

Agreement Between Hopelessness/Helplessness and Montgomery-Asberg Depression Rating Scale in Healthy Individuals and in Patients with Benign Breast Disease and Breast Cancer: A Prospective Case-Control Study in Finland

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Abstract. *Background:* The relation between scoring for hopelessness/helplessness and the Montgomery-Asberg Depression Rating Scale (MADRS) in healthy study subjects (HSS) and in patients with benign breast disease (BBD) and breast cancer (BC) has not been compared in a prospective study. We, therefore, investigated hopelessness and helplessness scores versus the MADRS in 115 patients. *Patients and Methods:* In the Kuopio Breast Cancer Study, 115 women with breast symptoms were evaluated for hopelessness and helplessness, and for the MADRS before any diagnostic procedures were carried out. *Results:* In the self-rating score (SRS), hopelessness/helplessness versus the MADRS were highly significantly positively correlated in the HSS, BBD and BC groups. In the SRS, the weighted kappa values for hopelessness/helplessness versus the MADRS in the HSS, BBD and BC groups were also statistically significant. There was also a significant positive correlation in the examiner-rating score (ERS) for hopelessness versus the MADRS in the HSS, BBD and BC groups and for helplessness versus the MADRS in the HSS, BBD and BC groups. The unweighted kappa values in the ERS for hopelessness versus the MADRS were statistically highly significant for the HSS, BBD and BC groups and those for helplessness versus the MADRS in the HSS and BBD groups were statistically significant. *Conclusion:* A new finding with clinical relevance in the present work is the agreement between hopelessness/

helplessness scores and MADRS in the SRS and ERS. In the breast cancer diagnostic unit, the identification of hopeless/helpless persons is essential in suicide prevention and it is important to assess and treat hopelessness/helplessness even though an individual may report few depressive symptoms.

Depression is one of the most common psychological disorders and cross-sectional studies have found an association between depression and depression-associated symptoms such as hopelessness/helplessness in terminally-ill cancer patients (1); hopelessness/helplessness may also occur as a precursor of depression (2-6). Hintikka *et al.* in Finland showed an 11.7% prevalence of depression in a general population sample (7) and 10-34% of women were shown to have depression and depression-like symptoms in a general population cohort (8). Many studies have clearly demonstrated that depression and depression-associated symptoms such as hopelessness/helplessness affect compliance with cancer therapy, and reduce survival and quality of life (7, 9-11).

The Montgomery-Asberg Depression Rating Scale (MADRS) was developed more than 20 years ago as an inventory for the rapid screening of depression by British and Swedish researchers, especially as an adjunct to the Hamilton Rating Scale for Depression (12). It is used to measure the severity of depressive episodes in patients with mood disorders.

We assessed hopelessness *versus* helplessness in patients with breast cancer (BC) and benign breast disease (BBD), and in healthy study subjects (HSS) (9, 10). Our results suggested a specific link between hopelessness and helplessness attitude characteristics in breast disease. However, the results of hopelessness/helplessness scores and MADRS in healthy study patients (HSS) and in patients with benign breast disease (BBD) and breast cancer (BC) has not been compared in a prospective study. Because BC is a hormonally-responsive neoplasm with great psychological

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Table I. Characteristics of the study participants. Results are shown for the patients with breast cancer (BC), for those with benign breast disease (BBD) and for the healthy study participants (HSS).

Variable	HSS (n=28)	BBD (n=53)	BC (n=34)	p-Value
Age (mean, years)	45.7	47.6	51.6	0.12
Height (mean, cm)	160.8	162.3	164.4	0.75
Body weight (mean, kg)	68.3	67.8	72.5	0.25
Age at menarche (mean, years)	13.4	13.4	13.4	0.99
Age at birth of first child (mean, years)	25.0	25.0	25.2	0.92
Age at menopause (mean, years)	50.0	48.9	47.9	0.53
No. of children (mean)	2.5	2.4	2.6	0.27
Parous	23 (82%)	44 (83%)	31 (91%)	0.50
Breast feeding (mean, months)	3.9	3.4	3.6	0.77
Use of oral contraceptives	18 (64%)	25 (47%)	13 (38%)	0.12
HRT	14 (50%)	36 (68%)	27 (79%)	0.44
Premenopausal	18 (64%)	28 (53%)	13 (38%)	0.10
Postmenopausal	10 (36%)	25 (47%)	21 (62%)	0.12
History of previous BBD	10 (36%)	22 (42%)	18 (53%)	0.37
Family history of BC	5 (18%)	5 (9%)	1 (3%)	0.21
Use of alcohol	13 (46%)	31 (58%)	21 (62%)	0.44
Smoker	10 (36%)	21 (40%)	15 (44%)	0.80

HRT, Use of hormonal replacement therapy.

impact, it is the tumor type most extensively investigated for possible psychological variables associated with risk and survival (13). Hormonal factors, such as early age at menarche, later age at menopause, later age at first full-term pregnancy and hormone replacement therapy, are known to be the main risk factors for sporadic BC (14-17). In addition, lifestyle factors, such as obesity, smoking, alcohol consumption and lack of physical activity, appear to contribute to an increased risk for this malignancy, although the results concerning such factors are inconsistent (18-20).

Psychological factors, such as stressful and adverse life events, are widely thought to play a role in the aetiology of BC (21-42). To our knowledge, the associations between hopelessness/helplessness scores and the MADRS are rarely considered together. Therefore, we carried out this prospective study to examine the concordance between hopelessness/helplessness score and the MADRS in women with breast symptoms referred by physicians to the Kuopio University Hospital.

Patients and Methods

The Kuopio BC Study was a multi-disciplinary cooperative project conducted by different departments of the University of Kuopio and Kuopio University Hospital, and included all women who were

referred to the hospital for breast examination between April 1990 and December 1995. The Kuopio BC Study followed the protocol of the International Collaborative Study of Breast and Colorectal Cancer coordinated by the European Institute of Oncology in Milan, and was initiated as a SEARCH program of the International Agency for Research on Cancer. The collaborative study is based on the assumption that BC and colorectal cancer may have common risk factors. Study centres for the BC study are situated in Canada, Finland, Greece, Ireland, Italy, Russia, Slovakia, Spain and Switzerland (43). The study participants showed BC symptoms (a lump in the breast or in the axilla, pain in the breast, bleeding from the nipple, nipple discharge or skin dimpling), or an abnormality of the breast and the indications for referral in this study were in line with our previous investigations in a BC Diagnostic Unit in Finland (44, 45).

This case-control study was an extension of the Kuopio BC Study (46, 47) and was approved by the Joint Committee of the University of Kuopio and Kuopio University Hospital (approval number 14/12/1989). Women referred from January 1991 to June 1992 were included. Participation was based on written consent. One hundred and fifteen women participated and were interviewed (to determine the level of emotional depression) by a psychiatrist (P.O.) before any diagnostic procedures, so neither the interviewer nor the patient knew the diagnosis at the time of the interview. The interviews were recorded and the ratings were completed before the final diagnosis. The clinical examination, mammography and biopsy showed BC in 34 (29.6%) patients, BBD in 53 (46.1%) patients and 28 (23.4%) HSS (Table I).

MADRS. The examiner (P.O.) completed the MADRS with 10 variables and the MADRS was used as a continuous variable in this study. The questionnaire items measuring depression in the MADRS test are following: apparent sadness; reported sadness; inner tension; reduced sleep; reduced appetite; concentration difficulties; lassitude; inability to feel; pessimistic thoughts; suicidal thoughts. Each MADRS item yields a score of 0 to 6, with the test total score ranging from 0 to 60. The final score was rated as follows: grade I: score 0, no depression; grade II: scores 1-6, little depression; grade III: score 7-19, mild depression; grade IV: score 20-34, moderate depression; and grade V: score 35-60, severe depression.

Scoring of hopelessness. The questionnaire items measuring hopelessness in the self-rating score (Hopelessness SRS) and in the examiners-rating score (Hopelessness ERS) were assessed before any diagnostic procedures for the HSS, BBD and BC groups and are given in detail in our earlier report of hopelessness (9). The mean duration (SD) of the interview for the patients with BC was 126.5 (21.6) minutes, for the patients with BBD was 127.3 (23.3) minutes, and for the HSS group 123.0 (23.3) minutes ($p=0.72$).

Scoring of helplessness. The questionnaire items measuring helplessness (10) in the SRS were: grade I, 'I feel self-supporting and have no helplessness' (true or false); grade II, 'I feel independent, but have a little helplessness' (true or false); grade III, 'I feel balanced, but have some helplessness' (true or false); grade IV, 'I feel dependent and have clear helplessness' (true or false) and grade V, 'I have strong helplessness' (true or false). The helplessness characteristics in the ERS for the HSS, BBD and BC groups were on a 5-point Likert-scale: grade I, no helplessness, self-supporting; grade II, little helplessness, independent; grade III, some helplessness, balanced; grade IV, clear helplessness, dependent and grade V, strong helplessness.

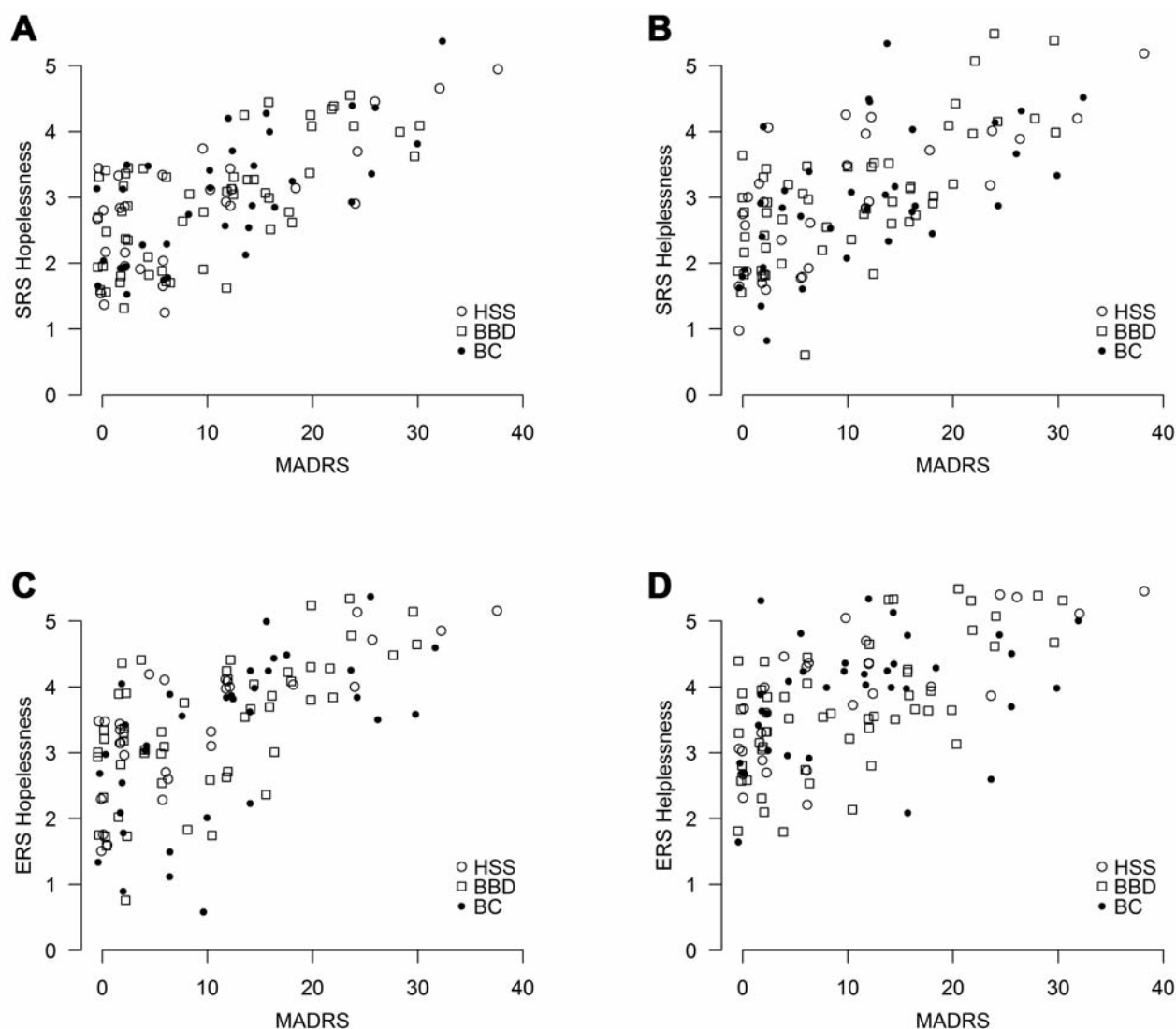


Figure 1. Scatter plots of the individual values of the self-rating scores (SRS) measuring hopelessness (A) and helplessness (B) and examiner-rating scores (ERS) measuring hopelessness (C) and helplessness (D) versus MADRS, as a continuous variable for healthy study participants (HSS), for those with benign breast disease (BBD) and for patients with breast cancer (BC).

Statistical analysis. Significance of the results was calculated with the SPSS/PC statistical package (SPSS Inc., Chicago, IL, USA). Correlations and differences between the study groups (BC, BBD and HSS groups) were measured with the two-sided chi-square test and non-parametric Kruskal-Wallis variance analyses. Results were considered statistically significant at a p -value <0.05 . The agreement between ERS and SRS was assessed using unweighted kappa statistic (Cohen's kappa), where all disagreements were arbitrarily regarded as having equal importance (48, 49), and the weighted kappa statistic, where weight matrix cells located on the diagonal (upper-left to bottom-right) represent agreement and thus contain zero (50). The kappa statistic provides a measure of agreement after exclusion of the proportion of agreement expected by chance, and can vary from +1, indicating perfect agreement, to 0, indicating agreement no greater than that expected by

chance, and can assume negative values up to -1 when agreement is less than expected by chance.

Results

Although the patients in the BC group were older than those in the BBD and HSS groups (51.5 *versus* 47.5 and 45.7 years, respectively), the age difference was not statistically significant ($p=0.12$). The majority of patients (85/115, 74%) were married or living in a steady relationship. The groups differed only slightly from each other as to the factors of the reproductive life of the women (Table I).

Table II. The Spearman correlation coefficients and kappa values between the self-rating score (SRS) for hopelessness and helplessness versus Montgomery-Asberg Depression Rating Scale (MADRS) and the examiner rating score (ERS) for hopelessness and helplessness versus the MADRS in the HSS, BBD and BC groups.

Group	Spearman (p-Value)	Kappa (p-Value)	Weighted kappa (p-Value)
Rating of hopelessness (SRS) vs. MADRS			
HSS	0.616 (<0.001)	0.383 (<0.001)	0.514 (<0.001)
BBD	0.710 (<0.001)	0.411 (<0.001)	0.524 (<0.001)
BC	0.691 (<0.001)	0.392 (<0.001)	0.518 (<0.001)
Rating of helplessness (SRS) vs. MADRS			
HSS	0.649 (<0.001)	0.341 (<0.001)	0.471 (<0.001)
BBD	0.662 (<0.001)	0.287 (<0.001)	0.437 (<0.001)
BC	0.580 (<0.001)	0.122 (0.239)	0.332 (<0.001)
Rating of hopelessness (ERS) vs. MADRS			
HSS	0.852 (<0.001)	-0.037 (0.673)	0.303 (<0.001)
BBD	0.693 (<0.001)	-0.048 (0.505)	0.229 (0.001)
BC	0.700 (<0.001)	-0.001 (0.989)	0.250 (0.008)
Rating of helplessness (ERS) vs. MADRS			
HSS	0.750 (<0.001)	-0.070 (0.343)	0.153 (0.015)
BBD	0.634 (<0.001)	-0.091 (0.138)	0.118 (0.020)
BC	0.422 (0.013)	-0.165 (0.019)	0.032 (0.549)

The Spearman correlation coefficients and kappa values for hopelessness/helplessness by the SRS *versus* MADRS in the HSS, BBD and BC groups are shown in Table II. In the SRS, hopelessness and the helplessness scores were highly significantly positively correlated with the MADRS in the HSS, BBD and BC groups. In the SRS, the weighted kappa values for hopelessness and helplessness *versus* the MADRS in the HSS, BBD and BC groups were also statistically significant.

The Spearman correlation coefficients and kappa values between hopelessness/helplessness by the ERS *versus* MADRS in the HSS, BBD and BC groups are also shown in Table II. There was also a significant positive correlation of ERS for hopelessness with the MADRS in the HSS, BBD and BC groups and of the ERS for helplessness with the MADRS in the HSS, BBD and BC groups. The unweighted kappa values between the ERS for hopelessness and the MADRS in the HSS, BBD and BC groups were statistically highly significant and those between the ERS for helplessness and the MADRS in the HSS and BBD groups were statistically significant.

Figure 1 shows the scatter plots of the individual values of the SRS and the ERS measuring hopelessness and helplessness *versus* MADRS as a continuous variable for the HSS, BBD and BC groups.

Discussion

The MADRS is one of the most widely used and validated rating scales monitoring the severity of depression (51-55). A higher MADRS score indicates more severe depression. There is also a self-rating version of this scale (MADRS-S) available for rapid screening of depression even in family practice and the MADRS-S correlates reasonably well with physicians' ratings (54). The MADRS is a short and concise scale designed to follow symptoms identified as selective and sensitive. The MADRS is a good instrument for the prediction of the treatment response to modern antidepressive medicines in patients with depression (55). Hermens *et al.* compared a face-to-face MADRS scale with a telephone MADRS rating in 66 primary-care patients with minor or mild/major depression (56). During a face-to-face interview at the patient's home a trained interviewer administered the MADRS rating. A few days later the MADRS rating was administered again but by telephone and by a different interviewer. The intra-class correlation coefficient (ICC) for the full rating was 0.65 and Hermens *et al.* concluded that the MADRS rating can be reliably administered by telephone.

The most common correlation coefficient is Pearson's correlation coefficient. However, the Pearson correlation coefficient is sensitive only to a linear relationship between two variables. Spearman's correlation coefficient is a rank correlation coefficient measuring the extent to which as one variable increases the other variable tends to increase. From a mathematical point of view, Spearman's correlation coefficient measures a different type of relationship from that by Pearson's correlation coefficient.

Although there are no previous reports with this study design available for sufficient comparison, some reports of the MADRS *versus* hopelessness/helplessness scoring can be obtained. In earlier studies, hopelessness was found to be associated with depression (57-59), and in a non-clinical cohorts it has been shown to be a predictor of depressive symptoms in the future (60, 61). It has been suggested that the identification of hopeless/helpless persons is essential in suicide prevention and it is important to assess and treat hopelessness/helplessness even though an individual may reports few depressive symptoms.

We assessed hopelessness/helplessness scoring *versus* the Beck Depression Inventory (BDI) in BC and BBD, and in HSS. Our results suggested a specific link between hopelessness/helplessness scores and the BDI in breast disease (62). However, the BDI is a self-rating scale, and relatively little is known about hopelessness/helplessness scores *versus* MADRS depression scale in breast cancer diagnosis. The purpose of the present study was to investigate scoring of hopelessness/helplessness compared to the MADRS in BC diagnosis and thus to increase awareness of this issue, since this knowledge may be useful in

preventive health care. This study shows that hopelessness and helplessness scores in the BC, BBD and HSS groups are reliably related to MADRS classification. We have earlier discussed that the development of suitable criteria for the identification of clinical symptoms and signs may lead to the reduction of the variability between observers (63, 64).

Conclusion

A new finding with clinical relevance in the present work is the agreement between hopelessness/helplessness scores and MADRS in the SRS and ERS. In the breast cancer diagnostic Unit, the identification of hopeless/helpless persons is essential in suicide prevention and it is important to assess and treat hopelessness/helplessness even though an individual may report few depressive symptoms.

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Conflicts of Interest

No conflicts of interest exists. The Authors alone are responsible for the content and writing of this article.

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