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Depression, Young Age, Chronic Marijuana Use and Inter-episodic symptoms Predict Psychological Distress In Patients with Cyclic Vomiting Syndrome

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Abstract

Background—Cyclic vomiting syndrome (CVS) is often triggered by stress. Patients report high degrees of psychological distress due to CVS but there is limited data on factors associated with psychological distress. We sought to determine the degree of psychological distress and its correlation with clinical characteristics in CVS.

Methods—The Brief Symptom Inventory (BSI), a validated tool to determine psychological distress, was administered prospectively to patients. The control population consisted of 719 normal subjects. Student's t test was used to compare population means and logistic regression analysis was performed to identify predictors of a GSI score ≥ 63 , indicating high degrees of psychological distress. Scores for the regression predictors were calculated using the maximum likelihood estimate for the logistic regression model and was called the DAME score (**D**epression, **A**ge 25–35, **M**arijuana use and **E**pisodic GI symptoms).

Key Results—Of 87 patients, 60% were female, 92% were Caucasian and mean age was 37 years. Forty-one % of patients had high degrees of psychological distress with the highest scores

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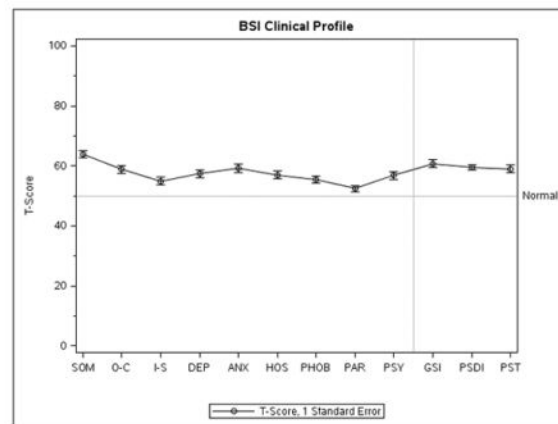
Disclosures

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for somatization. Independent predictors of psychological distress included depression, young age (25–35 years), chronic marijuana use and inter-episodic dyspepsia (called the DAME score). A score of 7 accurately predicted psychological distress in > 88% of patients.

Conclusions & Inferences—Psychological distress is common in CVS and can be predicted accurately using our proposed DAME score. Whether psychological distress is a cause or an effect of CVS needs to be determined. Addressing psychological distress can potentially improve overall health care outcomes in CVS.

Graphical Abstract



Keywords

cyclic vomiting; marijuana; depression; psychological distress

Cyclic Vomiting Syndrome (CVS) is a chronic functional gastrointestinal disorder characterized by episodic nausea and vomiting. A diagnosis of CVS in adults is made using Rome criteria which include 1) Stereotypical episodes of vomiting regarding onset (acute) and duration (less than one week) 2) Three or more discrete episodes in the prior year and 3) Absence of nausea and vomiting between episodes.¹ As with other functional gastrointestinal disorders (FGIDs) such as Irritable Bowel Syndrome, gastroparesis and non-ulcer dyspepsia, psychological disorders have previously been reported in patients with CVS.² In one study, as many as 78% of CVS patients screened positive for depression while 84% had symptoms of anxiety.³ The prevalence of anxiety and depression has varied from 14% – 47% in other studies.^{4, 5} The presence of psychological disorders can contribute to the development and propagation of gastrointestinal symptoms and increased health care utilization.⁶ In fact, lower levels of psychological distress have been associated with a better prognosis in patients with IBS.⁷ However, the degree of psychological distress and its correlation with clinical characteristics has not been systematically studied, especially in adults with CVS. We thus sought to examine the psychological profile of CVS patients compared to the general population and identify risk factors for high degrees of psychological distress in an ambulatory setting.⁸

Materials and methods

The Institutional Review Board at the Medical College of Wisconsin approved the study. After informed consent was obtained, the Brief Symptom Inventory (BSI), a validated and reliable tool for psychological assessment of individuals, was administered prospectively to patients diagnosed with CVS based on Rome III criteria in an ambulatory setting at a tertiary referral center located in Milwaukee, Wisconsin. All patients had undergone diagnostic testing including routine laboratory studies such as a complete blood count, hepatic panel and basic chemistry panel, an upper endoscopy and abdominal imaging to exclude other potential causes of vomiting. Exclusion criteria included pregnancy, presence of organic GI diseases such as inflammatory bowel disease, malignancy, and/or severe systemic illness. Details about patient demographics and clinical characteristics were obtained using a clinical intake questionnaire that was administered prospectively to patients. (See supplemental file 1) Data was collected utilizing an existing Research Electronic Data Capture (RedCap) database, a secure physician-patient portal.

The BSI consists of 53 questions and is used to evaluate nine symptom dimensions: somatization (SOM), obsessive-compulsive trait (O-C), interpersonal sensitivity (I-S), depression (DEP), anxiety (ANX), hostility (HOS), phobic anxiety (PHOB), paranoid ideation (PAR), psychoticism (PSY) as well as three global indices of distress: positive symptom total (PST), positive symptom distress index (PSDI) and global severity index (GSI). The BSI is based on the SCL-90-R and was designed to minimize time while maintaining validity and construct and has been used effectively in both clinical and research settings. A GSI score ≥ 63 is deemed to be clinically significant and serves as a predictor of psychological distress.⁹ A sample of 719 non-patient normal subjects was used for comparison.

Student's t-test was used to compare population means with a p value of < 0.05 considered significant. Logistic regression analysis was performed to identify predictors of a high GSI score ≥ 63 indicating high degrees of psychological distress. Scores for the regression predictors were calculated using the maximum likelihood estimate for the logistic regression model given by twice the estimate rounded to the nearest whole number. The sensitivity, specificity, positive and negative predictive values for this model were calculated. The Receiver Operating Characteristic (ROC) curve and the area under the curve (AUC) for this scoring model were also determined.

Results

Eighty-seven patients completed the study. Mean age was 37 ± 13 years, 52 (60%) were female and 80 (92%) were Caucasian. Sixty patients (69%) had a history of anxiety, 42 (48%) had a history of depression, and 37 (43%) reported chronic marijuana use over the last 6 months. Demographics and clinical characteristics of patients with CVS are shown in Table 1. Sixty-eight (78%) patients were seen in our clinic for the first time while the remainder was established patients receiving ongoing care in clinic. A high GSI T-score ≥ 63 indicating global psychological distress was seen in 36 (41%) patients. Based on BSI scores, patients with CVS had significantly higher degrees of psychological distress in all nine

primary symptom domains including SOM, O-C, IS, DEP, ANX, HOS, PHOB, PAR and PSY compared to 719 normal subjects ($p < 0.001$) (Figure 1).

Significant independent predictors of a high GSI score 63 included a history of depression, age group of 25–35 years, chronic marijuana use, and presence of inter-episodic GI symptoms (Table 2). Gender, history of anxiety, panic disorder, IBS, use of amitriptyline with dose of 75mg or higher and health care utilization measured by the number of hospitalizations and/or emergency department (ED) visits in the previous year were not associated with a high GSI score. There was also no difference in GSI scores between new and established patients.

Using a prediction model, scores were calculated and assigned for each of the significant predictors of a GSI 63. History of depression, which had the highest overall influence on the BSI score, received a score of 4, followed by age group of 25–35, which received a score of 3, history of chronic marijuana use a score of 2, and lastly presence of inter-episodic GI symptoms a score of 1. For short, we called this the DAME score, which stands for **d**epression, **a**ges between 25–35 years, **c**hronic **m**arijuana use and **i**nter-**e**pisodic **G**I symptoms. If a patient fit into more than one category, scores were summed together.

The sensitivity, specificity, positive and negative predictive values of the DAME score in predicting psychological distress with a GSI score 63 are shown in Table 3. A DAME score 7 accurately predicted the presence of significant psychological distress with a PPV of 100% and a negative predictive value of 67%. When a cut off DAME score 6 was chosen, the sensitivity and the negative predictive were higher with a slightly lower specificity and PPV. The ROC curve for the DAME score has an AUC of 0.837 as shown in Figure 2 showing good accuracy.

Discussion

In this study, we show that a large proportion of patients (41%) with CVS have high degrees of global psychological distress with a GSI score 63, as measured by the BSI, a validated tool for psychological assessment of individuals. This is similar to previously published studies in FGIDs such as Irritable Bowel Syndrome and non-ulcer dyspepsia, which demonstrate a strong association with psychiatric co-morbidities such as generalized anxiety disorder, panic disorder, major depression and psychological distress.^{2, 10} The prevalence of mental distress as measured by the General Health Questionnaire was 38% amongst patients with functional dyspepsia.¹¹ A cross-sectional study of 21,545 Swedish citizens showed that subjects with functional GI disorders have an 8 fold increased odds of having psychological illness and a higher risk of health care seeking behaviors when compared to somatic illness.¹²

Patients with CVS had the highest scores for somatization, which has been reported in other FGIDs. Of 327 patients who were seen in a tertiary referral center, patients with FGIDs were more likely to have a coexistent psychiatric diagnosis and somatization state.¹³ Somatization is the physical expression of multiple bodily symptoms involving different organ systems that cannot be explained by an organic illness. In one study, somatization was present in at

least a quarter of patients with IBS in a university setting but has also been reported in community settings.^{14, 15} Treating somatoform symptoms has been found to improve patient outcomes. The mean somatization score was 64 ± 10 and was the highest of all nine symptoms domains assessed by the BSI in this patient population. Reassuring patients and avoiding unnecessary and extensive investigations in search of an alternative organic illness is recommended in this patient group.

Independent predictors of psychological distress included history of depression, younger age (ages 25–35), chronic marijuana use, and presence of inter-episodic gastrointestinal symptoms. Other studies show that psychological disorders such as depression predicted the presence of FGIDs.¹³ Younger patients (25–35 years) were more likely to suffer higher degrees of distress in comparison to older patients in our study. Patients in this age group are subject to many uncertainties and stressors during this time period in their lives, which include completion of education, career building and beginning of family life; all of which could contribute to psychological vulnerability and distress.

Chronic marijuana use was also correlated with psychological distress in our study. Patients with CVS often use marijuana for its anti-emetic properties and in one Internet-based study, patients reported subjective improvement in overall well-being, appetite, nausea, vomiting and particularly stress levels. Marijuana users were also more likely to be male and have an associated anxiety disorder in the same study.¹⁶ Our study showed that chronic marijuana use was correlated with psychological distress. These findings must be interpreted with caution as these patients may be using marijuana to relieve symptoms rather than marijuana use leading to increased levels of distress. Whether marijuana is the cause or effect of increased psychological distress remains to be determined. Future studies to determine the clinical effects of chronic marijuana use in stress related disorders should clarify this question.

We also found that presence of inter-episodic dyspepsia was correlated with psychological distress, which can be easily explained. Almost a third of patients with CVS have inter-episodic nausea and dyspepsia and do not return to normal in between episodes. This phenomenon is referred to as coalescence of symptoms where patients continue to have low-grade symptoms interspersed with intense episodes of nausea and vomiting.¹⁷ Clearly those who return to completely normal health in between episodes are usually able to resume normal activities and thus may have less psychological distress.

Interestingly, health care utilization due to CVS symptoms as evidenced by the number of ED visits and hospitalizations in the year prior to presentation did not predict psychological distress. These findings are supported by some studies in other FGIDs: Talley et al showed that psychological distress was increased among patients with IBS in the community and was not associated with increased health care utilization in line with findings in our study. However there are contradictory reports where health care utilization was associated with psychological distress and vice versa. The finding that psychological distress is independent of health care utilization as shown in our study has important implications. Recognizing and treating underlying psychological distress and co-morbid psychological conditions would be important to achieve better health care outcomes rather than attributing psychological

distress to the underlying GI illness and associated health care visits. We were unable to determine association of psychological distress with severity of CVS given the lack of validated scales to assess severity of CVS.

To be able to readily identify patients with CVS who have high degrees of psychological distress, we used a logistic regression model to create a scoring system. We assigned specific point values to patient risk factors — history of depression (4), age group of 25–35 (3), history of chronic marijuana use (2) and presence of inter-episodic GI symptoms (1) - to predict individuals most likely to be affected by psychological distress. Using this scoring system, a score of 6 reliably predicted a GSI T-score of 63 in 67% of patients while a score of 7 predicted a high GSI T-score > 63 in 88–100% of patients. The AUC for this model showed good accuracy of the DAME score to ensure that the scoring system can be used in a busy clinic setting to identify CVS patients who are at risk for experiencing psychological distress. By focusing on these high risk patients, appropriate allocation of resources can be provided to those most in need of psychiatric evaluation and counseling. This simple scoring system, which we termed the DAME score (Depression, Age, Marijuana, Inter-episodic GI symptoms), can be used instead of extensive questionnaires that are expensive and potentially difficult to administer in clinic.

There are limitations to this study. Firstly, these patients were seen in a tertiary referral center and are not representative of patients with CVS in the community who may not have the same high degrees of psychological co-morbidity. However, arguably it is this very subset of patients who are most in need of intervention. Most of these patients were seen for the first time in our clinic and had not received a diagnosis of CVS nor started on specific treatment, which by itself can lead to increased psychological distress. Fleisher et al has shown that just receiving a diagnosis of CVS and validating the patient's symptoms can improve outcomes. It is possible that less knowledge about CVS and the absence of standard therapy in patients who were being seen for the first time in our clinic led to increased psychological distress given the uncertain and unpredictable nature of the illness. However, subgroup analysis did not show any differences between new and established patients though our study was not powered to detect such a difference.

In summary, a large proportion of patients with CVS have high degrees of psychological distress. Significant predictors of psychological distress included young age (25–35 years), depression, chronic marijuana use and absence of inter-episodic symptoms. Whether psychological distress is a cause or an effect of CVS remains unclear. Our findings underscore the need for a biopsychosocial model in treating CVS like other FGIDs. Given the often-busy GI clinic setting, we propose that clinicians use the DAME score, a simple scoring model that we developed, to identify patients who are likely to have high degrees of psychological distress. Steps to incorporate screening for psychological disorders and their treatment in such high risk groups should be undertaken and has the potential to improve health care outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key points

- Cyclic vomiting syndrome (CVS) is a chronic functional GI disorder (FGID) with episodes that are often triggered by psychological distress. The degree of psychological distress and predictors of distress in CVS have not been systematically studied.
- This cross-sectional study revealed that 41% of patients with CVS have high degrees of psychological distress with somatization being the most severe symptom domain. Independent predictors of psychological distress were a history of depression, younger age (ages 25–35), chronic marijuana use, and presence of inter-episodic GI symptoms (which we called the DAME score for short).
- A DAME score ≥ 7 accurately predicted psychological distress in most patients with CVS and can be used in a busy clinical setting to identify such high-risk groups.

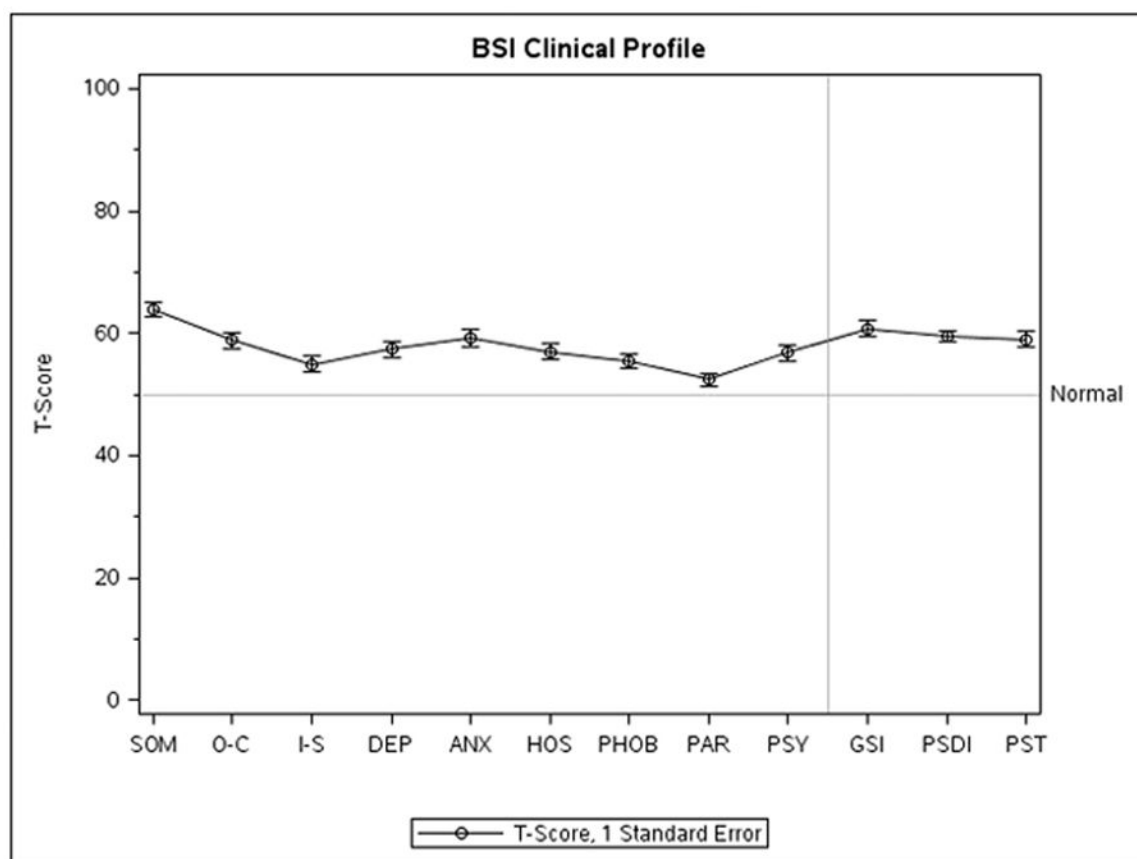


Figure 1.

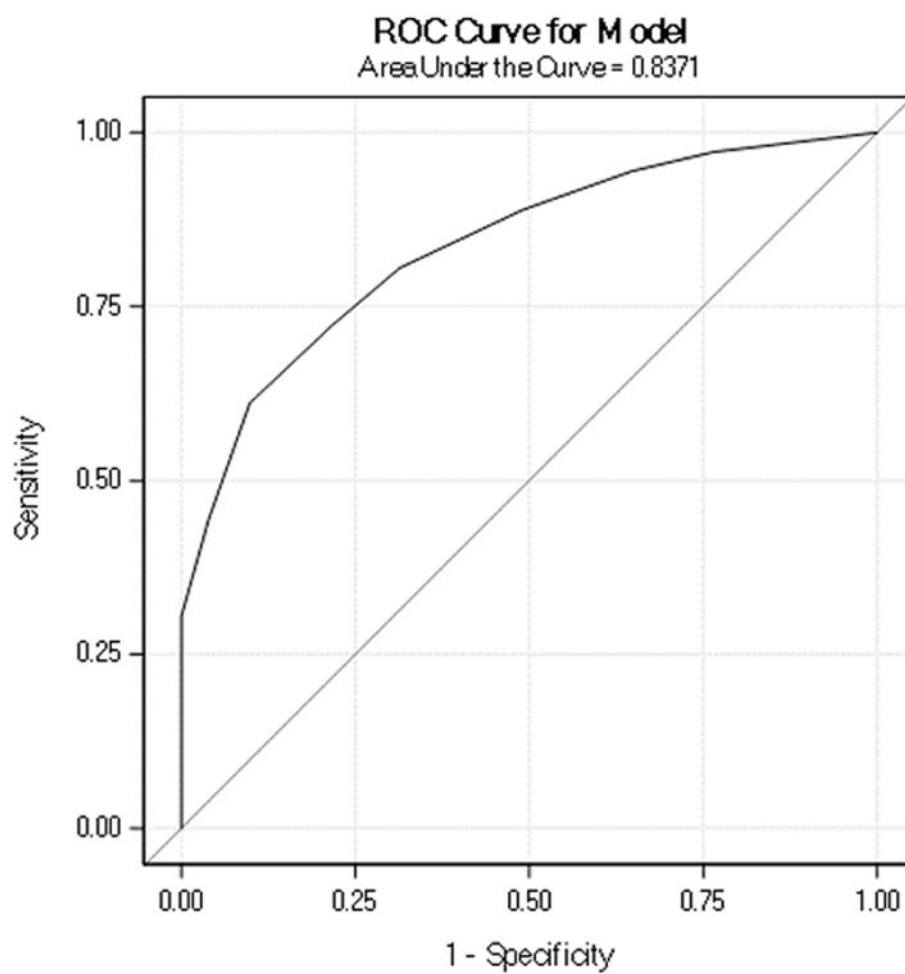


Figure 2.

Table 1

Baseline Characteristics of CVS patients

Patient Characteristics	Total n= 87
Age in years (<i>mean ± SD</i>)	37 ± 13
Gender	
•Female <i>n (%)</i>	52 (59.8%)
Race <i>n (%)</i>	
•Caucasian	80 (92.0%)
•African-American	7 (8.0%)
Established patients (receiving ongoing care in clinic) <i>n (%)</i>	18 (20.7%)
History of anxiety <i>n (%)</i>	60 (69.0%)
History of depression <i>n (%)</i>	42 (48.3%)
History of irritable bowel syndrome <i>n (%)</i>	20 (23.0%)
Current use of amitriptyline or nortriptyline <i>n (%)</i>	30 (34.5%)
Panic symptoms prior to episode onset <i>n (%)</i>	57 (65.5%)
History of current marijuana use <i>n (%)</i>	37 (42.5%)
Inter-episodic GI symptoms <i>n (%)</i>	28 (32.2%)

SD: Standard Deviation

Table 2

Significant predictors of psychological distress with a high GSI score ≥ 63 in patients with CVS

Variables	Score	Odds Ratio	Confidence Limit	P value
Depression	4	7.61	2.30–25.15	<0.001
Age				
•18–25 vs. 45+	0	0.88	0.15–5.12	0.89
•25–35 vs. 45+	3	5.43	1.19–24.89	0.03
•35–45 vs. 45+	0	0.81	0.172–3.81	0.79
Chronic marijuana use	2	3.29	1.05–10.30	0.04
Inter-episodic GI symptoms	1	2.05	1.11–3.79	0.02

Results from logistic regression model for GSI T-score ≥ 63 (vs. GSI T-score < 63) adjusting for age, depression, marijuana use, and health between episodes in 87 CVS patients. Scores for the regression predictors were calculated using the maximum likelihood estimate for the logistic regression model given by twice the estimate rounded to the nearest whole number.

Table 3

Sensitivity, specificity, positive and negative predictive value of the DAME score in predicting psychological distress in CVS patients

Variables	Global Severity Index T Score			P Value	Population (%)	Sensitivity (this score)	Specificity (this score)	PPV (this score)	NPV (this score)
	Total N=87 (%)	<63 N=51 (%)	>63 N=36 (%)						
DAME Score				< .001 C					
0	13 (100.0)	12 (92.3)	1 (7.7)		14.9	100.0	0.0	0.41379	-
1	7 (100.0)	6 (85.7)	1 (14.3)		8.0	97.2	23.5	0.47297	0.92308
2	10 (100.0)	8 (80.0)	2 (20.0)		11.5	94.4	35.3	0.50746	0.90000
3	8 (100.0)	5 (62.5)	3 (37.5)		9.2	80.6	68.6	0.64444	0.83333
4	12 (100.0)	9 (75.0)	3 (25.0)		13.8	88.9	51.0	0.56140	0.86667
5	10 (100.0)	6 (60.0)	4 (40.0)		11.5	72.2	78.4	0.70270	0.80000
6	9 (100.0)	3 (33.3)	6 (66.7)		10.3	61.1	90.2	0.81481	0.76667
7	8 (100.0)	0 (0.0)	8 (100.0)		9.2	30.6	100.0	1.00000	0.67105
8	2 (100.0)	0 (0.0)	2 (100.0)		2.3	30.6	100.0	1.00000	0.67105
9	7 (100.0)	2 (28.6)	5 (71.4)		8.0	44.4	96.1	0.88889	0.71014
10	1 (100.0)	0 (0.0)	1 (100.0)		1.1	30.6	100.0	1.00000	0.67105

C Chi-square test