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# Major depression and myocardial infarction in Italian adults

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**Summary**
The main aim of present work was to evaluate, for the first time in Italy, the weight of depression as a risk factor for cardiovascular disease (CVD), in particular for myocardial infarction (MI). Clinical data of 215 subjects (153 women, 62 men; mean age 51.75±15.74) with a mood disorder and no previous history of CVD, were collected. Percentages of MI in sample population, grouped by age classes, were compared to those reported for the Italian population by the Italian National Institute of Statistics. Statistical analyses were performed by the $\chi 2$ method. Prevalence for myocardial infarction in our study population was significantly higher than in ISTAT study (5.6% vs. 1.7%, $p<0.001$). When analysing data by gender, prevalence of MI resulted 4.6% vs. 1.1% in women ($p<0.001$) and 8% vs. 2.4% in men ($p<0.005$). Analysis by age and gender showed statistically significant results in the 45–54 and 65–69 age-classes (prevalence: 5.4% vs. 0.4% and 17.7% vs. 2.2%, respectively; $p<0.001$) for women, and in the 45–54 class (22.2% vs. 1.5%, $p<0.001$) for men. Even taking into account the small dimension of the study population, our results evidence that a previous history of major depression could be strongly and significantly linked to a subsequent episode of myocardial infarction.

**Key Words**
Major depression; myocardial infarction; Italian study.

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## Introduction

Major Depression (MD) is a condition characterized by a long-lasting depressed mood or marked loss of interest or pleasure (anhedonia) in all or nearly all activities. MD is a serious mental disorder that profoundly affects an individual's quality of life. Unlike normal bereavement or an occasional episode of "the blues", MD causes a lengthy period of gloom and hopelessness, and may rob the sufferer of the ability to take pleasure in activities or relationships that were previously enjoyable. Mental efficiency and memory are affected, causing even simple tasks to be tiring and irritating. MD is a common psychiatric illness with high levels of morbidity and mortality. It is estimated that 10% to 15% of the general population will experience clinical depression during their lifetime, and 5% of men and 9% of women will experience a depressive disorder in a given year (Richards, 2011).

In the last two decades, several studies have focused on the association between depression and organic conditions, such as aging, physical and psychological stress, chronic pain, metabolic disorders like diabetes, alcoholism and inflammatory condition (Silverstone, 1990; Wolkowitz et al., 2011; Prina et al., 2012).

Particularly, many investigations have been aimed to characterize the reciprocal relationship

between depression and cardiovascular disease (CVD) (Grippo & Johnson, 2009; Lippi et al., 2009); nevertheless, in spite of the great effort, such hypothetical association has not yet been properly defined due to several reasons:

(i) most of the researches focused on depression as a risk factor for cardiac events in patients with stable coronary heart disease (Carney et al., 2003; Barth et al., 2004; Pena et al., 2011);

(ii) only few scientists suggested depression as a risk factor for cardiovascular disease in healthy subjects although obtained results prevented to definitively confirm the MD-CVD correlation (Ford et al., 1998; Frasure-Smith & Lespérance, 2005);

(iii) the overall picture is further complicated by several individual factors, since this relationship is likely to be influenced by lifestyle choices (smoking, sedentary life style or unhealthy diet) that affect each subject independently (Baune et al., 2012).

Historically, several models have been proposed to explain the connection between depression and CVD (Mosovich et al., 2008 and reference quoted therein):

- in the first model CVD was considered as a risk factor for depression on account of several studies focusing on the investigation of the rate of depression in patients affected by myocardial infarction (MI) or by a stroke event (Hance et al., 1996; Gainotti et al., 1999).

- in the second model, the idea suggesting that depression was instead a risk factor for CVD raised from studies suggesting that a prior history of depression or depressive symptoms is strongly associated with subsequent development of ischaemic heart disease and MI (Rozanski et al., 2005).

- finally, more recently, a third integrated model hypothesized the occurrence of a common underlying factor for cardiovascular disease and depression. The specific mechanism would rest on the presence of a cytokine-mediated chain of events initiated by chronic stress that would lead to biodynamic outcomes (e.g. neurotoxicity, serotonin dysfunction, platelet hyper-reactivity) that, over time, could manifest themselves in severe clinical outcomes including depression and/or CVD (Miller & Blackwell, 2006).

Noteworthy, although coming from different points of view and approaches, somehow even contradictory, all authors ended up agreeing on confirmation of an undeniable evidence of a strong relation between the two conditions. Thus, even if the association between depression and CVD has been widely accepted, its real entity and direction are yet to be addressed, especially because the underlying mechanisms linking these two pathologies remain largely unclear (Carney & Freedland, 2007; Dawood et al., 2008; Nemeroff & Goldschmidt-Clermont, 2012).

The purpose of the present observational study, in our knowledge carried out for the first time in Italy, was to assess the importance of depression as a cardiac risk factor, in particular for myocardial infarction (MI). To this aim, we evaluated the rate of MI in 215 subjects affected by mood disorders but without a previous history of cardiovascular disease.

## Methods

The data collected and discussed in this paper refer to a survey carried out during 2007 by Dr. M.R. Seiti on patients suffering from mood disorders who, throughout 2006, applied to the "Centro Psico-Sociale (CPS)" of Romano di Lombardia (BG) for psychological/psychiatric support. Obtained results have been compared with the ISTAT data available at that time, i.e. "Condizioni di salute, fattori di rischio e ricorso ai servizi sanitari - anno 2005 (Health state, risk factors and access to health services - Year 2005)" by the Italian National Institute of Statistics (ISTAT), published in 2007.

### *Study population*

Clinical data of 215 patients were collected from September to November 2007. Study population consisted of 153 women and 62 men, with an age ranging from 22 to 85 years (mean 51.75±15.74), grouped into nine age-classes (< 24 years; 24–34; 35–44; 45–54; 55–64; 65–69; 70–74; 75–79; ≥ 80 years; Table 1), as in the Italian National Institute of Statistics (ISTAT) survey (ISTAT, 2007), in order to make a proper comparison between the results obtained by present research and the ISTAT report.

Diagnosis was reached through a clinical-anamnestic study to ascertain the presence of the criteria specified by DSM-IVTR (American Psychiatric Association, 2004). All patients underwent psychodiagnostic investigation in the following ways: HRSD-21 (Hamilton Rating Scale for Depression), HRSA (Hamilton Rating Scale for Anxiety), CGI (Clinical Global Impression), SCL-90 (Symptom CheckList-90), HCL-32 (Hypomania Check list). The subjects were recruited without regard to sex, age and food intake pattern. Exclusion criteria consisted of:

(i) diagnosis other than affective disorder;
(ii) prior history of CVD, stroke or cancer; and
(iii) full medical records not available.

| Age Groups | Women | Men | Total |
|---|---|---|---|
| <24 | 6 | 2 | 8 |
| 24-34 | 15 | 5 | 20 |
| 35-44 | 30 | 13 | 43 |
| 45-54 | 37 (2) | 9 (2) | 46 (4) |
| 55-64 | 19 (1) | 16 (2) | 35 (3) |
| 65-69 | 17 (3) | 6 (1) | 23 (4) |
| 70-74 | 13 (1) | 3 | 16 (1) |
| 75-79 | 10 | 2 | 12 |
| =80 | 6 | 6 | 12 |
| Total | 153 | 62 | 215 |

Table 1. Study population distributed by gender and age classes. Inside brackets numbers of subjects affected by myocardial infarction.

Percentages of patients affected by both fatal and nonfatal MI were compared to data reported by ISTAT (2007).

### *Statistical analysis*

The hypothesis that MI frequencies observed in our sample and in the Italian population survey by ISTAT were different was examined by using the $\chi^2$ test. A p-value less than 0.05 was considered statistically significant.

## Results

The prevalence of mood disorders in our study population was in line with the classical epidemiology distribution resulting in a predominance of Major Depressive Disorder (73 subjects, including 53 women and 20 men; incidence: 34%) and Major Depressive Episode (71 subjects, 50 women, 21 men; incidence: 33%) (data not shown but available on request). Typical prevalence of mood disorders in women was confirmed as well (observed women:men ratio was about 2.5:1).

Only twelve subjects (4 men and 2 women with Major Depressive Episode; 1 man and 5 women with Major Depressive Disorder) out of a total of 215, resulted to be exposed to myocardial infarction after a previously diagnosed mood disorder (Table 2). As shown in Table 3, data analysis revealed that in our sample (women+men) MI rate was significantly higher than that reported in the ISTAT study (5.6% vs. 1.7%, respectively, $p<0.001$). Moreover, when analysing data by gender, statistically significant results were obtained: 4.6% vs. 1.1% in women ($p<0.001$) and 8% vs. 2.4% in men ($p<0.005$). Analysis of data by age and gender showed statistically significant results in the 45–54 and 65–69 age-classes (5.4% vs. 0.4% and 17.7% vs. 2.2%, respectively; $p<0.001$) for women, whereas, only in the 45–54 class (22.2% vs. 1.5%, $p<0.001$) for men.

Such trends were also confirmed when aggregated results (women+men) were analyzed by age; the prevalence of MI in the study population with respect to ISTAT data was significantly higher in the 45–54 (8.7% vs. 0.9%, $p<0.001$), 55–64 (8.6% vs. 2.9%, $p<0.05$) and 65-69 (17.4% vs. 4.7%, $p<0.005$) groups.

As far as concerns patients ≥70 years, in our study population the more the age increases the more the number of subjects suffering from MI after the diagnosis of depression diminishes if compared to the ISTAT survey.

## Discussion

Although public health has often been conceptualized only as the prevention of physical illness, several recent data suggest that mental illnesses are increasingly relevant to the mission of disease prevention and health promotion (Chapman & Perry, 2008). Depression is a major cause of morbidity worldwide: lifetime prevalence varies widely, from 3% in Japan to 17% in the US. In most countries the number of people who would suffer from depression during their lives falls within an 8–12% range. In Italy, about 10% (~ 6 millions of people) of the general population will experience clinical depression during their lifetime, and about 3% (1.7% of men and 4.2% of women) will experience a depressive disorder in a given year.

Noteworthy, based on current trends, it is estimated that, by 2020, depression will be the second

| N. | Gender | Age | Diagnosis |
|---|---|---|---|
| 1 | Woman | 45 | Major Depressive Disorder |
| 2 | Woman | 53 | Major Depressive Episode |
| 3 | Man | 53 | Major Depressive Disorder |
| 4 | Man | 54 | Major Depressive Episode |
| 5 | Woman | 55 | Major Depressive Disorder |
| 6 | Man | 57 | Major Depressive Episode |
| 7 | Man | 58 | Major Depressive Episode |
| 8 | Woman | 65 | Major Depressive Disorder |
| 9 | Woman | 68 | Major Depressive Episode |
| 10 | Woman | 68 | Major Depressive Disorder |
| 11 | Man | 69 | Major Depressive Episode |
| 12 | Woman | 71 | Major Depressive Disorder |

Table 2. Gender, age and diagnosis of subjects affected by myocardial infarction.

cause of disease burden worldwide, being ischemic heart disease the leading cause (Lopez & Murray, 1998). Hence, assessing the actual weight of depression as risk factor for other health outcomes might be of relevant impact on future preventive and therapeutic health strategy. To this aim, present study was carried out to investigate the role played by major depression as a cardiac risk factor, in particular for myocardial infarction (MI).

Our results appear to support the hypothesis that mood disorders contribute to the progress of CVD and its outcomes. In our study population, the risk of developing ischemic heart disease linked to depression is particularly relevant, in both sexes, between 45 and 54 years, age at which individuals are still very much active and productive in all respects. Hence, if considering that the economic cost of depression is estimated at $30.4 billion a year, preventive action aimed at these subjects could reduce the health, social and economic negative effects of heart disease and depression (see http://www.psychiatry.wustl.edu/depression/depression_facts.htm). In this perspective, it would be of paramount importance that the Italian National Health Service devoted human and financial resources to improve treatment of psychiatric illness in order to ensure better overall quality of life and an important reduction of health service costs, especially if considering that the annual direct and indirect cost of CVD and stroke in the United States and in the European Union is about $297.7 and €169 billion, respectively (Roger et al., 2012).

In the 65–69 women age class, prevalence of MI was significantly higher than in the ISTAT study. Taking into account that women experience depression about twice as often as men, such data could be considered strongly related to the fact that, while cardiovascular disease and coronary heart disease for decades was understood as mainly a male disease group, through the last years it has become increasingly evident that it is now an important disease causing premature death also in the female populations throughout the Westernized world (Espnes & Byrne, 2008).

The very low prevalence of MI observed in ≥70 year age-classes might be the result of the scarce number of old patients whom clinical data were available for. In fact, in elderly people, the diagnosis of depression may be misled by two main causes: poor attention to symptoms of mood disorders, particularly by family, and/or misdiagnosis by physicians.

Namely, persons of ≥70 years can be hardly enrolled since they frequently depend for transportation on their relatives who, usually, consider mood disorders less relevant and tend not to worry very much about this condition in elders. Moreover, in older adults mood disorders may also be characterized by impairment in cognition, a syndrome sometimes referred to as pseudodementia, and by psychomotor agitation or retardation. As a result, symptoms of depressive disorder are frequently masked in older adults and may initially appear to be cognitive impairment or an early sign of neuroendocrine and related chronic disorders, which makes the diagnosis of depression for aged adults more difficult but, at the same time, important to their care (Chapman & Perry, 2008).

Alternatively, if depression is a real risk factor for CVD, it is most probable that the lower frequency of cases of heart failure in older people observed in our study sample could be an effect of the highest prevalence of cardiac disease occurring in the intermediate age groups and, consequently, of the increased related mortality within the same groups.

Although prevalence of major depression is generally thought to be lower among older adults than among young adults, understanding depressive disorders among elderly people not only remains vital to public health but also can be of some help in

| | | Age Groups | | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| | | <24 | 24-34 | 35-44 | 45-54 | 55-64 | 65-69 | 70-74 | 75-79 | =80 | |
| Women | ISTAT | 0.0 | 0.1 | 0.1 | 0.4 | 1.1 | 2.2 | 3.2 | 4.7 | 6.1 | 1.1 |
| | SP | 0.0 | 0.0 | 0.0 | 5.4* | 5.3 | 17.7* | 7.7 | 0.0 | 0.0 | 4.6* |
| Men | ISTAT | 0.0 | 0.0 | 0.3 | 1.5 | 4.8 | 7.7 | 8.6 | 12.1 | 11.1 | 2.4 |
| | SP | 0.0 | 0.0 | 0.0 | 22.2* | 12.5 | 16.7 | 0.0 | 0.0 | 0.0 | 8.0*** |
| Women+Men | ISTAT | 0.0 | 0.0 | 0.2 | 0.9 | 2.9 | 4.7 | 5.6 | 7.7 | 7.8 | 1.7 |
| | SP | 0.0 | 0.0 | 0.0 | 8.7* | 8.6** | 17.4*** | 6.25 | 0.0 | 0.0 | 5.6* |

Table 3. Percentages of subjects, grouped by age classes, affected by myocardial infarction in study population (SP) and Italian population (ISTAT). In the "Total" column percentages by gender, independently of age, are reported. *: $p<0.001$; **: $p<0.05$; ***: $p<0.005$.

preventing complications of other illnesses because of depression. Furthermore, rates of major depression rose markedly over the past decade, suggesting that future cohorts of older adults will have increasing numbers of people who have experienced or are contending with depressive disorders (Chapman & Perry, 2008).

Because of the potential utility of the intervention targets it would be very useful that future studies explore these relationships in more depth and use a sufficiently large, randomly selected sample. Moreover, future studies should assess this relationships through longitudinal data collection and/or data collection before and after interventions to improve coping strategies, self-efficacy and educational programs about CVD. In fact, interventions focused to promote stress management and healthy coping and to prevent and, later on, intensely treat mood disorders might lead to a significant reduction of CVD incidence and prevalence (Frasure-Smith & Lespérance, 2003; Nickels et al., 2009).

There is a clear need to identify the underlying mechanisms responsible for MD and their linkage to the heart and vascular system. Further knowledge of these items may pave the way for novel and perhaps relatively simple therapeutic strategies (e.g. β-blockers, central sympatho-inhibition with imidazoline binding drugs) to be administered in patients with MD to modify cardiac risk (Nickels et al., 2009). Indeed, defining therapeutic interventions that reduce cardiac risk will be an important step forward in alleviating the burden of depressive illness on the community.

## Conclusions

Obtained results showed that a previous history of major depression could be strongly and significantly linked to a subsequent episode of myocardial infarction.

Even taking into account the small dimension of our study population, nevertheless statistical significance of obtained results does underline that present study provides additional evidence of a relationship between MD and cardiovascular diagnoses and confirms the hypothesis that major depression is an independent risk factor for the development and progression of heart disease.

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