Depression in Survivors of Acute Myocardial Infarction

Aneta Spasovska Trajanovska¹, Jorgo Kostov², Zanina Perevska³

ABSTRACT

Introduction: There was growing evidence of increased cardiovascular risk in patients with depressive disorders. Aim: To determine the percentage of depression in the three investigated groups of patients with myocardial infarction and to determine the correlation between sociodemographic characteristic and level of depression in survivors of AMI. Methods: The study was designed as an observation cross-section including 120 patients treated at the University Clinic of Cardiology Skopje during 2018-2019 year, observed as 3 groups: group 1 was presented with patients during hospitalization for AMI, group 2 were patients survivors after 3 months of the acute coronary event and group 3 patients survivors after 12 months of the acute coronary event. Depression status was assessed using BDI. Results: The three groups presented almost equal representation of depression according BDI (X²=1,182, df=2, p=0,913) presented with 34,1 %, 30,8% and 30% respectively. The three groups of patients did not show significant difference according distribution of gender smoking , physical activity, stress, diabetes mellitus, age, mean BMI, Systolic BP, age of education and marital status. Only group 3 presented significantly higher diastole BP comparing in group 1 and group 2 (F=9,532, df=2,p< 0,001). The depression (BDI score) in examination groups was associated with sociodemographic and clinical parameters where female gender, higher education level, decreased BMI, smoking, decreased physical activity, younger age and single status are independent predictors of depression in patients who survived acute myocardial infarction. Conclusion: The results obtained in our study showed indicative representation of depression in patients survivors of AMI and significant association with sociodemographic and clinical parameters as predictors of depressive disorder. Regular screening for depression in patients survivors of AMI may improve the therapy decision, prognosis and the quality of patients’life. Keywords: patients, myocardial infarction, depression, sociodemographic parameters, therapy.

1. INTRODUCTION

During the last decade it was found that the history of depressive disorders increased the risk of acute myocardial infarction (AMI) according to the Epidemiological Catchment Area study (1, 2). Despite evidence that depression may be an independent risk factor for AMI, the relationship that underscores this significant association remains poorly understand (3, 4). One of the postulated path physiological mechanisms explain these findings with deregulation of the serotonin transporter leading to increased platelet activation in patients with depression, further accounting for increased coagulopathy and coronary obstruction (5). In some individuals with AMI a disruption in an atherosclerotic plaque and resulting platelet activation and aggregation leads to the development of a coronary thrombosis and an acute cardiovascular event (6). Platelets have the highest concentration of serotonin in the whole organism. There is similarity in serotonergic structures in platelets and in neuronal CNS. The difference is that the platelets do not synthesize serotonin because of that the total amount of serotonin in platelets occurs exclusively as a result of active intake (2). The serotonin transmitter SHTT located on the platelet membrane allows the insertion of serotonin from the blood plasma into the cytoplasm of the platelet. During the injection, a portion of the serotonin can be decomposed from an MAO enzyme, while the rest is stored in delta granules (vesicles),(6,1). The serotonin also participates in the complex process of blood coagulation. In this process, serotonin is released from the delta platelet granules through the process of
exocytosis resulting in released serotonin, which binds to the 5HT2A receptors located on the platelet membrane. By binding serotonin to the receptors, a platelet response occurs, such as change in the shape of the platelets with decreased synthesis of the inhibitor of aggregation; thus the change of the shape of the platelets results in structural changes of the platelet receptors, allow them to bind to molecules of fibrinogen and bridges to be created between the platelets aggregation and thrombosis. (6, 7). Several studies have found changes in platelet aggregation and platelet serotonin uptake, decreased platelet serotonin transporters in central nervous system and platelet membranes, and alterations in platelet serotonin binding in depressed individuals (4, 5)). This may indicated the existence of subgroup of AMI with depression that have a distinct underlying biological response to serotonin regulation in the both the brain and periphery in depression other healthy individuals (4). One of the greatest challenges in the research on the prospective association of depression with AMI is that atherosclerosis may facilitate depressive symptoms (vascular depression). Recurrent depression has considerably stronger association with AMI then single depressive episodes (4) as well as distinctive sociodemographic characteristic (8, 9).

2. AIM

Aim of this cross-sectional study was to determine the percentage of depression (BDI >10) of the three investigated groups of patients with myocardial infarction and to determine the correlation between sociodemographic characteristic and level of depression in survivors of AMI.

3. METHODS

The patients of this cross-section study were examination in the University Clinic of Cardiology Skopje during 2018-2019 year. The study was approved by the regional ethics committee for research. All participants gave written consent. We evaluated prevalence of depression in 120 patients—survivors of AMI. The patients were observed in the University Clinic of Cardiology Skopje during 2018-2019 year. The study was approved by the regional ethics committee for research. All participants gave written consent. We evaluated prevalence of depression in 120 patients—survivors of AMI. The patients were observed in 3 groups: group 1 was presented with patients during hospitalization for AMI, group 2 were patients survivors after 3 months of the acute coronary event and group 3 patients survivors after 12 months of the acute coronary event, For the collection of data we use medical documentation (history of illness and an outpatient diary). The sociodemographic data included in the analysis were: age, gender, marital status (single and married), education (years of schooling) The life-style characteristics were analyzed evaluating tobacco smoking status (smoker, non-smoker), psychical activity, stress. In our study we also evaluated blood pressure and body mass index (BMI). Depressive symptoms were measured using the Beck depression Inventory (BDI). The BDI is self—report 21-items screening instruments used to screen for assess the severity of depressive symptoms. The total BDI scores the sum of all items and ranges from 0—63. The score ≥10 of BDI considered positive for depressive symptoms, Acute myocardial infarction was diagnosed according to the European society of cardiology consensus guidelines. Criteria for AMI included specific clinical symptoms according to case history information (typical pains, changes in blood levels of cardiac enzymes and specified ECG changes). We excluded participants with cancer, asthma, diabetes mellitus, other endocrine disorders and autoimmune diseases. The differences between observed groups were tested with Chi-square (categorical data) and analysis of variance (ANOVA) for continuous variables and using Turkey test to define the significant inter groups difference. The correlation between BDI and the sociodemographic and clinical parameters was tested with p—Spearman coefficient. The association of the predictors (independent variables) with the dependent variable (BDI) was tested with multiple linear regression analysis. The data with non-parametric distribution were log transformed. The data analyses were performed using SPSS for Windows (ver. 25).

4. RESULTS

The three groups of patients did not show significant difference according distribution of gender (X²=2,368, df=2, P>0,05) smoking (X²=1,731, df=2, P>0,05) physical activity(X²=5,924 df=2, P>0,05), stress (X²=4,367, df=2, P>0,05), diabetes mellitus (X²=1,097 df=2, P>0,05), age(F=1,357 df=2, P>0,05), BMI (F=0,159 df=2, P>0,05), BDI (F=0,015 df=2, P>0,05), Systolic BP (F=0,049 df=2, P>0,05), age of education(F=0,996 df=2, P>0,05)and marital status (X²=5,315 df=2, P>0,05). Only group 3 presented significantly higher diastole BP comparing in group 1 and group 2 (F=11,095, p= 0,000), (table 1)

| Parameter                           | Group 1 (N=41) | Group 2 (N=39) | Group 3 (N=40) | p   |
|-------------------------------------|---------------|---------------|---------------|-----|
| Gender (m/f)                        | 70,7/29,3     | 84,6/15,4     | 80,0/20,0     | ns  |
| Age (years)                         | 63,546,2      | 61,449,2      | 60,748,5      | ns  |
| BDI                                 | 10,6±3,9      | 10,3±4,4      | 10,1±4,6      | ns  |
| Smoking (Y/N)                       | 66,7±33,3     | 62,2±57,8     | 52,5±47,5     | ns  |
| Physical activity (Y/N)            | 36,6±63,4     | 53,8±46,2     | 27,5±72,5     | ns  |
| Stress (Y/N) %                      | 78,0/22,0     | 74,4/25,6     | 57,5/42,5     | ns  |
| BMI (kg/m²)                         | 26,2±4,4      | 26,30±4,3     | 26,4±5,5      | ns  |
| DM (Y/N)%                           | 47,5/52,5     | 35,9/64,1     | 42,5±57,5     | ns  |
| Systolic BP (mmHg)                  | 148,4±17,7    | 144,4±17,6    | 144,6±17,3    | ns  |
| Diastolic BP(mmHg)                  | 90,248,5      | 92,848,8      | 107,824,9     | p<0,05 |
| Marital status M/S(%)               | 82,9%±11,7%   | 92,3%±7,7%    | 97,5%±2,5%    | n.s |
| Education (years)                   | 11,4±2,82     | 10,26±2,009   | 10,50±2,9     | ns  |

Table 1. Socio-demographic and clinical characteristics of patients who survived acute myocardial infarction. BMI—body mass index, DM—Diabetes mellitus, BP—blood pressure, M—married, S—single, *statistical difference between group 1 and group 2, **statistical difference between Group 1 and group 3, *statistical difference between group 2 and group 3

There was no significant difference (X²=1,182, df=2, P=0,915) between observed groups in n distribution according DBI>10 and DBI<10 in patient survivors of AMI between observed groups. In the study we got a small percentage of BDI 34,1 in group 1, 30,8 in group 2 and 30 in group 3 (Table 2).

| DBI     | Group 1 (N=41) | Group 2 (N=39) | Group 3 (N=40) | p   |
|---------|---------------|---------------|---------------|-----|
| ≤10     | 27            | 27            | 28            | 70  |
| >10     | 14            | 34,1          | 12            | 30  |

Table 2. The distribution of survivors of AMI according their BDI in the observed groups
Data obtained from all groups show significant positive association with depression in female patients. Moreover, there was positive but insignificant association of the patients’ age with depression in the observed groups. Smoking was positive and insignificantly associated with depression in patients during acute coronary event, but in survivors of AMI after 3 month and after 12 months after ACS smoking was significantly negatively associated with depression. Physical activity was significantly positive associated with depression in the group 1 and group 2, while in the group 3 it was insignificantly negative associated with depressive mood. Moreover, we got negative association of marital status with depression in all examination groups (Table 3).

5. DISCUSSION

The results obtained in our study showed presentation of depression (using DBI score) with almost equal distribution in patients during acute episode of myocardial infarction as well as in patients after period of three and twelve months of the acute coronary event). In fact, we did not register significant change of the number of depressive patients during prolonged time after the AMI. The results obtained in our study, although in a small percentage, are still indicative of the relationship between depression and coronary heart disease (AMI), so they report that depressive symptoms associated with risks for AMI. These results correlate with another research that reported that depression influence for the development of coronary artery disease. More recent studies have reported a similar association (9, 10), some authors also have found association between depression and heart disease (10, 11, 12). A meta analysis published in 2004 found that depression is associated with cardiac and all-cause mortality in post-AMI patients (13). The authors of a 25 systematic review, however concluded that it difficult to draw unambiguous conclusion about the association between depression and post-AMI mortality (14)

The present study revealed that 31.7% of patient in the first group were score of DBI ≥10. This results correlate with some study 20% (15); 30% (16); 32% (17); 35% (18); 20%; (19); 21% (20), but not correlate with another study 47% (21). In second group score of DBI≥10 was in 25.6% of patients and in third group 22.5%,.. This results correlate with some researcher reports 31,1% (25), DBI >10 after 4 month 48%(16), after 12 month 37% (22) ; after 6 month 30%, after 18 month 34% (20); after 12 month 30% (22). But not correlate with another study who reported that after 30 day of survive AMI 70% (23) of patients have DBI scores >10 and after 6–8 week of survive AMI 60% of patients have DBI >10 (18).

The results in our study between three groups of patients did not show significant differences according sociodemo-

| Parameter                   | Group 1 (N=41) | Group 2 (N=39) | Group 3 (N=40) | Total (N=120) |
|-----------------------------|---------------|---------------|---------------|--------------|
| Gender (m/f)                | p=0.362*      | p=0.403*      | p=0.368*      | 0.377**      |
| Age (Yr)                    | p=0.082       | p=0.236       | p=0.292       | 0.027        |
| Smoking (Y/N)               | p=0.291       | p=0.449**     | p=0.577**     | 0.290**      |
| Physical activity (Y/N)%    | p=0.314*      | p=0.403*      | p=0.305       | 0.128        |
| Stress (Y/N)                | p=0.079       | p=0.098       | p=0.220       | -0.111       |
| BMI (kg/m)                  | p=-0.328*     | p=-0.027      | p=-0.608**    | -0.349**     |
| DM (Y/N)                    | p=-0.115      | p=0.001       | p=0.140       | 0.014        |
| Systolic BP (mmHg)          | p=-0.596**    | p=0.061       | p=0.150       | 0.090        |
| Dyastolic BP (mmHg)         | p=-0.551**    | p=0.243       | p=0.158       | 0.35         |
| Marrital status             | p=0.075       | p=-0.390*     | p=-0.063      | 0.163        |
| Education                   | p=0.294       | p=-0.035      | p=0.396*      | 0.255**      |

Table 3. Association of the socio-demographic and clinical parameters with depression observed in the group with AMI, and groups after 3 and 12 months after acute coronary event BMI-body mass index, DM-Diabetes mellitus, BP-blood pressure

The observed sex difference in BDI scores (p<0,001) is in keeping with the common observation of higher prevalence of depression among women (24). Also the results in our study reported there females presented significant positive association with depression in the three groups of patients. This results not correlate with another study who present that higher BDI scores were associated with increased risk of AMI in both sexes (4). Some research reported that depression may be an especially important coronary disease risk form women (8, 9).

Depression is more prevalent in AMI patients older than age 65 years (12). Moreover, in our study there was positive but insignificant association of the patients’ age with depression in the observed groups.

Smoking was positively correlated with depressed affect among the women (10). This is undoubtedly related to the fact that patients with depression are three times more likely to be cigarette smokers (12). Also in our study smoking was positive and insignificantly associated with depression in patients during acute coronary event, but in survivors of AMI after 3 month and after 12 month of AMI smoking was significantly negatively associated with depression. This result is most likely due to the internist’s recommendations that it should be stopped by smoking cigars after AMI. However, the higher prevalence of depression in women and smoking positively correlation with depressed and it is important (24) because depression affect might act to foster coronary disease and early mortality (25).

Among patients depressive symptoms were positively associated with amount smoked and negatively associated with body mass index and systolic blood pressure (4). Moreover, in our study we got negatively association between depression and BMI in all examination groups. The results in group 1 of our study reported negative association of systolic and diastole BP but in group 2 and 3 we got normal level of systolic and diastole BP The results obtained are most likely due to the regular treatment of the prescribed blood pressure therapy as well as the medical recommendations surrounding the correct diet.

112

ORIgINAL PAPER • Mater Sociomed. 2019 Jun; 31(2): 110-114

Depression in Survivors of Acute Myocardial Infarction
In our study physical activity was significantly positive associated with depression in the group 1 and group 2, while in the group 3 it was insignificantly negative associated with depressive mood. These obtained results are most likely due to the inclusion of internists for reducing the physical activity after AMI. Some researches reported that between depression and single marital status exit correlation (12), in our study we also got association between single marital status and depression so the large number of the patients with BDI >10 were with poor social support.

However, in our study we got a small percentage of depression conduction but this results is very important because depressive symptomatology are associated with increased risk of MI and mortality in the patients with AMI (5). Some have argued that depression should be identified during the AMI hospitalization because depressed patients have a higher risk of morbidity and mortality after AMI (18, 24).

Some research has shown that depression predict total mortality and the prognosis of patients after MI (22), but evidence concerning the role of depression in the pathogenesis of coronary disease has been less clear. Because the factor that has complicated research in this area is the similarly between the symptoms of depression and the symptoms of coronary disease. Because both illnesses result in tiredness, feelings of weakness, etc, it is possible that manifestations of subclinical heart disease could be mistaken for depressive symptomatology (25). Therefore, it is important for studies to rely on hard outcomes such as documented AMI (26, 27). A second solution is to eliminate somatic symptoms from consideration when depression is assessed (6). Five of more of the nine symptoms must be present for diagnosis of depression. (DSM–IV criteria) (28).

Acute myocardial infarction practice guidelines recommend that the psychosocial status of patients be evaluated including inquiries regarding symptoms of depression (29). They most commonly used assessment methods for identifying patients with depression after AMI are structured clinical interview and questionnaire, particularly the Beck depression Inventory(BDI) ( 30). The authors in some studies suggest that patients who score 10 or above on the BDI should men be evaluated by a clinical psychologist or psychiatrist (30, 31).

Depression would be important to identify in AMI patients if it were show that patients should be treated differently than those who are not depressed. For example, patients with depression after AMI have increased platelet activation so in these patients should receive more aggressive antiplatelet therapy (31). The SSRI sertraline have been shown to be beneficial in the treatment of depression Increasing serotonin transporter affinity was associated with reduced odds of AMI among users of all. SSRI (p<0.01) but not tricyclic (p=0.77) or atypical (p=0.70) antidepressants. These data demonstrate that increasing serotonin transporter affinity correlates with greater AMI protection with SSRI but not with other antidepressant exposure (32). The SSRI exert a positive effect patient and also appear to reverse enhanced platelet activity seen in depressed patients with AMI. The available evidence suggests that there is significant need and merit to treat depression associated with AMI (29, 30).

Screening for depression in all AMI patients is also important. So the post AMI patients who are discharged from the hospital must be go to the rehabilitation facilities There nurses. Physical therapists and social workers have time to diagnoses and undertake treatment for depression in them (27, 28).

The results in early study reported on the results of group psychotherapy among 118 patients post AMI At 1-year followed-up, CAD events were reduced by 65% (12), Psychosocial intervention in 2320 male survivors of AMI were resulting with 23% reduction in CAD events. (12, 14) they found a four-fold increase in the death rate of men classified as socially isolated and as having a high degree of life stress. In the detailed review of the literature (12, 15) found that significant 50% of post AMI patients reduction in cardiac events in the intervention groups. They concluded that psychosocial interventions and stress management may offer solutions for both limiting interventional cardiologic expenses and improving the health of CAD patients (12).

When associated with AMI depression increases hospital LOS re-admission rates, and consequently the cost of medical care. Authors in some studies found that cost of medical care for the first 12 months after admission for a patients with AMI and depression was 11% higher than cost of treating patients without depression (7, 6) The also found that rehospitalization rates were higher in depressed patients with AMI. And the cost of care for patients hospitalized for MI are significant higher for patients with evidence of depression. So the treatment of depression with cognitive behavior therapy, psychotherapy, social support, supplemented with an SSRI antidepressant lowering the risk of reinfarction or mortality and reduce the cost of medical care (31, 32).

6. CONCLUSION

In our study we got a small percentage off depression condition but this results is very important because depressive symptomatology are associated with increased risk of MI and mortality in the patients with AMI. Sociodemographic and clinical independent predictors of depression may also be a clinical signal for the cardiologist for consultative psychiatric evaluation of patients with ischemic heart disease. So, acute myocardial infarction practice guidelines recommend that the psychosocial status of patients be evaluated including inquiries regarding symptoms of depression items with AMI. Screening for depression in all AMI patients is also important. Because that patients should be treated differently than those who are not depressed So the treatment of depression with cognitive behavior therapy, psychotherapy, social support, supplemented with an SSRI antidepressant lowering the risk of reinfarction or mortality and reduce the cost of medical care.

• Author’s contribution: Each author gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work. Each author had role in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and they agree to accountable for all aspects of the work in ensuring that questions.
related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

- Conflicts of interest: There are no conflicts of interest.
- Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms.
- Financial support and sponsorship: Nil.

REFERENCES

1. Pratt LA, Brody DJ. Depression in the United States household population, 2005-2006. NCHD Data Brief; 2008(7): 1-8.
2. Frasure-Smith N, Lesperance F, Irwin MR, et al. Depression, C-reactive protein and two-years major adverse cardiac events in men after acute coronary syndromes. Biol Psychiatry. 2007; 62(4): 302-308.
3. Grace SL, Abbey SE, Kapral MK, et al. Effect of depression on five-year mortality after an acute coronary syndrome. Am J Cardiol. 2005; 96(9): 1179-1185.
4. Schins A, Hamulyak K, Scharpe S, et al. Whole blood serotonin and platelet activation in depressed post-myocardial infarction patients. Life Sci. 2004; 76 (6): 657-650.
5. Blumenthal JA, Lett HS. Depression and cardiac risk. J Cardiopulm. Rehabil. 2005; 25(2): 78-79.
6. Libby P, Theroux P. Pathophysiology of coronary artery disease. Circulation. 2005; 111(25): 3481-3488.
7. Mendelson SD. The current status of the platelet 5-HT (2A) receptor in depression. J Affect Disord. 2000; 57(1-3): 15-24.
8. Brett T, Enc B, Daniel F, et al. Prevalence of depression in survivors of Acute Myocardial infarction. J Gen Intern Med, 2006; 21(1): 30-38.
9. John B, Marianne S. Symptoms of depression, acute myocardial infarction, and total mortality in a community sample. Circulation, 1996; 93: 1976-1980.
10. Carney RM, Blumenthal JA, Catellier D, et al. Depression as a risk factor for mortality after acute myocardial infarction. J Cardiol. 2005; 92: 1277-1281.
11. Ladwing KH, Kieser M, Konig J, et al. Affective disorders and survival after acute myocardial infarction. Results from the post-infarction late potential study. Eur Heart J. 1991; 12: 959-964.
12. Kaufmann MW, Fitzgibbons JP, Sussman EJ, et al. Relation between myocardial infarction, depression, hostility, and death. Am Heart J. 1999; 138: 959-964.
13. Barth J, Schumacher M, Herrmann-Lingen C, et al. Depression as a risk factor for mortality in patients with coronary heart disease: a meta analysis. Psychosom Med. 2004; 66: 802-813.
14. Sorensen CF, Friis-Nasche E, Haghfelt T, Beck P, et al. Post myocardial infarction mortality in relation to depression: a systematic critical review. Psychother Psychosom. 2005; 74: 69-80.
15. Bush DE, Ziegelstein RC, Tayback M, et al. Even minimal symptoms of depression increase mortality risk after acute myocardial infarction. Am J Cardiol. 2001; 88: 337-341.
16. Lane D, Carroll D, Ring C, et al. The prevalence and persistence of depression and anxiety following myocardial infarction. Br J Health Psychol. 2002; 7: 11-21.
17. Lesperance F, Frasure-Smith N, Talajic M. et al. Five-years risk of cardiac mortality in relation to initial severity and one year changes in depression symptoms after myocardial infarction. Circulation. 2002; 105: 1049-1053.
18. Davis T, Jensen L. Identifying depression in medical patients. Image J Nurs Sch. 1988; 20: 191-195.
19. Watkins LL, Blumenthal J, Cerney RM, et al. Association of anxiety with reduced baroreflex cardiac control in patients after acute myocardial infarction. Am Heart J. 2002; 143: 460-466.
20. Luutonen S, Holm H, Salminen JK. et al. Inadequate treatment of depression after myocardial infarction. Acta Psychiatr Scand. 2002; 106: 434-439.
21. Steeds RP, Bickerton D, Smith MJ, et al. Assessment of depression following acute myocardial infarction using the Beck Depression Inventory. Heart. 2004; 90: 217-218.
22. Barefflot JC, Brug MM, Carnery RM. et al. Aspects of social support associated with depression at hospitalization and follow-up assessment among cardiac patients. J Cardiopulm Rehabil. 2005; 23: 404-412.
23. Lauzon C, Beck CA, Huehn T, et al. Depression and prognosis following hospital admission because of acute myocardial infarction. CMAJ. 2005;168: 547-552.
24. Frasure-Smith N, Lesperance F, Talajic M. Depression following myocardial infarction: impact on 6-month survival. JAMA. 1993; 270: 1819-1825.
25. Ahem DK, Gorkin L, Anderson JL. et al. Biobehavioral variables and mortality or cardiac arrest in the cardiac arrhythmia pilot study. Am J Cardiol, 1990; 66: 69-72.
26. Monte M, Pascal JJ. Depression and acute myocardial infarction. Prev Card 2004; 7(2).
27. Zigmond AS, Snith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983; 67: 561-570.
28. Monte M, Pascal JJ. Depression and acute myocardial infarction. Prev Cardiol. 2004; 7(5).
29. Anda RF, Williamson DF, Escobedo LG. et al. Depression and the synanoc of smoking a national perspective JAMA, 1990; 264: 1514-1545.
30. Welin C, Lappas G, Wilhelmsson L. et al. Independent importance of psychosocial factors for prognosis after myocardial infarction. J Inter Med. 2000; 247: 629-639.
31. Anda R, Williams D, Jones D. et al. Depressed affect, hopelessness, and risk of oschemic heart disease in a cohort of US adults. Epidemiology,1995; 4: 285-294.
32. Shekelle RB, Vernon SW, Ostfeld AM. Personality and coronary heart disease. Psychosom. Med. 1991; 53: 176-184.