Methods of Screening for Depression in Outpatients with Heart Failure

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Abstract

Background: Depression is a syndromic clinical condition underdiagnosed in patients with heart failure. Several instruments are currently applied to screen for depression.

Objective: To determine the prevalence of depression and the agreement among screening methods for depression in patients with heart failure.

Methods: Cross-sectional study conducted between March 2015 and January 2017 including 76 outpatients following up at a clinic specialized in heart failure. Depression was screened with the Hamilton Depression Rating Scale (HAM-D), Beck Depression Inventory-II (BDI-II), and Patient Health Questionnaire-9 (PHQ-9). The agreement among the three instruments was analyzed with Fleiss' kappa coefficient (k_F), Krippendorff's alpha coefficient (C_k) and Cronbach's alpha coefficient. The accuracy, sensitivity, and specificity, as well as false-positive and false-negative results of the HAM-D and PHQ-9 were calculated considering the BDI-II as the gold-standard instrument in the diagnosis of depression.

Results: The prevalence rates of depression were 72.4% (n = 55) with the HAM-D, 67.1% (n = 51) with the BDI-II, and 40.8% (n = 31) with the PHQ-9 scales. The prevalence of depression simultaneously identified by all three instruments was 28.9% (n = 22) and the diagnostic agreement (presence or absence of depression) was 47.4% (n = 36). The analysis revealed a superficial agreement ($k_F = C_k = 0.27$) and moderate consistency (($\downarrow C = 0.602$, significantly not null, p = 0.000). Sociodemographic and clinical variables were not risk factors for depression in the evaluated sample.

Conclusion: The screening methods analyzed showed agreement and were useful in detecting depression among outpatients with heart failure. (Int J Cardiovasc Sci. 2018;31(4)414-421)

Keywords: Heart Failure; Depression / diagnosis; Depression / prevalence; Medical Records; Surveys and Questionnaires; Cross-Sectional Studies.

Introduction

Depression is a disorder of multifactorial nature.[1] When associated with heart failure (HF), depression compromises the functional capacity, quality of life, and survival of the patient.[2-7] It is necessary to explore the screening methods used to diagnose depression because despite the variety of applied instruments, no studies have been conducted to evaluate the agreement of these methods in patients with HF.[1,8]

The diagnosis of depression is established through the patient's clinical history and duration of signs and symptoms, as well as the application of specific scales.[1,8-9] There are approximately 49 scales used in the multidimensional assessment of depression,[10] including the Hamilton Depression Rating Scale (HAM-D),[11] Beck Depression Inventory-II,[12] and Patient Health Questionnaire-9 (PHQ-9),[13] among others.

A study conducted by Matias et al.[1] comparing the screening of depression with the PHQ-9 and the

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Geriatric Depression Scale of Yesavage concluded that both instruments are useful in identifying depression in elderly individuals, with a rho correlation of 0.387 (p < 0.000), kappa reliability 0.41 (p < 0.001), sensitivity 80%, specificity 44%, and moderate agreement.

A randomized study conducted by Freedland et al.[14] evaluated the efficacy of an integrative cognitive behavior therapy intervention for depression (measured by the scales BDI-II [46%] and HAM-D [51%]) and self-care in outpatients with HF (n = 158); the results of the study showed that the intervention was effective for depression, but not for self-care.

Another study,[15] conducted to determine the best sensitivity and specificity values of the BDI-II and HAM-D in patients (n = 73) seen at a reference center in neuropsychiatric showed that the BDI-II had higher sensitivity and specificity (94.4% and 90.6%, respectively) than the HAM-D (95% and 75.5%, respectively).

The BDI-II has been described as a gold-standard instrument to screen for depression in HF.[3,16] However, as a self-rating scale, the BDI-II has limited application in patients with cognitive impairment or low education level. In these cases, interviewer-rated scales may be applied by professionals experienced in interviewing depressed patients.[15,17]

The objective of this study was to determine the prevalence of depression and the agreement among methods of screening for depression in patients with HF.

Methods

Type of study

Cross-sectional study with a consecutive sample, carried out between March 2015 and January 2017 in a clinic specialized in HF in *Universidade Federal Fluminense* (UFF), Niterói, RJ, Brazil.

Participants

The participants were enrolled in a multidisciplinary program of a clinic specialized in HF (UFF).

The participants included in the study were patients enrolled in the clinic's program, diagnosed with HF according to the criteria by McMurray et al.[18], of both genders, and with the ability to answer the questionnaires. We excluded patients with cognitive impairment, as identified in their medical records, difficulty or inability of understanding the

instruments, and with a prior history of cognitive therapy or use of antidepressants.

In all, 76 patients comprised the final study sample and were assessed with three questionnaires for the screening of depressive symptoms: HAM-D, BDI-II, and PHQ-9.

The interview was conducted by a single interviewer, who followed the guiding protocol of the interviewer-rated questionnaire (HAM-D).[17]

The questionnaires BDI-II and PHQ-9 were applied as recommended in the literature.

The questionnaires were applied during the same interview, conducted by a single examiner. In the case of the self-rating questionnaires (BDI-II and PHQ-9), the patients were informed that these questionnaires were meant to evaluate their mental health status. They were then instructed to read the questionnaires attentively and mark the answers according to the intensity of their symptoms, with all following the same direction (i.e., the greater the severity of the symptom, the higher the score to be checked). There was no time constraint for the participants to complete the questionnaires and the examiner did not interfere with the reading of the questions to avoid a biased interpretation by the patient.

In regards to the HAM-D questionnaire, whose interview follows a protocol, the examiner conducted structured interviews and assigned a score to each response according to the intensity of the patient's signs and symptoms.

Instruments

Hamilton Depression Rating Scale

The HAM-D was the first interviewer-rated scale, i.e., applied by an interviewer. This scale was designed and developed by Hamilton at the end of the 1950s decade.[19] In 1994, the HAM-D was adapted to the Brazilian population as a valid instrument for an early diagnosis of a depressive episode. The HAM-D scale initially had 21 items but was subsequently reduced to a 17-item version after some items were removed (paranoid symptoms, obsessional symptoms, derealization, and diurnal variation), due to the low incidence or reliability of these items in relation to the measure of depression.[11,19]

In 1988, a structured manual was prepared for the HAM-D scale interview[20] to standardize the questions by the interviewer. Hamilton did not establish a cutoff value to discriminate normality from morbidity. Currently, it is accepted that scores with more than 25 points characterize

severely depressed patients, scores between 18 and 24 points characterize patients moderately depressed, and scores between 7 and 17 points characterize patients with mild depression.[17,19]

The items of the HAM-D scale focus on somatic symptoms (28%), cognitive symptoms (28%), motor symptoms (12%), anxiety (16%), mood (8%), and social symptoms (8%).[19]

This scale has been validated by several studies comparing the scores in groups of patients with diseases of different severity, including HF.[10]

Beck Depression Inventory-II

The BDI-II[12] has been validated in psychiatric inpatients and outpatients by comparison with the HAM-D, in which the BDI-II has been shown to be more effective.[12] The BDI-II is a self-rating instrument that screens for the presence of depressive symptoms using a scoring scale comprising 21 questions with four answer choices ranging from zero to three, ordered according to severity. To fill out the inventory, the individual selects the option that best fits the way he feels at the moment, with the scores ranging from zero (absence of symptoms) to three (highest intensity of the symptom).[21]

The overall BDI-II assessment is done by adding the numbers marked beside each question. A sum of 0-9 is considered normal, while 10-15 indicates mild depression, 16-23 indicates moderate depression, and 24 or more points indicate severe depression.

The screening properties of the BDI-II have been validated in Brazil. This scale is considered the gold-standard method for depression screening and has demonstrated good psychometric and operational characteristics.[3,10,12,16,21]

Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 evaluates the presence of depressive symptoms using a Likert-like scale comprising nine questions categorized into four response options ranging from "not at all" (zero points) to "nearly every day" (3 points) and a total score ranging from zero to 27 points. Thus, the higher the score, the worse the severity of the depressive signs. The PHQ-9 is a quick self-rating instrument that screens individuals at higher risk of presenting a major depressive episode.

The screening properties of this questionnaire were validated in the general Brazilian population in 2013,[22] and the questionnaire has demonstrated good psychometric and operational characteristics, with a sensitivity of 77% to 98% and specificity of 75% to 80%, having also been validated for the population of adults and elderly individuals.[1,23,24]

Procedures for data analysis

The descriptive analysis characterized the studied population according to frequencies and proportions. For quantitative variables, we used the statistics of minimum, maximum, mean, median, values, standard deviation, and coefficient of variation (CV). The variability of the distribution of a quantitative variable was considered low if $CV < 0.20$, moderate if $0.20 \leq CV < 0.40$, and high if $CV \geq 0.40$. In order to investigate the significance of the association between two qualitative variables, we used the chi-square test, and when this proved inconclusive, we applied Fisher's exact test for 2 x 2 tables.[25]

In the inferential analysis, complementary proportions were compared using the binomial test. The hypothesis of normality of a quantitative variable distribution was verified by the Kolmogorov-Smirnov (KS) and Shapiro-Wilk (SW) tests. The distribution was considered normal if both tests did not reject the null hypothesis of normality. In order to compare two independent groups when the variable had a normal distribution, we used unpaired Student's t test; otherwise, the comparison between the groups was performed with the Mann-Whitney non-parametric test.[25]

The agreement of the three instruments in diagnosing depression in the HF population was analyzed by Fleiss' kappa (k_F) and Krippendorff's alpha coefficients (C_k). The consistency of the three instruments in diagnosing depression in the HF population was assessed by Cronbach's alpha coefficient (C_c). Agreement and consistent were evaluated according to the Landis & Koch classification (1977).

We calculated the accuracy, sensitivity, specificity, and rates of false-positive and false-negative results of the HAM-D and PHQ-9 instruments considering the BDI-II as the gold-standard instrument in the diagnosis of depression (the definition of these concepts can be found in Medronho et al., 2009).

The statistical analysis was performed using the program Statistical Package for the Social Sciences (SPSS), version 20.0, and all analyses were carried out considering a maximum significance level of 5.0%.

Ethical procedures

The study was approved by the Research Ethics Committee of *Hospital Universitário Antônio Pedro/Universidade Federal Fluminense* with the number 630.078. The patients were informed about the objectives of the research, signed a free and informed consent form, and were assured about their right to data confidentiality and care in regards to the use of their information in written work. The patients presenting symptoms related to any mental disorder during the clinical interview of the main study were referred to a mental health service integrated into the clinic specialized in HF.

Results

A total of 76 patients participated in this study, of whom 40 (52.6%) were female and 36 (47.4%) were male. The binomial test showed no significant difference between these proportions (p = 0.731), i.e., the sample was balanced in relation to the distribution of men and women, and the observed prevalence of women was not significant. The age of the patients followed a normal distribution (p = 0.094 by the KS test and p = 0.467 by the SW test), with an interval of 35 to 91 years, a mean of 63.0 years, standard deviation of 11.6 years, and a median of 65 years. The CV of age (0.18) showed that the distribution of age had low variability in the sample.

The monthly income of the patients did not follow a normal distribution (p = 0.000) and ranged from R$ 500.00 to 3,000,00, with a mean of R$ 1,118.74 (standard deviation R$ 576.32 and median R$ 1,000.00). The CV of the income (0.51) showed that the distribution of income had high variability in the sample. The frequency distribution of the observed variables characterizing the patients are shown in Table 1.

Typically, all patients had a white self-declared color (67.1%), education level of Elementary School I (56.6%), NYHA functional class II (51.3%), hypertension (100%), dyslipidemia (81.6%), diabetes (56.4%), and obesity (44.8%). There was no significant difference between the age of men and women (p = 0.056) or between the incomes of men and women (p = 0.644).

The male and female groups did not differ in relation to the distribution of self-declared color (p = 0.641), education level (p = 0.352), and incidence of diabetes (p = 0.223), dyslipidemia (p = 0.827), chronic renal failure (CRF; p = 0.426), chronic obstructive pulmonary disease (COPD; p = 0.601), and stroke (p = 1.000).

Table 1 - Sociodemographic and clinical characteristics of outpatients with heart failure

Sociodemographic variables	n (76)
Gender	
Female	52.6% (n = 40)
Male	47.4% (n = 36)
Age (mean ± SD)	63.03 ± 13.5 years
Self-declared color	
White	67.1% (n = 51)
Black	28.9% (n = 22)
Indeterminate	3.9% (n = 3)
Education level*	
Literacy	2.6% (n = 2)
Elementary School I	56.6% (n = 43)
Elementary School II	36.8% (n = 28)
Middle School	3.9% (n = 3)
Family income in reais (mean ± SD)	1,118.74 ± 576.32
Functional class (NYHA)	
I	30.3% (n = 23)
II	51.3% (n = 39)
III	18.4% (n = 14)
Hypertension	100% (n = 76)
Dyslipidemia	81.6% (n = 62)
Diabetes	56.6% (n = 43)
BMI (kg/m²)	
Low weight	1.3% (n = 1)
Normal weight	23.7% (n = 18)
Overweight	14.5% (n = 11)
Pre-obesity	15.8% (n = 12)
Obesity I	30.3% (n = 23)
Obesity II	9.2% (n = 7)
Obesity III	5.3% (n = 4)
Anemia	19.7% (n = 15)
CRF	23.7% (n = 18)
COPD	3.9% (n = 3)
Stroke	5.3% (n = 4)

n: number of patients; SD: standard deviation; NYHA: New York Heart Association; BMI: body mass index; CRF: chronic renal failure; COPD: chronic obstructive pulmonary disease.

The prevalence rates of depression diagnosed by the instruments were: 72.4% (n = 55) by the HAM-D, 67.1% (n = 51) by the BDI-II, and 40.8% (n = 31) by the PHQ-9, as shown in Table 2. Considering a simultaneous diagnosis by all three instruments, the prevalence of depression was 28.9% (n = 22). The three instruments showed a diagnostic agreement (presence or absence of depression) in only 47.4% of the sample (n = 36).

Comparing the three instruments in terms of diagnosing depression in the HF population, there was superficial agreement ($k_F = C_k = 0,27$, as evaluated by Fleiss' kappa (k_F) and Krippendorff's alpha coefficients (C_k), and moderate consistency (significantly not null, p = 0.000), as assessed by Cronbach's alpha coefficient (C_C).

Table 3 shows the quality measures of the HAM-D and PHQ-9 instruments as diagnostic tests for depression in outpatients with HF, using the BDI-II as the gold-standard instrument. The HAM-D scale proved to be the best instrument to diagnose depression, as it showed higher accuracy and sensitivity and a lower percentage of false-negative results. The PHQ-9 instrument was conservative in diagnosing depression, with a high percentage of false-negative results and a low sensitivity in identifying patients who in fact had depression.

Considering the BDI-II as the gold-standard instrument in diagnosing depression, we investigated the association of depression with the patients' characteristics. There was no significant association between depression and the following factors: gender (p = 0.291), self-declared color (p = 0.976), education level (p = 0.918), obesity (p = 0.324), diabetes (p = 0.316), dyslipidemia (p = 0.056), COPD (p = 0.250), stroke (p = 0.296), and CRF (p = 0.536).

The age and income of the patients with and without depression were also not associated with depression (p = 0.862 [unpaired Student's t test] and p = 0.776 [Mann-Whitney test], respectively).

Therefore, none of the variables included in this study was associated with depression or was a risk factor for depression in outpatients with HF.

Discussion

This is the first study comparing screening methods for depression in outpatients in a multidisciplinary clinic specialized in HF. Depression has not been systematically analyzed in patients with HF, but when specifically researched, has been observed to be frequent in this population.[28-36] This condition affects between 14.0% and 26.0% of the patients without HF, but the incidence increases to 24.0% to 85.0% in patients with HF.[33,34]

The main findings of this study indicate a relevant prevalence of depression in HF patients when screened by the HAM-D, BDI-II, and PHQ-9 instruments. BDI-II has been considered the gold-standard instrument for depression screening in patients with HF, but in individuals with cognitive impairment or illiterate, this instrument is not recommended.[10,12,21] Therefore, the results of our investigation in relation to the internal

Table 2 - Prevalence (P) of depression in outpatients with heart failure	
Instrument	**Results**
HAM-D	72.4% (n = 55)
BDI-II	67.1% (n = 51)
PHQ-9	40.8% (n = 31)
Agreement among all three instruments	$k_↓F = C_↓k = 0.27$
Consistency of the three instruments	($↓C$ 0.602; p < 0.000)

n: number of patients; HAM-D: Hamilton Depression Rating Scale; BDI-II: Beck Depression Inventory-II; PHQ-9: Patient Health Questionnaire-9.

Table 3 - Quality measures of the HAM-D and PHQ-9 instruments as diagnostic tests for depression in outpatients with heart failure					
Instrument	**Accuracy**	**Sensitivity**	**Specificity**	**% of false-positives**	**% of false-negatives**
HAM-D	76.3	86.3	56.0	14.5	9.2
PHQ-9	55.3	47.1	72.0	9.2	35.5

HAM-D: Hamilton Depression Rating Scale; PHQ-9: Patient Health Questionnaire-9.

consistency of the scales show that the BDI-II, HAM-D, and PHQ-9 proved to be useful tools for application in patients with HF.

We observed in this study a possible agreement advantage of the HAM-D with the BDI-II, the gold-standard instrument. This is probably due to the number of items in both questionnaires. The significant agreement among the scales indicates an evaluation of the intensity of the symptoms in the same direction, i.e., the greater the score, the greater the severity.[37,40]

A possible explanation for the difference in prevalence identified in the PHQ-9 scale may be due to its self-rating features since they portray an individual's subjective response (as how he perceives his health and symptom). Although the instrument has already been tested in various levels of health care attention and different cultural contexts,[1] still limited research has been carried out in Brazil using the PHQ-9 to screen for depression in outpatients with HF. A study carried out in Minnesota applied the PHQ-9 scale to evaluate the occurrence of depression in a sample of 425 outpatients with HF and identified a prevalence of 42.1% (n = 179),[38] which is in line with our findings.

Self- and interviewer-rating scales should take into account several aspects, including the individual's educational level and time availability for the assessment, as well as the objective of the evaluation.

The BDI-II and HAM-D scales are instruments used in more than 50% of the studies;[10] the sensitivity and specificity of these instruments is approximately 0.84 and 0.72, respectively,[37,39] which is also in line with our results.

A review[9] has assessed the scales HAM-D, BDI-II, Zung Self-Rating Depression Scale, Geriatric Depression Scale of Yesavage, and Montgomery-Åsberg Depression Rating Scale (MADRS). The results showed relevance in the identification of signs and symptoms of depressive disorders, directing the attention to mental health interventions in the elderly.

We observed that the patients in the present study had important clinical comorbidities (diabetes, dyslipidemia, obesity, CRF, and hypertension), which were not associated with depression. In a study conducted by Aguiar et al. (2010) in hospitalized patients with HF (n = 43), patients with depression (55.8%, n = 24) according to the HAM-D scale did not differ from non-depressed ones in regards to gender, age, anemia, and renal function, factors that are known to influence the occurrence of clinical manifestations.

Depression is an important risk factor associated with HF,[2] a syndromic clinical condition. When depression is not specified, it is mistaken and underdiagnosed in these individuals,[35] probably due to the superposition of symptoms of HF (dyspnea, weight change, sleep, fatigue) and the neurovegetative symptoms of depression (insomnia, psychomotor slowing, and decreased energy, concentration, and appetite).[36]

A study conducted by Freedland et al.[32] in a sample of 682 patients with HF showed that 245 (36%) patients had clinically significant depression (according to the Diagnostic and Statistical Manual of Mental Disorders [DSM-IV] criteria), while 436 (64%) were classified as non-depressed. Patients with depression also were not significantly affected by the presence of other important comorbidities, such as diabetes or kidney disease, or by the presence of only one of these conditions. These results are aligned with those of our study and differ in some aspects from the observations described in the literature. However, considering that depression emphasizes the clinical manifestations and worsens the progression of patients with HF, more attention should be dedicated to this condition, including to its screening. The importance of this initiative has been increasing in clinics specialized in HF, since studies have documented that the treatment of depression promotes improvement of the symptoms and quality of life of the patients.[2]

Limitations

This study presents limitations due to its experimental, observational, and cross-sectional design, which did not allow us to establish the variables predicting depression in HF. However, through the data presented, it becomes evident the importance of this discussion, because different depression scales are applied in this population.

This research demonstrates a need for further work on the screening of depression in outpatients in practices specialized on HF, due to the relevant prevalence of and damage from this association. It is important to highlight the need to deepen the knowledge of the association of depression with the sociodemographic and clinical characteristics present in this population for the development of preventive work in outpatients with HF.

Conclusions

Based on the results of this study on the prevalence of depression associated with HF, we found the following:

Int J Cardiovasc Sci. 2018;31(4)414-421
Original Article

Guerra et al.
Screening: depression in heart failure

420

1) depression has a relevant prevalence in outpatients with HF; 2) the diagnosis and detection of depression are obtained through the use of questionnaires in outpatients with HF; 3) the three questionnaires evaluated have a superficial agreement and moderate consistency in the diagnosis of depression in the population with HF; 4) the HAM-D scale proved to be the best instrument in diagnosing depression, since it showed greater accuracy and sensitivity, and a lower percentage of false-negative results; 5) the PHQ-9 instrument was conservative in diagnosing depression, with a high percentage of false-negative results and low sensitivity to identify patients who are in fact depressed.

In the present study, the HAM-D questionnaire showed greater accuracy in the diagnosis of depression, due to its convenience in grading this condition and for demonstrating (in several studies) the ability to evaluate the severity of the depression.

These conclusions identify areas with gaps requiring further research, in addition to new questions in the screening of depression, and adds more information on the prevalence of depression in HF, guiding researchers and clinicians in terms of screening for depression and issues relevant to the association of these two pathologies, depression and HF.

Author contributions

Conception and design of the research: Guerra TRB, Mendlowicz MV, Mesquita ET, Cavalcanti ACD;

Acquisition of data: Guerra TRB, Venancio ICD, Pinheiro DMM; Analysis and interpretation of the data: Guerra TRB, Mesquita ET, Cavalcanti ACD; Statistical analysis: Guerra TRB; Obtaining financing: Mesquita ET, Cavalcanti ACD; Writing of the manuscript: Guerra TRB, Pinheiro DMM; Critical revision of the manuscript for intellectual content: Mendlowicz MV, Mesquita ET, Cavalcanti ACD.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Hospital Universitário Antônio Pedro under the protocol number 630.078. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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