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**Screening of depression in cardiology:
a study on 617 cardiovascular patients.**

Valentina Tesio^{1,2}, Sebastiano Marra^{1,3}, Stefania Molinaro^{1,4}, Riccardo Torta^{1,4},
Fiorenzo Gaita^{1,3}, Lorys Castelli^{1,2}.

Corresponding author: Tesio Valentina; email: valentina.tesio@unito.it.

c/o Department of Psychology, University of Turin, Via Po 14, 10123 Turin, Italy;

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Key words: cardiovascular disease; depression; coronary artery disease;
acute coronary syndrome; HADS; screening.

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² Department of Psychology, University of Turin, Via Po 14, 10123, Turin, Italy.

³ Division of Cardiology, University of Turin, “Città della Salute e della Scienza” Hospital, Corso Bramante 88, 10126, Turin, Italy.

⁴ Clinical Psychology and Psycho-Oncology Unit, University of Turin, “Città della Salute e della Scienza” Hospital, Corso Bramante 88, 10126, Turin, Italy.

Abstract

Background

Depression screening in the cardiovascular disease (CVD) care setting is under-performed, also because the issue of the optimal screening tools cut-off is still open. We analysed which HADS (Hospital Anxiety and Depression Scale) total score cut-off value shows the best properties in two groups of 357 Acute Coronary Syndrome (ACS) and 260 Chronic Coronary Artery Disease (CAD) hospitalized patients.

Methods

A Receiver Operating Characteristics (ROC) curve was plotted for both groups using the Montgomery-Asberg Depression Rating Scale (MADRS) as the criterion. Accuracy, positive (PPV) and negative (NPV) predictive values were computed for different cut-off scores.

Results

The ROC curves confirmed the excellent/very good accuracy of the HADS in both groups, with an area under the curve of .911 for the ACS and .893 for the CAD patients. The cut-off of 14 showed the best compromise between high sensitivity and good specificity in both groups, with high negative predicted values (95.5% and 92.4%, respectively).

Conclusion

Using a cut-off value of 14, the HADS could be considered a good screening tool to identify hospitalized CAD and ACS patients requiring a more accurate depression assessment, in order to promptly plan the most appropriate treatment strategies and prevent the negative effects of depression in CVD patients.

1. Introduction

A recent systematic analysis of the “Global Burden of Disease Study 2013” underlined once again that cardiovascular deaths still account for almost a third of all deaths globally [1].

There is extensive evidence that cardiovascular disease (CVD) and depression reinforce each other, with a downward spiral association [2]. Depression results in an 80–90% increased risk of CVD onset [3] and is strongly linked with adverse outcomes, negatively contributing to the progression and prognosis of the disease. Furthermore, CVD itself could increase the risk of developing depressive disorders [2], with Major Depressive Disorder (MDD) showing a prevalence of 20% to 30% in coronary heart disease (CHD) patients [4].

Although several clinical guidelines recommend early screening and evaluation for treatment of depression [5], clinical cardiologists often do not take into account depression as a negative risk factor, underestimating its negative effect. What is more, routine screening in the hospital care setting is still under-performed, also because of conflicting and confused findings regarding the optimal tool [4,6,7]. A recent systematic review analysed the diagnostic accuracy of different screening tools, including the “Hospital Anxiety and Depression Scale” (HADS), in detecting MDD in CHD patients [4]. Although it highlighted that the HADS is a useful self-report instrument in CVD patients [4], other studies call into question the diagnostic accuracy of the two subscales separately, but strongly suggest the use of the HADS total score (HADS-Tot) [8-11]. On these bases, the general aim of this study is to provide clinicians with the optimal HADS cut-off to identify depressed patients. We thus investigated the concurrent validity of the HADS-Tot with a clinician-rated scale, assessing depression in two groups of cardiac hospitalized patients - Acute Coronary Syndrome (ACS) and chronic Coronary Artery Disease (CAD).

2. Methods

2.1. Patients and procedure

The study was proposed to all consecutive patients hospitalized in the Cardiology Unit of the “Città della Salute e della Scienza” Hospital of Turin. All patients who gave their written informed consent and completed the HADS had a clinical interview with an expert psychologist who filled in the Montgomery-Asberg Depression Rating Scale (MADRS). From a pool of 1049 inpatients who completed the HADS, the data of 357 patients with ACS and 260 with chronic CAD were analysed. Patients were classified into the ACS or CAD group by expert cardiologists according to the Canadian Cardiovascular Society grading of angina pectoris [12].

2.2. Measures

The MADRS, a semi-structured clinical interview rated by an expert clinical psychologist/psychiatrist, is one of the gold-standard clinician-rated diagnostic tools [13]. Following the widely-accepted recommendations, the cut-off value of 11 was used to tally a patient as depressed (≥ 11) or not (< 11) [13,14].

The HADS is a brief self-rating instrument composed of 14 items rated between 0-3, widely used in physically ill patients [15,16]. It evaluates the presence of depressive and anxiety symptoms. According to the more recent methodological studies published on the matter, the total score was used as an index of psychological distress [9].

2.3. Statistical analyses

All statistical analyses were performed using the Statistical Package for Social Science (SPSS-23). A Receiver Operating Characteristics (ROC) curve was plotted separately for ACS

and CAD patients, using the results of the MADRS as the criterion.

Positive (PPV) and negative (NPV) predictive values, accuracy and distance (d) to the optimal (0,1) point were computed for different cut-off scores. To determine the optimal cut-off score, both the “point of curve closest to the (0,1)” criteria (d value) and visual assessment of the score combining high sensitivity with good specificity were considered.

3. Results

Table 1 shows the demographic characteristics of the two groups. ACS and CAD patients reported a mean (SD) HADS-Tot raw score of 10.7 (7.5) and 11.8 (7.4) respectively, with 19% (68) of patients in the former group and 29.6% (77) in the latter showing clinically relevant depressive symptoms according to the MADRS (**Table 1**).

The ROC curve analyses showed an excellent/very good accuracy of the HADS-Tot in both groups, with an area under the curve (AUC) of .911 for the ACS and .893 for the CAD group (**Table 2**). Between the possible cut-off values with the lowest d values, visual inspection of the data revealed that the cut-off of 14 showed the best compromise between high sensitivity and good specificity in both ACS and CAD patients, with high NPVs (95.5% for ACS and 92.4% for CAD) (**Table 2**).

4. Discussion

Depressive symptoms have a negative role in CVD, increasing the risk of new cardiac events and negative outcomes, and worsening patients' quality of life [2]. Indeed, post-myocardial infarction (MI) depression is associated with a 1.5- to 2.7-fold increased risk for both post-MI

mortality and new cardiac events [17]. Despite the negative effects of depression on cardiac patients, its assessment is still underused, especially in the Italian cardiology hospital setting.

The opportunity to screen for and treat depression in hospitalized cardiac patients should not be missed, also because the risk of mortality or new cardiovascular events in cardiac patients with depression increases mainly in the first two years after the original cardiac event [18].

Accurate assessment of depressive disorders with a semi-structured interview, such as the Structured Clinical Interview for DSM disorders (SCID-I) or the MADRS, would be costly for the healthcare system in terms of both time (more than 30 minutes) and money, and may not suit the routine of the hospital setting. This is why clinical guidelines [5,19] usually recommend a two-step procedure: first, screening with a self-report scale; then, evaluation with a more accurate assessment (i.e. MADRS) of positive patients. So it is crucial to choose a rapid self-administered tool allowing easy but accurate first-step screening, in order to accurately identify those patients requiring further psychological assessment. The HADS is a clinical tool specifically developed to assess depressive and anxiety symptoms in physically ill patients [20]. It has the advantage of being an easy and rapid self-report instrument (no more than 5 minutes) that can be administered during admission or in a waiting room and takes no longer than a minute to be scored by the clinician. The HADS screening procedure could easily be inserted into the hospital routine, allowing the screening of all patients and reducing drop-out, since discharged patients are often unwilling to return for further scheduled medical appointments.

To this aim, recent evidence suggests using the HADS total score, but not the two subscales score separately [8-11]. This indication has both a clinical and a methodological rationale. Clinically, in depressive, as well as in anxiety disorders properly so-called (DSM criteria), both depressive

and anxiety symptoms often co-occur, even if to a different extent. Indeed, symptoms of anxiety and depression could both be considered parts of that multidimensional continuum called psychological distress, which ranges from normal feelings of vulnerability, sadness and fears to problems that could become disabling, such as depressive disorders. A valid first-step screening tool should therefore account for the overall psychological distress [11].

From a methodological standpoint, recent confirmatory factor analysis (CFA) suggests that the HADS is saturated by a single general distress factor (explaining over 70% of the variance), with the two subscales showing weak item loadings separately [9,10]. These data provide psychometric evidence against the internal consistency of the two subscales in favor of the reliability of the HADS-Tot [9,10]. What is more, a recent study shows that the HADS-Tot is a valid measure and that it is predictive of future symptoms of distress, healthcare costs and quality of life in a CHD population [11].

The data of the present study show that, compared to the MADRS, the HADS-Tot has good reliability and accuracy for ACS and CAD patients. In both groups, 14 is the cut-off with the best psychometric properties to screen those patients with clinically relevant levels of psychological distress who should be submitted to a more in-depth assessment for depression. This cut-off provides not only high sensitivity, but also high specificity, with about 4 out of 5 patients correctly classified, as shown by the accuracy values. What is more, this cut-off shows high NPVs (95% for ACS and 92% for CAD), meaning that 9 out of 10 patients who, according to the HADS-Tot, did not present a clinically relevant level of psychological distress and therefore did not require further psychological investigation, were correctly identified (i.e. they really were non-depressed, according to the MADRS). Clinically, these screening

procedures allow the healthcare provider to correctly reduce the number of patients requiring more in-depth depression assessment procedures (clinical interviews) with a considerable reduction in time and money spent. What is more, using a unique cut-off for both pathologies could increase the practicality of this tool, allowing an immediate scoring of the HADS, independently of the cardiac diagnosis. Even if a cut-off of 13 would have allowed increasing the sensitivity (from 83.8% to 91.2%) of the HADS-Tot for ACS patients, we think that this increase had not been enough to compensate the decrease in the specificity (from 80.3% to 76.5%). This is the reason why we think that the cut-off of 14 represents the best compromise between high sensitivity and specificity. While this cut-off is the same proposed by other studies (see for example Bunevicius and colleagues [21]), it is higher than 12, the one proposed by Palacios and colleagues [11]. Given the clinical relevance of this issue, further studies are needed to confirm and reinforce this result in order to come to a clear implementation of this cut-off in the clinical practice.

Limitation of the study

Given the negative role that an anxiety disorder could have on cardiac patients, further studies should evaluate the validity of the HADS total score as a screening tool also for the presence of anxiety disorders, by means of a specific gold standard clinical interview. This would also allow evaluating if the lower cut-off found by Palacios and colleagues [11] could be due to its comparison with both a diagnosis of depression and anxiety.

In conclusion, the data of the present study suggest that, using a cut-off value of 14, the HADS could be considered a good first-step screening tool in order to identify CAD and ACS

inpatients with a relevant level of psychological distress, who risk developing depressive disorders, and thus require a deeper second-step assessment.

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Table 1. Demographic and clinical characteristics of the 617 CVD patients.

Variable	ACS (N=357)	CAD (N=260)
Age (Mean (SD))	67.3 (11.4)	69 (9.8)
Sex (N (%))		
<i>Male</i>	269 (75.4)	190 (73.1)
<i>Female</i>	88 (24.6)	70 (26.9)
Educational level (Mean (SD))	9.6 (4.4)	9.7 (4.1)
Marital status (N (%))		
<i>Single</i>	25 (7)	18 (6.9)
<i>Married/cohabiting</i>	264 (74.4)	200 (76.9)
<i>Divorced</i>	21 (5.9)	21 (8.1)
<i>Widowed</i>	45 (12.7)	21 (8.1)
Employment status (N (%))		
<i>Employed</i>	97 (29.3)	50 (19.9)
<i>Unemployed/homemaker</i>	22 (6.7)	22 (8.8)
<i>Retired</i>	212 (64)	179 (71.3)
MADRS	6.8 (5.9)	8.6 (6.2)
<i>Above cut-off (Cases) (N (%))</i>	68 (19)	77 (29.6)
HADS-Tot	10.7 (7.5)	11.8 (7.4)
HADS-D	4.9 (4.2)	5.7 (4.1)
HADS-A	5.8 (4.2)	6.2 (4.1)

ACS: Acute Coronary Syndrome; CAD: chronic Coronary Artery Disease;

MADRS: Montgomery-Asberg Depression Rating Scale;

HADS-Tot: Hospital Anxiety and Depression Scale – total score;

HADS-D/-A: Hospital Anxiety and Depression Scale – depression/anxiety subscale.

Table 2. Psychometric properties at each cut-off value of the HADS total score for the screening of clinically relevant depressive symptoms in

Acute Coronary Syndrome (ACS) and Coronary Artery Disease (CAD) patients.

	N (%)	Sensitivity		Specificity		d		PPV		NPV		Accuracy		AUC	
			% (95% CI)		% (95% CI)		% (95% CI)		% (95% CI)		% (95% CI)	%	(95% CI)	%	(95% CI)
	≥11	164 (45.9)	94.1 (84.9-98.1)	65.4 (59.6-70.8)	0.351	39 (31.6-47)	97.9 (94.4-99)	70.8							
Acute	≥12	150 (42)	94.1 (84.9-98.1)	70.2 (64.6-75.4)	0.303	42.7 (34.7-51)	98.1 (94.8-99.4)	74.8							
Coronary	≥13	130 (36.4)	91.2 (81.1-96.4)	76.5 (71.1-81.2)	0.251	47.7 (38.9-56.6)	97.4 (94.1-98.9)	79.3							.911
Syndrome	≥14	114 (31.9)	83.8 (72.5-91.3)	80.3 (75.1-84.6)	0.255	50 (40.5-59.5)	95.5 (91.8-97.6)	80.9							(.875-.947)
(ACS)	≥15	99 (27.7)	79.4 (67.5-87.9)	84.4 (79.6-88.3)	0.259	54.5 (44.3-64.5)	94.6 (90.9-96.9)	83.5							
	≥16	89 (24.9)	77.9 (65.9-86.7)	87.5 (83-91)	0.253	59.6 (48.6-69.7)	94.4 (90.7-96.7)	85.7							
	≥11	132 (50.8)	92.2 (83.2-96.8)	66.7 (59.3-73.3)	0.342	53.8 (44.9-62.4)	95.3 (89.6-98.1)	74.2							
Coronary	≥12	115 (44.2)	88.3 (78.5-94.2)	74.3 (67.2-80.3)	0.283	59.1 (49.6-68.1)	93.8 (88.2-96.9)	78.5							
Artery	≥13	100 (38.5)	84.4 (74-91.3)	80.9 (74.3-86.2)	0.247	65 (54.7-74.1)	92.5 (87-95.9)	81.9							.893
Disease	≥14	89 (34.2)	83.1 (72.5-90.4)	86.3 (80.3-90.8)	0.217	71.9 (61.2-80.7)	92.4 (87.1-95.7)	85.4							(.848-.937)
(CAD)	≥15	81 (31.2)	77.9 (66.8-86.3)	88.5 (82.8-92.6)	0.249	74.1 (62.9-82.9)	90.5 (85-94.2)	85.4							
	≥16	70 (26.9)	68.8 (57.1-78.6)	90.7 (85.3-94.3)	0.326	75.7 (63.7-84.8)	87.4 (81.6-91.6)	84.2							

HADS: Hospital Anxiety and Depression Scale; $d = \sqrt{[(1 - \text{Sensitivity})^2 + (1 - \text{Specificity})^2]}$; PPV: positive predictive value;

NPV: negative predictive value; AUC: area under receiver operating curve.

Optimal cut-off values in **bold**.