

Relationship between Electrocardiogram with Diabetes Mellitus and Metabolic Syndrome in Japanese-Brazilians

Luigi Brollo¹, Maria Teresa Nogueira Bombig¹, Cleber do Lago Mazzaro¹, Yoná Afonso Francisco¹, Francisco Antonio Helffenstein Fonseca¹, Antonio Carlos Camargo Carvalho¹, Helena Harima^{2,3}, Amélia Hirai^{2,3}, Rui Povoá¹

Departamento de Medicina, Disciplina de Cardiologia, Unifesp-EPM¹; Departamento de Medicina Preventiva - Unifesp-EPM²; Japanese-Brazilian Diabetes Study Group (JBDSG)³, São Paulo, SP - Brasil

Summary

Background: When the Japanese immigrated to the Americas, they were subjected to Westernization, with a great change in lifestyle, specially in dietary habits, and this may explain the increase in the incidence of diabetes mellitus (DM), metabolic syndrome (MS) and cardiovascular disease among them.

Objective: To study the presence of myocardial necrosis and left ventricular hypertrophy (LVH) in a population of Japanese-Brazilians, using the ECG and its relationship with DM and MS.

Methods: This was a cross-sectional study which evaluated 1,042 Japanese-Brazilians aged 30 or over, 202 of them born in Japan (Issei) and 840 of them born in Brazil (Nissei), from the second phase of the Japanese-Brazilian Diabetes Study Group initiated in 2000. MS was defined according to the NCEP-ATP III criteria modified for the Japanese. DM and MS were associated with the presence of myocardial necrosis (according to the Minnesota criteria) and LVH (according the Perugia score on the ECG). The statistic chi square method was used to reject the null hypothesis.

Results: Of the 1,042 participants, 35.3% had DM (38.6% of the Issei and 34.5% of the Nissei); 51.8% had MS (59.4% of the Issei and 50.0% of the Nissei). The presence of an inactive zone in the diabetic Issei group was not statistically significant when compared to the non-diabetic group, but among the diabetic Nissei group an inactive zone was present in 7.5% of them. There was a statistically significant correlation between MS and LVH in the Issei and Nissei groups.

Conclusion: Metabolic disorders presented a high prevalence in Japanese-Brazilians with significant correlations with necrosis and hypertrophy on the ECG. (Arq Bras Cardiol 2009;92(5):351-355)

Key words: Asia Brazilians; metabolic syndrome; diabetes mellitus; myocardial hypertrophy, left ventricular.

Introduction

There have been continuous population emigrations throughout history, with varying impacts on the interaction between these groups and their new societies. In the first half of the twentieth century, a significant number of Japanese landed in Brazil, and today they are the largest Japanese community outside of Japan (around 1 million and 300 thousand people), with 65% of them living in the State of São Paulo¹.

The Japanese immigration to the Americas (United States and Brazil) brought about major changes in the dietary habits and life style of this group, resulting in a higher intake of protein, fats and non-complex carbohydrates²⁻⁴, reduced physical activity and elevated levels of stress. This process was called "Westernization"⁵⁻¹⁰.

The consequences of that "Westernization" were increases in the incidence of type 2 diabetes mellitus (DM 2), above

the rates found in Japan and even in Brazil¹¹⁻¹³, the resistance to insulin with a resulting increase of insulinemia^{9,10} and the incidence of metabolic syndrome (SM).

Takeuchi et al¹⁴, using the NCEP-ATP III¹⁵⁻¹⁷ criteria modified for the Japanese (normal waist circumference < 90 cm for women and 85 cm for men), found a 25.3% incidence of MS in male Japanese residents of Hokkaido, Japan. Rosebaum et al¹⁸ using the NCEP criteria for Asians (90 cm and 85 cm for men and women, respectively), found a 56.8% incidence of MS (three times higher than the incidence found in the U.S. population)^{19,20} and an increase in abdominal obesity in Japanese-Brazilians of the first (Issei) and second (Nissei) generations living in the city of Bauru, São Paulo. Gimeno et al²¹ found a high incidence of cardiovascular mortality in patients with diabetes and glucose intolerance in the same population.

Epidemiological studies using the electrocardiogram (ECG), as the GUSTO IV²², showed the importance of left ventricular hypertrophy (LVH) as a predictor of acute coronary syndrome. The Rifle Pooling Project²³ and the NIPPON DATA80²⁴ studies emphasized the importance of abnormal q-waves of myocardial necrosis as markers of risk for cardiovascular disease, particularly of ischemic diseases.

Our goal was to assess the prevalence of metabolic

Mailing address: Luigi Brollo •

Departamento de Medicina – Disciplina de Cardiologia Unifesp-Escola Paulista de Medicina. Rua Julio Verne 266, 04725-060, São Paulo, SP – Brasil
E-mail: lbrollo@uol.com.br

Manuscript received June 11, 2008; revised manuscript received July 23, 2008; accepted August 4, 2008

disorders, such as diabetes mellitus and metabolic syndrome, in two generations of Japanese-Brazilians, and their relationship to LVH and myocardial necrosis, using a practical and inexpensive tool, such as the ECG.

Methods

Patients

This study was approved by the ethics committee of the Unifesp, with the written consent of the participants, and it included patients of the second phase of the Japanese-Brazilian Diabetes Study Group, initiated in 1993 to evaluate the prevalence of DM in a non-mixed population of Japanese-Brazilians living in the city of Bauru²⁵. In the year 2000, 1,042 Japanese-Brazilians were recruited: 202 Issei (first generation, born in Japan) and 840 Nissei (second generation, born in Brazil), aged over 30 years.

We considered diabetics those with fasting plasma glucose > 126 mg/dl or plasma glucose \geq 200 mg/dl, two hours after an overload of 75 grams of glucose (KGMM WHO CONSULATION-1998).

The metabolic syndrome was defined by the NCEP-ATP III criteria modified for the Japanese (abdominal circumference \geq 90 cm for women and \geq 85 cm for men)¹⁷.

The weight was measured with the patients wearing light clothes and without shoes; the waist circumference was measured at the level of the navel, and the BMI was calculated by dividing weight by height.

We made three blood pressure (BP) measurements and took into account the average of the last two, using an automatic device, OMRON HEM-712c.

The 12-Lead ECG was carried out using a ESAOTE BIOMEDICA P80 electrocardiograph.

The myocardial necrosis ("QS") on the ECG was defined by the Minnesota²⁶ criterion for LVH and the Perugia²⁷ index.

Total cholesterol and triglycerides levels in the blood fractions were obtained through automatic analysis, and the blood glucose was obtained with the use of a glucosidase colorimetric assay kit.

Statistical analysis

The subgroups of patients with diabetes and metabolic syndrome in each generation were associated with the ECG results, taking into account the presence of electrically inactive areas and LVH, and they were compared and analyzed by the chi-square statistical method. We chose $p < 0.05$ as the level of significance to reject the null hypothesis.

Results

The sample consisted of 1042 patients: 481 (46.1%) males and 561 (53.9%) females, average age 57.0 ± 12.5 years; among the Issei the average age was 69.7 ± 9.0 years; and among the Nissei, the average age was 54.0 ± 11.1 years. Other population characteristics are described in Table 1.

368 were considered diabetic subjects (35.3%), 38.6% of

them Issei and 34.5% of them Nissei. Twenty-nine (7.8%) of the diabetics had "qs" waves of necrosis on the ECG, while only 25 (3.7%) of the non-diabetic patients had those waves ($p = 0.003$). Among the diabetic Issei, necrosis was present in 12.8%, and among the non-diabetics, in 7.2% ($p = 0.66$). In Nissei diabetics and non-diabetics, the presence of necrosis was 7.5% and 2.18% respectively ($p = 0.0018$).

In the total population of Japanese-Brazilians, LVH was present in 13.0% of the diabetics, and in 9.2% of the non-diabetics ($p = 0.04$). Among the Issei, 12 (15.3%) diabetic patients and 13 (10.4%) non-diabetic patients had LVH ($p = 0.30$), while among the Nissei, LVH was found in 37 (12.7%) of the diabetics and 48 (8.7%) of the non-diabetics ($p = 0.06$) (Table 2).

The MS was present in 540 (51.8%) participants, 59.4% of them Issei, and 50% of them Nissei. Of these 540 participants, 5.7% had "qs" waves of necrosis on the ECG, while among those without the MS necrosis occurred in 4.6% of participants ($p = 0.16$). Among the Issei with "qs" waves on the ECG, 9.1% had MS and 6.1% did not have MS ($p = 0.40$). In the 420 Nissei patients with MS, necrosis was present in 5.0% of them, and in those without MS, necrosis occurred in 4.0% of them ($p = 0.49$).

Of the 540 patients with MS, 13.3% had LVH on the ECG, while among those without MS, LVH occurred in only 7.6% of them ($p = 0.0001$). 13.3% of the Issei patients with MS had LVH, compared to 10.9% of those without MS ($p = 0.58$). Among the Nissei with MS, 13.3% had LVH, compared to 6.9% of those without MS ($p = 0.0018$) (tab.3).

Discussion

Studies that can identify cardiovascular risk factors in special populations to determine the need of an intervention are very important. However, the use of certain diagnostic methods in large populations may be costly or impractical; therefore the search for practical and inexpensive tools that can aid in this identification becomes necessary. The electrocardiogram is one of those tools. It is one of the most practical and inexpensive tools that can be used in the risk stratification of

Table 1 – Demographic, clinical and electrocardiographic characteristics of the 1,042 Japanese-Brazilians

Demographic Characteristics	Issei (n=202)	Nissei (n=840)	p
Age (years) average \pm SD	69.7 \pm 9.0	54.0 \pm 11.1	0.001
Gender n%			
Male	104 (51.3)	373 (44.4)	0.086
Female	98 (48.7)	467 (55.6)	
Diabetes n%	78 (38.6)	290 (34.5)	0.312
Metabolic syndrome n%	120 (59.4)	420 (50.0)	0.020
Myocardial necrosis on ECG n%	16 (7.9)	38 (4.5)	0.078
LVH (Perugia score) n%	25 (12.3)	85 (10.1)	0.359

Issei - first generation Japanese (born in Japan). Nissei - second generation Japanese-Brazilians (born in Brazil). LVH: myocardial hypertrophy. $p < 0.05$.

Table 2 – Relationship between diabetes mellitus (DM) and the presence of myocardial necrosis and LVH on the ECG

ECG	Total (n=1,042)			Issei (n=202)			Nissei (n=840)		
	DM+	DM–	p	DM+	DM–	p	DM+	DM–	p
n%	368 (35.3)	674 (64.7)		78 (38.6)	124 (61.4)		290 (34.5)	550 (65.5)	
Necrosis n%	29 (7.8)	25 (3.7)	0.003*	7 (12.8)	9 (7.2)	0.66	22 (7.5)	16 (2.18)	0.0018*
HVE n%	48 (13.0)	62 (9.2)	0.04*	12 (15.3)	13 (10.4)	0.30	37 (12.7)	48 (8.7)	0.06

Issei - first generation Japanese (born in Japan). Nissei - second generation Japanese-Brazilians (born in Brazil). DM+: presence of diabetes mellitus. DM–: absence of diabetes mellitus. p<0.05.

Table 3 – Relationship between metabolic syndrome (MS) with the presence of myocardial necrosis and LVH on the ECG

ECG	Total (n=1,042)			Issei (n=202)			Nissei (n=840)		
	MS+	MS–	p	MS+	MS–	p	MS+	MS–	p
n%	540 (51.8)	502 (48.2)		120 (59.4)	82 (40.6)		420 (50.0%)	420 (50.0%)	
Necrosis n%	31 (5.7)	23 (4.6)	0.16	11 (9.1)	5 (6.1)	0.40	21 (5.0)	17 (4.0)	0.49
LVH n%	72 (13.3)	38 (7.6)	0.0001*	16 (13.3)	9 (10.9)	0.58	56 (13.3)	29 (6.9)	0.0018*

Issei - first generation Japanese (born in Japan). Nissei - second generation Japanese-Brazilians (born in Brazil). MS+: presence of metabolic syndrome. MS–: absence of metabolic syndrome. LVH: left ventricle hypertrophy. p<0.05.

a specific population, aiming at the diagnosis of myocardial necrosis and left ventricular hypertrophy.

In this study we observed that the prevalence of diabetes was very high among Japanese-Brazilians, reaching values seven times higher than those found in Japan (35.3% compared to 5.0%), and surpassing the values found in similar populations in the United States^{9,10,28,29}. These values were 1.5 to 2.0 times higher than those found in the Brazilian population^{11,13}, and these changes are probably related to the so-called “Westernization”, associated with a genetic dysfunction of pancreatic beta-cells favoring the existence of this phenotype^{9,28,29}. The adoption of different lifestyles was observed in genetically homogeneous populations such as the Pima Indians, who emigrated from Mexico to the United States and had a six-fold increase in the incidence of diabetes. Additionally, this population also had a genetic defect which facilitated the emergence of diabetes^{30,31}.

Our data showed that Japanese-Brazilian patients had a significant association with atherosclerotic coronary heart disease, evidenced by the frequent presence of waves of myocardial necrosis on the ECG. Epidemiological studies of coronary artery disease and strokes in Japanese men living in Japan and Japanese-Americans living in Hawaii and California (Los Angeles) observed a higher incidence of myocardial infarction and death by coronary disease^{5,32,33}, in these groups, as well as a higher prevalence of risk factors for high blood pressure than in non-Japanese Americans^{23,34}.

The Italian population study Rife Pooling Project (Risk Factors and Life Expectancy)²³ followed 22,553 Italian men and women (asymptomatic and over 30 years) for six years. It was observed that the presence of abnormalities in the initial ECG was associated with significant mortality and incidence of coronary heart disease in asymptomatic patients,

suggesting a high prevalence of silent heart disease. In that study, the presence of “qs” waves of necrosis on the ECG was the strongest predictor of fatal events. Similarly, the NIPPON DATA80 Research Group²⁴ study, conducted among the Japanese, observed that patients with abnormal “qs” waves on the ECG showed a high risk of mortality from all causes. In these studies the code of Minnesota was used to identify myocardial necrosis (“qs”).

Our study had not the intention of comparing the two generations of Japanese-Brazilians, since it was impossible to compare these two groups in terms of age, gender and number. However, it is noteworthy that the association of diabetes and necrosis in the electrocardiogram observed in these groups was more intense in the Nissei subgroup, who were certainly more Westernized than their parents. The Issei group, in spite of also presenting high rates of diabetes, showed no significant association with necrosis on the ECG. In our opinion, due to the small number of participants and the older average age of that generation, the Issei group was comprised of “survivors” of heart disease or other illnesses that affect this group of Japanese-Brazilians.

The “Westernization” of Japanese-Brazilians, with the accompanying changes in dietary habits and lifestyle, and associated with intrinsic factors of this population, resulted in an increase in blood glucose, abdominal obesity, blood pressure levels and dyslipidemia, which characterize the MS; MS is found in twice as many individuals in the population of Japanese living in Brazil as those living in Japan^{14,18}. In Japanese-Americans, visceral fat is associated with a greater prevalence of high blood pressure³⁵, and the greater prevalence of MS is due to the presence of genetically influenced factors (lipids, glucose and high blood pressure)³⁶. Unlike diabetics, MS patients showed no significant association with myocardial

necrosis observed on the ECG.

The ECG changes suggestive of myocardial necrosis found in a significantly greater number of patients with DM than in those with MS confirm the results of the ARIC³⁷ study, which assessed 15,792 Americans of both genders and concluded that the MS and its components are predictors of cardiovascular disease and DM, although the prevalence of cardiovascular disease is higher among diabetics.

The myocardial hypertrophy was associated with components of the MS^{38,39} such as insulin resistance, high blood pressure and abdominal obesity, and their presence suggests a high risk for death from cardiovascular disease, ischemic or not, as we have seen in observational studies such as the GUSTO IV ACS (Global Utilization of Strategies to Open occluded arteries)²², carried out among women, and the NHANES II (Second National Health and Nutrition Examination Survey Mortality Study)⁴⁰, conducted in the general population.

In our study, the prevalence of LVH among the Japanese-Brazilians with metabolic syndrome was very high, both in the entire group and in the Nissei subgroup. Among the Isseis, there were more individuals with MS and LVH on the ECG, although, in this group, a selective removal must have occurred, thus reducing its actual prevalence.

This study objectively showed that, in the population of first and second generation Japanese-Brazilians, similarly to what happens among Japanese-Americans, DM and MS are present in a very aggressive manner, with high prevalence of myocardial necrosis and left ventricular hypertrophy.

The cardiac changes resulting from that aggression could be observed on the ECG, a reproducible and inexpensive method that is widely used in clinical studies.

Conclusion

DM and MS are common in Japanese-Brazilians, and the electrocardiogram is very useful in the search for cardiac

abnormalities, such as necrosis or hypertrophy, specially in studies involving large populations.

Addendum 1

JBDSG (Japanese-Brazilians Diabetes Study Group).

Members of the group: AT Hirai, K Osiro, LJ Franco, LC Iochida, M Lunes (in memoriam), SRG Ferreira, SGA Gimeno (Department of Preventive Medicine, UNIFESP, São Paulo, SP); LK Matsumura, RS Moisés (Department of Internal Medicine, UNIFESP, São Paulo, SP); N Barros Jr. (Department of Surgery, UNIFESP, São Paulo, SP); DDG Lerario (Department of Medicine, Discipline of Endocrinology, UNIFESP, São Paulo, SP); M Kikuchi (University of São Paulo, SP); MA Cardoso (Department of Epidemiology and Public Health, Medical School of São José do Rio Preto, São Paulo); N Tomita (School of Odontology, University of São Paulo, Bauru, SP); R Chaim (School of Nutrition, Sagrado Coração University, Bauru, SP); K Wakisaka (Japanese-Brazilian Study Center, São Paulo, SP).

Limitations of the Study

When this study was conducted, the Issei population was small, due to several reasons, hindering the representativeness of the group.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

This study was funded by FAPESP.

Study Association

This article is part of the thesis of doctoral submitted by Luigi Brollo, from UNIFESP – Escola Paulista de Medicina.

References

1. Ferreira SRG, Lunes M, Franco LJ, Iochida LC, Hirai A, Vivolo MA, the Japanese-Brazilian Diabetes Study Group. Disturbances of glucose and lipid metabolism in first and second generation Japanese-Brazilians. *Diabetes Res Clin Prac* 1995;34:559-63.
2. Freire RD, Cardoso AM, Gimeno SGA, Ferreira SRG for the Japanese-Brazilian Diabetes Study Group. Dietary Fat Is Associated With Metabolic Syndrome in Japanese-Brazilians. *Diabetes Care* 2005;28: 1779-85.
3. Sartorelli DS, Freire RD, Ferreira, Cardoso MA for the Japanese-Brazilian Diabetes Study Group. Dietary Fiber and Glucose Tolerance in Japanese-Brazilians. *Diabetes Care* 2005;28:2240-42.
4. Bertolino CN, Castro TG, Sartorelli DS, Ferreira SRG, Cardoso MA The Japanese-Brazilians Diabetes Study Group Influência do consumo alimentar de ácidos graxos trans no perfil de lipídios séricos em nipo-brasileiros de Bauru, São Paulo, Brasil. *Cad Saúde Pública* 2006; 22(2):357-64.
5. Marmot MG, Syme SL. Acculturation and coronary heart disease in Japanese-Americans. *Am J Epidemiol* 1976;104(3):225-47.
6. Hara H, Egusa G, Yamakido M. Incidence of non-insulin-dependent diabetes mellitus and its risk factors in Japanese-Americans living in Hawaii and Los Angeles. *Diabet Med* 1996;13(9):S133-142.
7. Ueshima H, Okayama A, Saitoh S, Nakagawa H, Rodriguez B, Sakata K et al; INTERLIPID Research Group. *J Hum Hypertens* 2003;17(9):631-9.
8. Reed D, McGee D, Cohen J, Yano K, Syme SL, Feinleib M. Acculturation and coronary heart disease among Japanese men in Hawaii. *Am J Epidemiol* 1982;115(6):894-905.
9. Nakanishi S, Okubo M, Yoneda M, Jitsuiki K, Yamane K, Kohno N. A comparison between Japanese-Americans living in Hawaii and Los Angeles and native Japanese: the impact of lifestyle westernization on diabetes mellitus. *Biomed Pharmacother* 2004;58(10):572-7.

10. Hara H, Egusa G, Yamakido M, Kawate R. The high prevalence of diabetes mellitus and hyperinsulinemia among the Japanese-Americans living in Hawaii and Los Angeles. *Diabetes Res Clin Pract* 1994;24:S37-42.
11. Franco LJ. Diabetes in Japanese-Brazilians – influence of the acculturation process. *Diabetes Res Clin Pract* 1996;34:S51-57.
12. Lunes M, Franco LJ, Wakisaka K, Iochida LC, Osiro K, Hirai AT et al. Self-reported prevalence of non-insulindependent diabetes mellitus in first (Issei) and second (Nissei) generation of Japanese-Brazilians over 40 years of age. *Diabetes Res Clin Pract* 1994;24:S53-57.
13. Malerbi DA, Franco LJ. Multicenter study of the prevalence of diabetes mellitus and impaired glucose tolerance in urban Brazilian population aged 30-69 years The Brazilian Cooperative Group on the Study of Diabetes Prevalence. *Diabetes Care* 1992;15:1509-16.
14. Takeuchi H, Saitoh S, Takagi S, Ohnishi H, Ohhata J, Isoe T et al. Metabolic Syndrome and Cardiac Disease in Japanese Men: Applicability of the Concept of Metabolic Syndrome Defined by the National Cholesterol Education Program-Adult Treatment Panel III to Japanese Men – The Tanno and Sobetsu Study. *Hypertens Res* 2005;28(3):203-8.
15. National Cholesterol Education Program: Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001;285:2486-97.
16. New criteria for “obesity disease” in Japan. *Circ J* 2002; 66: 987-92.
17. Matsuzawa Y. Metabolic Syndrome-Definition and Diagnostic Criteria in Japan. *J Atheroscler Thromb* 2005;12:301.
18. Rosebaum P, Gimeno SGA, Sanudo A, Franco LJ, Ferreira SRG for the Japanese-Brazilian Diabetes Study Group. Analysis of criteria for metabolic syndrome in population-based study of Japanese-Brazilians. *Diabetes Obes Metab* 2005;7:352-9.
19. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutritional Examination Survey. *JAMA* 2002;287:356-9.
20. I Diretriz Brasileira de Diagnóstico e Tratamento da Síndrome Metabólica. *Arq Bras Cardiol* 2005, 84, suppl 1.
21. Gimeno SGA, Osiro K, Matsumura L, Massimino FC, Ferreira SRG for the Japanese-Brazilians Diabetes Study Group. Glucose intolerance and all-cause mortality in Japanese migrants. *Diabetes Res Clin Pract* 2005;68:147-54.
22. Westerhout CM, Lauer MS, James S, Fu Y, Wallentin L, Armstrong PW; GUSTO IV ACS Investigators. Electrocardiographic left ventricular hypertrophy in GUSTO IV: an important risk marker of mortality in women. *Eur Heart J* 2007;28(17):2064-9.
23. Menotti A, Seccareccia F. Electrocardiographic Minnesota code findings predicting short-term mortality in asymptomatic subjects. The Italian RIFLE Pooling Project (Risk Factors and Life Expectancy). *G Ital Cardiol* 1997;27(1):40-9.
24. Horibe H, Kasagi F, Kagaya M, Masutani Y, Okayama A, Ueshima H; The NIPPON DATA80 Research Group; Working Group of Electrocardiography Coding for the National Survey of Circulatory Disorders, 1980. *J Epidemiol* 2005;15(4):125-34.
25. Gimeno SGA, Ferreira SRG, Franco LJ, Hirai AT, Matsumura L, Moisés RS. Prevalence and 7-year incidence of Type II diabetes mellitus in a Japanese-Brazilian population: an alarming public health problem. *Diabetologia* 2002 45:1635-38.
26. Prineas R, Crow R, Blackburn H. The Minnesota code manual of electrocardiographic findings. Littleton (Mass): John Wright-PSC, Inc., 1982.
27. Verdecchia P, Schillaci G, Bongiorno C, Ciucci A, Gattobigio R, Zampi I et al. Prognostic value of a new electrocardiographic method for diagnosis of left ventricular hypertrophy in essential hypertension. *JACC* 1998;31:383-90.
28. Fujimoto WY, Bergstrom RW, Boyko EJ, Chen K, Kahn SE, Leonetti DL et al. Type 2 diabetes and the metabolic syndrome in Japanese Americans. *Diabetes Res Clin Pract* 2000;50:S73-6.
29. Fujimoto WY. Nature, nurture, and the metabolic epidemiology of diabetes - - the saga of Japanese in America. 59th Annual Scientific Sessions of ADA, San Diego, CA 1999.
30. Schulz LO, Bennett PH, Ravussin E, Kidd KK, Esparza J, Valencia ME. Effects of traditional and western environments on prevalence of type 2 diabetes in Pima Indians in Mexico and the U.S.. *Diabetes Care* 2006;29(8):1866-71.
31. Williams DE, Knowler WC, Smith CJ, Hanson RL, Roumain J, Saremi A et al. The effect of Indian or Anglo dietary preference on the incidence of diabetes in Pima Indians. *Diabetes Care* 2001;24(5):811-6.
32. Marmot MG, Syme SL, Kagan A, Kato H, Cohen JB, Belsky J. Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California: prevalence of coronary and hypertensive risk associated risk factors. *Am J Epidemiol* 1975;102(6):514-25.
33. Robertson TL, Kato H, Rhoads GG, Kagan A, Marmot M, Syme SL et al. Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California. Incidence of myocardial infarction and death from coronary heart disease. *Am J Cardiol* 1977;39(2):239-43.
34. Imazu M, Sumida K, Yamabe T, Yamamoto H, Ueda H, Hattori Y et al. A comparison of the prevalence and risk factors of high blood pressure among Japanese living in Japan, Hawaii and Los Angeles. *Public Health Rep* 1996;111:S59-61.
35. Hayashi T, Boyko EJ, Leonetti DL, McNeely MJ, Newell-Morris L, Kahn SE et al. Visceral adiposity and the prevalence of hypertension in Japanese Americans. *Circulation* 2003;108(14):1718-23.
36. Austin MA, Edwards KL, McNeely MJ, Chandler WL, Leonetti DL, Talmud PJ et al. Heritability of multivariate factors of the metabolic syndrome in nondiabetic Japanese Americans. *Diabetes* 2004;53(4):1166-9.
37. Ballantyne CM, Hoogeveen RC, McNeill AM, Heiss G, Schmidt MI, Duncan et al. Metabolic syndrome risk for cardiovascular disease and diabetes in the ARIC study. *Int J Obes* 2008; 32 Suppl 2:S21-4.
38. Ferrara LA, Guida L, Ferrara F, De Luca G, Staiano L, Celentano A et al. Cardiac structure and function and arterial circulation in hypertensive patients with and without metabolic syndrome. *J Hum Hypertens* 2007;21(9):729-35.
39. Grandi AM, Maresca AM, Giudici E, Laurita E, Marchesi C, Solbiati F et al. Metabolic syndrome and morphofunctional characteristics of the left ventricle in clinically hypertensive nondiabetic subjects. *Am J Hypertens* 2006;19(2):199-205.
40. Brown DW. Left ventricular hypertrophy as a predictor of coronary heart disease mortality and the effect of hypertension. *Am Heart J* 2000;140(6):848-56.