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Hemodynamic changes in depressive patients

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Abstract: Objective: This study is aimed at exploring the relationship between hemodynamic changes and depressive and anxious symptom in depression patients. Methods: The cardiac function indices including the left stroke index (LSI), ejection fraction (EF), heart rate (HR), diastolic pressure mean (DPM), systolic pressure mean (SPM), left ventricle end-diastolic volume (LVDV), effective circulating volume (ECV), resistance total mean (RTM) and blood flow smooth degree (BFSD) were determined in 65 patients with major depressive disorders and 31 healthy normal controls. The clinical symptoms were assessed with Hamilton depression scale (HAMD) and Hamilton anxiety scale (HAMA). Results: In patients with depression without anxiety, LSI, EF, LVDV, DPM, SPM, ECV, BFSD were significantly lower than those in controls, while RTM was higher than that in controls. Patients with comorbidity of depression and anxiety showed decreased LVDV, ECV, BFSD, and increased HR in comparison with the controls. The anxiety/somatization factor score positively correlated with LSI, EF, LVDV, but negatively correlated with RTM. There was negative correlation between retardation factor score and DPM, SPM, LVDV. Conclusion: The study indicated that there are noticeable changes in left ventricle preload and afterload, blood pressure, peripheral resistance, and microcirculation in depressive patients, and that the accompanying anxiety makes the changes more complicated.

Key words: Depression, Anxiety, Heart function tests
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INTRODUCTION

In recent years, more attention has been paid to the relationship between major depressive disorder and cardiovascular disease, relevant studies mainly focused on epidemiological investigation (Black and Markides, 1999; Penninx *et al*., 2001) and pathophysiological mechanism exploration (Laghrissi-Thode *et al*., 1997; Agelink *et al*., 2001; Lespérance *et al*., 2004). To our knowledge, there are no reports on the impairment of cardiovascular function when patients are in depressive state. Therefore, by applying heart function detecting technique without wounds, we examined 9 cardiovascular indices in 65 patients with depression to explore which indices of cardiac function were abnormal as well as the relationship among these indices and the depressive and accompanying anxiety symptoms from the hemodynamic visual angle.

SUBJECTS AND METHODS

Patients and samples

Sixty-five patients aged 19 to 55 years old (mean (37±10) years; 30 men and 35 women) who were outpatients or inpatients from the Department of Psychiatry, the Second Affiliated Hospital, School of Medicine, Zhejiang University, China from Jan. 2003 to Mar. 2004 were included in our study. They were diagnosed as major depression patients according to the third China diagnostic criteria of mental disorders, they must have total score of over 20 in Hamilton depression scale (HAMD, 24 items) and no other mental disorders; those suffering from a combination of any disease of the heart, brain, liver and kidney were excluded. All subjects had not taken any antidepressants and drugs which can affect the cardiovascular function within two months before cardiovascular function examination.

In order to know whether anxiety can bring out different effect on cardiac function, we divided the patients into depression without anxiety group (HAMA<14) and depression accompanying anxiety group (HAMA≥14) according to their total score of Hamilton anxiety scale (HAMA). The former comprised 34 cases (16 men and 18 women) aged from 19 to 54 years old (mean (35±10) years), the latter comprised 31 cases (14 men and 17 women) aged from 19 to 55 years old (mean (39±10) years).

Thirty-one healthy volunteers were recruited from the adults who took health examination in our hospital and were proved to have no any psychiatric and/or somatic disease (15 men and 16 women, aged 21~60 years, mean (38±10) years). Their total HAMD and HAMA scores were all less than 7. There were no significant difference in age and sex among the three groups.

Scales evaluation

The clinical symptoms of the subjects were assessed with HAMD and HAMA by one psychiatrist before their indices of cardiovascular function were examined.

Cardiovascular function examination

All subjects performed the tests at 9~10 o'clock of morning, and must sit silently more than 15 min before their blood pressure, body height and weight were measured. After that, they were required to lie down and hold their breath for 10 s while a senior lab experimenter collected their 4 physio-signal of body surface with a cardiac function analysator of QXG-IIIA type: arterial tracing, phlebogram, electrocardiogram and cardiac sound (Zhang and Lou, 1998). The data were processed by microcomputer. We mainly observed 9 indices: left stroke index (LSI), ejection fraction (EF), heart rate (HR), diastolic pressure mean (DPM), systolic pressure mean (SPM), left ventricle end-diastolic volume (LVDV), effective circulating volume (ECV, is the effective blood volume participating in the general circulation which is determined by the total blood volume and the volume of the vascular bed), resistance total mean (RTM) and blood flow smooth degree (BFSD, reflects if the blood flow is uniform and advantageous for the exchange of nutritive substance in the microcirculation).

Statistical analysis

All the data in the study were processed by SPSS 11.0 package. Pearson's correlation analysis was first used to find the dependability among the total score and factor score of HAMD and all indices. One-way ANOVA was used for comparing the differences in all indices among each group. Statistical significance was defined as $P<0.05$.

RESULTS

Correlation analysis of each cardiac function index and the HAMD score

Table 1 shows the anxiety/somatization factor score positively correlated with LSI, EF, LVDV, but negatively correlated with RTM. There was negative correlation between retardation factor score and DPM, SPM, LVDV, total score, with other factor score having no correlation with each index.

Comparison of cardiac function indices among two patient groups and controls

Form Table 2, the analysis results by ANOVA showed significant group differences in all indices

Table 1 Correlation analysis of each cardiac function index and the HAMD score in 65 patients with depression (*r*)

HAMD factor	*LSI*	*EF*	*HR*	*DPM*	*SPM*	*LVDV*	*ECV*	*RTM*	*BFSD*
Total score	0.276	0.253	0.075	−0.139	−0.051	0.104	−0.176	−0.103	0.178
Anxiety/somatization	0.397*	0.447#	0.023	0.152	0.320	0.410*	0.046	−0.370*	0.171
Weight	0.046	0.033	−0.136	−0.049	−0.028	−0.042	−0.296	−0.114	−0.106
Cognition disorder	0.295	0.229	0.080	−0.135	−0.031	0.119	−0.143	−0.164	0.135
Day and night change	−0.187	−0.265	−0.087	−0.152	−0.247	−0.311	0.019	0.297	−0.026
Depression/retardation	−0.118	−0.156	−0.029	−0.353*	−0.401*	−0.331*	−0.203	0.053	−0.005
Sleep disorder	−0.208	−0.155	−0.075	0.162	0.073	0.047	0.159	0.310	0.198
Feeling of despair	0.173	0.084	0.199	−0.311	−0.292	−0.146	−0.255	0.061	−0.027

*$P<0.05$; #$P<0.01$

except HR (P<0.01 or 0.05). Further multiple comparison showed that in patients with depression without anxiety, the LSI, EF, DPM, SPM, LVDV, ECV, BFSD indices were significantly lower than those in controls, while RTM was higher than that in controls (P<0.01 or 0.05). The patients with comorbidity of depression and anxiety showed decreased LVDV, ECV, BFSD, and increased HR in comparison with the controls (P<0.01 or 0.05). Other interclass differences had no statistical significance. LSI, EF, SPM and LVDV in patients with depression without anxiety were lower than those in patients with comorbidity of depression and anxiety, but RTM was higher (P<0.01 or 0.05).

DISCUSSION

Epidemiologic studies proved that depression is an independent risk factor for cardiovascular disease, and can cause higher morbidity and mortality rates especially in patients with coronary disease (Penninx *et al*., 2001; Thornton, 2001).

At first, we carried out correlation analysis of each cardiac function index of 65 patients and of the HAMD score. The results showed that only the anxiety/somatization factor score positively correlated with LSI, EF, LVDV, but negatively correlated with RTM, which showed that the more serious the anxiety is, the less the afterload, the bigger the preload and the larger the cardiac output is, with the patients showing more somato-complaint symptoms. Whereas there was negative correlation between retardation factor score and DPM, SPM, LVDV, which indicates that the more serious the depression is, the less the preload and the lower the blood pressure is. The total score and other factor score having no correlation with the indices reveals that the factors which mainly influence patient's cardiovascular function are the core symptoms of major depression and the accompanying anxiety.

In general, major depression and anxiety occur simultaneously (Nutt, 1997). The above results of correlation analysis reveal that depression and anxiety might bring out different, even opposite, effects on cardiovascular function, so we divided the patients into depression without anxiety group and depression accompanying anxiety group to study.

Patients with depression invariably have the symptoms of decreased appetite and loss of weight, etc., which can induce hypovolemia. Recent studies found that platelets aggregation can increase (Laghrissi-Thode *et al*., 1997), the function of endotheliocytes can be activated (Lespérance *et al*., 2004) and lipid metabolism processes can be mixed up (Olusi and Fido, 1996) when depression occurs. All these can slow down BFSD and thereby make returned blood volume further decreased, and finally cause decreased LVDV, leading to decreased left ventricle preload, weakened myocardial contractility, and decreased stroke volume, which can explain the consequently decreased LSI and EF in patients with depression without anxiety.

This study on heart rate variability showed that there are autonomic function disturbances in depressive patients, showing decreased cardiac vagal function, relatively higher sympathetic activity and increased catecholamine secretion (Stein *et al*., 2000;

Table 2 Comparison of cardiac function indices among two patient groups and controls ($\bar{x}\pm s$)

Indices	Depression without anxiety	Depression accompanying anxiety	Controls	ANOVA	
				F	P
LSI (ml/m^2)	41.3±12.4^{a,d}	49.9±15.0	50.6±8.5	4.649	0.013
EF	0.54±0.10^{b,c}	0.62±0.11	0.60±0.06	5.278	0.007
HR (times/min)	70.4±6.9	74.2±12.2^{e}	68.0±9.0	2.758	0.070
DPM (mmHg)	74.3±6.6^{c}	77.1±9.5	79.4±5.6	3.366	0.040
SPM (mmHg)	92.1±9.7^{a,c}	100.0±14.7	97.6±7.2	3.301	0.043
LVDV (ml)	111±9^{a,d}	117±11^{f}	129±6	33.62	0.000
ECV (ml)	2528±610^{c}	2340±623^{f}	2880±540	5.849	0.004
RTM (N·S/cm^5)	17.1±4.0^{a,c}	14.9±3.5	14.9±2.3	3.880	0.025
BFSD	0.15±0.05^{d}	0.15±0.00^{f}	0.26±0.05	47.88	0.000

Depression without anxiety group compared to depression accompanying anxiety group: ^{a}P<0.05, ^{b}P<0.01; Depression without anxiety group compared to controls: ^{c}P<0.05, ^{d}P<0.01; Depression accompanying anxiety group compared to controls: ^{e}P<0.05, ^{f}P<0.01

Agelink *et al*., 2001), to make the peripheral vas constricted, and increase peripheral resistance. Increased cardiac afterload further decreases the output to inevitably induce decrease of blood pressure especially diastolic pressure, although systolic pressure can still be influenced by peripheral resistance. In our study, the rise of systolic pressure due to increase of RTM was not sufficient for compensating for the decreased systolic pressure due to decreased cardiac output, so DPM in patients with depression without anxiety decreased. This finding disagrees with Light *et al*.(1998)'s results which indicated both diastolic pressure and systolic pressure increased when the depressive patients were in quiescent condition.

Many studies showed that there were increased sympathetic activity (Yeragani *et al*., 1995; Cohen *et al*., 2000) and enhancement of the hypothalamus-pituitary-adrenal axis (Gerra *et al*., 2000) when patients were in the anxiety state, which can result in enhanced myocardial contractility, increased cardiac output and high blood pressure. Binding correlation analysis, different results of comparison among two patient groups and controls, regarding LSI, EF, LVDV, DPM, SPM and RTM have explained that anxiety causes adverse effects compared with depression alone, and that the last results are related to the degree of the depression and the accompanying anxiety.

Carney *et al*.(1999)'s study showing that the resting heart rate increased in patients with coronary heart disease accompanied by depressive symptoms, but without difference in heart rate between the patients with depression without anxiety and controls in our study may be related to the heterogeneity of subjects and serious degree of depression. In our study, HR in the patients with depression accompanying increasingly significant rise in anxiety may indicate that the additive effect of depression and anxiety on sympathetic activity induced the HR increase at last.

CONCLUSION

Because of the limited cases of patients, we did not group and conduct research on the patients according to the times of depression episode and the course of the disease. But the initial results showed that there are noticeable changes in left ventricle preload and afterload, blood pressure, microcirculation, peripheral resistance in patients with depressive episode, and the accompanying anxiety would make it more complicated. The continuing changes of cardiovascular function would develop to organic damage at last if depression were not treated in time. Therefore, it is necessary and very important to treat the major depression disorder promptly and thoroughly not only for improving emotion, but also for decreasing the morbidity and mortality of cardiovascular disease.

References

Agelink, M.W., Majewski, T., Wurthmann, C., Postert, T., Linka, T., Klieser, E., 2001. Autonomic neurocardiac function in patients with major depression and effects of antidepressive treatment with nefazodone. *J. Affect. Disord.*, **62**(3):187-198. [doi:10.1016/S0165-0327(99)00202-5]

Black, S.A., Markides, K.S., 1999. Depressive symptoms and mortality in older Mexican Americans. *Ann. Epidemiol.*, **9**(1):45-52. [doi:10.1016/S1047-2797(98)00025-8]

Carney, R.M., Freediand, K.E., Veith, R.C., Cryer, P.E., Skala, J.A., Lynch, T., Jaffe, A.S., 1999. Major depression, heart rate, and plasma norepinephrine in patients with coronary heart disease. *Biol. Psychiatry*, **45**(4):458-463. [doi:10.1016/S0006-3223(98)00049-3]

Cohen, H., Benjamin, J., Geva, A.B., Matar, M.A., Kaplan, Z., Kotler, M., 2000. Autonomic dysregulation in panic disorder and in post-traumatic stress disorder: application of power spectrum analysis of heart tate variability at rest and response to recollection of trauma or panic attacks. *Psychiatry Res.*, **96**(1):1-13. [doi:10.1016/S0165-1781(00)00195-5]

Gerra, G., Zaimovic, A., Zambelli, U., Timpano, M., Reali, N., Bernasconi, S., Brambilla, F., 2000. Neuroendocrine responses to psychological stress in adolescents with anxiety disorder. *Neuropsychobiology*, **42**(2):82-92. [doi:10.1159/000026677]

Laghrissi-Thode, F., Wagner, W.R., Pollock, B.G., Johnson, P.C., Finkel, M.S., 1997. Elevated platelet factor 4 and beta-thromboglobulin plasma levels in depressed patients with ischemic heart disease. *Biol. Psychiatry*, **42**(4):290-295. [doi:10.1016/S0006-3223(96)00345-9]

Lespérance, F., Frasure-Smith, N., Theroux, P., Irwin, M., 2004. The association between major depression and levels of soluble intercellular adhesion molecule 1, interleukin-6, and C-reactive protein in patients with recent acute coronary syndromes. *Am. J. Psychiatry*, **161**(2):271-277. [doi:10.1176/appi.ajp.161.2.271]

Light, K.C., Kothandapani, R.V., Allen, M.T., 1998. Enhanced cardiovascular and catecholamine responses in women with depressive symptoms. *Int. J. Psychophysiol.*, **28**(2):157-166. [doi:10.1016/S0167-8760(97)00093-7]

Nutt, D.M., 1997. Management of patients with depression associated with anxiety symptoms. *J. Clin. Psychiatry*, **58**(Suppl 8):11-16.

Olusi, S.O., Fido, A.A., 1996. Serum lipid concentrations in patients with major depressive disorder. *Biol. Psychiatry*, **40**(11):1128-1131. [doi:10.1016/S0006-3223(95)00599-4]

Penninx, B.W., Beekman, A.T., Honig, A., Deeg, D.J., Schoevers, R.A., van Eijk, J.T., van Tilburg, W., 2001. Depression and cardiac mortality: results from a community-based longitudinal study. *Arch. Gen. Psychiatry*, **58**(3):221-227. [doi:10.1001/archpsyc.58.3.221]

Stein, P.K., Crney, R.M., Freedland, K.E., Skala, J.A., Jaffe, A.S., Kleiger, R.E., Rottman, J.N., 2000. Severe depression is associated with markedly reduced heart rate variability in patients with stable coronary heart disease. *J. Psychosom. Res.*, **48**(4-5):493-500. [doi:10.1016/S0022-3999(99)00085-9]

Thornton, L.A., 2001. Depression in post-acute myocardial infarction patients. *J. Am. Acad. Nurse Pract.*, **13**(8):364-367.

Yeragani, V.K., Pohl, R., Srinivasan, K., Balon, R., Ramesh, C., Berchou, R., 1995. Effects of isoproterenol infusions on heart rate variability in patients with panic disorder. *Psychiatry Res.*, **56**(3):289-293. [doi:10.1016/0165-1781(95)02608-Y]

Zhang, M.F., Lou, F.Q., 1998. Investigation of risk factors in 95 patients with decreasing ejection fraction. *Chin. J. Cardiac. Func.*, **10**(3):160-162 (in Chinese).