis.
4) Measures of periodontal diseases: some studies have used the total dental index, which is a combination of probing measures, furcation involvement and dental caries infections. Some others have used Russell's periodontal index, or RPI, which is a non-probing index. One study has used bone loss[2], and several other studies have used self-reported periodontal diseases [10]

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Linseed Trial in Hyperlipidemic Patients

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Abstract

Background - Hyperlipidemia is an important cause of coronary artery diseases. Linseed contains large amounts of omega-3 fatty acids, and it has a major role in lowering serum lipid levels. This study evaluated the effect of linseed powder in patients who did not respond to regular diet regimens.

Methods - We conducted an interventional study (before and after) of 56 patients with hyperlipidemia that had not responded to a 3-month regular diet and had serum levels of total cholesterol >240 or TG>300 or LDL>160 or HDL<30 (mg/dl). We prepared the dose of 6 gr/day of linseed powder in the form of a biscuit and gave it to the patients for 3 months plus their regular diet regimen. The serum levels of lipids were measured before and after the 3-month intervention program. The data were analyzed using SPSS software with paired t-test.

Results - The mean (±SD) of serum level of total cholesterol before treatment was 258 (±55.59) mg/dl and afterwards was 232.05 (±41.47) mg/dl (P=0.0001). The mean serum triglyceride level before and after treatment was 289.92 (±126.57) mg/dl, and 225.07 (±82.58), respectively (P=0.0001). Also, the mean serum LDL decreased from 173.82 (±52.87) to 141.12 (±39.94) mg/dl (P=0.0001). However, no significant difference on HDL levels was found before and after intervention (43.89 (±25.66) vs. 43.53 (±13.84), P=0.85). Overall, the linseed powder regimen for 3 months decreased the total cholesterol by 10.2%, serum triglyceride by 22.33% and LDL cholesterol level by 18.8%. HDL level increased by 1.45%.

Conclusion - Linseed powder plus regular diet decreased the lipoprotein levels significantly. Thus, we recommend roughly 6 gr. daily consumption of linseed as a compliment of regular diet regimen in lowering the level of serum lipids ***(Iranian Heart Journal 2005; 6 (1,2): 37-42).***

Key words: hyperlipidemia ■ linseed ■ cholesterol ■ triglyceride■ LDL■ HDL■ diet

Cardiovascular diseases are a common cause of mortality and morbidity in the world, and hyperlipidemia is the major risk factor of these diseases. Primary and secondary cares showed that with interventional programs which result in decreasing serum lipid levels, the risk of coronary events will be decreased and also lead to regression of atherosclerotic plagues in coronary arteries.

Thus, the National Center of cholesterol in United States recommended interventional program in the general population.

This recommendation first emphasizes on diet and physical activities.

Due to the genetic susceptibility, many subjects with hyperlipidemia may not respond to regular diet regimens alone.

In this case, drug therapy for lowering lipid levels is recommended.

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step for controlling lipid levels.

The presence of fat in the diet is necessary for health status, and it provides the required energy, fatty acids and vitamins for bodily activities.[1]

Published studies confirm that cholesterol and triglyceride (TG) of serum has a direct relationship with the type and amount of daily fat consumption. Saturated fatty acids elevate the level of total cholesterol, and polyunsaturated and monounsaturated fatty acids decrease the cholesterol level.[2-4] The required fatty acids include omega-6 linoleic acid (LA) and omega-3 alpha linolenic acid (LNA). These fatty acids with polyunsaturated fatty acids (PUFA) must be provided through daily diet consumption.[5] WHO and FAO recommend that at least 15% of the daily-received energy be provided from fatty acids. Also, the ratio of LA to LNA must be between 5:1 and 10:1, and linoleic acid must provide 10 to 40% of daily energy supply.[1]

Linseed, or *Linum usitatissimum*, is a plant cultivated for extracting oil from its seed or using its fiber. Linseed oil is supplied from linolenic acid (LNA), and its combination is different in relation to type, size, seed and climatic conditions. In a study, 35g linseed oil (20.7g omega-3 LNA and 4.9g omega-6 LA) was extracted from each 100 grams of linseed.[6] In another study, it was shown that 52% fatty acid supplied in linseed was made from LNA and 17% from LA, and that also the ratio of PUFA to saturated fat was 6/9.[7] Linseed is the only plant oil which contains more than 50% LNA[8-10], and the rate of omega-3 fat of linseed is three times greater than that of fish oil.[6]

Published studies on the effect of omega 3 fat on serum lipids have almost always used fatty acid extracted from seafood (fish). There are a few studies of the effect of linseed on lipids of serum, and their results also are somewhat contradictory. Since linseed is the main source of omega 3 fatty acid, this interventional study was conducted to determine the effect of linseed powder on decreasing lipid levels in patients who did not respond to regular diet regimen.

Methods

We conducted an interventional study (before and after) in patients with hyperlipidemia who did not respond to the recommended 3-months regular diet regimens alone without drug therapy; i.e. their lipid levels (TG, Chol, LDL, HDL) did not change toward the normal level. In our formal definition, regular diet was defined as formal diet without animal oil, plant oil, red meat and any other internal components of sheep such as liver, kidney, etc., and the maximum consumption of yolk (of egg) allowed was 1 egg per week. We recruited 75

patients consecutively with convenience sampling method. All these patients gave informed consent before undergoing our linseed intervention program plus regular diet. We included subjects into the study whose cholesterol was >240 or TG>300 or HDL <30 and LDL>160. Subjects who did not give an informed consent, those who did not tolerate drug therapy due to any side effects and also patients with diagnosis of coronary artery diseases or cerebrovascular diseases or any other systematic diseases were excluded from our study.

The preparation of linseed oil is difficult and problematic and should be done in conditions without light. The lin fiber invokes bile acids and results in modifying the cholesterol level. In addition, consumption of linseed powder alone has an unpleasant taste. Thus, the linseed powder was converted to biscuit form for convenience and compliance of the subjects under study. Our laboratory analysis for determining the oil combination of linseed and preparation of biscuit package was conducted by The Iranian Agricultural and Industrial Company, Ghoncheh.

The laboratory analysis showed that linseed contained 39.3% oil, which was combined with linolenic acid (56.49%) and linoleic acid (10.08%). In the north of Iran, Ghoncheh Company is responsible for preparing linseed and the process of its disinfection. First, linseed is changed to powder and then converted to biscuits in formats of 12 gr. Each biscuit contains white wheat flour (2.008g), sugar powder (3.05g), vitamin C (0.24g), baking powder (0.001g), vanillin (0.001g) and water (0.7mL). Each package of biscuits contains 33 pieces for consumption, which was handed to the subjects. The daily dose of consumption for each subject was 6g linseed powder, prepared as 12g biscuits. These biscuits in addition to regular diet were used for 3 months in our intervention program.

The serum lipid level of each subject was measured before and after the 3-month regimens. LDL and HDL were measured by calorimetric end point, and TG and CHOL were measured by the end-point method. Out of the 75 subjects under study, 19 patients were excluded: 9 due to a lack of tolerating the taste of the biscuits and 10 patients were lost to follow up. The data of 56 subjects, whose compliance was confirmed by the accompanying person in our follow-up, were analyzed using SPSS software, and we used the paired t-test to determine the significant effect of our intervention program in decreasing the lipid levels.

Results

The mean age (±SD) of the participants was 56.2 (±6.9) years, with the range of 30-79 years, and 19 cases were male and 37 cases were female. The results showed that the mean cholesterol was 258.44 before and 232 after 3-months' intervention (P=0.0001). The mean difference was 26.39 mg/dl, and the decreasing rate was 10.2% (Table I). The mean difference in TG level was 64.85mg/dl, a decrease of 35%. The mean difference in LDL level was 32.7 mg/dl (P=0.0001), a decrease of 18.8%. The mean difference in HDL was 0.64 mg/dl, a 1.45% decrease (P>0.05).

Table I. The mean (SD) of serum lipids before and after intervention with linseed powder.

Serum lipid	Before treatment Mean ± SD (g/dl)	After treatment Mean± SD (g/dl)	P value
Total Cholesterol	258.44±55.95	232.05±41.47	0.0001
TG	289.92±126.57	225.07±82.54	0.0001

LDL	**173.82±52.87**	**141.12±39.94**	**0.0001**
HDL	**43.89±25.66**	**44.53±13.89**	**0.85**

Discussion

Our findings indicate that the consumption of linseed powder plus regular diet regimens significantly decreased the mean cholesterol, TG and LDL in both male and female subjects, but HDL level increased significantly only in females. These results are consistent with those reported that the consumption of polyunsaturated fatty acid leads to a decreased total cholesterol level.[2,4,11,12] In particular, the consumption of omega-3 fatty acid decreases the total cholesterol level.[13] However, Alekseeva et al.[14] and Eristland et al.[15] did not find any significant effect of linseed and omega 3 fatty acid on cholesterol level. These differences might be due to the difference in social factors, genotype with respect to the hyperlipidemia, background diet, dose, method of prescription and the duration of follow-up. Moreover, Kim et al. reported that the consumption of linseed in patients with hyperlipidemia caused a decrease in total cholesterol level up to 25%.[6] This figure is much more than those we estimated in our study (10.2%).We used the least possible dose of linseed in order to prevent any side effect. Thus, the differences essentially might be due to the prescribed dose of linseed which we used. Although the consumption of omega 6 fatty acid induces a relative increase in serum cholesterol level,[16] linseed mostly contains omega 3 fatty acids.[9,10] According to many clinical researchers, this type of fatty acid is expected to decrease the plasma level of triglyceride. Our findings showed that the mean difference of TG was 64.8 mg/dl, a decrease of 22.3%. These results also corresponded to those reported about the effect of omega 3 fatty acid and linseed on TG plasma level.[7,9,10,17,18,19] Our findings did not correspond with those reported by Alekseeva et al., who showed that the consumption of linseed did not change TG level of plasma.[14] Kim et al. also reported that the daily consumption of linseed led to a 65% decrease in serum TG level.[6] We found that this figure was 22.3%. This difference might be due to the dose of linseed prescribed in our study (we used the least dose).

Our findings also revealed that LDL level significantly decreased by a mean of 32.7mg/dl, or 18.8%. This result is also consistent with those reported in the literature.[16,17,20-22] In contrast, Alekseeva et al. and Eristland et al. did not find any significant effect of omega 3 fatty acid on LDL levels.[15,16] The reasons we discussed already can explain these different results.

Published studies reveal that the consumption of omega 6 fatty acid leads to lowering in HDL level[23, 24] and that omega 3 fatty acid increases HDL level or does not change it at all. We also did not find any significant difference on overall HDL level. These findings also corresponded with those reported by Eristland et al,[15] while other published data in the literature have reported a significant increase in HDL level using omega 3 fatty acids.[17, 22]

In addition, when we conducted stratified analysis with respect to the gender, the findings revealed that our intervention program was effective in decreasing the total cholesterol, TG and LDL level in both males and females; however, HDL level tended to decrease in men. This might be due to the small number of men in the study, and also it did not achieve statistical significance. On the other hand, HDL levels increased significantly in females.

A limitation of using linseed oil is that it must be kept in a closed space and packed in dark houses since it is extremely susceptible for oxidation. Also, some kinds of linseed might contain unflavored combinations which could be toxic, such as glucose cyanogen. In

particular, linseed used for cultivation of linen has greater risk than linseed oil, and oil linseed is much less susceptible for such toxigenic activity. The risk of this toxin is greater in premature seed than mature seed, and it can lead to cyanotoxin through hybridization.
According to the report of the Industrial Nutrition Institute of Iran, the major oil consumption in Iranian families is hydrogenous vegetable oil, which accounts for 22% of the total required daily energy. In addition, PUFA comprises only 1.5% of total energy, and its rate of consumption is much lower than recommended levels.[1,2] Taking into account that roughly 40% of mortality is due to cardiovascular diseases,[1] the pattern of consumption of nutrients, especially oil has an important role on overall health. Thus, a community-based intervention program and changing diet behavior, particularly in urban areas is required to modify the present pattern of oil consumption. In this regard, we recommend roughly 6g daily consumption of linseed powder as a compliment of the regular diet regimen for lowering lipid levels.

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Transcatheter Occlusion of PDA by Detachable Coil Occluder and Amplatzer Device

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Abstract

Background- The aim of this study was to report the results of using PDA occluders (coil occluder and Amplatzer device), which has continued since December 1999 at the pediatric department of Rajaee Heart Center.

Methods- Between December 1999 and September 2002, 193 cases of PDA were admitted at the pediatric ward. Seventy cases underwent transcatheter occlusion of PDA by the detachable coil occluder, and in 53 cases PDA was occluded by the Amplatzer device.

Results- Successful coil placement was accomplished in 68 cases. Two cases of intravascular hemolysis were observed due to residual shunt .In one of them, acute tubular necrosis ensued, and peritoneal dialysis was performed. However, after surgical PDA closure, the renal performance was recovered eventually. Also, two cases of coil detachment to the LPA were observed with no long-term sequala on pulmonary function. Fifty-two of the 53 Amplatzer occlusions were successful. Only one failure was observed due to the small size of the Amplatzer in comparison to the duct diameter.

Conclusion- Retrograde and antegrade transcatheter closure of the PDA by the detachable coil occluder and Amplatzer device has been performed successfully in our department. The problem that we face has been PDA sizing and also the retrieval of detached coils ***(Iranian Heart Journal 2005; 6 (1,2): 43-47).***

Key words-Patent ductus arteriosus ■ transcatheter occlusion ■coil occluder ■ Amplatzer device

Patent ductus arteriosus (PDA) is one of the most common congenital heart defects.[1] In the USA the incidence of PDA in children born at term is between 0.002% and 0.006% of live births. The incidence increases in children born prematurely, children with a history of perinatal asphyxia and possibly, children born at high altitudes. A large number of surgical and transcatheter techniques for the interruption or closure of PDA have been reported as a safe alternative to surgery.[2] The earliest report of catheter closure was in 1966. Since then, many devices have been used to achieve closure.

The different types of devices used include the buttoned device, the botalloccluder device, the Gianturco Grifka Vascular Occlusion Device (GGVOD), the amplatzer duct occluder and the Gianturco coils[3] For small PDAs, the coil is the choice number one; however; for moderate to large PDAs, the Amplatzer device is the first choice.[4,5] There has been a high rate of embolization of the coil to the peripheral pulmonary arteries, which is not release controlled.

Recently, this problem has been resolved with controlled –release Jackson coils, and they have become widely used by pediatric cardiology centers.[6,7] In this study, the immediate and short term outcomes of transcatheter closure of PDA by the detachable coil occluder and the Amplatzer duct occluder device are assessed.

Methods

Between December 1999 and September 2002, 193 cases of PDA were admitted to the pediatric ward, and 123 patients underwent percutaneous PDA closure at Shaheed Rajaee Heart Center. The inclusion criteria for the coil occluder device were small PDAs with a diameter of equal or less than 2 mm at angiography and a body weight of more than ten kilograms. The inclusion criteria for the Amplatzer device were clinical and echocardiographic features of moderate to large PDAs with an internal diameter of more than 4 mm. Occlusion was achieved via the anterograde arterial and venous approach. Follow-up valuations were performed by 2D-Echocardiogram, color flow mapping and Doppler measurement of the descending aorta and left pulmonary artery velocity at 24 hours and 1, 3, 6 and 12 months after ... 23 ... by ... (38 female and 15 male) PDA was occluded by the Amplatzer device, and in the remaining patients, the PDAs were occluded surgically.

Results

Of 70 procedures of PDA occlusion by the coil occluder device, 66 were completely successful (94%). Pulmonary–systemic flow ratio (QP/QS) was 1.15-1.5 (mean1.3). The smallest internal dimension ranged from 1.5 mm to 4 mm (average 2.4 mm). Thirty patients had PDA closure with the smallest available coil (IMWC-3-PDA-4). Twenty-four had closure with the midsize coil (IMWC-5-PDA-4 or 5-PDA-5). Sixteen patients received large-sized PDA coils (IMWC-6.5-PDA-4). Five patients received two or three coils, and the other PDAs were occluded with one coil.

We experienced two cases of intravascular hemolysis 12 hours after the procedure due to residual shunt. In one of these cases, acute tubular necrosis ensued, and peritoneal dialysis was performed. Fortunately, the hemolysis was relieved after the complete surgical closure of the residual PDA, and renal performance returned to normal

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eventually. We also experienced two cases of coil detachment into the LPA that could not be retrieved, but at follow-up no pulmonary residual problem was observed. Complete closure was accomplished by ortography 10-15 minutes after the procedure in at least 51 patients, and color flow imaging study 24 ours after the procedure showed no residual leak in 9 patients in whom post implantation angiogram had shown small residual leak. Complete closure was confirmed in 7 after 7 days and in 3 patients up to one month later. Follow-up revealed 2 insignificant residual shunts that had disappeared spontaneously at six months. After one year's follow-up, no patient had persistent residual leak that necessitated surgical or interventional procedure (100% closure). None of the patients underwent additional catheterization. During the study period, 53 PDAs were occluded by the Amplatzer device, and the results were excellent. The mean duct diameter was 4.7 mm. The pulmonary to systemic flow ratio (QP/QS) varied between 1.9-2.2 (mean 2.04). No displacement of the Amplatzer occurred, and there was only one failure due to the small size of the Amplatzer in comparison to the PDA diameter. At the angiography 10-15 minutes after the procedure, 37 patients had no residual shunts.

At 24 hours' follow –up by color flow mapping, only one residual leak was observed, which was relieved at one week's follow–up, and at 6 months' follow-up no residual shunt was observed (Table I).

Table I: Patients and Data

Procedure	Coil	Amplatzer
Sex	Female (47) Male (23)	Female (38) Male (15)
Age	0.7-17 yr (5.2)	0.7-17 yr (5.6)
Weight	5-45 kg (18 kg)	5-45 kg (18.5 kg)
PDA Diameter	1.5-4 mm (2.4)	2-12 mm (4.7)
Coil and Amplatzer Size	4-8 (5 loop)	4-16 mm (6.6 mm)
Complication	2	1
Residual Shunt	20	0
Unsuccessful	0	1

Discussion

Embolization of the device, residual shunt, stenosis and reversion to surgery are potential risks associated with the closure of PDAs with devices. Over a 33-month period, a total number of 70 percutaneous PDA occlusions were performed. Two major problems were encountered during this period. One was residual shunt and hemolysis as the consequence of the shunt (which was observed in two patients 12 hours after implantation of the detachable coil) and the other was embolization of the coil to the left pulmonary artery (LPA). A study by Jaeggi et al.[8] compared the Cook detachable coil with a preceding series of Rashkind umbrella series. Long term shunt persistence after single coil deployment in moderate sized ducts was as frequent as that with the Rashkind device; and the use of multiple coils was advocated.

Residual leaks are high with the Rashkind device[9], and there is a high risk of embolization with multiple coils.[10] Bulbul et al.[11] demonstrated that the closure of PDA was more complete when using coils compared with the Rashkind device.[12, 13] In a report by Jaeggi et al., a visible residual shunt at post– implant angiography in moderate ducts was associated with a high incidence (59%) of long term echocardiographic shunt patency and a need for repeat interventions for audible residual shunts. (32%) More recently, Wang et al. reported a series of 55 patients who underwent transcatheter PDA closure using Gianturco coils For patients with small PDA (<3mm), the authors reported 100% successful coil deployment, and no distal device embolizations. However, as the PDA size increased, so too did the rate of unsuccessful coil deployment, residual left-to-right shunt and, most importantly, coil embolization (37%) in patients with ductal diameter >4mm)[14].

As seen in our study, the two cases with residual shunts were of moderate PDAs sized 4 mm. Residual leak led to hemolysis, but after PDAs had been ligated surgically and the shunt had been removed, no permanent renal dysfunction was observed at one year's follow-up.

In 1996, Tometzki et al.[15] published a six- center British study. Implantation of the Duct-Occlud device was feasible in 44 of 51 cases with persistent arterial ducts. The minimum diameter of the PDA ranged from 1.0 to 4.3 mm (mean 2.1 mm) The PDA in the remaining 7 patients was judged too large for the device and Rashkind devices used. In 39 patients, coil implantation was performed using the transvenous route. In five patients, the device was deployed from the aorta. Embolization of the Duct-Occlud device occurred in three cases (5.8%). In one patient, the device embolized hours after placement, and a second-procedure was required for removal. In one patient, the device could not be retrieved from a distal branch of the right pulmonary artery, so it was left in place. In another patient, a 3-mm fragment of the device became entangled in the tricuspid apparatus. The patient had another device successfully deployed, and after

12 months' follow-up the fragment remained in situ with no evidence of tricuspid valve regurgitation. In 40 (91%) of the 44 patients in whom the Duct-Occlud device was used, complete occlusion at 24 hours could be demonstrated on color flow Doppler Echocardiography. Another nation-wide multicenter trial of Duct-Occlud was reported by Oho et al.[16] in 1998. The Duct-Occlud was used in 35 patients aged 0.5to 27.2 years (median 7.6 years). The smallest diameter of PDA was 2.0 0.7 mm (range 1.0 to 3.3 mm). Pulmonary– systemic flow ratio (QP: QS) was 1.3 0.3 (range 1.0 to 2.2). The coils were successfully implanted in 32 (91%) of patients. Of 31 patients who were followed 6 months after the procedure, 26 (84%) had no residual shunt, and five (16%) had a trivial residual shunt. One patient had infective endocarditis 1 month after the procedure but recovered completely. There were no incidences of coil embolization, hemolysis, late coil migration or obstruction of the pulmonary artery or the aorta.

In our study, only two cases of coil detachment to the LPA were observed. Unfortunately, they could not be retrieved because of a lack of suitable devices. But at one year's follow–up, no residual pulmonary problem was encountered.

As it is emphasized by other reports [6,7,10] the selection of the most suitable device (coil occluder versus Amplatzer device) according to the duct diameter is a very important component influencing the result. Lee et al.[17] and Arora et al.[18] published the only previous series of PDA closure using the Amplatzer Duct Occluder in adult patients. In their series of 5 patients with PDA, Lee et al. reported a procedural success rate of 100%. Complete echocardiographic closure was seen in all the patients within 24 hours, and there were no complications. Similarly, in a series of 27 patients with PDA, Arora et al. reported only one unsuccessful placement of an Amplatzer Duct Occluder device. Furthermore, complete occlusion without a residual shunt was observed in 100% of patients within 24 hours of device placement, and no complications were seen. In our series of patients, we observed similar favorable results. Of 193 patients with PDAs of a wide variety of sizes, 53 had occlusion by the Amplatzer device, and 100% success was observed. In over 67 % of the cases, immediate angiographic closure was observed. By 24 hours post-procedure, complete closure was observed in 98% of the cases, and by 6 months post-procedure, complete closure was observed in 100% of the cases. Unfortunately, late follow-up on one of the patients who did not have complete closure by 24 hours is not available. Of the patients who completed 6-months' and 1-year's follow- up, 100% had complete closure of their PDAs. The complication rate was low, and none were attributed to the implantation of the Amplatzer device but rather to the catheterization procedure itself (groin complications and allergic reaction).

Conclusion

We believe that the selection of an appropriate device for the closure of PDA in children should depend on the angiographic diameter of the ductus. If the PDA is small with a diameter <3 mm, then, depending on the operator's preference, either coil closure or the Amplatzer device may be considered. For patients with a PDA >3 mm, we believe that the Amplatzer device deployed from the venous side is the best available option.

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Atrio-Ventricular Plane Displacement in Ischemic Heart Disease

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Abstract

Background- Whether atrio-ventricular plane displacement (AVPD) in echocardiography findings may help to diagnose ischemic heart disease (IHD) in the presence of normal systolic function is not clear. This study aimed to assess the relationship between AVPD and ischemic heart disease (IHD) in a group of IHD patients.

Method- One hundred two outpatients (65 male and 37 female) aged 58.9±11.4 were examined for IHD by echocardiography, stress test and angiography, and 61 patients were found to have IHD. Echocardiographic findings, including AVPD, LVEF and RWMA, were compared in normal and IHD patients.

Results- Comparison of echocardiography findings in the ischemic patients to the normal subjects showed that the subjects with IHD had significantly lower AVPD, LVEF and higher RWMA. Results of a logistic regression analysis indicated that AVPD was an independent predictor of IHD (OR=0.61, 95%CI= 0.46-0.79).

Conclusion- These data suggested that low AVPD was associated with increased risk of IHD. AVPD may help diagnose IHD when more sophisticated techniques are not available and/or applicable ***(Iranian Heart Journal 2005; 6 (1,2): 48-51).***

Key words: AVPD ■ echocardiography ■ IHD

There are many stress tests: stress imaging tests (radionuclide and stress echo study) and new imaging modalities (eg. CT-angio, MR) for the determination of the prognosis of ischemic heart disease (IHD). While these diagnostic tests are improving rapidly, many people in low-income countries do not have access to these expensive tests. Echocardiography is one of the basic heart evaluations. Whether simple and reliable techniques such as atrioventricular plane displacement (AVPD) in echocardiography findings may help diagnose IHD is not clear.

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AVPD is an indicator of longitudinal fiber function, and is used in assessing systolic left ventricular (LV) function.[1-3]
The long axis shortening of the LV is related to LV function and can be measured by AVPD. Determination of left AVPD is a reliable, reproducible, readily mastered, quickly performed and, thus inexpensive method that can be used in almost all patients for evaluation of LV function, as well as for prognostic implications in heart failure (HF). Left AVPD reflects both systolic and diastolic LV functions.
Simplified echocardiography is useful for screening of asymptomatic patients at risk of developing HF, and for routine diagnostic purposes in patients with symptoms suggestive of HF.[4] AVPD was independently correlated with both left ventricular systolic function and diastolic filling in patients with CAD. Thus, given the same degree of ejection fraction, it was found that the greater the impairment in diastolic filling, the lower the AVPD.[5] Echocardiographically-determined AVPD is a clinically useful, independent prognostic tool in patients with stable CAD.[6] It is not currently a diagnostic tool for the diagnosis of IHD.[7] Considering that the subendocardium is more vulnerable to ischemic damage than mid-myocardium and subepicardium,[8] we hypothesized that AVPD might help detect IHD in patients with normal systolic function. This study aimed to assess the association of AVPD with the risk of IHD in a cross-sectional design.

The subjects were 102 outpatients (65 male and 37 female) aged 58.9± 11.4 admitted in Heshmat Heart Clinic in Rasht, Iran. The subjects were examined for IHD. Data on age, history of previous myocardial infarction and coronary revascularization (PCI and CABG) were collected using questionnaires. Four subjects were found to have atrial fibrillation and were excluded from the study. None of the patients had mitral valve replacement, repair, mitral annulus calcification or any localized aneurysm in the basal portion of the LV. The subjects gave written consent for participation in this study.
The equipment for echocardiography was a Vingmed 750-echocardiography system and a 2.5 MHz transducer.
A complete echocardiography study including parasternal long and short axis, apical four, five and two- chamber views was carried out. Sixteen segment wall motion abnormality and modified Simpson's LVEF were measured. AVPD measurement was done using the method described by Alam, et al. [1]
AVPD was measured in the long axis apical two-chamber view for anterior and posterior walls and in the long axis apical four-chamber view for lateral and septal walls. The distance between AV plane and apex was measured in millimeters in systole and diastole, and the difference between these two measurements was assigned as AVPD. The M-mode cursor was placed at the anterior, posterior, lateral and septal orientation at the AV plane and is connected to the fix point of the apical portion of the LV (fix portion is that part of the LV apex that has the lowest displacement relative to the chest wall, Fig. 1).

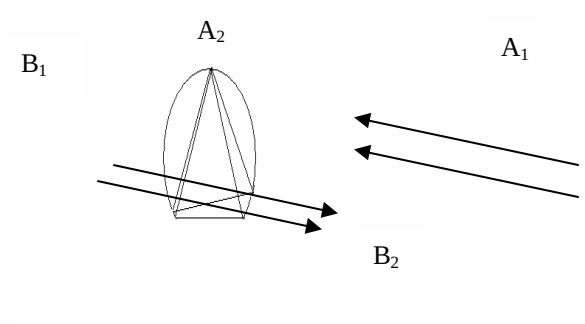

Fig. 1. schematic AVPD measurement in apical two-chamber view in systole and diastole

AVPD (ant) =A_1- A_2, AVPD (post) =B_1- B_2

The distance in each plane was measured twice, and the mean was calculated. Mean AVPD was calculated by adding four planes measurements divided by four.

CAD was defined by definite ECG findings, history of revascularization or positive diagnostic tests (stress test and coronary angiography). According to the history of revascularization and electrocardiography data (Q-waves indicating myocardial infarctions), 28 patients had documented CAD. The investigation was continued on 70 patients by either exercise stress test (n=28), stress imaging tests (n=38) or coronary angiography (n=4). Finally, 61 patients had proved IHD, and 37 subjects were normal.

Statistical analysis

Mean AVPD, LVEF, RWMA and age between the two groups were compared by Student's t test. The Pearson correlation of coefficients between the measured variables was calculated. A backward stepwise logistic regression analysis was also performed to model the predictors of IHD. Values are given as the mean ± standard deviation. P-value less than 0.05 were considered as the level of significance. Analyses were performed using the statistical package SPSS software, version 10.01 for windows (SPSS Inc®, Chicago, USA).

Results

Echocardiography data and age of the subjects in the two groups are given in Table I. Subjects with IHD had significantly lower AVPD, LVEF and higher RWMA than subjects without IHD. These data showed that AVPD was positively correlated to LVEF (r=0.635 p=0.0001) and negatively correlated to age (r=-0. 241 p=0.005) and RWMA (r=-0.44 p=0.0050).

Table I. Comparison of echocardiography data and age in the study population

	IHD (n=61)	normal (n=37)	P-Value
AVPD (mm)	8.9± 2.6	12.1 ± 2.1	P<0.0001
LVEF (%)	51.3 ± 10.0	59.9 ± 7.3	P = 0.006
RWMA (n)	1.8 ± 0.3	1.3 ± 0.4	P<0.0001
Age (y)	60.0 ± 11.6	56.7 ± 11.2	P = 0.17

Results of a backward stepwise logistic regression analysis showed that AVPD is an independent predictor of IHD in this study (Table II).

Table II. The final result of a backward stepwise logistic multiple regression analysis with LVEF, AVPD, RWMA, age and sex as independent variables and IHD as the dependent variable.

Variables in the equation	B ± SD	OR	CI	P-Value
AVPD (mm)	- 0.48 ± 0.13	0.61	0.46 - 0.79	0.003
RWMA	1.46 ± 0.06	4.32	1.33 - 14.0	0.01
SEX (Male)	1.67 ± 0.61	5.3	1.5 - 17.6	0.006
LVEF (%)	- 0.27 ± 0.45	0.97	0.88 - 1.06	0.544
Age (y)	- 0.007 ± 0.027	0.99	0.94 - 1.04	0.799

Discussion

It is well known that under resting conditions patients with coronary artery disease may have normal left ventricular function. If no permanent myocardial damage occurs and the ventricle is not ischemic at the time of examination, routine echocardiography study does not reveal the underlying coronary artery disease.[9] Our findings showed that AVPD might serve as a predictor of IHD in the study population. Rydberg et al. have previously indicated that low AVPD is in high agreement with the results of angiography in assessing IHD.[10] The present data indicated that the association between low AVPD and the risk of IHD is independent of LVEF and RWMA. It has been recently suggested that decreased AVPD despite normal LVRWM may be a true sign of myocardial dysfunction, predominantly indicating subendocardial dysfunction.[11] High sensitivity of longitudinal muscle (subendocardial and papillary muscle fibers) to ischemia explains the association between AVPD and IHD.

Measurement of AVPD in four planes in apical two and four-chamber views using 2 D-guided M-mode echocardiography is a simple technique and can be performed by a simple echocardiography system. Such a technique does not take a long time to perform, and it is highly reproducible.[12] More studies are needed to elucidate the role of AVPD in diagnosing IHD.

In conclusion, our data suggested that abnormal AVPD was associated with IHD and that it might have a role in predicting IHD. This finding might have important diagnostic implications in developing countries, where more sophisticated diagnostic techniques are not available everywhere in the country.

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Acute Myocardial Infarction in the Young

M. H. Soltani, MD; M. Sadr, MD; M. Rafee, MD; M. Imami, MD; M. Motafakker, MD; A. Andishmand, MD and M. Nemayandeh, MD.

Abstract

Background- **The purpose of this study was to assess frequency, risk factors, complications and mortality rate of young patients with acute myocardial infarction (AMI), in Yazd.**

Methods- **From a database of 815 consecutive patients admitted to Yazd hospitals with AMI between 2001 and 2002, we compared care, risk factors, complications and outcome of patients, divided into two age groups: £ 45 years, (young) and >45 years (old). Risk factors, type of AMI, management, complications and hospital outcomes of the 2 groups were evaluated.**

Results- **The young patients represented 11.6% of all cases, and 10% of these individuals were female. Smoking (60.2% vs. 33.6%, P. value=0.000), positive family history (40.2% vs. 28.6%, P. value=0.017) and obesity (25% vs. 13.9% P. value=0.022) were more common in the young group. Diabetes mellitus (24.1% vs. 46.9%, P. value=0.000) and hypertension (15.1% vs. 43.3%, P. value=0.000) were more common in the old patients. Young male patients had less in-hospital mortality (1.2% vs. 9.1%, P. value=0.005) than old male patients, but in the females the difference of mortality between young and old was not significant (10% vs. 19.9%, P. value=0.3).**

Conclusion- **In this study, about one-tenth of the patients with AMI were £ 45 years old. Smoking, obesity and positive family history were more common in the young patients, and overall mortality rate was low in the young** *(Iranian Heart Journal 2005; 6 (1,2): 52-54).*

Key words: **Yazd ■acute myocardial infarction ■ young**

Acute myocardial infarction (AMI) is a common cause of disability and death, and when it happens in young individuals, it causes more social and economic disadvantages. About 10% of all patients with AMI are <45 years old [1, 2]. Their risk factors vary in different countries. In most studies, smoking is the most prevalent risk factor in young patients[1-2-3-4-5-6] Positive family history of coronary artery disease (CAD) has been important in some studies.[3,6,7] Hypertension and diabetes mellitus are more common in older patients in most studies.[2,4,6]

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Methods

815 patients with AMI, admitted to all coronary care units of Yazd between 2001 and 2002, were studied. The diagnosis of AMI was confirmed with standard ECG criteria and at least three fold increment in consecutive CPK levels.

We compared risk factors, care, in hospital complications and mortality rate in patients ≤45 years (young group) and >45 years (old group).
Risk factors were defined as follows:
Hypertension: **History of hypertension (BP ≥ 140 / 90 at least two split measurement) or drug use for hypertension.**
Diabetes mellitus: **History of diabetes mellitus or drug use for diabetes, or at least one BS 3 200 mg/dl via random venous sampling.**
Cigarette smoking: **Ten cigarettes per day for at least one year.**
Hypertriglyceridemia: **Fasting triglyceride more than 200 mg/dl.**
Hypercholesterolemia: **Fasting LDL-C more than 130 mg/dl.**
Low HDL: **HDL-C lower than 35 mg/dl.**
Positive family history: **Sudden death or AMI in young first degree relatives (men ≤ 55, women ≤ 65 years old).**
Obesity: **BMI more than 30.**
Data analysis was performed with the chi square, Fisher's exact test and T test using SPSS software.

Results

815 patients with AMI were enrolled in this study. Ninety-five patients (11.6%) were £ 45 years old (90% male, 10% female). 720 patients (88.4%) were >45 years old (77% male, 23% female).
The frequency of risk factors is shown in Table I.
Smoking, positive family history and obesity were more prevalent in the young patients, and hypertension and diabetes mellitus were more prevalent in the old patients.
Hypercholesterolemia and hypertriglyceridemia were more common in the young group, but the difference was not significant.
Thrombolytic drug (streptokinase) was used in 67.7% of the young vs. 54% of the older patients (p value=.008).
Mean levels of cholesterol, LDL. C, HDL. C and triglyceride were 197±71 vs. 191±50, (p value=0.158); 128±36 vs. 118±43, (p value=0.62); 41±11 vs. 39±10, (p value=0.72); and 176±118 vs. 164±118, (p value=0.136) in the young and old patients, respectively.

The frequency of major in-hospital complications is shown in Table II.
The in-hospital mortality rate was 2/2% in the young vs. 14/7% in the older patients. It was 1/.2% in the young males vs. 9.1% in the young females (P. value=0.005) and 10% in the old males vs. 19.9% in the old females (P. value=0.385).
The mortality rate in the young male patients was very low, but in the young females and old patients it was relatively high.

Discussion

Acute myocardial infarction (AMI) is a common cause of disability and death in many countries[8] and causes more disadvantages, when it happens in young patients. Therefore, the diagnosis of major risk factors and their modification may prevent AMI in young individuals.
In this research, 11.6% of all the patients with AMI were £ 45 years old. In the Doughty M study in USA [(1)] and Morillas PJ in Spain[2], the frequency of young patients (£45 years old) with AMI was 10% and 6.8%, respectively. It appears that more patients in our study were young. Smoking, obesity and positive family history were major risk factors in our patients.
In the Doughty M study in USA,[1] Morillas PJ in Spain,[2] Von Eyben FW in Denmark[3] Miyamoto S in Japan,[4] Ranjith N in South

Africa[5] and Zimmerman FH in USA[6] cigarette smoking is a common risk factor in young patients with AMI.
Positive family history was an important risk factor in our young patients as it was in the Von Eyben FE[3], Zimmerman FW[6] and Friedlander Y[7] studies.
Obesity was also more common in our young patients as it was in the Miyamoto S study.[4]

Table I. risk factor frequency in two age groups

Risk factors	Frequency of risk factor (%)		P. value
	Young(28-45)	Old(46-100)	
Diabetes mellitus	24.4%	46.7%	0.000
Hypertension	15.1%	43.3%	0.000
Positive family history	40.2%	28.6%	0.017
Hypercholesterolemia	52.4%	36.2%	0.11
Hypertriglyceridemia	31.3%	26.2%	0.197
Smoking	60.2%	33.6%	0.000
Obesity	25%	13.9%	0.002
Low HDL	24.2%	35.9%	0.133

Table II: frequency of major in-hospital complication in two age groups

Complication	Frequency (%)		P. value
	Young(28-45)	Old (46-100)	
Cardiogenic shock	9.5%	18.2%	0.113
VSD	0%	3.2%	0.270
Acute pulmonary edema	4.8%	15.6%	0.06

In our study, Hypercholesterolemia and hypertriglyceridemia were more common in the young group, but the difference was not significant. In some studies,[2-3-4-5] high cholesterol is an important risk factor in young patients with AMI, but the difference of cholesterol level between the young and old patients with AMI in our study was not statistically significant.
Hypertension and diabetes mellitus were more common in our old patients as it was in most other studies.[2-4- 6]
The in-hospital mortality rate of the young male patients in this study was low as it was in other studies[1-2], but the in-hospital mortality rate of the young females and old patients was relatively high.

In conclusion, cigarette smoking, positive family history and obesity were more common in young patients with AMI (in comparison with old patients), and overall in-hospital mortality rate was low in young patients with AMI.

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QT Dispersion in Children with Congenital Heart Disease after Open-Heart Surgery

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Abstract

Background- A number of publications has shown a relation between increased QT dispersion and death from a cardiac cause. However, there are no published data on the value of QT interval dispersion after open-heart surgery in the pediatric age group.

Methods- Three electrocardiograms (pre-operation, on the day of operation and the second day post-operation) were obtained from 18 children (11 males, 7 females), three to 14 years of age. Measurements were carried out from standard 12- lead ECGs recorded at a speed of 25 mm/s at rest. The QT and preceding RR intervals of at least one sinus beat (range one to three) were measured in a range of nine to 12 leads, and the mean QT and RR intervals were calculated. The corrected QT interval was calculated by Bazett's method ($QTc = QT/\sqrt{RR}$). QT intervals were measured from the onset of the QRS complex to the end of

the T wave. Dispersion of the QT and QTc were defined by the difference between the maximum and minimum QT and QTc intervals occurring in any of the 12 leads.

Results- The mean QT dispersion in patients before surgery was 53 ± 22 ms, 72±31 ms on the day of operation and 65±27 one day after operation, and mean QTc dispersion before surgery was 62±22 ms, 95±27 ms on the day of operation and 97±41 ms on the day after operation. There was a significant increase in mean QT and QTc immediately after surgery ($p<0.001$). Although it decreased on the first day after surgery, it remained significantly high as compared to before surgery ($p<0.02$).

Conclusion- QT interval dispersion may increase after open-heart surgery, which may result in death following an arrhythmia. Open-heart surgery may have an independent role in the genesis of QT dispersion prolongation and should be considered as one of the mechanisms of arrhythmia after surgery ***(Iranian Heart Journal 2005; 6 (1,2): 55-59).***

Key words: QT dispersion ■ open-heart surgery ■ arrhythmia

QT interval dispersion is an indirect measure of the heterogeneity of ventricular repolarisation.[1,2] A potential application of this inter-lead difference from standard 12-lead electrocardiograms (ECGs) was first proposed by Day et al. in 1990.[3]

More recently, there has been an increasing interest in what has become known as QT dispersion, which is defined as the difference between the maximum

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reduced as a result of certain drug treatments.[4-9]

On the other hand, increased QT dispersion has been shown not to be associated with increased cardiac death in patients with idiopathic dilated cardiomyopathy.[10]

It has also been suggested that increased dispersion has been reported as a non-invasive marker of an electrophysiological arrhythmogenic substrate, and it has been associated with high risk of ventricular arrhythmias and sudden death in various cardiac disorders.[11-12] Altogether, within the last decade, QT dispersion has been proposed as a descriptor of ventricular repolarization and, as such, as a potential prognostic tool in the detection of future ventricular tachyarrhythmic events and death.[13] In a recent study, it has been found that not only QT-interval dispersion but also other indices measured on the whole QRS-T complex, especially the JT index and T peak-T end, could be used in the quantitative assessment of the dispersion of ventricular repolarisation.[14] However, there has been only a limited amount of data published on the use of indices other than the QT interval, and also there are few published data on the value of QT interval dispersion in the pediatric age group. Hence, this study was carried out to determine the changes of QT, QTc, JT and JTc dispersion in children with congenital heart disease who undergo open-heart surgery.

Methods

Three electrocardiograms (pre-operation, on the day of operation and the second day post-operation) were obtained from 18 children (11 males, 7 females), three to 14 years of age (mean: 8.4 ± 3.4 years). The children had at least one type of congenital heart disease necessitating open-heart surgery.

Study Protocol

Measurements were carried out from standard 12- lead ECGs, recorded at a speed of 25 mm/s at rest. A one-channel electrocardiographic recorder (Hewlett Packard, model 4745 A) was used. The QT and preceding RR intervals of at least one sinus beat (range one to three) were measured in a range of nine to 12 leads, and the mean QT and RR intervals were calculated. The corrected QT interval was calculated by Bazett's method ($QTc = QT/\sqrt{RR}$).[15] The mean QT and the mean RR were used to calculate the mean QTc for each lead. Heart rate was derived from the mean of the RR intervals. The QT and RR intervals were measured manually with calipers by a single observer. QT intervals were measured from the onset of the QRS complex to the end of the T- wave. The end of the T- wave was defined as the point of return to the isoelectric line. When a U wave was present, the QT interval was measured to the nadir of the curve between the T and U wave.[16] Leads with non indeterminate end of the T- wave were excluded from the calculation. Dispersion of the QT and QTc were defined in two ways: (1) the difference between the maximum and minimum QT and QTc intervals occurring in any of the 12 leads (QTD, QTcD), and (2) the standard deviation of the QT and QTc interval in the leads that could be measured (QT-SD, QTc-SD).[17] RR variation was also calculated in a same manner (RRD and RR-SD, respectively).

All the data are expressed as mean ± SD. Paired and unpaired Student's *t* tests were used where appropriate. Correlations were assessed by Pearson's coefficients. A two- tailed p value < 0.05 was considered significant.

Results

The study group consisted of 18 children, 11 of whom were male and the remainders were female. The mean age was 8.4 ± 3.4 years, with the mean weight of 20.5 ± 7.6 kg. All the patients in the study group had undergone open-heart surgery due to one or more of the following congenital heart diseases: tetralogy of Fallot, ventricular septal defect, atrial septal

defect and partial AV canal with patent foramen ovale or patent ductus arteriosus. The ECG data before, immediately after and one day after open-heart surgery are presented in Table I.

Table I. QT measurements before, just after and one day after open-heart surgery.

	Before	**Just after**	**One day after**	**P values***
RR mean (ms)	644(101	507(90)	563(115)	p<0.001
QT mean (ms)	342(38)	336(34)	336(79)	p<0.001
QT Dispersion (ms)	53(22)	72(31)	65(27)	p<0.001
QTc mean (ms)	424(33)	476(32)	437(88)	p<0.001
QT cDispersion (ms)	62(22)	95(27)	97(41)	p<0.001
JT mean (ms)	256(27)	257(24)	266(31)	NS
JT Dispersion (ms)	51(21)	57(28)	68(30)	NS
JTc mean (ms)	337(25)	363(28)	362(33)	p<0.001
JT cDispersion (ms)	62(26)	97(41)	86(26)	p<0.001

* p values refers to comparison between before and just after surgery measurements.

The mean QT dispersion in patients before surgery was 53 ± 22 ms, 72±31 ms on the day of operation, and 65±27 ms on the day after operation.
QTc dispersion before surgery was 62±22 ms, 95±27 ms on the day of operation, and 97±41ms on the day after operation.
There was a significant increase in QT and QTc dispersion immediately after surgery ($p<0.001$).
Although it decreased on the first day after surgery, it remained significantly high as compared to before surgery ($p<0.02$).
Individual QT dispersion values are shown in Fig. 1 before and one day after open-heart surgery.
QT dispersion values have shown to be increased in two-thirds of patients and to be decreased in the rest.

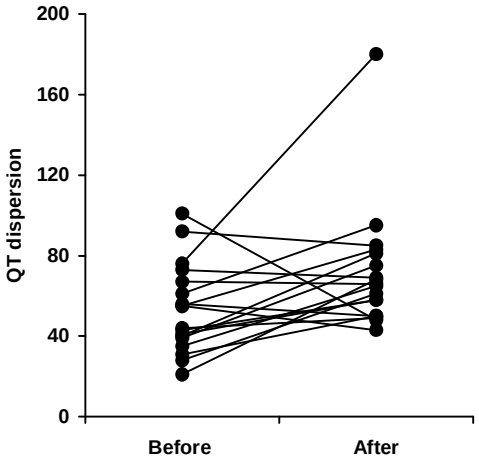

Fig. 1. Individual QT dispersion values before and one day after open-heart surgery.

Discussion

It is well-established that ventricular repolarization characteristics play an important role in arrhythmogenesis.[18] In the assessment of ventricular repolarization, prolongation of the QT-interval duration is known to contribute to the triggering of arrhythmias.[19] The dispersion of ventricular repolarisation, measured from the surface ECG and defined as the interlead variability of the QT-interval, has been reported as a new method for analyzing ventricular repolarization. Dispersion of repolarization is thought to reflect regional heterogeneity of the recovery process within the myocardium, which is believed to be important in the genesis of ventricular arrhythmias.[20] The concept that QT interlead variability reflects the dispersion of ventricular repolarization is supported by the close correlation between changes in dispersion of repolarization from ventricular monophasic action potential recordings and changes in QT-interval variation produced by ventricular pacing.[1] Furthermore, dispersion of ventricular repolarization has been shown to be increased in various cardiac disorders known to be complicated by ventricular arrhythmias, such as long QT syndrome, drug toxicity and dilated and hypertrophic cardiomyopathies.[12]

There are few published data on the value of QT interval dispersion in the pediatric age group. In the study of Macfarlane et al.[21] in the pediatric age group, overall QT dispersion was 24.52±8.7ms (10-44 ms). This study showed that open-heart surgery increased QT-interval dispersion in children. One of our patients who showed the most increment in QT dispersion died with arrhythmia after surgery. Little is known about the etiology of increased QT dispersion in patients after open-heart surgery, but sympathetic tone and excitation-contraction coupling may be important. As in the majority of studies of QT dispersion, all QT-intervals in our study were measured manually. There is evidence that manual measurement is superior to automatic measurement of QT dispersion, which usually needs some form of manual editing[22] and gives different results.[23]

Conclusion

We found that in children, QT-interval dispersion might increase after open- heart surgery, which may result in death following an arrhythmia. Hence, open- heart surgery may have an independent role in the genesis of QT dispersion prolongation and should be considered as one of the mechanisms of arrhythmia after surgery.

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Stenting Cerebral Arteries with Emboli-Protection Device: Report of 5 Cases and Six-Month's Follow-Up

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Abstract

Background- Carotid endarterectomy is superior to medical management for the prevention of stroke in patients with carotid and vertebral artery stenosis, but stenting with the use of emboli-protection devices is less invasive. We report our results with carotid artery stenting in five patients.

Methods- Stenting was done in five symptomatic male patients (mean age = 66.8 years), 20% and 40% of whom were diabetic and hypertensive, respectively, and 60% had coronary artery involvement. Indications for stenting were prior stroke in one, vertigo in one and transient ischemic attack in three patients.

Results- Stenting with self-expandable stents was technically successful in all the cases. No stroke, restenosis or death occurred.

Conclusion- Stenting cerebral arteries are feasible with a high degree of technical success ***(Iranian Heart Journal 2005; 6 (1,2): 60-63).***

Key words: carotid artery stenosis ■ vertebral artery stenosis ■ stenting ■ stroke ■ prevention

Atherosclerotic stenosis of the carotid artery causes about 20% of all ischemic strokes and transient ischemic attacks.[1] The advantage of carotid endarterectomy over medical therapy in patients with significant carotid stenosis has been established in several clinical trials.[2, 4] Shorter hospitalization, avoidance of anesthesia and surgical incision make carotid angioplasty and stent placement attractive.[3] Over the past decade, carotid angioplasty with stenting has been used to treat high surgical risk patients.[4] But an important concern is intra-procedural embolization. Emboli-protection devices have been developed to reduce this problem.[4]

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We report our experience of carotid and vertebral artery stenting with the emboli-protection device in five patients and their follow-up for a period of six months.

Methods

From March 2003 to March 2004, five male patients, 60 to 72 years old (mean = 66.8), underwent carotid and vertebral angioplasty and stenting at Imam Reza (A.S.) Hospital (Mashhad, Iran). All the patients (100%) had symptomatic cerebral artery stenosis of at least 70% of the luminal diameter on color duplex ultrasonography.

One patient (20%) had diabetes mellitus, two others (40%) had hypertension and three patients (60%) had severe coronary artery disease. Indications for intervention were a prior stroke in one patient, vertebrobasilar ischemia related symptoms (vertigo attacks) in another patient and hemispheric transient ischemic attack in three others. Clinical characteristics and demographic data are shown in Table I.

Table I. Patient characteristics

Characteristics	No.	Percent
Patients	**5**	**100%**
Mean age (year)	**66.8**	**-**
Sex (male/female)	**5/0**	**100% Male**
Diabetes mellitus	**1**	**20%**
Hypertension	**2**	**40%**
Coronary artery disease	**3**	**60%**
Stroke	**1**	**20%**

All patients underwent pre-procedural transthoracic echocardiography and four-vessel, selective carotid and vertebral angiography. Significant angiographic stenosis was defined as more than 70% diameter stenosis. All the patients received aspirin 100 mg/day and ticlopidine 250 mg/BID or clopidogrel 75 mg/day for one week before the procedure. Angiography and stenting were performed with local anesthesia via the femoral approach. After arterial access, 5000-10000 IU heparin was administered. No sedation was used before and during the procedure. Hemodynamics were monitored continuously. The stenotic lesions were crossed with a protection device (filter wire EZ) placed 2cm distal to the lesions and expanded before the stents were deployed. All the lesions were treated with self-expandable stents (Carotid Wallstent, Boston Scientific). After stent deployment, post-dilation with a balloon 5 mm in diameter was performed. Just before balloon inflation, atropine 1 mg was administered to prevent bradycardia. At the end of the procedure, the emboli-protection device containing the captured emboli was collapsed and removed. Carotid and vertebral angiography was performed in all the patients to assess technical results and the presence of distal spasm (Fig. 1).

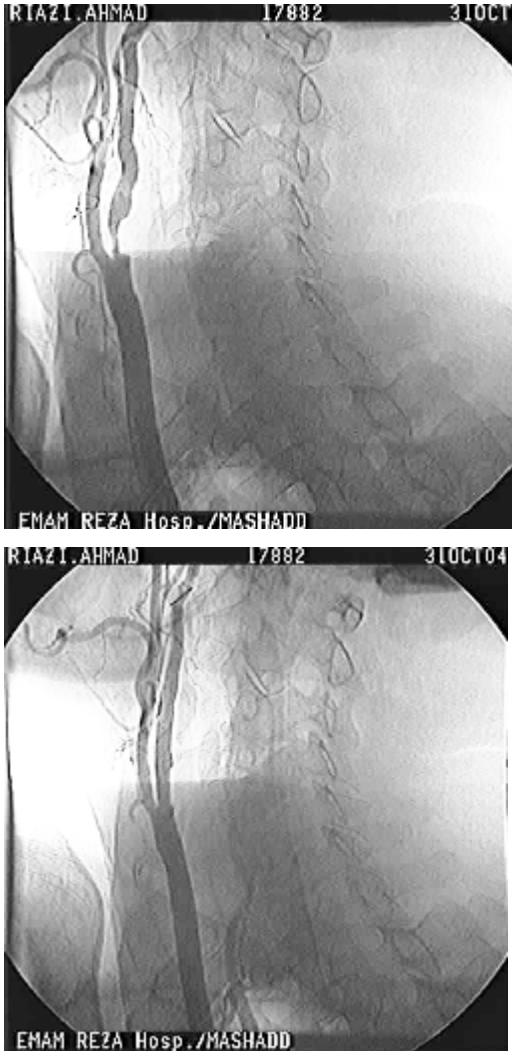

Fig.1. **Angiograms demonstrating left internal carotid artery ostial stenosis in a 70-year-old man with history of hypertension, who presented with transient ischemic attack. Color Doppler ultrasonography revealed 70% stenosis in the left internal carotid artery (Fig 1-A). The final result after stenting (Fig. 1-B).**

After the procedure, all the patients were observed in CCU for 48 hours with blood pressure and heart rate monitoring. The patients were usually discharged after 48 hours and after examination by a neurologist and were prescribed ticlopidine 250 mg/BID or clopidogrel (75mg/day) for 3 months

and aspirin 100 mg/day for an unlimited time. Outpatient follow-up was done at 30 days, 3 and 6 months after the procedure. Six months after the procedure, color duplex ultrasonography was repeated in all the patients.

Post-stenting residual stenosis equal to or greater than 30% and recurrent or residual in-stent stenosis with more than 50% diameter reduction, determined by duplex ultrasonography, were defined as technical failures.

Angiographic results

Most lesions were located at the proximal portion of the vessels. Treated cerebral arteries were the left vertebral artery in one patient, the right internal carotid artery in three patients and left internal carotid artery in one patient. Technically successful procedures were achieved in all the patients. No significant residual stenosis and no immediate neurological problems occurred after cerebral artery stenting. Two patients had hypertensive instability due to internal carotid artery balloon dilation. No stroke, myocardial infarction or death occurred during a 30- day follow-up. During 1 to 6 months' follow-ups, all the patients remained neurologically unchanged, and color duplex ultrasonography revealed that all the stents were patent without residual or recurrent stenosis.

Discussion

According to the findings of European Carotid Surgery Trial (ECST)[5] and North American Symptomatic Carotid Endarterectomy Trial (NASCET),[6] the most common cause of cerebral artery stenosis is atherosclerosis. Carotid surgery is the standard treatment for severe symptomatic carotid artery stenosis. In ECST and NASCET, the 30 days' stroke and death rates in patients in the surgical group were 7.0% and 6.5%, respectively.[5,6] There have been many reports on the percutaneous interventional treatment of cerebral arteries on the basis of the CAVATAS Trial. Angioplasty is better than surgery because it reduces the risks related to the incision in the neck and general anesthesia. Also, according to CAVATAS, there is no significant difference in the major risks of balloon angioplasty or stenting and carotid surgery (10% frequency of death or any stroke in both groups). According to the SAPPHIRE trial,[4] stenting was not inferior to surgery, and the rate of death and stroke within 30 days was 4.8% in the stenting group and 9.8% in the endarterectomy group. Wholey and colleagues reported that carotid stenting had a complication rate of stroke and death of 5.8% within 30 days of treatment. However, cerebral embolization is currently considered as the major risk associated with carotid artery stenting.[7] Most strokes after carotid angioplasty are the result of plaque fracture in the carotid artery at the time of balloon inflation with subsequent thrombosis and embolism. For this reason, primary stenting seems to be safer than simple balloon angioplasty.[1] Stents will also prevent a free intimal flap from dissection. Improved dilation achieved by stenting than with balloon angioplasty might also reduce the rate of stroke in the short-term after treatment.[1] In addition, distal protection devices reduce intra-procedural embolization during carotid artery stenting.[8] In our study, primary carotid and vertebral stenting with the emboli-protection device was done successfully in all the patients, without any complications. Short-term follow-up showed no residual stenosis or restenosis. In conclusion, cerebral artery stenting can be performed safely and may provide an alternative to endarterectomy, especially in patients

with high surgical risk. Long-term follow-up, however, is required.

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Implications of Atrial Fibrillation after Coronary Artery Bypass Surgery

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Abstract

Background- Postoperative atrial fibrillation (AF) is a common complication of coronary artery bypass graft surgery (CABG) and is associated with an increased incidence of other complications and an increased hospital length of stay. Prevention of AF is a reasonable clinical goal. The aim of this study is to determine the predictive value of multiple clinical, hemodynamic and operative variables for the occurrence of postoperative AF.

Methods- This research is a descriptive study. Patients scheduled for elective CABG between 1997 and 1999 were recruited. The patients underwent holter monitoring for 3 consecutive days. Information was collected by a questionnaire. Statistical analysis was based on the SPSS software and was done through the descriptive statistical method.

Results- 200 patients underwent isolated CABG between 2001 and 2003. The patients with a mean age of 55±8 years old underwent holter monitoring for 3 days. AF occurred in 20% of the patients, postoperatively. 30% of the patients converted to sinus rhythm spontaneously, 60% converted with amiodarone and 10% of the patients required electric shock.

Conclusion- Beta blockers are the first line of medication for the prevention of postoperative AF. The incidence of AF during the first postoperative week after CABG varies between 5-40%; prolonged mechanical ventilation after CABG significantly increases the incidence of postoperative AF ***(Iranian Heart Journal 2005; 6 (1,2): 64-67).***

Key words: atrial fibrillation Ë coronary artery bypass surgery

Cardiac arrhythmias occur in 11-40% of patients after coronary artery bypass graft surgery (CABG), atrial fibrillation (AF) being the most common supraventricular arrhythmia.[1] Postoperative AF has a negative effect in terms of perioperative morbidity (myocardial infarction, stroke), 30 days and 6 months' mortality, stays in the intensive care unit (ICU) and hospital costs.[2] Perioperative intravenous[3] or oral amiodarone[4] has been shown to decrease the occurrence of AF after cardiac surgery. Magnesium prophylaxis for postoperative AF has also been reported, with certificating conclusions.[5]

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The aim of this study, conducted on cardiac patients, was to diagnose those suffering from AF after CABG.

Methods

This is a descriptive study, performed in Shahid Madani Heart Hospital in Tabriz, Iran, between 1997 and 1999 on 200 patients who underwent CABGs.
Data were collected through completing a questionnaire consisting of age, sex, results of angiography and echocardiography, number of grafts, duration of mechanical ventilation and the manner of the conversion of AF to normal sinus rhythm.
The statistical analysis was based on the SPSS software and was carried out through the descriptive statistical method.

Results

This prospective study was performed in Shaheed Madani Heart Hospital between 1997 and 1999 on 200 patients who underwent coronary artery bypass graft surgery.
In this study, 84.5% were male and 15.5% female. Mean age of the patients was 57.4±7.8 years old. AF was identified in 20% of the patients, and it was more frequent in older patients. No difference was observed in the occurrence of AF when the patients were stratified according to sex or angiographic EF (ejection fraction).
Postoperative AF in patients with EF>30% was 24% versus 19.6% in patients with EF<30% (P=0.05). Duration of mechanical ventilation showed the strongest correlation, with 40% postoperative AF versus 16% with less than 20 hours' ventilation (P= 0.00008). There was no difference in the occurrence of post-CABG AF with the increasing numbers of grafts or grafts to the left versus right coronary systems. 30% of the patients converted to normal sinus rhythm spontaneously, 60% with intravenous amiodarone. Only 10% of the patients with hemodynamic instability required electrical cardioversion.

Discussion

The incidence of AF during the first postoperative week after CABG varies between 5 and 40%.[6] In our study, AF occurred in up to 20% of the patients, postoperatively. Previous studies[7-9] reporting increased age as a predictor of postoperative AF in patients who had CABG found AF in 4% of patients less than 40 years of age and in 30% of those who were 70 years old or older.[8] This is in accordance with our study, in which the mean age of the patients who had postoperative AF was greater than that of the patients who did not: 27.6% in patients more than 65

years of age versus 15% in patients less than 65 years (P=0.007). However, all of the above studies include patients with a history of preoperative antiarrhythmic drugs, atrial arrhythmia, diabetes mellitus, chronic obstructive lung disease, chronic renal failure or severely reduced ejection fraction. If we include the disorders that per se could be associated with an increased incidence of AF, age will not be a predictive factor for postoperative AF, a finding that is in accordance with other studies.[10] the pathogenesis of atrial fibrillation after cardiac surgery is multifactorial. Atrial injury or intra- pericardial pneumonectomy decreases the atrial fibrillation threshold for 7-10 days operatively. Other factors such as intraoperative atrial ischemia, postoperative increases in circulating catecholamines, hypoxia and electrolytes also may contribute to increased vulnerability of atria to reentrant tachyarrhythmias.[11] Ormerod and coworkers also concluded that older age was not a risk factor for postoperative arrhythmia.[12] Roffman and Fieldman found that patients with AF were older than patients who maintained sinus rhythm.[13] It has been postulated that abrupt cessation of propranolol after surgery increases the frequency of AF because of possible hypersensitivity to adrenergic stimulation after the withdrawal of medication.[14] Risk of postoperative AF increases in patients with more than 20 hours of mechanical ventilation: 40% vs. 16% (P=0.00008). It has been postulated that obstructive lung disease increases the incidence of postoperative AF.
In a study on 570 consecutive patients undergoing CABG,[15] the overall incidence of AF was 33%. Multivariate logistic regression analysis identified increasing age (more than 70 years), male gender, hypertension, need for intraoperative aortic balloon pump, postoperative pneumonia, ventilation for more than 24 hours and return to the intensive care unit as independent predictors of postoperative AF; congestive heart failure and

preoperative heart rate greater than 100 beats per minute were identified as risk factors. Several other factors have been associated with the development of AF following CABG. These include bypass for right coronary artery disease, the presence of pulmonary disease and sleep apnea.[15,16]

Stephen et al. studied the efficacy of supplemental magnesium in reducing AF after CABG.[17] They found that prophylactic magnesium does not significantly reduce atrial and ventricular arrhythmias.[17] Amit and coworkers evaluated epicardial atrial defibrillation for the treatment of postoperative AF. They found that temporary atrial defibrillation to resynchronize patients in postoperative atrial fibrillation was safe and effective. [18]

Comments

Postoperative AF remains the most common complication after cardiac surgery.[19] Medical management of postoperative AF using antiarrhythmic agents has shown to have some benefits.[20-22] Postoperative AF increases hospital stays, cost and morbidity. It converts to the sinus rhythm spontaneously, by drugs or DC shock.

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The Frequency of Human Leukocyte Class II Antigens in Patients with Rheumatic Heart Disease in an Iranian Population

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Abstract

Background- With respect to the high incidence of rheumatic heart disease (RHD) and the almost identical racial background of the western population of Iran and the importance of investigation on HLA typing as a new research tool, this study was conducted with the aim of better understanding the mechanisms involved.

Methods- The frequencies of class II HLA antigens (DQ, DR) in 35 patients with a diagnosis of RHD were studied and compared with a control group of 36 healthy individuals.

Results- An increase was found in the frequency of HLA-DR53 (57.1% in the patient group versus 16.7% in the control group: P=0.00099, RR=6.66), HLA-DR2 (31.4% in the patient group versus 2.8% in the control group: P=0.0037, RR=16.04) and HLA-DR15 (28.6% versus 2.8%: P=0.007, RR=14). The increased frequency of HLA-DQ2 and HLA-DQ5 in the patients compared with the control group was also significant (P<0.05); however, frequency differences for other antigens was not significant.

Conclusion- HLA-DR53, HLA-DR2 and HLA-DR15 may be markers for susceptibility to RHD in our patients. These results could be explained by genetic differences resulting from racial or geographical diversity ***(Iranian Heart Journal 2005; 6 (1,2): 83-88).***

Key words: RHD ■ HLA Class II antigens ■ Iran

Acute rheumatic fever (ARF) develops in only a relatively small percentage of patients (3%) following even the most virulent bouts of streptococcal pharyngitis, and not all patients with ARF develop rheumatic heart disease (RHD). Therefore, the question of host predisposition is often raised by investigators. [1,2,3]

For more than a century, researchers have tried to determine a genetic pattern of susceptibility to RHD and RF. Cheadle in 1889 assigned an increased susceptibility to RHD or RF.[4] Some researchers have assumed an autosomal recessive model.[5]

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Occurrence of RF or RHD in identical twins suggests that if a Mendelian pattern is present, penetrance must be incomplete.[6] Recent studies have tried to uncover specific markers for RHD or RF susceptibility.

Some studies have analyzed human leukocyte class I antigens, but no consistent association of these antigens with RF has been found.

Subsequent studies of class II antigens have disclosed an association with different HLA-DR alleles according to the population analyzed.[7]

Therefore, considering the high incidence of RHD and the almost identical racial background of the population in western Iran and the importance of research in this field, this study was conducted with the aim of better understanding the mechanisms involved.

Methods

Patients

To determine the frequencies of class II antigens, HLA typing was performed in 35 patients with rheumatic heart disease. In all the cases, the diagnosis was made by a cardiologist and was supported by echocardiography, cardiac catheterization and histological findings (in patients who underwent surgery for heart valve replacement). The patients were from the western regions of Iran and were aged 20-63 years old (mean age, 40.17). There were 32 females and 3 males.

The control group comprised 36 healthy individuals, racially and geographically similar to the patient group, who were 20-57 years old. HLA class II typing was performed in all the patients and controls.

HLA typing

The HLA class II antigens were determined by the microlymphocytotoxicity test using specific DQ and DR anti-sera (Pel-Freez). This test is achieved by the isolation of mononuclear cells from the peripheral blood and purification of the peripheral blood B cells by adherence to nylon wool columns [Teresi method[8]]. Tests were performed on fresh blood samples in all the cases.

Statistical analysis

The frequencies of HLA class II antigens were compared using Yates`s correction X^2 test and Fischer Exact test when the number of the individuals with a specified antigen was less than five. Probability values and relative risk (RR) were calculated.

Results

Detailed results are presented in Table I.

Table I. Frequency of HLA-DQ and HLA-DR antigens in patients and controls

YC=Yates' correction
FE= Fisher Exact test
RR=Relative risk
NS= Not significant

HLA	Patients (n=35) (%)	Controls (n=36) (%)	P value (YC)	P value (FE)	RR
DQ1	11.4	55.5	NS	-	…
DQ2	57.1	25.0	0.0119	-	4
DQ3	42.58	22.2	NS	-	…
DQ4	2.85	2.77	-	NS	…
DQ5	22.8	5.55	-	0.038	5.03
DQ7	11.4	13.8	-	NS	…
DR1	0.0	5.55	-	NS	…
DR2	31.4	2.77	0.0037	-	16.04
DR3	2.85	13.88	-	NS	…
DR4	14.28	8.3	-	NS	…
DR5	11.4	8.3	-	NS	…
DR6	14.2	5.5	-	NS	…
DR7	37.1	19.4	NS	-	…
DR8	8.57	13.88	-	NS	…
DR9	0.0	8.2	-	NS	…
DR10	5.7	2.8	-	NS	…
DR11	8.5	8.35	-	NS	…
DR12	8.6	8.3	-	NS	…
DR13	5.8	8.2	-	NS	…
DR15	28.57	2.77	0.007	-	14
DR52	57.1	47.2	NS	-	…
DR53	57.1	16.66	0.00099	-	6.66

The class II HLA antigens were typed in 35 patients with RHD and compared with a control group of 36 healthy individuals. HLA-DR53 was positive in 20 patients (57.1%) compared with 16.7% in the control group (P=0.00099, RR= 6.66). The frequencies of HLA-DR2 (31.4% in patients versus 2.8% in the control group: P=0.0037, RR=16.04) and HLA-DR15 (28.6% in patients versus 2.8% in the control group: P=0.007, RR= 14) were found to have increased. Also, HLA-DQ2 and HLA-DQ5 frequencies were found to be higher (P<0.05) in the patients compared with the control group, but as for the other antigens, the frequency difference was not significant.

Discussion

Although an abnormal response following streptococcal infection has been mentioned to be a potential cause of RF and RHD, the exact mechanism has not yet been clarified. HLA antigens interfere in the presentation of the rheumatogenic determinants of beta-hemolytic streptococci to T lymphocytes, and certain HLA alleles increase the responsiveness to beta-hemolytic streptococci and the immune response against streptococci causes tissue damage, especially in the heart, due to cross-reaction of streptococcal antigens with heart valve antigens. Therefore, investigators have attempted to establish an association between HLA antigens and RF/RHD. Other immunological factors of RF and RHD are under investigation.[3,9]

HLA class II typing, first performed in the 1980s, has led to conflicting results. Jhinghan studied an Indian population and described a positive association between RF with HLA-DR3 and HLA-AW33 and a negative association with HLA-DR2 (in contrast to our results).[7] Anastasiou Nana described a higher frequency of HLA-DR4 and a lower frequency of HLA-DRW6 in Caucasian patients with RHD. Monplaisir showed a significant decreased in HLA-BW14 and BW42 frequencies and an increase in HLA-B35 and HLA-DR1 frequencies.[3] Ayoub et al. disclosed an association of RF with HLA-DR2 in black patients, and with HLA-DR4 and HLA-DRW9 in Caucasian patients.[10] Rajapakse defined HLA-DR4 as a genetic marker of RHD in the Saudi Arabian population.[11] In Ozkan's study, an increased frequency of DR3, DR7 and B16 phenotypes and a decreased frequency in DR5 was reported.[12]

Afana suggested an increased frequency of HLA-B17, HLA-B21 and HLA-CW4 phenotypes in patients with rheumatic myocardium.[13] Reddy found an increased frequency of DR3 phenotype and decreased frequency of DR2 in RHD patients.[14] Guilherme et al. found that HLA-DR7 and HLA-DR53 were markers for susceptibility to RF and RHD in Brazil.[9]

Gu et al., having studied the genetic susceptibility of HLA-DQA1 alleles to RF or RHD in Chinese Hans by PCR-PAGE and then silver dyeing, suggested that DQA1*0101 contributes to genetic susceptibility for RF and RHD in Guangdong Hans.[15] Guedez et al. studied class II allele/haplotype distribution in patients with RHD and found significant increases in DRB1*0701 and DQA1*0201 alleles and DRB1* 0701-DQA1 *0201 haplotypes.[16] Maharaj et al. performed HLA-A , HLA- B HLA-DR and HLA-DQ surveys in Indian patients with severe chronic rheumatic heart disease requiring cardiac surgery and found that there was no significant difference in HLA-A, HLA-B, HLA-DR and HLA-DQ frequencies between patients and controls.[17]

Koyanagi et al. performed DNA typing of HLA class II genes (DRB1, DQA1, DQB1 and DPB1) in patients with RHD and suggested that the susceptibility to mitral stenosis is in part controlled by a gene (or genes) in close linkage disequilibrium with HLA-DQA1*0104 and DQB1*05031.[18] Carlquist et al. examined HLA-DR frequencies in rheumatic heart disease by a meta-analysis study that showed a significant negative association with DR4 in all studies, increased DR1 and DR6 in black patients, increased DR3 in Eastern Indian patients, decreased DR2 (in contrast to our results) and DR5 and increased DR4 in American whites.[19] Bhat et al. studied the distribution of HLA class I (A,B,C) and class II (DR and DQ) antigens in patients with rheumatic heart disease in Kashmir. They found that susceptibility to RHD in

the studied population was HLA- related, with HLA-DR4 influencing its occurrence and HLA-B5 conferring protection against disease.[20] Guedez et al. reported a significant increase in DRB1*0701 and DQA1*0201 alleles and DRB1*0701-DQA1*0201 haplotypes in patients with RHD and decreased frequency of DQA1*0103 allele and absence of DQB1*0603 allele and concluded that certain class II alleles/ haplotypes were associated with risk for or protection from RHD.[21]

Guilherme et al. in their study reported that T cells sensitized in the periphery by M5 protein during streptoccocal infection, in particular the M5 (81-96) peptide in HLA DR7 and DR53-positive RHD patients, migrated to the heart and initiated heart tissue damage after activation due to cross- reactive recognition of the relevant heart antigen.[22]

The present work is the first study on the population of the west of Iran in order to determine HLA phenotype frequencies in patients with RHD. In this research, the frequencies of HLA-DR53, HLA-DR52 and HLA-DR15 were found to have significantly increased in the patients with RHD compared with the control group. The frequency of HLA-DR53 was especially higher, and this finding is similar to Guilherme's report.[9] HLA-DR9, which is included in the HLA-DR53 group, was absent in the patient group. Frequencies of HLA-DR4 and HLA-DR7 (other antigens in the HLA-DR53 group) were not statistically significantly different. The high frequency of HLA-DR2 and statistical significance of this is in concordance with Ayoub's results[10] and in contrast with Reddy's results[14].

The frequencies of HLA-DQ2 and HLA-DQ5 in the present study were also high and notable ($P<0.05$), but the increased frequency of HLA-DR4 which has been found in other populations[9,23] was not high in the present study. HLA-DR1 and HLA-DR9 were absent in our patients.

Based on these results, HLA-DR53, HLA-DR2 and HLA-DR15 antigens or a gene out of the MHC complex, which has preferential motivation with this, may be involved in an abnormal immune response against streptococcal antigens, causing valvular damage and rheumatic heart disease. The difference between our results and those in other reports is probably related to geographical or racial differences in populations and different patterns of reactivity to allo-antisera.

Consequently, we can conclude that HLA-DR53, HLA-DR2 and HLA-DR15 may be markers for susceptibility to RHD, but other genetic factors might have roles in determining this susceptibility. Indeed multiple genetic factors may be interacting to define this susceptibility.

On the other hand, we cannot underestimate the role of non-genetic factors, such as social and economic factors in the analysis of RHD and RF, as well as different streptococcal strains that may elicit different patterns of immune response.

Conclusion

According to the present study and other reports, genetic difference resulting from racial and geographical variations must have a role in susceptibility to RHD, but major influence must be in the form of a "susceptibility gene" situated in or near the HLA-DR locus.

Further studies and evaluation of all the important limbs of the immune system, cellular and humoral immune parameters, as well as immunogenetic profiles may provide convincing evidence in the pathogenesis of rheumatic heart disease and rheumatic fever.

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Prevalence of Atheromatous Aortic Plaques in Patients with Ischemic Stroke Using Transesophageal Echocardiography

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Abstract

Background- Nowadays, the pathogenic role of atherosclerosis of the aorta in embolic stroke is well understood. TEE continues to play a prominent role in the evaluation of patients with stroke and finding the source of emboli. TEE shows that the incidence of strokes presumed to have a cardioembolic origin varies from 13-40% and that atherosclerotic

disease of the aortic arch has been found in 40-60% of cerebral emboli. We investigated the prevalence and severity of atherosclerotic aortic plaques in patients with embolic stroke to ascertain their role as a risk factor for ischemic cerebral events.

Methods- Using TEE, we performed a cross-sectional study of the frequency and severity of aortic plaques in 60 patients admitted with ischemic stroke. Major atherosclerotic risk factors and the presence of coronary artery disease and carotid plaques were also surveyed.

Results- TEE detected at least one potential source of embolism in 48 patients, aortic plaques in 29, carotid plaques in 11 and cardiac pathologies in 19. Atrial fibrillation and valvular heart diseases (mostly mitral stenosis) were the most prevalent cardiac anomalies. The remaining 12 patients were regarded as cryptogenic cases. Fifty patients had at least one major risk factor of CAD. The majority of the plaques were detected in the arch and ascending aorta; of these 13.7% were complicated (grade III). There was a significant relation between aortic plaques and hypertension, male sex and CAD. Aortic calcification in CXR was strongly predictive of aortic plaques but not a sensitive criterion.

Conclusion- Abnormalities are commonly found by TEE in patients with stroke. The results indicate a strong, independent association between atherosclerosis of the aorta and risk of stroke. TEE should be considered in patients after stroke as a routine test and ultimately for prophylaxis and treatment of stroke ***(Iranian Heart Journal 2005; 6 (1,2): 72-77).***

Key words: transesophageal echocardiography (TEE) Ë atheromatous aortic plaque Ë ischemic stroke.

Stroke is the third cause of mortality in the world.[1] Investigations as to the underlying cause of ischemic stroke reveal cardioembolic causes in 13-40% but fail to define any cause in about 30% of cases.[2] Until recently, atherosclerosis of the aorta was not regarded as a potential source of emboli.[3]

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have shown atherosclerotic aortic plaques in 40% of cases.[4]

The advent of transesophageal echocardiography (TEE) has made it possible to detect aortic plaques and reveal their morphologic characteristics with the risk of stroke and other vascular events.[5]

In particular, atherosclerotic disease of the aorta may simply be a marker for general atherosclerotic disease, as coronary artery disease (CAD) or carotid plaques.[6]

The aim of our study was to determine with TEE the frequency of plaques in the aorta in patients admitted with brain infarction.

Methods

This was an observational, analytic study with a cross-sectional design. Sixty-five patients with ischemic stroke who were hospitalized in the neurology ward between 2003 and 2004 were enrolled in the study. f e e

the presence of abrupt neurological deficit accompanied by territorial infarction pattern visualized by either brain CT scan or MRI. A complete patient history and atherosclerotic risk factors were recorded. In addition, a careful physical examination of each patient was performed on admission. Routine hematologic and biochemical tests, urine analysis, chest X-ray and 12-lead ECG were obtained. Each patient underwent an examination of carotid arteries by a radiologist using duplex sonography. Written consent forms were taken from all the patients. Within two weeks of the onset of acute symptoms, TEE was performed for all

the patients after local oral and pharyngeal anesthesia with 2% lidocaine spray, using a 5MHz multiplanar probe on a Ving Med device. All the images were recorded on videotapes for further evaluation. Whenever necessary, the patient was sedated with 1-3 mg IV midazolam. Agitated saline was injected to all the patients to evaluate any intracardiac shunts. TEE examination included visualization and evaluation of valves, chambers and aorta. Intraaortic plaques were described with regard to their location as ascending, arch and descending, and also to their severity as follows: Grade I = mild irregularity and intimal thickening, Grade II = moderate irregularity and intimal thickening <5 mm and Grade III = severe irregularity and intimal thickening >5 mm, and mobile, protruding, ulcerated or calcified plaques.

Statistical Analysis

Quantitative variables were shown as mean ± SD. T-test was used for their comparison. To compare qualitative variables, we used Chi-square for 2×2 tables and ANOVA (F-test) for more complex tables. Primary significant differences were further assessed by the Post Hoc (Tukey method) test. All the calculations were performed by SPSS 10.0 package. Statistical significance was set at $p< 0.05$.

Results

We examined sixty patients (35 males, 25 females) 27-75 years of age (mean age 55.7±8.8). Fifty patients (83%) had at least one of the major risk factors for atherosclerosis; of these 23 (38%) had history of hypertension (HTN) irrespective of their treatment status, 17 (28%) had hyperlipidemia, 14 (23%) were diabetic, 24 (40%) had history of previous or recent cigarette smoking and 7 (13%) had history of CAD in their first-degree relatives (See Table I).

Table I. Demographic and paraclinical variables in the study population.

No. of patients	60
Age (yr , mean ± SD)	55.7 ± 8.81
Range of age (yr)	27 - 75
Sex (male/female)	35/25 (58% / 42%)
Hx. of CVA / TIA	4 (6.7%)
Hx. of IHD	11 (18.3%)
Atherosclerosis risk factors	50 (83%)
Hypertension	23 (38.3%)
Hyperlipidemia	17 (28.3%)
Diabetes Mellitus	14 (23.3%)
Cigarette Smoking	24 (40%)
Family History	8 (13.3%)
Cardiac findings by TEE	19 (31.6%)
Aortic calcification in CXR	10 (16.6%)
Aortic plaque by TEE	29 (48.3%)
Carotid plaque by Duplex sono	11 (18.3%)
Lab data (mean ± SD)	
FBS	111.5 ± 26.7
BUN	27.2 ± 7.1
Cr	1.03 ± 0.2
TG	210.3 ± 77.4
T.Chol	198.9 ± 57.2
HDL	58.5 ± 9.1
LDL	116.6 ± 52.4

In 10 patients (16%), there was calcification of parts of the aorta in chest X-ray; 9 of them also had aortic plaques in TEE (Pearson chi-square = 0.003). As to the cause of stroke, we found cardiac sources in 31.6%, carotid disease in 18.3% and aortic plaques in 48.3%. Even with the above-mentioned investigations, no cause could be found in 12 patients (20%). Of all the cardiac sources, 9 patients were in atrial fibrillation rhythm, 10 had valvular heart disease (all of them mitral stenosis), 3 had left atrial appendage clot, one had left ventricular clot (in a patient with extensive anterior myocardial infarction), Spontaneous echo contrast (smoke) was observed in six cases with mitral stenosis and also in the patient with extensive anterior myocardial infarction. Severity, frequency and location of the carotid artery disease are shown in Fig.1.

Fig.1. Frequency and severity of carotid plaques.

Carotid plaques were detected in both left and right carotids simultaneously in three patients. Aortic plaques were detected in 29 (48.4%) patients (Fig.2

Fig. 2. Severity and location of aortic plaques.

As it is seen, simultaneous disease in both the arch and descending portion of the aorta is more frequent than other segments, so the frequency of plaques in the descending aorta, either alone or with other areas, is as high as 86%. The severity of aortic plaques was G I = 52%, G II = 34% and G III = 14%. Age distribution of aortic and carotid plaques is shown in Figs.3 and 4.

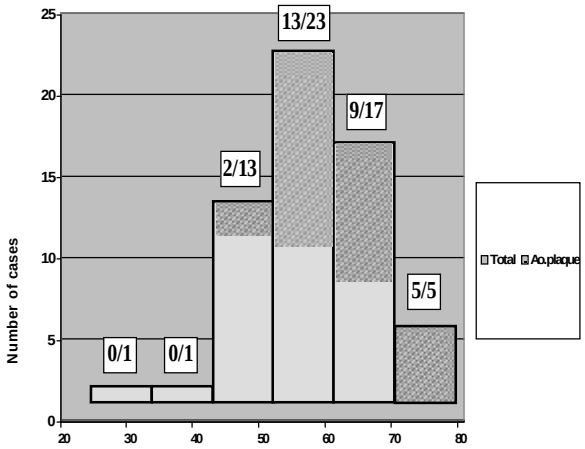

Fig. 3. Age distribution of aortic plaques.

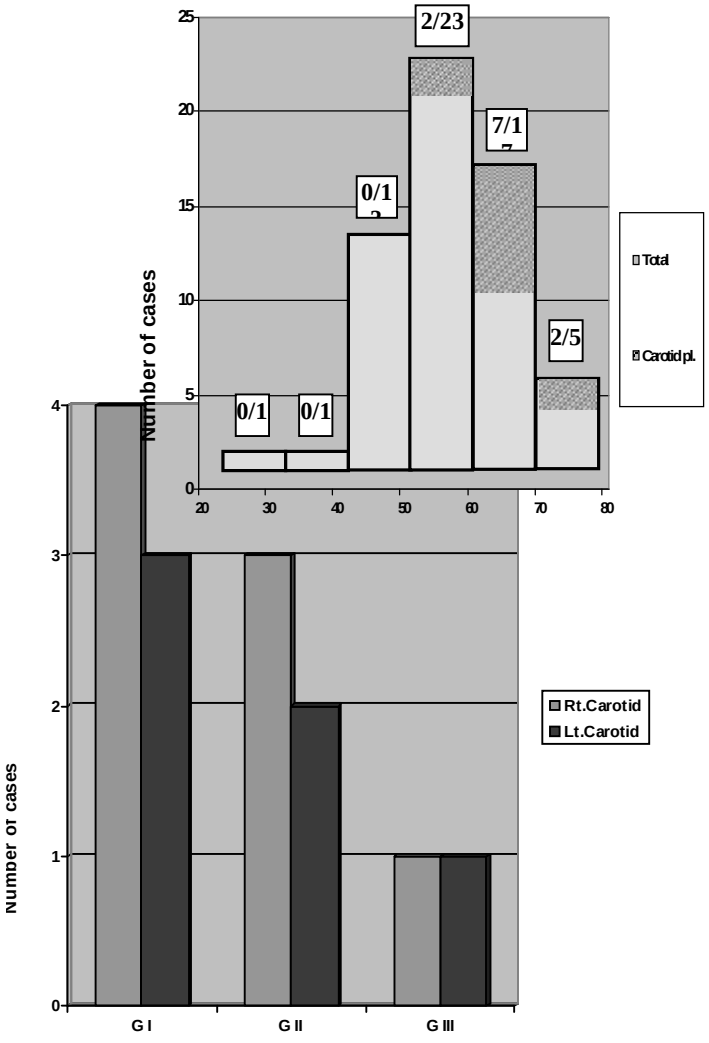

Fig. 4. Age distribution of carotid plaques

Aortic plaque prevalence was significantly different between the males and females (21% vs. 8%, respectively, p =0.03). A significant association between the major atherosclerotic risk factors and aortic plaques was found only for HTN (p = 0.002). Ten of the 11 patients with history of CAD also had aortic plaques (p =0.003), but the association was not significant between carotid and aortic plaques.

Discussion

Atherosclerotic disease is inherent in the aging process. In view of the high medical

and economic burden of stroke, it is prudent to search for its causes to plan for appropriate treatment and prophylaxis. TEE is a non-invasive procedure that poses little or no risk to the patient, and its accessibility, ease of use and low cost has made it a useful investigative tool to evaluate cardiovascular sources of embolism. It has the potential to detect the lesions in the aorta more accurately than plain radiography,[7] computed tomography,[7] angiography[7,8] and, of course, TTE.[9] Plaques located proximal to the ostium of the left subclavian artery have been found in 60% of patients 60 years of age or older with ischemic stroke.[10] In our study, most of the lesions were found in the descending and arch of the aorta, whereas the ascending aorta appeared to be the least prevalent site of atherosclerosis involvement. This finding is consistent with previous necropsy and echocardiographic studies.[11,12] It has been proposed that the lack of vasa vasorum in the descending aorta makes this segment vulnerable to the atherosclerotic process, and this could be a probable cause for this difference in the distribution of plaques.[13] Several studies have shown that aortic plaques are highly associated with the presence of CAD, with acceptable positive and negative predictive values.[14,15,16] The present study also showed a high association between the history of CAD and the presence of aortic plaques in patients with stroke. Consequently, it is reasonable to routinely perform TEE at least in patients with a history of CAD. Amarenco et al. showed the significance of plaque morphology in risk stratification for overall vascular events, especially ischemic stroke, and their mortality. Several morphologic characteristics of plaques have been proposed to be as associated with increased risk of stroke. The most increased relative risk is attributed to the plaques with a thickness of more than 4 mm, although ulceration, lack of calcification and the presence of hypoechoic pattern in plaques are also markers of increased risk.[17] The term "vulnerable" refers to these high risk, unstable plaques, which are most prone to rupture and thrombosis. In all the previous studies with TEE for the evaluation of stroke patients, echo was performed only in those who exhibited no evidence of carotid atherosclerotic disease,[18] although it is possible to find atherosclerotic plaques both in the aorta and the carotid arteries. Thus in our study, we did not exclude those with carotid plaques in order to be able to find such co-morbidities. A negative TEE examination does not rule out the possibility of cardiogenic embolism, and even if a definite abnormality such as thrombosis or vegetation can be identified, this does not prove that the abnormality is the actual source of the embolism.[8] According to the present knowledge, there is no general agreement for continuing the evaluation by TEE if another reasonable source of stroke has been detected. Although finding such aortic plaques in these patients may not change the therapeutic management, these plaques are highly valuable for determining the prognosis and recurrence rate of stroke and other vascular events, e.g. renal and peripheral emboli. In other words, it is unwise to accept a patent foramen ovale, atrial septal aneurysm or even a low risk carotid plaque in an old age stroke patient with a history of CAD. Our study showed the association of aortic plaques and major risk factors only for HTN, but it is acceptable to find this association also for other risk factors by choosing a larger sample volume and a more precise study design. Meanwhile, it is evident that diagnosis and prompt modification of these risk factors can be highly effective in reducing the incidence and mortality of any vascular events- as it has been so in recent years- generally speaking, better primary and secondary

prevention. The aorta is recognized as the first and most severe site for atherosclerosis, with lesions occurring there long before one is able to detect atherosclerotic plaques in coronary or carotid arteries.[14] With respect to the senile process of atherosclerosis, it is logical to find plaques more prevalently in older ages. The peak prevalence for aortic and carotid lesions is in the 6^{th} and 7^{th} decades, respectively. This can be explained by the earlier beginning of atherosclerotic processes in the aorta than in the carotid artery. The frequency of aortic plaques in the 8^{th} decade (100%) is significantly more common than carotid (40%) plaques. It can be associated to a bias in patient groups because of more frequent mortality in patients with carotid lesions compared to aortic ones.

Conclusion

Atherosclerotic disease of the aorta has recently been considered as a source of emboli. It is highly prevalent in stroke patients, so the evaluation of the aorta by TEE could be included in the work up of all these patients. A further aspect of our research relates to the therapeutic consequences of aortic plaques; therefore, it is advisable to conduct prospective cohort studies to ascertain the natural course of these plaques and plan appropriate therapeutic modalities.

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Comparison of the Hemodynamic Effects of Human and Sheep Atrial Extracts in Anesthetized Rats

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Abstract

Background- Atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) belong to a family of hormones that have structural similarities and some biological actions in common, such as natriuresis and vasodilatation. Previous studies have revealed the presence of ANP and BNP in the sheep atrial extract and ANP in the human atrium. The aim of the present study was to compare the hemodynamic effects of the two atrial extracts on blood pressure and hematocrit in anesthetized rats.

Methods- Human and sheep atrial extracts were prepared using saline and acid milieu method. The femoral arteries and jugular veins were cannulated for recording blood pressure and drug administration, respectively. To measure the hematocrit, we collected blood samples from the rats' eyes at the beginning and once again after 45 minutes of extract administration.

Result- The rats' mean arterial blood pressure (MAP) was reduced by the sheep atrial extract ($p<0.05$), whereas the human atrial extract did not have any significant effect on MAP. The hypotensive effect of the sheep atrial extract was higher than that of the human extract ($p<0.05$). Both extracts increased the rats' hematocrit significantly ($P<0.05$).

Discussion- The obtained results suggest that the difference between the hemodynamic effects of the two extracts could be due to the differences between the ANP and BNP clearance, cardiac output fall and the negative feedback inhibition ***(Iranian Heart Journal 2005; 6 (1,2): 78-82).***

Key words: ANP ■ BNP■ human ■ sheep ■ atrial extract ■ mean blood pressure ■ hematocrit

It has been known for a long time that the atria play an important role in the regulation of volume balance. Natriuretic peptides have been found to exist in mammalian atrial extracts. The natriuretic peptides play important roles in cardiovascular homeostasis. Three isoforms, i.e. atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP) and C-type natriuretic peptide (CNP) constitute the natriuretic peptide family.[1] In humans, ANP and BNP are mainly produced in cardiac atria and ventricles, respectively.

CNP is most strongly expressed in the brain but also is produced in vascular endothelial cells.[2,3,4] The combined actions of natriuretic peptides on vasculature, kidney, and adrenal glands serve both acutely and chronically to reduce systemic blood pressure as well as intravascular volume. The reduction in blood pressure is the consequence of reduced peripheral vascular resistance (mediated in part by direct relaxation of vascular smooth

muscle), diminished cardiac output and decreased intravascular volume.

In the kidneys, natriuretic peptide acts on specific receptors in renal microvasculature and tubule epithelium to induce hyperfiltration, the inhibition of sodium transport and the suppression of renin release, all of which are effects responsible for natriuresis and

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Spontaneous Coronary Artery Dissection in a Young Male: A Case Report and Review of the Literature

Rezayat Parvizi, MD; Bahram Sohrabi, MD; Hadi Hakim, MD; Naser Aslanabadi, MD and Jahanbakhsh Samadikhah, MD

Abstract

Spontaneous coronary dissection (SCDis) is a rare entity which has been increasingly reported over the last two decades. About 150 cases were described from 1931 to 2000, of which fewer than 50 cases were in male patients without any evidence of coronary atherosclerosis.
We describe a case of SCDis in a 32-year-old man who presented with low-threshold angina and without evidence of coronary atherosclerosis ***(Iranian Heart Journal 2005; 6 (1,2): 89-92).***

Key words: coronary artery ■ dissection ■myocardial infarction■ atherosclerosis

Spontaneous coronary dissection is a rarely identified entity whose exact incidence, etiology, pathogenesis and optimal treatment have not yet been firmly established. The clinical presentation often involves sudden onset of acute ischemia or infarction, which mimics that seen in traditional coronary atherosclerotic disease. Sudden cardiac death is unfortunately a common presentation of spontaneous coronary dissection, occurring in up to 70% of patients.

Case report

We describe a case of SCDis in a 32-year- old man who presented with low-threshold angina from one month before. He had a history of anteroseptal MI 4 months previously in another center without receiving thrombolytic therapy. Past medical history was negative for chest trauma, intense physical exercise and cocaine abuse. Physical examination was unremarkable except for mild obesity and an audible S4 in the apex. ECG showed poor R progression from V1-V4 without significant ST changes in other leads.

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Echo study showed hypokinetic septum and apex without visible clot and left ventricular ejection fraction (LVEF) of about 45%. Coronary angiography showed a 20-25mm long coronary dissection in the proximal portion of the left anterior descending artery (LAD) extending to mid-portion. An intimal plaque with about 90% obstruction was demonstrated (Fig. 1).

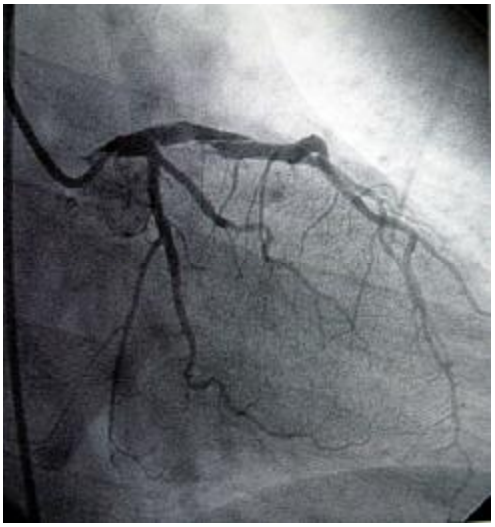

Fig 1. Spontaneous coronary artery dissection in the proximal portion of the LAD in RAO caudal view.