Factors influencing heart rate variability power spectral analysis during controlled breathing in patients with chronic heart failure or hypertension and in healthy normotensive subjects

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ABSTRACT

A decreased LFP (low-frequency power) spectral component of HRV [HR (heart rate) variability] is a risk factor for sudden death in patients with CHF (chronic heart failure). In the present study, we evaluated factors (age, arterial pressures and HR) influencing LFP and HFP (high-frequency power) components in short-term recordings during controlled breathing in patients with CHF or hypertension, and healthy normotensive subjects. In patients with CHF, we also compared LFP values with known markers of sudden death [NYHA (New York Heart Association) class, HR and ejection fraction]. All HRV measures were significantly lower in patients with CHF than in hypertensive and normotensive subjects ($P < 0.001$), and in hypertensive than in normotensive subjects ($P < 0.05$). Stepwise multiple regression analysis showed that, in patients with CHF, LFP was inversely associated with NYHA class ($\beta = -0.5, P < 0.0001$) and HR ($\beta = -0.2, P = 0.001$) and was positively associated with ejection fraction ($\beta = 0.28, P < 0.0001$). In patients with CHF, LFP remained unchanged with age. In normotensive and hypertensive subjects, HFP decreased with age, but in patients with CHF it did not. In the $\geq 60 < 70$ and $\geq 70$ years of age subgroups, we found no difference between HFP in the three groups studied. Hence, in normotensives and hypertensives, LFP tended to diminish with age ($\beta = -0.4, P < 0.0001$ in normotensives; $\beta = -0.4, P < 0.001$ in hypertensives) and was inversely associated with HR ($\beta = -0.2, P = 0.002$ in hypertensives). Conversely, in patients with CHF, LFP is predominantly influenced by NYHA class, HR and ejection fraction, but not by age. LFP might therefore increase the sensitivity of factors already used in stratifying the risk of sudden death in patients with CHF.

INTRODUCTION

For more than two decades short-term power spectral analysis of HRV [HR (heart rate) variability] has been used to assess autonomic control of HR. Recently, it has also been used to stratify the risk of sudden death in subjects with CHF (chronic heart failure). Spectral analysis of recordings in normotensive healthy subjects during controlled breathing shows two distinct components of HRV: HFP (high-frequency power) [1],

Key words: aging, autonomic nervous system, heart failure, heart rate variability, spectral analysis.
Abbreviations: BMI, body mass index; LFP, low-frequency power; HR, heart rate; HRV, HR variability; CHF, chronic heart failure; HFP, high-frequency power; NYHA, New York Heart Association; TP, total power; VLFP, very-low frequency power.
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which synchronizes with breathing activity and therefore reflects vagal modulation of the sinus node, and LFP (low-frequency power) oscillating at approx. 0.1 Hz [1] influenced also, although not solely [2,3], by sympathetic modulation of the sinus node [1]. Among factors that strongly influence autonomic control of the sinus node and HRV are aging [4–6], hypertension [1,4,7] and CHF [1,8–11]. In particular, CHF causes a marked increase in catecholamine concentrations [12], accompanied by a decrease in β-adrenergic receptor function [13], and a marked decrease in baroreflex sensitivity [8,14] and vagal activity [8,15]. The more prominent these changes, the higher is the risk of sudden death due to the onset of malignant ventricular arrhythmias [16]. In short-term power spectral recordings, these conditions markedly decrease both spectral components of HRV [8–11]. Rather than increasing LFP of HRV as one might expect, excessive sympathetic stimulation decreases it [8–11,17].

The current need for more information on LFP of HRV arises from a prospective study conducted by La Rovere et al. [17] showing that LFP < 13 ms² is a risk factor for sudden cardiac death in patients with CHF. Hence we designed the present study to assess the effect of age on the two main spectral components of HRV, LFP and HFP, in subjects with CHF or hypertension and in healthy normotensive subjects. We elected to record spectral variables during controlled breathing because (i) this condition makes it easier to distinguish the two spectral components; (ii) patients allowed to breathe freely tend to be unaware of a respiratory rhythm that alters the spectral profile [18,19]; and (iii) LFP values obtained during controlled breathing are predictive of sudden death [17]. We have not reported normalized values, because normalization tends to annul spectral variance, TP (total power), between subjects with wide total variability [1] (e.g. between young persons and adults and between subjects without and with CHF) thus risking, especially in patients with CHF, confounding effects owing to the paradoxic increase in normalized units of HFP [8].

**METHODS**

**Study subjects**

In the present study, we selected 90 outpatients (49 men and 41 women) who had stable CHF secondary to primitive or ischaemic dilated cardiomyopathy, 123 hypertensive subjects attending the outpatients clinic (82 men and 41 women) and 190 healthy normotensive control subjects (105 men and 85 women). To exclude the presence of ischaemic cardiomyopathy, normotensive and hypertensive subjects underwent exercise stress testing. None of the patients with CHF had asthma, malignancy, primary valve disease, atrial fibrillation, frequent extra-systole (one extrasystole/min was permitted) or other arrhythmias likely to interfere with assessments. The clinical characteristics of the study subjects are shown in Table 1. Patients with CHF were taking standard medications for CHF, including enalapril (73 subjects: from 2.5–10 mg/day), losartan (17 subjects: 50 mg/day), furosemide (90 subjects: from 25–250 mg/day), spironolactone (82 subjects: from 25–50 mg/day), carvedilol (62 subjects: from 6.25–50 mg/day), digoxin (52 subjects: 0.125–0.250 mg/day) and acetylsalicylic acid (85 subjects: 100 mg/day). Of the 90 patients with CHF, 22 belonged to NYHA (New York Heart Association) class II, 59 to class III and 9 to class IV. The severity of anxiety was determined using the Kawachi Symptoms Score [20].

All participants gave their informed consent to the procedures, and the Ethics Committee of the Department of the Science of Ageing, University of Rome, “La Sapienza” approved the study. The study complied with the ethical rules for human experimentation stated in the Declaration of Helsinki.

**Study protocol and data acquisition**

In accordance with the testing protocol, at approx. 09.00 hours, after a 30 min rest lying down, the subject underwent assessment of HRV. During the present study all subjects had to breath at 15 breaths/min in time with a metronome, and each subject underwent a simultaneous recording from a single ECG lead (Telemetria Mortara Rangoni) and respiratory rate (strain-gauge belt). Under conditions of free breathing, subjects in all three study groups breathed at a rate of approx. 13 ± 3 breaths/min.

The two analogical signals (ECG and respiratory rate) were acquired simultaneously and digitally converted with a custom-designed card (Keithley Metrabyte – DAS

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CHF patients</th>
<th>Hypertensive subjects</th>
<th>Normotensive controls</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>26 ± 0.4</td>
<td>26 ± 0.4</td>
<td>26 ± 0.3</td>
<td>NS</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>84 ± 1*</td>
<td>72 ± 1</td>
<td>69 ± 1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>133 ± 1</td>
<td>142 ± 1</td>
<td>115 ± 1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Diastolic pressure (mmHg)</td>
<td>73 ± 1</td>
<td>88 ± 1</td>
<td>74 ± 1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Anxiety symptom score</td>
<td>1 ± 0.1</td>
<td>1 ± 0.1</td>
<td>1 ± 0.1</td>
<td>NS</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>25 ± 0.4*</td>
<td>62 ± 0.05</td>
<td>64 ± 0.4</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
Figure 1  Power spectral analysis of HRV in two normotensive subjects of different ages during controlled breathing
Upper panel, spectrum for a 50-year-old subject; lower panel, spectrum for an 80-year-old subject. The abscissa represents the frequency in Hz, the ordinate the spectral power. Note that all spectral power components were decreased in older patients. PSD, power spectral density.

Figure 2  Power spectral analysis of HRV in two patients with CHF during controlled breathing
Upper panel, spectrum from a subject who had an ejection fraction of 18% and belonged to NYHA class IV. Lower panel, spectrum from a subject who had an ejection fraction of 30% and belonged to NYHA class II. The abscissa represents the spectral frequency in Hz, and the ordinate the spectral power. In the latter subject, note that all the spectral components are decreased but, most importantly, LFP is lower than 13 ms².

1200 Series) at a sampling frequency of 500 Hz/channel with 12-bit precision.

For recognition and measurement of the RR intervals, blood pressure and respiratory rate, we used a software developed in our laboratory and based upon an automated derivative/threshold algorithm.

Stationary 256–512 beat segments (5 min) of ECG and respiratory recordings were analysed with an autoregressive algorithm [1]. We then determined TP of RR intervals, and the total spectral density of these variables. For RR intervals we calculated the following spectral components: an HFP component (oscillating approx. 0.25 Hz equivalent), an LFP component (approx. 0.1 Hz equivalent) and a VLFP (very-low frequency power) component (below 0.03 Hz equivalent; Figures 1 and 2) [1]. The resulting spectral data were transformed into the natural logarithm of the variable [1,4,6].

Data and statistical analysis
Unless otherwise indicted, all data are expressed as means ± S.E.M. All data were evaluated with database SPSS-PC+. One-way ANOVA was used to compare the general characteristics and other linear data in the study groups. To detect possible statistical differences related to age, we divided each of the three study groups into five age subsets: < 40 years of age; ≥ 40 < 50 years of age; ≥ 50 < 60 years of age; ≥ 60 < 70 years of age; and ≥ 70 years of age. Because patients with CHF who have LFP values ≤ 13 ms² are at increased risk of sudden death [17], we subdivided the CHF group into two groups: one group with LFP > 13 ms² and the other with LFP values ≤ 13 ms². We then determined possible differences in HR, ejection fraction and NYHA class between these two groups.

Because spectral data are non-linearly distributed, to compare spectral data in the three study groups we used the Kruskal–Wallis and Mann–Whitney tests. Possible associations between variables were studied with regression analysis and stepwise multiple regression models. For stepwise multiple regression analysis, we transformed the spectral data (non-linear) into their natural logarithm and considered as a dependent variables ln LFP and ln HFP, and as independent variables for each study group (CHF, hypertensive subjects and normotensive controls) age, HR, systolic and diastolic arterial pressures, BMI (body mass index), anxiety scores, NYHA class and ejection fraction. P < 0.05 was considered to indicate statistical significance.

RESULTS
Age, BMI, sex distribution or anxiety symptom scores did not differ significantly between the three study groups, whereas HR, systemic arterial pressures and ejection fractions differed significantly (Table 1). All five subgroups had similar mean intergroup age (Table 2).
### Table 2  Mean age of subjects in the different age groups

<table>
<thead>
<tr>
<th>Age groups</th>
<th>CHF patients</th>
<th>Hypertensive subjects</th>
<th>Normotensive controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>90</td>
<td>123</td>
<td>190</td>
</tr>
<tr>
<td>&lt; 40 years of age</td>
<td>33 ± 1 (n = 12)</td>
<td>34 ± 1 (n = 13)</td>
<td>32 ± 1 (n = 40)</td>
</tr>
<tr>
<td>≥ 40 &lt; 50 years of age</td>
<td>44 ± 0.6 (n = 13)</td>
<td>44 ± 0.5 (n = 23)</td>
<td>44 ± 0.5 (n = 34)</td>
</tr>
<tr>
<td>≥ 50 &lt; 60 years of age</td>
<td>54 ± 0.5 (n = 20)</td>
<td>54 ± 0.5 (n = 31)</td>
<td>54 ± 0.5 (n = 32)</td>
</tr>
<tr>
<td>≥ 60 &lt; 70 years of age</td>
<td>64 ± 0.5 (n = 30)</td>
<td>64 ± 1 (n = 26)</td>
<td>64 ± 0.5 (n = 50)</td>
</tr>
<tr>
<td>≥ 70 years of age</td>
<td>76 ± 0.5 (n = 15)</td>
<td>77 ± 1 (n = 30)</td>
<td>76 ± 1 (n = 34)</td>
</tr>
</tbody>
</table>

### Table 3  Spectral variables for HRV in patients with CHF, hypertensive subjects and normotensive controls

Values are median (interquartile range). Interquartile range is calculated as 75th percentile — 25th percentile. Central frequencies of LFP and HFP are expressed in Hz equivalents (Hz Eq) as means ± S.D. P values refer to ANOVA calculated between the three study groups. *P < 0.05 and **P < 0.001 compared with hypertensive subjects and normotensive controls; †P < 0.05 compared with normotensive controls. NS, not significant.

<table>
<thead>
<tr>
<th>Variables</th>
<th>CHF patients</th>
<th>Hypertensive subjects</th>
<th>Normotensive controls</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>90</td>
<td>123</td>
<td>190</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>RR interval (ms)</td>
<td>714 (87)**</td>
<td>845 (179)</td>
<td>882 (153)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>TP (ms²)</td>
<td>216 (102)**</td>
<td>542 (526)</td>
<td>743 (791)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LFP (ms²)</td>
<td>28 (26)**</td>
<td>190 (231)</td>
<td>255 (313)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LFP central frequency (Hz Eq)</td>
<td>0.100 ± 0.0001</td>
<td>0.999 ± 0.0002</td>
<td>0.101 ± 0.0002</td>
<td>NS</td>
</tr>
<tr>
<td>HFP (ms²)</td>
<td>35 (30)*</td>
<td>59 (87)†</td>
<td>82 (104)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HFP central frequency (Hz Eq)</td>
<td>0.251 ± 0.0001</td>
<td>0.252 ± 0.0002</td>
<td>0.250 ± 0.0001</td>
<td>NS</td>
</tr>
<tr>
<td>LFP/HFP</td>
<td>0.7 (0.8)**</td>
<td>3 (5)</td>
<td>5 (4)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

### Table 4  LFP values according to age

Values are median (interquartile range). Interquartile range is calculated as 75th percentile — 25th percentile. P values refer to ANOVA calculated between the various study groups of the same age. Between-group analysis indicated that there were significant differences between the values obtained in CHF patients compared with hypertensive subjects and normotensive controls in each of the age groups. *P < 0.05 compared with ≥ 40 < 50, ≥ 50 < 60 and ≥ 60 < 70 years of age groups; †P < 0.001 compared with ≥ 70 years of age group; ‡P < 0.05 compared with the ≥ 70 years age group.

<table>
<thead>
<tr>
<th>Age group</th>
<th>CHF patients</th>
<th>Hypertensive subjects</th>
<th>Normotensive controls</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>90</td>
<td>123</td>
<td>190</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>&lt; 40 years of age</td>
<td>24 (24) (n = 12)</td>
<td>340 (394) (n = 13)**†</td>
<td>413 (455) (n = 40)**†</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>≥ 40 &lt; 50 years of age</td>
<td>24 (29) (n = 13)</td>
<td>224 (173) (n = 23)‡</td>
<td>323 (400) (n = 34)‡</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>≥ 50 &lt; 60 years of age</td>
<td>23 (28) (n = 20)</td>
<td>169 (258) (n = 31)</td>
<td>251 (263) (n = 32)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>≥ 60 &lt; 70 years of age</td>
<td>35 (32) (n = 30)</td>
<td>178 (238) (n = 26)</td>
<td>201 (231) (n = 50)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>≥ 70 years of age</td>
<td>30 (10) (n = 15)</td>
<td>132 (193) (n = 30)</td>
<td>129 (318) (n = 34)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

All spectral variables had significantly lower values in patients with CHF than in normotensive healthy controls and hypertensive subjects. The values were also lower in hypertensive subjects compared with control subjects (TP, P < 0.05; LFP, P < 0.05; and HFP, P < 0.05; Table 3).

The age-related effects on the two spectral power components of HRV differed in each study group. In patients with CHF, neither LFP nor HFP differed in the various age subgroups (Tables 4 and 5). Conversely, in hypertensive and normotensive controls, LFP was significantly higher in the < 40 years of age group than
in the other age groups and significantly higher in the 40–50 years of age groups than in the oldest age group (≥70 years; Table 4). In normotensive subjects, HFP was significantly higher in those <40 years of age than in all the other age groups, and was higher in the 40–50 years of age group compared with the two oldest age decades (Table 5). By contrast, in hypertensive subjects, HFP behaved differently: HFP values in the two younger age groups were significantly higher only when compared with subjects ≥70 years of age.

No difference was found in the central frequency of LFP either in the three study groups or in the age subsets (Table 3).

Of the 90 patients with CHF, 72 had LFP ≥13 ms², whereas 18 had LFP ≤13 ms²: the group with lower LFP had a significantly lower ejection fraction (19 ± 0.7 compared with 26 ± 0.4% respectively; P < 0.001) and a higher HR (91 ± 1.5 compared with 82 ± 0.6 beats/min; P < 0.001). Of the 18 subjects with LFP ≤13 ms², nine belonged to NYHA class III and nine to class IV. In patients with CHF, multiple stepwise regression identified only three variables as significantly associated with ln LFP (R² = 0.4, P < 0.0001): NYHA class (b = −0.9 ± 0.1, β = −0.5, t = −8, P < 0.0001), the ejection fraction (b = 0.0 ± 0.02, β = 0.28, t = 4, P < 0.0001) and HR (b = −3.0 ± 0.01, β = −0.2, t = −3, P = 0.001); constant term (b = 7.0 ± 1.0, t = 7, P < 0.0001). Linear regression analysis identified similar associations (Figure 3). Stepwise regression considering ln HFP as the dependent variable failed to confirm the significance of these variables (NYHA class: b = −0.3 ± 0.2, β = −0.2, t = −2, P = 0.109; ejection fraction: b = 0.02 ± 0.02, β = 0.1, t = 0.9, P = 0.362; and HR: b = 0.008 ± 0.015, β = 0.062, t = 0.5, P = 0.6).

In both groups without CHF, ln LFP was negatively associated with HR (for both groups r = −0.3, P < 0.0001; Figure 4).
(b = −0.02 ± 0.007, β = −0.3, t = −3, P = 0.002); constant term (b = 8 ± 0.687, t = 12, P < 0.0001).

The normotensive group showed the same associations (R² = 0.2, P < 0.0001): age (b = −0.03 ± 0.004, β = −0.4, t = −6, P < 0.0001) and HR (b = −0.02 ± 0.007, β = −0.2, t = −3, P = 0.002); constant term (b = 8 ± 0.579, t = 14, P < 0.0001) (Figure 4). In normotensive and hypertensive subjects, no other significant differences were found between LFP and the other non-spectral variables studied. Stepwise regression detected no significant differences in ln HFP among the three study groups.

**DISCUSSION**

The two spectral components of HRV studied (HFP and LFP) were both lower in patients with CHF than in hypertensive subjects and healthy normotensive controls. In patients with CHF, LFP, whose decrease seems to be the most predictive marker of sudden cardiac death [9,17], diminished as the HR and NYHA class increased and the ejection fraction decreased, but showed no relationship with age. Conversely, in subjects without CHF (hypertensive subjects and normotensive controls), LFP was inversely related to age and HR.

Precisely why LFP decreased paradoxically in our patients with CHF is unclear. One explanation might be oversaturation of spectral signal, reflecting autonomic control of HR [10,21,22]. Although spectral analysis provides a qualitative and quantitative assessment of RR interval oscillations, in the presence of sympathetic overactivity, for example in CHF, the sympathetic spectral component (LFP) loses its characteristic oscillations at frequencies at approx. 0.10 Hz (Mayer waves) and, therefore, seems to diminish [10]. In patients with CHF, a paradoxical decrease in LFP [9–11] below a threshold value of 13 ms² is a risk factor for sudden cardiac death from malignant arrhythmias [17].

Given that LFP below the threshold of 13 ms² is a highly sensitive marker for selecting patients at risk for sudden cardiac death, the present findings suggest that the currently accepted risk factors (NYHA class, ejection fraction and HR) assessed singly are not sufficiently precise. Using 13 ms² as the threshold LFP value to identify patients with CHF at risk of sudden cardiac death [17], we found that as many as nine out of 59 (15 %) patients belonging to NYHA class III had values below the threshold and should therefore be at greater risk of sudden death (Figure 3). Furthermore, the patient who had the lowest LFP value (0 ms²), presumably therefore at higher risk of sudden death, was not the patient with the lowest ejection fraction (Figure 3). As equally important, although all subjects in the CHF group studied who had LFP under the threshold risk value had HRs exceeding 90 beats/min, some subjects whose LFP exceeded 13 ms² also had HRs ≥ 90 beats/min (Figure 3). Including the

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LFP variable among the accepted factors already used in stratifying the risk of sudden death in patients with CHF might therefore increase their diagnostic sensitivity.

The age-related decline in LFP observed in hypertensive and normotensive subjects is consistent with the association of low LFP and a greater risk of death from all causes in a cohort of elderly persons observed over 10 years in the Framingham retrospective study [23]. The Kaplan–Meier survival curves showed a direct relationship between tertiles of LFP and survival: the tertile with LFP < 218 ms² had a significantly higher overall risk of death than subjects in the first (LFP > 219.9 < 415.5 ms²) and second tertiles (LFP > 415.8 ms²). In the present study, in the group of subjects older than 60 years of age, who did not belong to the CHF group, 60% (84 of 140) had LFP < 218 ms². Although the Framingham data obtained with different methods are hard to compare with those in the present study, we consider that current findings warrant investigation in a prospective study.

Another characteristic phenomenon was the lack of correlation between age and HFP in patients with CHF (non-significant stepwise regression analysis). We found significant differences in HFP values only in the three youngest age groups (< 40, ≥ 40 < 50 and ≥ 50 < 60 years of age); no difference between HFP values in the two older groups (≥ 60 < 70 and ≥ 70 years of age; Table 5). Hence, as would be expected, vagal modulation of the sinus node seems depressed in patients with CHF, exactly as it is in elderly normotensive and hypertensive subjects. This phenomenon may have more than one explanation. The first possibility is that among apparently healthy subjects or those with systemic hypertension alone some have coronary artery disease that exercise testing leaves undisclosed and, thus, a spectral profile similar to patients with CHF [24]; or more likely aging, or the decreased physical activity that often accompanies aging, could diminish vagal modulation of the sinus node as it does in CHF. Because healthy elderly subjects and elderly patients with CHF have similar HFP values, HFP probably has no prognostic value in elderly persons with CHF; low HFP values might nevertheless have prognostic value in younger patients with CHF.

The present study also yielded interesting information on the factors influencing the two spectral power components in subjects without CHF (hypertensive and normotensive subjects). Even though the HFP and LFP components, especially LFP, diminished substantially with age in both groups, due to the wide data dispersion despite log-transformation, the association between LFP and age had a low correlation coefficient (see Results section and Figure 4). An age-related decrease has already been described for LFP [4] and also for other spectral variables, including baroreflex sensitivity or α index [25,26], and probably has the same clinical meaning [27]. This age-related trend probably reflects differences in data dispersion in the various age subgroups. Data dispersion did not diminish with age (Table 4), especially in normotensive subjects. On the contrary, healthy subjects in the ≥ 70 years of age subgroup had more widely dispersed LFP values than their middle-aged counterparts (> 50 < 60 and ≥ 60 < 70 years of age).

Another finding of interest is the spectral differences in HRV between hypertensive and normotensive subjects. All subjects with higher arterial pressures than normotensive subjects had a significant decrease in all spectral variables and in TP (Table 3). These differences, which have already been reported by others [4], were not associated with a particular age range (Tables 4 and 5).

The data from the present study indicate that, whereas in hypertensive and normotensive subjects LFP tends to diminish with age, in young patients with CHF, LFP is already so low that it remains unchanged with age. The prognostic importance of these findings merits verification in future prospective studies.

REFERENCES


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