
Comorbidity Between Physical Disorders and Depression: Prevalence and Risk Factors.

Authors: M. T. Amboage-Paz, J. A. Díaz-Peromingo (*).

Center: Departments of Psychiatry and Internal Medicine (*). Complejo Hospitalario Universitario de Santiago. Santiago de Compostela (A Coruña). Spain.

Correspondence:

José Antonio Díaz-Peromingo.

Department of Internal Medicine.

Complejo Hospitalario Universitario de Santiago.

Santiago de Compostela (A Coruña). Spain.

Abstract

Introduction:

The presence of two or more chronic disorders in the same patient or comorbidity, is increasingly common nowadays. Comorbidity between depression and physical disorders is variable and can lead to a worsening of the associated physical diseases. Our objective is to assess the prevalence of depression and comorbidity in patients with physical diseases and the possible associated risk factors.

Material and methods:

We included 2659 patients with comorbidities according to the Charlson Comorbidity Index (CCI) who were also evaluated for the coexistence of hypertension, atrial fibrillation, anemia, depression, smoking and alcohol intake. In patients with reported depression, the most frequent associated comorbidities were studied.

Results:

Mean age was 73 years old (59.3% women), 11.6% were smokers and 11.3% referred alcohol intake. Mean CCI score was 3. Prevalence of depression reached 28.5%. The variables most frequently associated with depression were hypertension, anemia, atrial fibrillation, cerebrovascular disease, ischemic heart disease, heart failure, diabetes mellitus, dementia, liver disease, chronic kidney disease, COPD, thromboembolic disease, cancer, and peripheral vascular disease.

Conclusions:

Comorbidity is common in patients with depression. The high frequency of arterial hypertension, anemia, atrial fibrillation, ischemic heart disease, heart failure, diabetes mellitus and dementia is remarkable in our patients. On the other hand, patients with arterial hypertension, cerebrovascular disease, thromboembolic disease, COPD, liver disease, diabetes mellitus, hemiplegia, atrial fibrillation, and anemia have a higher risk for depression. Identifying these patients can be useful in the prevention and early diagnosis of patients with depression.

Keywords: Depression; comorbidity; physical disease.

INTRODUCTION:

The term comorbidity refers to the concomitant existence of two or more disorders in the same patient, which can be both physical and mental, for a certain period of time. Thanks to the adequate control of many acute diseases, especially in developed countries, chronic diseases have acquired a preponderant role, also increased by the increase in the population's life expectancy. Thus, the fact that there are more elderly people lead to a higher probability of developing chronic pathologies (1), which implies that there is greater comorbidity in many patients.

The prevalence of comorbidity in patients with mental disorders is very variable, reaching 79% in relation to the existence of comorbid mental illnesses (2). However, with respect to comorbidity between depression and physical disorders, lower comorbidity rates have been described, such as 29% for high blood pressure, 22% for acute myocardial infarction, 30% for epilepsy, 31% for cerebrovascular disease, 27% for diabetes mellitus, 33% for cancer, 44% for AIDS and 46% for tuberculosis, compared to the general population (10%) in studies conducted in the USA (2, 3).

The term depression refers to an alteration of mood that leads to loss of positive affect marked decrease in interest and the ability to enjoy activities that were previously perceived in a pleasant way, and a variety of emotional, cognitive and behavioral symptoms such as anhedonia, sleep and appetite disorders, self-care impairment and recurrent ideas of death (4). The World Health Organization (WHO) has predicted that depression will be the main cause of disease in the year 2030 (5).

There is increasing evidence showing that depression and physical illnesses coexist frequently in the same patient (6). Comorbidity between physical illnesses and depression results in a worsening of quality of life, a poor evolution of physical illnesses, an increase in mortality and disability, a greater functional impact and an increase in health costs, compared to patients with depression or physical diseases presented separately (7).

The association between depression and physical comorbidities, both from the point of view of depression and its aggravation as well as the presence of a physical illness as a cause of secondary depression, deserves deeper attention. In the present study, we analyzed the comorbidity between physical illnesses and depression, in terms of prevalence and associated risk factors. Early recognition of patients with physical illnesses, vulnerable to suffering from depression, or physical disorders that most frequently can be associated with depression, can be useful when planning a more accurate and personalized attention in this group of comorbid patients.

MATERIAL AND METHODS:

A population of 2659 patients consecutively admitted to the Department of Internal Medicine between 01-01-2018 and 12-31-2018 was studied. The following variables were analyzed: sex, age, smoking, (in smokers the number of packages/year smoked was quantified), alcohol intake, comorbidities that make up the Charlson Comorbidity Index (CCI, Table 1) (8) with age

correction (9), and the presence of hypertension, anemia, atrial fibrillation and depression. Patients diagnosed with major or minor depression, who had been diagnosed by a Psychiatrist or a Family Physician were included, according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-V) (10). Statistical analysis: a cross-sectional, descriptive study of the variables included in the study was carried out. The association between qualitative variables was analyzed by using the Pearson's Chi-square test and for quantitative variables the Student's T test was performed. To assess the risk of suffering depression according to the comorbidity, the hazard ratio was analyzed with a 95% confidence interval.

Ethics: The study was carried out in compliance with the Declaration of Helsinki, 2013 version. As it was a retrospective observational study, patients were not informed in writing. Patients' information that could be identified was encrypted and analyzes were performed anonymously. Therefore, the approval of the study by the ethical committee was not considered necessary.

RESULTS:

Patients diagnosed with depression accounted for a total of 452 (59.3%) women and 308 (40.4%) men. The most frequent comorbidities in patients diagnosed with depression are shown in Figure 1. Regarding quantitative variables, the average age was 73 years (range 20-98), average packets/year smoked 7.82 (range 0- 200), average CCI 3 (range 0-16) and average CCI modified by age 6 (range 0-19). Table 2 shows the probability of suffering from depression regarding to the different comorbidities included.

Female sex was associated with a higher probability of suffering depression in the qualitative analysis ($p < 0.001$) as well as smoking ($p = 0.041$) and alcoholism ($p = 0.024$). In the quantitative analysis, both female sex, a higher number of packages/year smoked as well as high scores in both the ICC and the age-corrected ICC, were associated with a higher prevalence of depression ($p < 0.001$ for all variables, Student's T test).

DISCUSSION:

The present study shows that patients diagnosed with depression have a high comorbidity index (3 points, 6 points after correcting by age). The prevalence of depression in our study was 28.5% (758 patients). The most frequent comorbidities in depressed patients were hypertension, anemia, atrial fibrillation, cerebrovascular disease, ischemic heart disease-AMI, heart failure, diabetes mellitus and dementia. The variables that showed a greater association with the risk of suffering from depression were arterial hypertension, cerebrovascular disease, thromboembolic disease, COPD, mild liver disease, diabetes mellitus without target organ involvement, hemiplegia, atrial fibrillation and anemia. Being a woman, smoking and drinking alcohol, was associated with a higher probability of suffering from depression.

The presence of depression is frequent in patients with physical illnesses, and especially when several of them occur in the same patient, the so called comorbidity. A study in patients with chronic diseases showed that they were almost 3 times more likely to suffer from depression than their healthy comparators (11). In addition, in large studies, the prevalence rises to 23% in patients with two or more physical illnesses associated with depression (7).

The association between depression and alcoholism has been widely studied. Davidson et al. found that depression-alcohol comorbidity is found in 16-88% of patients (12). In our study, alcoholic patients had a higher risk of comorbidity with depression ($p = 0.024$) and among patients diagnosed with depression the prevalence of alcoholism was 11.3%. Depression can precede alcoholism or occur in a known alcoholic patient. When alcoholism comes first, the risk of developing depression is considered 2-3 times greater than in the general population (13).

Regarding to cardiovascular diseases, in patients who have suffered a stroke, it has been described that 31% of those who survive, suffer from depression (14). In a Korean study, a prevalence of 25.5% was found (15), similar to our study (28.6%). Patients with an acute coronary syndrome suffer depression during hospitalization by up to 19.8% (16). Kang et al found a prevalence of depression of 21.7% in patients who had had an acute coronary syndrome (15). In our study this prevalence rises to 25.7%, and cardiovascular disease in a broad sense, including hypertension, atrial fibrillation, cerebrovascular disease, ischemic heart disease, heart failure and thromboembolic disease, make up the bulk of patients who have associated depression.

With respect to cancer, the prevalence of depression in patients with cancer disease was 12% in our patients, similar to that published in the literature of 10.8% (17). If we disaggregate patients with cancer according to whether they have extended disease or not, the prevalence of depression was 6.6% in those who did not have distant metastases and 5.4% in those who had metastases ($P = 0.536$, NS). Other cancer diseases collected in our study, in accordance with the ICC, were leukemia (0.7% of patients; 0.9% of comorbidity with depression) and lymphoma (1.5% of patients). In these patients, comorbidity with depression was found in 1.7%.

Special mention should be made for the association between depression and anemia. In our study, patients diagnosed with depression had a prevalence of anemia of 43.2%, very high. Due to the methodology of the study, it would be plausible that patients with cancer, cardiovascular diseases with associated anticoagulant therapy or chronic kidney disease, all entities that may have a certain degree of anemia, should be included in this group. On the other hand, among patients with anemia, the hazard ratio of depression was 1.485 (95% CI 1,250-1,765), suggesting that anemia, in itself, implies a greater probability of comorbid depression. In addition, Vulser et al. studied the relationship between depression and anemia in a cohort of 44,173 healthy people (63% men and with an average age of 38 years). People suffering from depression had anemia more frequently compared to those who were not diagnosed with depression, even after adjusting for sex, age, marital status, level of education, profession, alcohol or tobacco consumption, level of physical activity and body mass index (HR 1.36; 95% CI 1.18 - 1.57). In addition, the prevalence of anemia increased with the severity of depression (18). Thus, the relationship between anemia and depression is not completely clear, but it seems that both of them are entities that are more closely linked to each other than previously thought.

Dementia affects 21.4% of the patients analyzed in the present study, globally, without establishing differences between Alzheimer's disease or other types of dementia. Elderly patients

suffering from depression frequently have complaints or cognitive deficits that may result from depression or indicate the coexistence of a disease such as Alzheimer's disease or Parkinson's disease. The distinction between both situations has important implications for the treatment and evolution of these disorders (19).

Patients with type 2 diabetes mellitus have a higher prevalence of depression than the general population (20) and, in addition, patients with depression have a greater predisposition to develop diabetes mellitus throughout their lives (20,21). It has been described that patients with depression have an increased risk of 32–41% of developing diabetes and between 8–15% of diabetic patients are diagnosed with depressive symptoms (22,23). In our study, the prevalence of diabetes in patients with depression was 21.7%, however, there were differences according to the degree of diabetes evolution. Patients with diabetes mellitus without target organ involvement had a depression rate of 12.2% compared to those who did have target organ involvement (nephropathy, retinopathy, neuropathy) in which the frequency of depression was 9.5% ($p = 0.012$). In addition, the relative risk of depression was increased in the former ($p = 0.002$) and not in the latter ($p = 0.716$).

Chronic liver disease has also been associated with depression (24) and clinical studies have reported that some patients with chronic liver disease have more severe depressive trends than healthy people of the same age and sex (25). Through the use of the Hamilton depression scale in patients with chronic liver disease, a prevalence of depression of 62.9% has been reported (26). In our series, the prevalence of liver disease was 18.6% with a clear predominance of those patients with mild liver disease (13.7%) with respect to those with moderate-severe liver disease (4.9%), ($p = 0.023$). The presence of depression was associated with the existence of mild liver disease ($p = 0.001$) but not with moderate to severe liver disease ($p = 0.278$). Thus, depression can negatively affect the evolution and prognosis of patients with chronic liver disease.

In our study, patients with chronic kidney disease accounted for 16.3% of the total and the presence of depression was not associated with this disease ($p = 0.790$). However, depression also affects patients with chronic kidney disease. On the one hand, in its final stage associated with dialysis, due to the biological and psychosocial changes associated with this procedure (27), but it has also been reported that patients with chronic renal failure without associated dialysis have depression rates up to 3 times higher than the general population. In addition, depression worsens the quality of life and prognosis of patients with chronic kidney disease on dialysis or not (28-31). Probably, one of the causes for which we have not found association in our study is due to the low number of patients included and the non-differentiation between dialysis patients or not.

Chronic obstructive pulmonary disease (COPD) is a very prevalent condition with great morbidity and mortality. Depression and anxiety frequently accompany COPD and increase the risk of exacerbations, admissions to emergency services and hospitalizations with increased length of hospital stay (32-34). In addition, depression may be a risk factor for mortality in patients with COPD, especially in men (35). In our study, 16.2% of patients with COPD were

included, with a statistical association between COPD and depression ($p = 0.007$). The association between COPD and depression could be, in part, secondary to the social isolation suffered by patients with more severe COPD, but the prevalence of depression associated with COPD seems to be higher than in other chronic disabling diseases (36, 37). As a common link in many patients, there is tobacco. Smoking is the most important risk factor for developing COPD and is also frequently associated with depression (38). In our patients, smoking was relatively uncommon, 11.6%, and 20.4% were ex-smokers. Most of our patients (68%) were non-smokers. Despite this, smoking or having been an ex-smoker was associated with a higher probability of suffering from depression ($p = 0.041$). In patients hospitalized for an exacerbation of COPD, a prevalence of depression ranging from 9.5% to 85.6% (39) has been described, with a significant increase in readmissions in patients with associated depression (40,41), with an increase in post-hospitalization mortality due to exacerbation of COPD in patients with depression (40-42). In the meta-analysis of Atlantis et al. it has been shown that not only COPD increases the risk of developing depression (RR 1.69; 95% CI 1.45-1.96), but also depression increases the risk of poor prognosis and mortality of COPD patients (RR 1.43; 95% CI 1.20-1.71) (43).

Depression can affect the both prognosis and mortality or use of health resources in patients with physical comorbidities. The high prevalence of depression observed in patients with physical disorders suggests that it can significantly affect the evolution of these diseases. In this sense, it has been reported that patients with depression in association with chronic physical illnesses have a worse score on the quality of life scales than patients with isolated depression (7). On the other hand, patients with chronic diseases associated with depression also have greater functional impairment both objective and subjective, and treatment for depression improves not only depressive symptoms but also functionality (11, 36). With respect to mortality, it has been seen that having an associated depression increases mortality in cancer patients (44), in those who have suffered a stroke (45) and in those who have suffered an acute myocardial infarction (46) or suffer from COPD as described above (35). It has also been documented that patients with chronic diseases and associated depression use health services more frequently and consume more resources, which leads to an increase in costs derived from health care (13, 47).

The present study has a number of limitations. On the one hand, it is a retrospective study and does not include prevalent diseases and with a known association with depressive symptoms such as tuberculosis. Comorbidity has been studied using mainly the CCI that includes a series of prevalent pathologies but they do not necessarily have to be associated more with an increased prevalence of depression.

From our study data we can deduce that patients with cardiovascular disease, including hypertension, cerebrovascular disease, thromboembolic disease and atrial fibrillation, diabetes mellitus, liver disease, hemiplegia, COPD and anemia, have a high rate of comorbid depression. Conversely, patients with depression have a high CCI score. This means that several physical diseases are associated in these patients. Early identification of those patients who have physical illnesses, many of them chronic, which may be associated more frequently with the development

of depression, been negatively affected by this comorbidity, can facilitate a correct assessment and treatment of these patients by doctors involved in their attention.

REFERENCES:

- WHO. Innovative care for chronic conditions (Doc.: WHO/MNC/CCH/01.01). Geneva, WHO, 2001.
- Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, Wittchen HU, Kendler KS. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey. *Arch Gen Psychiatry*. 1994; 51: 8-19.
- Tarsitani L, Bertolote JM. Major depressive comorbidity in epilepsy as a reactive process to a chronic condition. *Epilepsy Behav*. 2006; 8: 343-344.
- Andrews G. Should depression be managed as a chronic disease? *BMJ*. 2001; 322: 419-421.
- World Health Organization. The global burden of disease: 2004 update. Geneva, Switzerland: WHO Press, 2008.
- Katon W, Lin EH, Kroenke K. The association of depression and anxiety with medical symptom burden in patients with chronic medical illness. *Gen Hosp Psychiatry*. 2007; 29: 147-155.
- Moussavi S, Chatterji S, Verdes E, Tandon A, Patel V, Ustun B. Depression, chronic diseases, and decrements in health: results from the World Health Surveys. *Lancet*. 2007; 370: 851-858.
- 8.- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40: 373-383.
- Charlson ME, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol*. 1994;47: 1245-1251.
- American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders. 5th ed. (DSM-V), APA, Washington, D.C., 2013.
- Egede LE. Major depression in individuals with chronic medical disorders: prevalence, correlates and association with health resource utilization, lost productivity and functional disability. *Gen Hosp Psychiatry*. 2007; 29: 409-416.
- Davidson KM, Ritson EB. The relationship between alcohol dependence and depression. *Alcohol Alcohol*. 1993; 28: 147-155.
- Mimura M. Comorbidity of depression and other diseases. *JMAJ*. 2001; 44: 225-229.

- Hackett ML, Pickles K. Part I: frequency of depression after stroke: an updated systematic review and meta-analysis of observational studies. *Int J Stroke*. 2014; 9: 1017-1025.
- Kang HJ, Kim SY, Bae KY, Kim SW, Shin IS, Yoon JS, Kim JM. Comorbidity of depression with physical disorders: research and clinical implications. *Chonnam Med J*. 2015; 51: 8-18.
- Thombs BD, Bass EB, Ford DE, Stewart KJ, Tsilidis KK, Patel U, Fauerbach JA, Bush DE, Ziegelstein RC. Prevalence of depression in survivors of acute myocardial infarction. *J Gen Intern Med*. 2006; 21: 30-38.
- Ng CG, Boks MP, Zainal NZ, de Wit NJ. The prevalence and pharmacotherapy of depression in cancer patients. *J Affect Disord*. 2011; 131: 1-7.
- Vulser H, Wiernik E, Hoertel N, Thomas F, Pannier B, Czernichow S, Hanon O, Simon T, Simon JM, Danchin N, Limosin F, Lemogne C. Association between depression and anemia in otherwise healthy adults. *Acta Psychiatr Scand*. 2016; 134: 150-160.
- Wilkins CH, Mathews J, Sheline YI. Late life depression with cognitive impairment: evaluation and treatment. *Clin Interv Aging*. 2009; 4: 51-57.
- Semenkovich K, Brown ME, Svrakic DM, Lustman PJ. Depression in type 2 diabetes mellitus: prevalence, impact, and treatment. *Drugs*. 2015; 75: 577-587.
- Kawakami N, Takatsuka N, Shimizu H, Ishibashi H. Depressive symptoms and occurrence of type 2 diabetes among Japanese men. *Diabetes Care*. 1999; 22: 1071-1076.
- Holt RI, de Groot M, Lucki I, Hunter CM, Sartorius N, Golden SH. NIDDK international conference report on diabetes and depression: current understanding and future directions. *Diabetes Care*. 2014; 37: 2067-2077.
- de Groot M, Golden SH, Wagner J. Psychological conditions in adults with diabetes. *Am Psychol*. 2016; 71: 552-562.
- Patten SB, Williams JV, Lavorato DH, Modgill G, Jetté N, Eliasziw M. Major depression as a risk factor for chronic disease incidence: longitudinal analyses in a general population cohort. *Gen Hosp Psychiatry*. 2008; 30: 407-413.
- Mullish BH, Kabir MS, Thursz MR, Dhar A. Review article: depression and the use of antidepressants in patients with chronic liver disease or liver transplantation. *Aliment Pharmacol Ther*. 2014; 40: 880-892.
- Popović DDj, Čulafić DM, Tepavčević DB, Kovačević NV, Špuran MM, Djuranović SP, Jovičić IA, Krstić MN, Perišić MD, Pekmezović TD. Assessment of depression and anxiety in patients with chronic liver disease. *Vojnosanit Pregl*. 2015;72: 414-420.

- Kimmel PL. Psychosocial factors in dialysis patients. *Kidney Int.* 2001; 59: 1599-1613.
- Palmer S, Vecchio M, Craig JC, Tonelli M, Johnson DW, Nicolucci A, Pellegrini F, Saglimbene V, Logroscino G, Fishbane S, Strippoli GF. Prevalence of depression in chronic kidney disease: systematic review and meta-analysis of observational studies. *Kidney Int.* 2013; 84: 179-191.
- Cukor D, Fruchter Y, Ver Halen N, Naidoo S, Patel A, Saggi SJ. A preliminary investigation of depression and kidney functioning in patients with chronic kidney disease. *Nephron Clin Pract.* 2012; 122: 139-145.
- Lee YJ, Kim MS, Cho S, Kim SR. Association of depression and anxiety with reduced quality of life in patients with predialysis chronic kidney disease. *Int J Clin Pract.* 2013; 67: 363-368.
- Tsai YC, Chiu YW, Hung CC, Hwang SJ, Tsai JC, Wang SL, Lin MY, Chen HC. Association of symptoms of depression with progression of CKD. *Am J Kidney Dis.* 2012; 60: 54-61.
- Ouellette DR, Lavoie KL. Recognition, diagnosis, and treatment of cognitive and psychiatric disorders in patients with COPD. *Int J Chron Obstruct Pulmon Dis.* 2017; 12: 639-650.
- Ng TP, Niti M, Tan WC, Cao Z, Ong KC, Eng P. Depressive symptoms and chronic obstructive pulmonary disease: effect on mortality, hospital readmission, symptom burden, functional status, and quality of life. *Arch Intern Med.* 2007; 167: 60-67.
- Laurin C, Moullec G, Bacon SL, Lavoie KL. Impact of anxiety and depression on chronic obstructive pulmonary disease exacerbation risk. *Am J Respir Crit Care Med.* 2012; 185: 918-923.
- Cuijpers P, Vogelzangs N, Twisk J, Kleiboer A, Li J, Penninx BW. Comprehensive meta-analysis of excess mortality in depression in the general community versus patients with specific illnesses. *Am J Psychiatry.* 2014; 171: 453-462.
- van den Bemt L, Schermer T, Bor H, Smink R, van Weel-Baumgarten E, Lucassen P, van Weel C. The risk for depression comorbidity in patients with COPD. *Chest.* 2009; 135: 108-114.
- Von Korff M, Katon WJ, Lin EH, Ciechanowski P, Peterson D, Ludman EJ, Young B, Rutter CM. Functional outcomes of multi-condition collaborative care and successful ageing: results of randomised trial. *BMJ.* 2011; 343: d6612.

- Matte DL, Pizzichini MM, Hoepers AT, Diaz AP, Karloh M, Dias M, Pizzichini E. Prevalence of depression in COPD: A systematic review and meta-analysis of controlled studies. *Respir Med.* 2016; 117: 154-161.
- Lecheler L, Richter M, Franzen DP, Rampini SK, Cheetham M, Jenewein J, Battegay E, Nowak A. The frequent and underrecognised co-occurrence of acute exacerbated COPD and depression warrants screening: a systematic review. *Eur Respir Rev.* 2017; 26. pii: 170026.
- Almagro P, Barreiro B, Ochoa de Echaguen A, Quintana S, Rodríguez Carballeira M, Heredia JL, Garau J. Risk factors for hospital readmission in patients with chronic obstructive pulmonary disease. *Respiration.* 2006; 73: 311-317.
- Papaoannou AI, Bartzioakas K, Tsikrika S, Karakontaki F, Kastanakis E, Banya W, Haniotou A, Papis S, Loukides S, Polychronopoulos V, Kostikas K. The impact of depressive symptoms on recovery and outcome of hospitalised COPD exacerbations. *Eur Respir J.* 2013; 41: 815-823.
- Abrams TE, Vaughan-Sarrazin M, Van der Weg MW. Acute exacerbations of chronic obstructive pulmonary disease and the effect of existing psychiatric comorbidity on subsequent mortality. *Psychosomatics.* 2011; 52: 441-449.
- Atlantis E, Fahey P, Cochrane B, Smith S. Bidirectional associations between clinically relevant depression or anxiety and COPD: a systematic review and meta-analysis. *Chest.* 2013; 144: 766-777.
- Pinquart M, Duberstein PR. Depression and cancer mortality: a meta-analysis. *Psychol Med.* 2010; 40: 1797-1810.
- Ayerbe L, Ayis S, Crichton S, Wolfe CD, Rudd AG. The long-term outcomes of depression up to 10 years after stroke; the South London Stroke Register. *J Neurol Neurosurg Psychiatry.* 2014; 85: 514-521.
- Lichtman JH, Froelicher ES, Blumenthal JA, Carney RM, Doering LV, Frasure-Smith N, Freedland KE, Jaffe AS, Leifheit-Limson EC, Sheps DS, Vaccarino V, Wulsin L; American Heart Association Statistics Committee of the Council on Epidemiology and Prevention and the Council on Cardiovascular and Stroke Nursing. Depression as a risk factor for poor prognosis among patients with acute coronary syndrome: systematic review and recommendations: a scientific statement from the American Heart Association. *Circulation.* 2014; 129: 1350-1369.

Bhattarai N, Charlton J, Rudisill C, Gulliford MC. Prevalence of depression and utilization of health care in single and multiple morbidity: a population-based cohort study. Psychol Med. 2013; 43: 1423-1431.

FIGURE 1:
Most frequent disorders in patients diagnosed with depression. Results are expressed as a percentage (%).

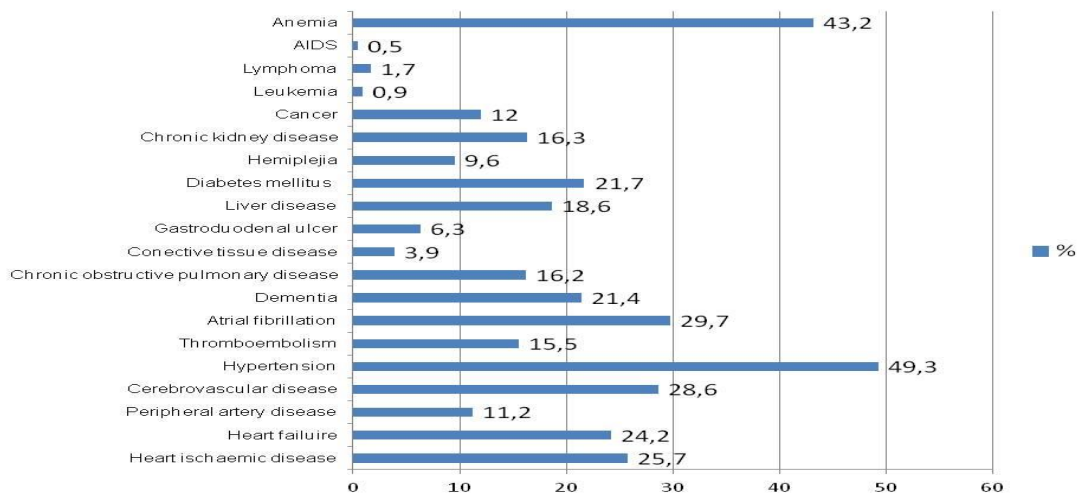


TABLE 1:
Charlson Comorbidity Index (CCI). Score and age correction.

| CHARLSON COMORBIDITY INDEX | POINTS |
|---|--------|
| Myocardial infarction | 1 |
| Congestive heart failure | 1 |
| Peripheral vascular disease | 1 |
| Cerebrovascular disease | 1 |
| Dementia | 1 |
| Chronic pulmonary disease | 1 |
| Connective tissue disease | 1 |
| Ulcer disease | 1 |
| Liver disease, mild | 1 |
| Diabetes | 1 |
| Hemiplegia | 2 |
| Renal disease, moderate or severe | 2 |
| Diabetes with end organ damage | 2 |
| Any malignancy | 2 |
| Leukemia | 2 |
| Malignant lymphoma | 2 |
| Liver disease, moderate or severe | 3 |
| Metastatic solid malignancy | 6 |
| Acquired immunodeficiency syndrome (AIDS) | 6 |

Age (years) correction to be added to the final score: < 50: 0; 50-59: 1; 60-69: 2; 70-79: 3; 80-89: 4; ≥ 90: 5.

Table 2: Association between depression and the different comorbidities included. Results are expressed as hazard ratio (HR) and statistical significance ($p < 0.05$).

| Variable | HR and CI 95% | P-value |
|--|---------------------|---------|
| Myocardial infarction | 1.025 (0.778-1.351) | 0.861 |
| Coronary artery disease | 0.982 (0.778-1.240) | 0.880 |
| Heart failure | 1.147 (0.944-1.393) | 0.167 |
| Peripheral artery disease | 0.915 (0.699-1.199) | 0.520 |
| Cerebrovascular disease | 0.567 (0.466-0.689) | <0.001* |
| Hypertension | 1.329 (1.123-1.574) | 0.001* |
| Venous thromboembolic disease | 0.382 (0.292-0.499) | <0.001* |
| Dementia | 0.921 (0.749-1.132) | 0.434 |
| Chronic obstructive pulmonary disease | 1.358 (1.087-1.697) | 0.007* |
| Connective tissue disease | 1.038 (0.676-1.596) | 0.864 |
| Peptic ulcer | 0.795 (0.557-1.136) | 0.207 |
| Mild liver disease | 0.598 (0.460-0.776) | <0.001* |
| Diabetes mellitus without target organ involvement | 1.475 (1.151-1.889) | 0.002* |
| Hemiplegia | 0.615 (0.453-0.835) | 0.002* |
| Moderate to severe chronic kidney disease | 0.969 (0.772-1.218) | 0.790 |
| Diabetes mellitus with target organ involvement | 0.948 (0.710-1.265) | 0.716 |
| Tumor without metastatic disease | 1.100 (0.786-1.538) | 0.578 |
| Leukemia | 0.567 (0.215-1.496) | 0.246 |
| Lymphoma | 0.826 (0.424-1.609) | 0.573 |
| Moderate-severe liver disease | 0.800 (0.535-1.198) | 0.278 |
| Tumor with metastatic disease | 0.961 (0.661-1.397) | 0.834 |
| AIDS | 1.600 (0.533-4.801) | 0.398 |
| Atrial fibrillation | 0.820 (0.680-0.988) | 0.036* |
| Anemia | 1.485 (1.250-1.765) | <0.001* |

* $p < 0.05$, statistically significant.