Übersicht HRV – Diabetes II und Diabetes I

Association between cardiac autonomic dysfunction and inflammation in type 1 diabetic patients: effect of beta-blockade.

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AIMS: To assess the relationship between cardiac autonomic dysfunction and inflammation in patients with type 1 diabetes and whether beta-blocker therapy might improve both abnormalities in these patients. METHODS AND RESULTS: We studied 49 patients with type 1 diabetes (age 50.5 +/- 11 years, 33 men). Serum levels of high-sensitivity C-reactive protein, as a marker of inflammation, and frequency-domain heart rate variability (HRV) on 24 h Holter monitoring, as a measure of cardiac autonomic function, were assessed in all patients. Twenty-one patients with depressed HRV were subsequently randomized to receive atenolol (50 mg daily) or no-beta-blockade. HRV and C-reactive protein were re-assessed after 3-4 weeks from randomization. An inverse correlation was found between C-reactive protein levels and HRV parameters, with the highest r coefficient shown with low-frequency (LF) power (r = -0.38; P = 0.007). Furthermore, C-reactive protein serum levels were significantly higher in patients with bottom quartile values of LF power compared with patients with values in the three top quartiles (4.64 +/- 2.8 vs.1.79 +/- 1.6 mg/L, respectively; P = 0.003), also after adjustment for potential confounding variables (P = 0.013). HRV parameters improved significantly in patients treated with atenolol, but not in the no-atenolol group. Furthermore, C-reactive protein levels decreased in the beta-blockade group, but not in the no-beta-blockade group (P = 0.04 for changes between groups). CONCLUSION: In type 1 diabetic patients, serum C-reactive protein levels are significantly associated with depressed HRV; the favourable effects of beta-blockade on both HRV parameters and C-reactive protein serum levels suggest that autonomic nervous system may have significant modulator effects on inflammation.

PMID: 17371783 [PubMed - in process]

Heart rate variability: short-term studies are as useful as holter to differentiate diabetic patients from healthy subjects.

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BACKGROUND: The definitive incorporation of heart rate variability (HRV) as a clinical tool depends on the development of more confident techniques of measurement. The length of the studies is a critical issue. Whereas Holter studies allow the monitorization at different hours and activities, short-term recordings allow the control of environmental conditions. Recording length is also strongly related to the procedure of analysis; for instance, some time-domain indexes are strongly affected by the duration of the study. Meanwhile, spectral analyses require stationary conditions, only achieved in short-term studies. Our main goal was to determine if HRV indexes obtained from short-term analyses were as useful as those from Holter monitoring for diagnosis of reduced HRV in diabetes. METHODS: We studied two
groups: one with impaired HRV (15 diabetic patients) and another with normal HRV (15 healthy subjects). HRV indexes obtained from 24-hour Holter recordings (SDNN, rMSSD, and the power of LF and HF bands), were correlated with analog indexes obtained from 10-minute digital acquired studies within each group. Besides, we compared the diabetic and control groups using the indexes obtained with both methodologies. Results: The correlation was high (0.70<or=r <or= 0.85, P <or= 0.0032) in the diabetic group, but was poor in the control group. HRV values were significantly lower in the diabetic group either for 24-hour or short-term studies (P <or= 0.0113). CONCLUSION: We conclude that short-term studies are at least as powerful as Holter to differentiate the diabetic group (impaired HRV) from the control group.

PMID: 14516288 [PubMed - indexed for MEDLINE]

High serum high-sensitivity C-reactive protein concentrations are associated with relative cardiac sympathetic overactivity during the early morning period in type 2 diabetic patients with metabolic syndrome.

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Sympathetic activation is associated with metabolic syndrome (MS) and increased risk of cardiovascular disease. The aim of this study was to investigate whether cardiac autonomic activity or sympathovagal balance, as estimated by a 24-hour power spectral analysis of heart rate variation, is associated with serum concentrations of high-sensitivity C-reactive protein (hs-CRP), a sensitive predictor for cardiovascular events, in type 2 diabetic patients with and without MS. We studied 104 type 2 diabetic patients (50 female and 54 male). The diagnosis of MS was based on the National Cholesterol Education Program Adult Treatment Panel III criteria. Based on the serum hs-CRP, diabetic patients were also divided into 3 groups: low risk (CRP < 1.0 mg/L), moderate risk (1.0 < or = CRP < or = 3.0), and high risk (CRP > 3.0). Heart rate variation was determined automatically every 5 minutes over 24 hours using an ambulatory Holter electrocardiographic recording. Power spectral analysis of the R-R intervals was performed by fast Fourier transformation. Low frequency (LF, both sympathetic and parasympathetic activities), high frequency (HF, pure parasympathetic activity), and the ratio of LF to HF, an index of sympathovagal balance, were used as indices of cardiac autonomic activity. Blood concentrations of hs-CRP, interleukin 6, and plasminogen activator inhibitor 1 were higher in diabetic patients with than in those without MS (P < .0001, P = .0056, and P < .0001, respectively). Both the 24-hour mean LF and the LF-to-HF ratio were also significantly higher in diabetic patients with than in those without MS (P = .0397 and P = .0483, respectively). The LF-to-HF ratio at 6:00 am was significantly higher in diabetic patients with a high CRP concentration than in those with a low or moderate CRP concentration (P < .001 and P < .01, respectively). Only urinary albumin and hs-CRP were independent factors predicting the LF-to-HF ratio at 6:00 am in diabetic patients. In conclusion, type 2 diabetic patients with MS have elevated markers of inflammation and evidence of cardiac sympathetic predominance. High serum concentrations of hs-CRP are associated with relative cardiac sympathetic overactivity during the early morning in type 2 diabetic patients.

PMID: 16839835 [PubMed - indexed for MEDLINE]
Power spectral analysis of heart rate variation in diabetic patients with neuropathic foot ulceration.

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OBJECTIVE: To evaluate the relationship between diabetic autonomic neuropathy and diabetic neuropathic foot ulceration, we used power spectral analysis (PSA) of heart rate variation, which provides the accurate simultaneous quantification of parasympathetic and sympathetic activities, to assess autonomic function in diabetic patients. RESEARCH DESIGN AND METHODS: We studied 55 NIDDM patients including 10 diabetic patients without neuropathy, 23 diabetic patients with neuropathy and no history of foot ulceration, and 22 diabetic patients with neuropathic foot ulceration. We performed PSA of 100 R-R intervals at rest and analyzed the results by fast Fourier transformation. RESULTS: The low frequency (LF) power, which reflects sympathetic activity, and the high frequency (HF) power, which reflects parasympathetic (vagal) activity, were inversely correlated with the duration of diabetes and the fasting plasma glucose (FPG) levels. By multiple regression analysis, the FPG remained with significant influence on both LF and HF powers. The LF and HF powers were positively correlated with motor nerve conduction velocity (MCV) and sensory nerve conduction velocity (SCV) in the upper and lower limbs and the coefficient of variation of R-R intervals. The LF and HF powers were significantly reduced in patients with neuropathy and patients with foot ulceration compared with patients without neuropathy. Although the median MCV and SCV were similar between diabetic patients with neuropathy and patients with foot ulceration, both the LF and HF powers were significantly decreased in patients with foot ulceration compared with patients with neuropathy. There was no difference in the value of the LF:HF ratio, an index of sympathovagal balance, among three subgroups. We observed a positive correlation between LF and HF power in all subjects; however, the LF and HF powers were not correlated in the subgroups of patients with foot ulceration. CONCLUSIONS: These results showed that diabetic patients with neuropathic foot ulceration have a greater impairment in spectral indexes of autonomic activity obtained by PSA than patients with neuropathy and no history of foot ulceration, whereas no difference was present in nerve conduction velocities.

PMID: 9653615 [PubMed - indexed for MEDLINE]

Role of heart rate variability in the early diagnosis of diabetic autonomic neuropathy in children.

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BACKGROUND: Diabetic autonomic neuropathy (DAN) is a major complication of diabetes. DAN has been shown to be closely related to glycemic control. To contribute significantly to the morbidity and mortality of the disease, and to be indicative of an increased risk of cardiovascular events. Tests assessing the function of the autonomic nervous system, such as the response of heart rate and blood pressure to maneuvers stimulating the autonomic nervous system, including deep breathing. Valsalva maneuver and standing, allowed to detect signs of DAN in adolescents; however, the sensitivity of such tests in revealing an early impairment of the autonomic nervous system proved low. Several studies found heart rate variability (HRV)
to be useful in assessing the dysfunction of the autonomic nervous system in diabetic children and adolescents, but only few HRV parameters were evaluated in most of them. OBJECTIVE: To study cardiac autonomic nervous system in diabetic children, and to investigate whether the duration of diabetes and the degree of metabolic control are determinants for the development of DAN in children. PATIENTS AND METHODS: We analyzed HRV in 50 asymptomatic patients with insulin-dependent diabetes mellitus (IDDM) and 30 healthy children matched for age and sex. RESULTS: Patients with a history of diabetes > 8 years showed significant alterations of the autonomic nervous system (significant reduction of r-MSSD, pNN50, HF and increase in LF/HF). Conversely, only a reduction in pNN50 was found in patients with a disease duration < 8 years. Furthermore, we also observed significant HRV abnormalities in patients with an impaired metabolic control of diabetes. Compared to controls, patients with glycosylated hemoglobin blood levels (HbA(1C)) > 8% showed a significant reduction of r-MSSD, pHH50 and total power spectrum, whereas no HRV abnormalities were detected in patients with an HbA(1C) < 8%. CONCLUSIONS: HRV analysis can detect early subclinical alterations of the autonomic nervous system in asymptomatic patients with IDDM, which seem to consist mainly in a parasympathetic impairment. Autonomic dysfunction is associated both with the duration and an inadequate metabolic control of the disease.

PMID: 12574897 [PubMed - indexed for MEDLINE]

Relationship between diabetic autonomic neuropathy and peripheral neuropathy as assessed by power spectral analysis of heart rate variations and vibratory perception thresholds.

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To investigate the relationship between diabetic autonomic and peripheral neuropathies, we carried out power spectral analysis (PSA) of heart rate variations and determined the vibratory perception threshold (VPT) in diabetic subjects (DM). The VPT, measured with a Suzuki-Matsuoka Vibrometer (SMV-5), was greater in diabetic subjects than in controls. The low frequency (LF) component of the PSA which represents sympathetic nervous activity and the high frequency (HF) component of the PSA which indicates parasympathetic nervous activity were significantly decreased in diabetic subjects when compared to values in the controls. In addition, there were significant inverse correlations between the LF and HF components of the PSA of heart rate variations and the VPT. These results suggest that the PSA of heart rate variations and the measurement of VPT are useful tools for evaluating diabetic autonomic and peripheral neuropathies.

PMID: 7924888 [PubMed - indexed for MEDLINE]

Incipient cardiovascular autonomic imbalance revealed by wavelet analysis of heart rate variability in Type 2 diabetic patients.

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AIM: Incipient cardiovascular autonomic imbalance is not readily diagnosed by conventional methods. Spectral analysis of heart rate variability (HRV) by wavelet transform (WT) was used to measure cardiovascular autonomic function in patients with Type 2 diabetes.
METHODS: Thirty-two diabetic patients without (D), 26 with cardiovascular autonomic
neuropathy (DAN) and 72 control subjects (C) participated. A 30-min HRV time series was analysed by wavelet transformation and four characteristic frequency intervals were defined: I (0.0095-0.021 Hz), II (0.021-0.052 Hz), III (0.052-0.145 Hz) and IV (0.145-0.6 Hz).

RESULTS: When compared with C, in both D and DAN the normalized power and amplitude of interval II were increased and of interval IV decreased, resulting in a significantly higher II/IV ratio. Furthermore, in DAN the normalized power and amplitude of interval I were increased and of interval III decreased when compared with the D and C groups. The diabetic patients were divided in two equal subgroups according to HbA(1c) < 8.0% and > or = 8.0%. In the subgroup with HbA(1c) > or = 8.0%, normalized power in interval II was significantly higher and in interval IV significantly lower than in the subgroup with HbA(1c) < 8.0%. In D, but not in DAN patients prescribed ACE inhibitors, the absolute amplitude and power of oscillations were significantly higher than in patients not taking ACE inhibitor therapy.

CONCLUSIONS: Patients with diabetes have increased sympathetic and decreased parasympathetic cardiac activity regardless of the presence of autonomic neuropathy. Glycaemic control and treatment with ACE inhibitors may favourably influence HRV in diabetic patients without autonomic neuropathy.

PMID: 17227320 [PubMed - indexed for MEDLINE]

Total power and high frequency components of heart rate variability and risk factors for atherosclerosis.

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INTRODUCTION: Low heart rate variability, HRV, is associated with diabetic neuropathy and with ischemic heart disease, IHD. The time context points to diabetes preceding changes in HRV, while changes in HRV precede the development of atherosclerosis and IHD. The purpose of the study was to analyse the association between the physiological risk factors of IHD and HRV in a prospective design. METHODS: In 1998 and 2002, data was gathered in a study concerning the risk factors for atherosclerosis. From among the participants it was possible to include 50 women and 24 men in a sub-study concerning HRV. Heart rate variability was measured partly during a clinical examination with exposure to a simple stress test, and partly during the first 4 h of sleep. The clinical examination, which lasted 45 min, resulted in 9, 5-minute HRV measurements, while the sleep period was divided into 2 periods of 2 h each, for which average HRV measurements were calculated. The associations between HRV and risk factors for IHD were analysed using the GLM, repeated measures method. As the dependent variables in the GLM analyses 11 levels (9 while awake and 2 while sleeping) of total power and high frequency variability, respectively, were used. The included risk factors were: body mass index, waist-hip ratio, systolic blood pressure, fibrinogen, cholesterol, HDL-cholesterol, HbA1c, testosterone, DHEAs, cortisol and catecholamines. Catecholamines were measured in urine and only in 1998. Cortisol was measured in both urine and saliva in 1998, but only in saliva in 2002. The results were adjusted according to the starting time of the measurements. RESULTS: Among the women, waist-hip ratio and HbA1c were significantly and negatively associated with both TP and HF. Stress hormones were not associated with HRV. Among the men, waist-hip ratio, HbA1c, and fibrinogen in 2002, and cortisol and noradrenaline in 1998 were significantly and negatively associated with TP and HF. CONCLUSION: The study showed gender differences in the observed associations. In both gender, waist ratio and HbA1c were negatively associated with TP and HF. Furthermore, in the men, but not in the women, stress hormones in 1998, i.e. cortisol and noradrenaline, was negatively associated with TP and HF. The presented data give rise to
Heart rate variability in an ageing population and its association with lifestyle and cardiovascular risk factors: results of the SAPALDIA study.


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AIMS: (i) To report associations between cardiovascular risk factors and heart rate variability (HRV) in a general population and (ii) to provide normal values for various HRV measurements in a healthy European general population sample aged > or = 50. METHODS AND RESULTS: Twenty-four-hour electrocardiograms were recorded in 1742 randomly selected SAPALDIA (Swiss cohort study on Air Pollution and Lung Diseases in Adults) participants aged > or = 50. In multivariate regression analyses, women (n=895) had a 6.1% lower standard deviation of all normal RR (NN) intervals (SDNN), a 11.4% lower total power (TP), and a 27.2% lower low-frequency (LF) power than men (n=847). Per unit increase in BMI, SDNN decreased by 0.7% and TP decreased by 1.2%. Persons with high blood pressure had a 9.2% lower LF than normotensive persons and current smokers a 15.5% lower LF than never smokers. Each hour of heavy physical exercise was associated with a 2.0% increase in SDNN, a 3.6% increase in the high frequency (HF) range power and a 4.2% increase in LF power. Higher levels of uric acid, high-sensitive C-reactive protein and non-HDL-cholesterol were associated with lower TP, HF and LF. Percentiles of TP and LF/HF as a function of age were calculated for an asymptomatic subsample of participants (n=499) free of cardioactive medications. CONCLUSION: Heart rate variability in a general population sample shows expected associations with all known cardiovascular risk factors, although not identically for all HRV domains. Together with our percentile estimates for HRV as a function of age, these findings could assist scientists in interpreting 24 h HRV values and factors influencing them in an ageing population.

PMID: 16798766 [PubMed - indexed for MEDLINE]

Heart rate variability in diabetes patients.

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Diabetes mellitus can cause cardiovascular autonomic neuropathy and is associated with increased cardiovascular deaths. We investigated cardiovascular autonomic neuropathy in diabetics and healthy controls by analysis of heart rate variability. Thirty-one diabetics and 30 age- and sex-matched controls were included. In the time domain we measured the mean R - R interval (NN), the standard deviation of the R - R interval index (SDNN), the standard deviation of the 5-min R - R interval mean (SDANN), the root mean square of successive R - R interval differences (RMSSD) and the percentage of beats with a consecutive R - R interval difference > 50 ms (pNN50). In the frequency domain we measured high-frequency power...
(HF), low-frequency power (LF) and the LF/HF ratio. Diabetes patients had lower values for
time-domain and frequency-domain parameters than controls. **Most heart rate variability parameters were lower in diabetes patients with chronic complications than in those without chronic complications.**

PMID: 16866023 [PubMed - indexed for MEDLINE]

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**Decreased heart rate variability may predict the progression of carotid atherosclerosis in type 2 diabetes.**

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Heart rate variability (HRV), a measure of autonomic function, can predict survival outcomes. Cardiovascular disease is a known complication of diabetes, and we aimed to determine if autonomic dysfunction was associated with carotid artery atherosclerotic plaques in type 2 diabetic patients. We assessed frequency domain HRV from power spectral analysis of 24 h Holter ECG recordings, expiration/inspiration (E/I) ratio during deep breathing, acceleration index (AI) of R-R interval in response to head-up tilt, and the degree of carotid artery atherosclerosis in 61 type-2 diabetic patients (39 males, 45-69 years). Studies were carried out 5-6 years after diagnosis (baseline) and repeated 8 years after diagnosis (follow-up). At baseline, patients diagnosed with autonomic neuropathy, with abnormal E/I ratio and abnormal AI measurements, had decreased low frequency (LF) HRV. Baseline E/I ratio correlated with day (r = 0.34; P < 0.001) and night-time (r = 0.44; P < 0.001) LF power. Night-time HRV did not differ in patient with and without autonomic neuropathy. Reduced common carotid artery diameter and atherosclerotic intima-media thickness (IMT) both correlated with HRV at baseline. At follow-up, all HRV variables decreased significantly. Furthermore, patients with lower LF power at baseline, had a larger increase in the thickness of the carotid bulb intima-media at follow-up. **Our results show that LF HRV power is associated with the extent and progression of carotid atherosclerosis in type 2 diabetes. A low LF HRV may predict the progression of atherosclerosis in these patients.**

PMID: 16763752 [PubMed - indexed for MEDLINE]

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**Heart rate variability and circadian variations in type 1 diabetes mellitus.**

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Diabetic autonomic neuropathy (DAN) commonly complicates diabetes and is associated with increased mortality rates over 5 yr. This fact denotes the significance of DAN prevention, mainly with effective glycemic control. However, total prevention of autonomic neuropathy in diabetic patients is not achievable. Thus, the timely detection of DAN and the use of effective means to improve autonomic nervous system function or slow down its progression become of utmost significance. Heart rate variability (HRV) is a technique that measures the beat-to-beat variability in RR intervals, which reflects changes in autonomic activity and their impact on cardiovascular function. Circadian variation in time and frequency domains of heart variability has been shown to correlate with circadian rhythm of ambulatory ischemia and suggests that relative changes in vagal and sympathetic tone at different times during the day may have a direct relationship to the severity of clinical events. Forty-seven (21 boys and 26
girls) type I insulin-dependent diabetics and 46 control subjects (19 boys and 27 girls) were included in the study. Our investigation demonstrated that overall HRV is markedly depressed in diabetes mellitus (DM). All time domain parameters except standard deviation of all 5-min mean RR intervals and all frequency domain indices maintain significant circadian variation. These changes in overall HRV and HRV circadian rhythms reflect significant reductions in cardiac parasympathetic activity and, possibly, increased sympathetic tone.

PMID: 16489974 [PubMed - indexed for MEDLINE]

Cardiac autonomic activity and Type II diabetes mellitus.

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CAN (cardiac autonomic neuropathy) is a common complication of diabetes. Meta-analyses of published data demonstrate that reduced cardiovascular autonomic function, as measured by heart rate variability, is strongly associated with an increased risk of silent myocardial ischaemia and mortality. A major problem in ischaemia-induced impairment of vascular performance in the diabetic heart is unrecognized cardiac sympathetic dysfunction. Determining the presence of CAN is based on a battery of autonomic function tests and techniques such as SPECT (single-photon emission computed tomography) and PET (positron emission tomography). Nevertheless, spectral analysis of heart rate variability seems to remain the primary technique in evaluating CAN, due to its low cost, easy use and good intra-individual reproducibility.

PMID: 15476437 [PubMed - indexed for MEDLINE]

Heart rate variability from 24-hour electrocardiography and the 2-year risk for sudden death.

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BACKGROUND. Low heart rate variability has been implicated as a risk factor for sudden death. However, no large epidemiological studies using sudden death as an outcome event have been reported. METHODS AND RESULTS. A total of 6,693 consecutive patients who underwent 24-hour ambulatory ECG were followed up for 2 years; of these, 245 patients died suddenly. Clinical data at the time of 24-hour ambulatory ECG were collected for all patients who died suddenly and for a random sample of 268 patients from the study cohort. In all patients in sinus rhythm with or without occasional supraventricular arrhythmias at the 24-hour ECG (193 patients who died suddenly and 230 patients from the sample), heart rate variability parameters were derived. Patients with low short-term RR interval variability (mean during 24 hours of per-minute standard deviations [SD] of RR intervals < 25 msec) had a 4.1-fold higher risk (95% confidence interval [CI], 2.6, 8.1) for sudden death than patients with high short-term variability (> or = 40 msec); after adjustment for age, evidence of cardiac dysfunction, and history of myocardial infarction, the relative risk was 2.6 (95% CI, 1.4, 5.1). The crude relative risk of long-term RR interval variability (SD during 24 hours of per-minute means of RR intervals < 8 msec) was 4.4 (95% CI, 2.6, 7.7); after adjustment for the same risk factors, it was 2.2 (95% CI, 1.2, 4.1). Patients with a minimum heart rate > or = 65 beats per minute had a double risk of sudden death compared with those with a minimum heart rate < 65 beats per minute (adjusted relative risk, 2.1; 95% CI, 1.3, 3.6).

CONCLUSIONS. These findings support the theory that patients with low parasympathetic
activity (low short-term RR interval variability) have an increased risk for sudden death independent of other risk factors.

PMID: 8319331 [PubMed - indexed for MEDLINE]

Cardiac autonomic nervous dysfunction in diabetic patients with a mitochondrial DNA mutation: assessment by heart rate variability.

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OBJECTIVE: To elucidate the degree and characteristics of cardiac autonomic nervous dysfunction in diabetic patients associated with a mitochondrial DNA mutation at base pair 3243.

RESEARCH DESIGN AND METHODS: We investigated heart rate variability using 24-h Holter monitoring in 10 diabetic patients with the mutation compared with 55 ordinary diabetic patients and 45 nondiabetic control subjects.

RESULTS: Age and sex were similar in the three groups. Between patients with the mutation and ordinary diabetic patients, the duration of diabetes and blood glycemic levels were not different. In the time domain analysis of heart rate variability, patients with the mutation and ordinary diabetic patients had significantly smaller SDNN index and pNN50 than control subjects. Compared with ordinary diabetic patients, patients with the mutation had smaller SDNN index (P < 0.02), but rMSSD and pNN50 were not different. In the frequency domain analysis, total, low frequency (LF), and high frequency (HF) spectra were significantly smaller in patients with the mutation and ordinary diabetic patients than in control subjects. Compared with ordinary diabetic patients, patients with the mutation had smaller total and LF spectra (P < 0.02). However, HF spectra were not significantly different. Notably, the LF/HF spectra ratio was lower in patients with the mutation than in ordinary diabetic patients and control subjects (P < 0.05), but this ratio was similar in ordinary diabetic patients and control subjects.

CONCLUSIONS: Our results suggest that diabetic patients with the mitochondrial DNA mutation have more severely impaired cardiac autonomic nervous function with sympathovagal imbalance, as compared with ordinary diabetic patients.

PMID: 12453978 [PubMed - indexed for MEDLINE]