

# Coronary Heart Disease Clinical Manifestation and Risk Factors in Japanese Immigrants and their Descendents in the City of São Paulo

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**Objective** – To assess whether a difference exists in coronary heart disease clinical manifestations and the prevalence of risk factors between Japanese immigrants and their descendents in the city of São Paulo.

**Methods** – Retrospective analysis of coronary artery disease clinical manifestations and the prevalence of risk factors, comparing 128 Japanese immigrants (Japanese group) with 304 Japanese descendents (Nisei group).

**Results** – The initial manifestation of the disease was earlier in the Nisei group (mean = 53 years), a difference of 12 years when compared with that in the Japanese group (mean = 65 years) ( $P < 0.001$ ). Myocardial infarction was the first manifestation in both groups ( $P = 0.83$ ). The following parameters were independently associated with early coronary events: smoking ( $OR = 2.25$ ; 95%  $CI = 1.35-3.77$ ;  $P < 0.002$ ); Nisei group ( $OR = 10.22$ ; 95%  $CI = 5.64-18.5$ ;  $P < 0.001$ ); and female sex ( $OR = 5.04$ ; 95%  $CI = 2.66-9.52$ ;  $P < 0.001$ ).

**Conclusion** – The clinical presentation of coronary heart disease in the Japanese and their descendents in the city of São Paulo was similar, but coronary heart disease onset occurred approximately 12 years earlier in the Nisei group than in the Japanese group.

**Keywords:** coronary heart disease, diabetes mellitus, hypercholesterolemia, hypertriglyceridemia, systemic arterial hypertension

Immigration of large population groups to regions with characteristics different from those of their places of origin allows the study of biological and psychosocial changes occurring through the interaction of these groups with the new environments<sup>1</sup>. Several studies on Japanese immigrants in the United States of America have placed mortality due to cardiac disease in Nisei individuals of California and Hawaii at an intermediate level between that observed in Japan and that of the North American population of Caucasian heritage. From 1965 onwards, the Ni-Hon-San study<sup>2</sup> compared the differences of cardiovascular disease between Japanese males aged from 45 to 69 years living in Japan (Hiroshima and Nagasaki) and groups of Japanese immigrants living in California and Hawaii. Of the latter, approximately 40% had originally come from Hiroshima and the southwestern region of Japan, which provided similar genetic patterns in the 3 cohorts<sup>3</sup>. Compared with the Japanese cohort, the Californian and Hawaiian cohorts had a greater prevalence and incidence of coronary heart disease and a greater prevalence of risk factors for that disease<sup>4</sup>. Mortality due to coronary heart disease was also greater in the Californian and Hawaiian groups<sup>2-6</sup>, which, in addition, also had a greater incidence of myocardial infarction as compared with that of the Japanese group living in Japan<sup>7</sup>. In our country, as in the United States, 2 waves of Japanese immigration occurred as follows: from 1908 to 1933, 110,191 individuals, and from 1950 to 1959, approximately 34,266 individuals. In Brazil, the Japanese immigrants concentrated in the southern and southeastern regions, mainly in the State of São Paulo, which has the largest Japanese community in Brazil, estimated at 1,400,000 inhabitants, 326,000 of whom live in the municipality of São Paulo<sup>8</sup>. In regard to coronary heart disease in immigrants, an intermediate mortality rate between those of the Japanese and the population of São Paulo was observed<sup>9,10</sup>. Similar values were reported in a rural population in the Brazilian State of Paraná<sup>11</sup>. The risk

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factors for coronary heart disease were also greater in Japanese descendants in the city of Campo Grande in the Brazilian State of Mato Grosso do Sul as compared with those of the Japanese who founded that colony<sup>12</sup>. The objective of this study was to evaluate whether differences exist in the clinical presentation of coronary heart disease and the prevalence of its risk factors between the Japanese immigrants and their descendants in the city of São Paulo.

## Methods

Patients of Japanese origin who sought medical care in the outpatient clinics of the Chronic Coronary Heart Disease Clinical Unit of the Instituto do Coração of the Medical School of the University of São Paulo were retrospectively studied. A total of 432 Japanese and Japanese descendants were selected through information obtained from their medical records considering ethnicity, family name, place of birth, and name of parents. Those patients had sought the outpatient clinics from July 1977 to April 1998 and had been clinically and angiographically diagnosed with coronary heart disease. After selection through the medical records, the patients were divided into 2 groups as follows: Japanese group - comprising the individuals who had been born in Japan and immigrated to Brazil; and the Nisei group - comprising the Brazilian children of those Japanese. The Japanese group comprised 128 patients, 82 males and 46 females. The Nisei group comprised 304 patients, 80 females and 224 males. Data were then collected and the following variables of interest for the comparative study were obtained: sex, nationality, date, and age of the patients on the day of the first ambulatory consultation. The age at which coronary heart disease began was determined by the first event or its first suggestive manifestation, either characterized by angina pectoris or myocardial infarction<sup>13,14</sup>. The cases with the associated diagnosis of valvular heart diseases and those with no clinical diagnosis of coronary heart disease were excluded. For the electrocardiographic diagnosis of myocardial infarction and silent ischemia on stress electrocardiography, the classical criteria<sup>15,16</sup> were applied to data referring to the first medical consultation or first coronary event.

The following variables of clinical history and laboratory findings were chosen for analysis: 1) familial antecedents, considering the report of sudden death or myocardial infarction among the parents or first-degree relatives before the age of 55 years for males and 65 years for females<sup>17-1</sup>; 2) body mass index obtained according to the formula  $BMI = \text{weight}/(\text{height})^2$ , values between 18.0 and 24.9 kg/m<sup>2</sup> being considered normal<sup>20</sup>; 3) smoking, when present at the time of the initial consultation and independent of the amount of cigarettes smoked per day and the duration of the smoking habit; 4) diastolic (DBP) and systolic (SBP) blood pressures obtained on the day of the first consultation and considering the borderline values of normality (normal systolic blood pressure 139 mmHg and normal diastolic blood pressure 89 mmHg<sup>21</sup>); 5) diabetes mellitus, reported

by the patient on the first consultation or the presence of a high glycemia value (<sup>3</sup> 126 mg/dL, with the normal range between 70 and 110)<sup>22,23</sup>; and 6) cholesterolemia and triglyceridemia related to the first consultation, with normal values established as < 200 mg/dL and < 150 mg/dL, respectively<sup>24</sup>.

The numeric variables were analyzed with the Student *t* test, *P* < 0.05 being the significance level adopted. For the nonnumerical variables, the chi-square test or the Fisher exact test was used with the same significance level (*P* < 0.05)<sup>25</sup>. After the comparative analysis between the groups, and considering that the result obtained was a lower mean age for the initial manifestation of coronary heart disease in the Nisei group, we considered it appropriate to complement our study with the analysis of the variables that could be influencing this finding. To know the effect of all variables on the clinical presentation of coronary heart disease in the 2 groups using the technique of logistic regression<sup>26</sup> as a predictive model of analysis, a dependent variable, the early coronary event, was established. An early coronary event was defined as the appearance of coronary heart disease before the age of 55 years for males and 65 years for females. This way and with this criterion established, the patients were separated into 2 groups according to the presence or absence of an early coronary event. Then, through univariate analysis and with the same level of significance adopted, the early coronary event variable and the numerical and nonnumerical variables were compared. The variables that proved significant were submitted to the multivariate approach model. Finally, with the latter variables, ie, those with statistical significance, an odds ratio was calculated for each factor.

## Result

Table I shows the distribution of the patients in the groups according to sex. The proportion of females in the Japanese group (36%) was greater than that in the Nisei group (26%), and this difference was significant (*P* = 0.045). Table II shows that the difference between the mean ages of coronary heart disease onset in the Nisei and in the Japanese groups was at least 10 years, both for males and females. Figures 1 and 2 depict the distribution of the age of coronary heart disease onset in the groups. The overall mean age of coronary heart disease manifestation was 12 years earlier in the Nisei group. In the curve for accumulated distribution of ages, the greater incline of the curve represen-

Table I - Sex distribution in the Japanese and Nisei groups

Group		Males	Females
Japanese	Number	82	46
	Proportion	64%	36%
Nisei	Number	224	80
	Proportion	74%	26%
Chi-square test, <i>P</i> = 0.04.			

ting the Nisei group represents a greater number of patients with early manifestations of coronary heart disease than in the Japanese group. Table III shows the initial coronary heart disease event. No difference was observed in the clinical presentation of the disease between the 2 groups.

The distribution of risk factors, which were considered variables of analysis in the 2 groups, is shown in table IV. Because some variables were not available in all medical records, the analysis was carried out with different numbers

for each variable: familial antecedents, 329 cases; diabetes mellitus, 428; active smoking, 369; body mass index, 413; systolic and diastolic blood pressures, 425; glycemia, 420; cholesterolemia and triglyceridemia, 348.

Table V shows the results and the odds ratio for each factor. In regard to statistically significant variables, with smoking, on average, a 2.25-fold greater probability existed for the occurrence of an early coronary event. Being Nisei had a 10.2-fold greater probability of an early coronary event than did being Japanese; likewise, being female had a 5-fold greater probability of an early coronary event than that of being male.

## Discussion

Our results showed that coronary heart disease appeared approximately 1 decade earlier in the Nisei group, which had a 10-fold greater probability of an early coronary event than did the Japanese group. This temporal difference in the clinical presentation of coronary heart disease may be attributed to the greater degree of acculturation reached by the descendents of the Japanese in São Paulo, resulting in the greater prevalence of the risk factors for coronary heart disease in that population. The studies on acculturation of Japanese groups in California<sup>27,29</sup> and Hawaii<sup>29</sup>, showing that the patients with a greater degree of acculturation have a greater prevalence and incidence of coronary heart disease, corroborate our assertion. The initial manifestation of coronary heart disease in the 2 groups was similar and comprised angina pectoris and myocardial infarction, and only 1 patient was diagnosed with silent ischemia. Considering that the Nisei group had a greater degree of acculturation, and according to the results found in the Californian<sup>27,29</sup> and Hawaiian<sup>29</sup> studies, and in the study by Mizushima et al<sup>12</sup>, we might have expected a greater prevalence of angina or myocardial infarction in the Nisei group and also in the Japanese and their descendents in Campo Grande and São Paulo. These differences regarding the results of prevalence between ours and that of the other studies may be explained by the fact that, in our study, the prevalence considered was that at the moment of the initial manifestation of the disease.

The results of the Ni-Hon-San study<sup>2</sup> showed a greater prevalence of smoking in the Japan group (75%) as compared with the Hawaii (44%) and the California (35%) groups. That study also found that, among Japanese, a greater consumption of cigarettes per day was not associated with an increa-

**Table II – Distribution of the quartiles and age of coronary disease onset (in years) in the Japanese and Nisei groups according to sex**

	Quartiles	Age	
		Japanese	Nisei
Males	Minimum	40	32
	Quartile 25%	56	45
	Median (50%)	64	52
	Quartile 75%	71.3	58
	Maximum	84	85
	Mean	63.6	52.7
	Mean Standard Error	1.04	0.59
	Number	82	223
Females	Minimum	48	39
	Quartile 25%	63	52
	Median (50%)	70	56
	Quartile 75%	75.5	62.8
	Maximum	85	74
	Mean	68.7	56.6
	Mean Standard Error	1.3	0.91
	Number	45	80
	Minimum	40	32

p<0.001

**Table III – Initial coronary heart disease event in the Japanese and Nisei groups**

Initial event	Japanese n = 128 (%)	Nisei n = 304 (%)
Stable angina	61(48)	129(42)
Unstable angina	21(16)	63(21)
Myocardial infarction	46(36)	111(36)

Fisher exact test, P = 0.835.

**Table IV - Distribution of the percentages and mean values of risk factors for coronary heart disease in the Japanese and Nisei groups**

Risk factors	Japanese	Nisei	P value
Familial antecedents	33%	37%	0.45
Diabetes mellitus	45%	45%	0.97
Active smoking	36%	48%	0.04
Body mass index*	24.7	25.9	0.002
Systolic blood pressure**	141.5	138.8	0.29
Diastolic blood pressure**	85.6	87	0.35
Glycemia*	126	128.4	0.62
Cholesterolemia*	223.9	233.9	0.11
Triglyceridemia*	243.8	261.4	0.56

\* values in kg/m<sup>2</sup>, \*\* values in mmHg, \*\*\* values in mg/dL.

**Table V - Representation of the significant variables in multivariate analysis with early coronary event**

Factor	Coefficient	P value	Odds ratio	[exp(coef.)] Confidence interval for odds ratio
Smoking (Yes/No)	0.814	0.002	2.258	[1.351; 3.773]
Nisei/Japanese group	2.325	<0.001	10.223	[5.642; 18.540]
Females/Males	1.617	<0.001	5.040	[2.667; 9.524]

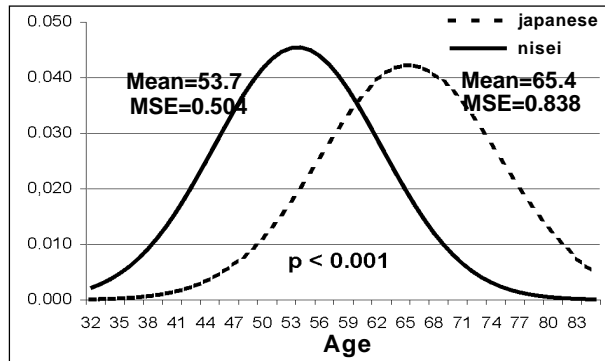


Fig. 1 – Distribution of the age of coronary heart disease onset in the Japanese and Nisei groups.

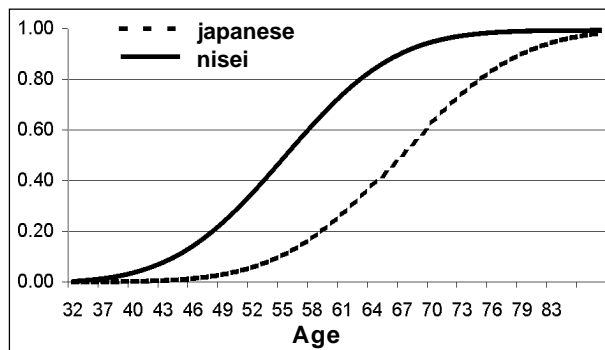


Fig. 2 – Accumulated distribution of the age of coronary heart disease onset in the Japanese and Nisei groups.

se in the incidence of coronary heart disease; on the other hand, in the Hawaiian group, smoking was an important risk factor for coronary heart disease<sup>28,30,31</sup>. In the study by Mizushima et al<sup>12</sup>, the Japanese group also had a greater prevalence of smoking. On the other hand, our findings showed a significant proportion of smokers in the Nisei group. The greater prevalence of smoking in the Nisei group and the greater probability of occurrence of an early coronary event in smokers in our study contributed towards making smoking an important risk factor for coronary heart disease among Nisei. The greater prevalence of hypercholesterolemia, hypertriglyceridemia, and a greater body mass index in the Nisei group agreed with the findings of Reed et al<sup>28</sup> in comparing the already acculturated Japanese immigrants in Hawaii and California with the individuals in the Japan group<sup>4</sup>. They reflect the greater consumption of unsaturated fat and a larger amount of animal protein by the Nisei<sup>32</sup>, also reported by Car-

dosio et al<sup>33</sup> in a study about dietary patterns in the Nisei population of São Paulo. In regard to glycemia, our patients had extremely elevated mean values (> 125 mg/dL in both groups), a large number of patients having values above those of the normal limit (around 50%), but with no difference between the 2 groups. Likewise, an increased incidence (45%) of diabetes mellitus was found in both groups. The prevalence of hyperglycemia in the Ni-Hon-San study<sup>2</sup>, both in Hawaii and California, is similar and greater than that observed in Japan<sup>4</sup>, but lower than that observed in our study. Ferreira et al<sup>34</sup>, studying the population of the Brazilian city of Bauru, reported overall prevalence values of noninsulin-dependent diabetes mellitus of 12% in the Japanese group and 16% in the Nisei group. A study carried out in Brazil<sup>35</sup> reported a greater prevalence of diabetes mellitus (17%) in coronary patients as compared with that in the general population. That value is greater than the prevalence of diabetes (7%) and glucose intolerance (7%) found in the urban Brazilian population<sup>36</sup>. The greater intake of noncomplex carbohydrates may be a cause of that finding, as it has been used to explain hyperglycemia in those patients<sup>32</sup>. The proportion of our patients with increased body mass index, more than 37% of the cases, may justify our findings but not such an elevated percentage of diabetes mellitus. Another explanation may be the greater glucose intolerance observed in patients with metabolic syndrome<sup>37</sup>. Therefore, diabetes mellitus should be carefully considered an important risk factor for coronary heart disease in the Japanese and their descendants in Brazil. In another analysis of the Ni-Hon-San study<sup>38</sup>, greater blood pressure levels were found in the Californian cohort than in the Japanese cohort; the values in the Hawaiian cohort occupy an intermediary position, the increase in blood pressure relating to the increase in body weight. These findings are similar to those of Mizushima et al<sup>12</sup>. In our study, both groups had similar mean systolic and diastolic blood pressures, and the proportions of patients with systolic and diastolic blood pressures considered elevated were also similar in both groups.

Finally, our study comprised a population that sought medical care at our institution. Considering the period from 1977 to 1998 and the number of patients studied, our results do certainly provide information regarding these 2 groups, the Japanese and their descendants, mainly in regard to the difference in the age of coronary heart disease onset for the same degree of coronary impairment.

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