

## Association between Self-Reported Depression with Severe Symptom Burden

Associação entre Depressão Auto-referida com Sobrecarga de Sintomas Graves

Asociación entre Depresión Autoinformada y Carga Grave de Síntomas

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### Abstract

**Objective:** To assess the prevalence of factors associated with a severe ESAS score of 7 points or more in one or more of its domains. **Method:** Patients admitted to medical clinic wards for three days or more were evaluated. Sociodemographic and clinical data and the ESAS questionnaire were collected. The ESAS has 10 domains, one of which is related to depression. ESAS was used with 10 domains and 9 domains (no depression domain). ESAS was classified as severe (with a score equal to or greater than 7 points in at least one domain) and not severe. Multivariate statistical evaluation identified the independent variables associated with severe and severe ESAS without the depression domain. **Results:** 93 patients were included in the study, 40 (43.01%) were female. The mean age was  $53.11 \pm 18.28$  years, religion was considered very important by 74 (79.56%), non-white ethnicity was identified in 70 (75.83%) and depression in 16 (17.20%). Severe ESAS was present in 52.69% of patients. The final multiple logistic regression model showed self-reported depression as the only factor associated with severe ESAS in the 10-domain protocol ( $p = 0.02$ ; OR = 4.30 (95% CI 1.21-15.24)) and as the only factor associated with severe ESAS without the depression domain ( $p = 0.04$ ; OR = 3.41 (95% CI 1.01-11.53)). **Conclusion:** The prevalence of severe ESAS was high and the only independent factor associated was self-reported depression. It is necessary to incorporate the assessment of symptoms into the routine of hospital care, especially in patients with self-reported depression.

**Keywords:** Symptom assessment; Depression; Adjustment disorders.

### Resumo

**Objetivo:** Avaliar a prevalência de fatores associados ao escore ESAS grave de 7 pontos ou mais em um ou mais de seus domínios. **Método:** Foram avaliados pacientes internados em enfermarias de clínica médica por três dias ou mais. Foram coletados dados sociodemográficos, clínicos e o questionário ESAS. A ESAS possui 10 domínios, sendo um deles relacionado à depressão. ESAS foi utilizada com 10 domínios e 9 domínios (sem domínio depressão). ESAS foi classificada como grave (com pontuação igual ou superior a 7 pontos em pelo menos um domínio) e não grave. Na avaliação estatística multivariada, foram identificadas as variáveis independentes associadas à ESAS grave e grave sem o domínio depressão. **Resultados:** Foram incluídos no estudo 93 pacientes, sendo 40 (43,01%) do sexo feminino. A média de idade foi  $53,11 \pm 18,28$  anos, religião considerada muito importante por 74 (79,56%), etnia não branca foi identificada em 70 (75,83%) e depressão em 16 (17,20%). ESAS grave esteve presente em 52,69% dos pacientes. O modelo final de regressão logística múltipla mostrou a depressão autorreferida como único fator associado à ESAS grave no protocolo de 10 domínios ( $p = 0,02$ ; OR = 4,30 (IC 95% 1,21-15,24)); e também, como único fator associado à ESAS grave sem o domínio depressão ( $p = 0,04$ ; OR = 3,41 (IC 95% 1,01-11,53)). **Conclusão:** A prevalência de ESAS grave foi alta e o único fator independente associado foi a depressão autorreferida. É necessário incorporar a avaliação dos sintomas na rotina do atendimento hospitalar, principalmente naqueles pacientes com depressão autorreferida.

**Palavras-chave:** Avaliação de sintomas; Depressão; Transtornos de ajustamento.

### Resumen

**Objetivo:** Evaluar la prevalencia de factores asociados a un puntaje ESAS severo de 7 puntos o más en uno de sus dominios. **Método:** Se evaluaron pacientes ingresados en salas de clínica médica por tres días o más. Datos recogidos: sociodemográficos,

clínicos y cuestionario ESAS. ESAS tiene 10 dominios, uno de los cuales está relacionado con la depresión. Se utilizó ESAS con 10 dominios y 9 dominios (sin dominio de depresión). La ESAS se clasificó en grave (con una puntuación igual o superior a 7 puntos) y no grave. En la evaluación estadística multivariada se identificaron las variables independientes asociadas a ESAS severo y severo sin el dominio depresión. Resultados: 93 pacientes fueron incluidos en el estudio, 40 (43,01%) eran del sexo femenino. La edad media fue de  $53,11 \pm 18,28$  años, la religión fue considerada muy importante por 74 (79,56 %), se identificó etnia no blanca en 70 (75,83 %) y depresión en 16 (17,20 %). La ESAS grave estuvo presente en el 52,69% de los pacientes. El modelo de regresión logística múltiple final mostró la depresión autoinformada como el único factor asociado con ESAS grave en el protocolo de 10 dominios ( $p = 0,02$ ; OR = 4,30 (IC del 95%: 1,21-15,24)); y también como único factor asociado a ESAS grave sin el dominio depresión ( $p = 0,04$ ; OR = 3,41 (IC 95% 1,01-11,53)). Conclusión: La prevalencia de ESAS grave fue alta y el único factor independiente asociado a este fue la depresión autorreferida. Es necesario incorporar la evaluación de los síntomas a la rutina de atención hospitalaria, especialmente en pacientes con autoinforme de depresión.

**Palabras clave:** Evaluación de síntomas; Depresión; Trastornos adaptativos.

## 1. Introduction

Population aging has been increasing in Brazil and other countries. This phenomenon has a profound impact on the entire health care system, from primary care to the assistance offered in the hospitals (Silva et al.,2019; Aliberti et al.,2019; Arcanjo et al.,2018; Avelino et al.,2014). Thus, all health care professionals involved in the treatment of these elderly patients and/or those with severe comorbidities need to incorporate knowledge and competencies related to symptom control and palliative care (PC). Also, the PC approach is associated with improved survival, better quality of life and/or reduction of costs involved in the care of different patient populations (Temel et al.,2010; Iyer et al.,2019; Schichtel et al.,2019).

However, it is known that knowledge and competencies in the PC area are facing a big deficit regarding health care professionals. This deficit is related to the structures of the courses offered during graduation and residency programs in all areas of health care (Lemos et al.,2017; Edwards et al.,2018). Consequently, we expect that symptom control in elderly patients or those with more severe disease (such as hospitalized ones) is not optimized (Falk et al., 2016; Nipp et al.,2017; Roldi & Moritz,2016).

In this scenario, the use of scales is very important to facilitate symptom evaluation and treatment effects. One of the most often used scales worldwide is the *Edmonton Symptom Assessment System* (ESAS) (Paiva et al.,2015). However, in Brazil, there are only approximately ten articles related to ESAS and published in the PUBMED database (Paiva et al.,2015; Soares et al.,2018; Perez-Cruz et al.,2018; Marcucci et al.,2016; Hui et al.,2015). Surprisingly, none has focused on the characterization of associated factors of inpatients (in internal medicine wards) suffering severe symptoms based on ESAS (one or more domains with 7 points or more), as similarly described by Wajnberg et al (Wajnberg et al.,2013).

Considering all these aspects, it is very important to evaluate the prevalence of severe symptoms (one or more domains of ESAS with a score of 7 points or more), and their possible associated factors, including self-reported depression. This knowledge can be used in the future for a faster evaluation of patients that show a higher probability of suffering severe symptoms and, consequently, need a more urgent approach based on PC and symptom control.

## 2. Methods

This article shows a cross-sectional analysis of the characteristics of hospitalized patients at admission. It was carried out in a public teaching hospital with 133 beds in internal medicine ward units (and its subspecialties). The patients were included from April 8 to 12 of 2019, taking into account the dynamics of each unit, similarly to other studies involving hospitalized individuals (Falk et al.,2016; Hammond et al.,2017; Sigurdardottir et al., 2008). The sample size consisted of all hospitalized patients that met the eligibility criteria.

Inclusion criteria were patients hospitalized in internal medicine wards. In addition, exclusion criteria comprised patients younger than 18 year, patients who refused to participate in the study, patients/proxy who did not adequately answer the questionnaire (e.g., did not speak Portuguese, deafness not corrected by hearing aid, etc.), patients coming from long-term care institutions (institutionalized), patients hospitalized for 3 days or less. We excluded patients with a short hospital length of stay (LOS) because they probably had lower symptom severity and comorbidities, and so the cutoff of prolonged LOS was set at 4 days, as similarly described for prolonged LOS in our state and in other studies (Nipp et al.,2017; Castro et al.,2002; Lovadini et al.,2019)

The previously trained researcher applied a structured data collection questionnaire to patients who met the eligibility criteria. In situations where the patients showed cognitive impairment OR delirium, the questionnaire was applied through the help of a proxy-respondent, as previously described in similar studies (Wajnberg et al.,2013; Borkenhagen et al.,2018). This contact always occurred in the morning. The data collected were Age (numerical in years old), Sex, self-perception of Religion importance (categorized as very important OR not), Ethnicity (categorized as non-white OR white), marital status (Married OR not), level of Schooling (categorized as  $\leq 8$  years OR more), self-reported Depression (present OR not), Charlson Comorbidity Index (numerical), Diagnosis (categorized as non- infectious OR infectious disease) and LOS (categorized as  $\leq 30$  days OR more) (Castro et al.,2002).

Moreover, the Brazilian version of the ESAS questionnaire was also applied to the hospitalized patients (Paiva et al.,2015; Bruera et al.,1991). The ESAS (containing 10 domains) was classified as severe (a score of 7 points or more in at least one of 10 domains) and non-severe, as previously published (Wajnberg et al.,2013). Finally, ESAS without the depression domain (containing 9 domains) was also classified as severe (score of 7 points or more in at least one of 9 domains) and non-severe. The use of ESAS without the depression domain aimed at avoiding the double interference of depression in the final analysis, because the self-reported depression is a variable that would be used to explain severe ESAS, related to the previous depression diagnosis.

Similarly, SOFA without a renal domain is used to assess the association between SOFA and the renal outcome (Leite et al.,2015; Stads et al.,2019).

The statistical analysis was performed using the SPSS program, version 20. Numerical variables are shown as mean and standard deviation (SD); and categorical ones as absolute and relative frequencies. Variables with p value  $<0.20$  in the bivariate analysis were initially included in the multiple logistic regression model (via stepwise elimination), with a p value of retention of 0.05. Thus, the variables independently associated with severe ESAS and also with severe ESAS without the depression domain, were identified. Statistical significance was considered with a p level of 0.05.

The institutional research ethics committee approved the present study. The individuals received information related to the research purpose and signed the informed consent form if they agreed to participate. Additionally, Brazilian human research ethical principles were taken into consideration when the study was carried out.

### **3. Results**

The study initially assessed all the 133 individuals hospitalized in the internal medicine wards for possible study entry. A total of 40 individuals were excluded from the study after the exclusion criteria were applied: 1 for being under the age of 18 yr., 1 patient who refused to participate in the study, and 38 patients who were hospitalized for 3 days or less. Consequently, 93 patients were included in the present study.

The main sociodemographic and clinical information regarding all included individuals (N=93) are shown in this paragraph. Mean age was  $53.11 \pm 18.28$  yr., 40 (43.01%) patients were females, religion was considered very important by 74

(79.56 %) patients, the self-reported ethnicity was non-white for 70 (75.83%) patients, 45 patients (48.38 %) were married, the level of schooling was  $\leq 8$  years in 56 (60.21%), Charlson Comorbidity Index was  $3.01 \pm 2.43$ , self-reported depression was identified in 16 patients (17.20%), 51 (54.83%) had a diagnosis of non-infectious disease, and LOS  $\leq 30$  days was observed in 72 patients (77.41%) .

Tables 1 and 2 showed the variables associated with severe ESAS in the bivariate analysis. Table 1 contains sociodemographic and clinical findings in the group with Severe symptom and non-severe symptoms on ESAS. Then, Table 2 brings the sociodemographic and clinical findings in the group with Severe Symptoms (without the depression domain) and non-severe symptoms on ESAS.

**Table 1** – Sociodemographic and clinical findings in the group with Severe symptom and non-severe symptoms on ESAS (N = 93)

| Variables                       | Severe ESAS<br>(n = 49) | Non severe ESAS<br>(n = 44 ) | p value* | OR (95% CI)*          |
|---------------------------------|-------------------------|------------------------------|----------|-----------------------|
| Age in Years Mean $\pm$ SD      | 51.29 $\pm$ 20.55       | 55.14 $\pm$ 15.35            | .310     | -                     |
| Female gender, n(%)             | 23 (57.5)               | 17 (42.5)                    | .420     | -                     |
| Religion – very important, n(%) | 39 (52.7)               | 35 (42.3)                    | .986     | -                     |
| Non-white ethnicity, n (%)      | 37 (52.9)               | 33 (47.1)                    | .822     | -                     |
| Married, n(%)                   | 26 (57.8)               | 19 (42.2)                    | .342     | -                     |
| Schooling $\leq 8$ years, n(%)  | 32 (57.1)               | 24 (42.9)                    | .186     | 1.778 (0.757 – 4.174) |
| Self-reported Depression, n(%)  | 12 (75)                 | 4 (25)                       | .058     | 3.243 (0.961-10.949)  |
| CCI , Mean $\pm$ SD             | 3.14 $\pm$ 2.70         | 2.86 $\pm$ 2.10              | .579     | -                     |
| Non-infectious Diagnosis, n(%)  | 23 (45.1)               | 28 (54.9)                    | .108     | 0.505 (0.220-1.161)   |
| LOS $\leq 30$ days, n (%)       | 34 (47.2)               | 38 (52.8)                    | .056     | 0.357 (0.124-1.026)   |

CCI: Charlson Comorbidity Index; LOS: Hospital Length of Stay. ESAS: Edmonton Symptom Assessment System. Severe ESAS=presence of a score of 7 points or more in at least one of the domains. \*Bivariate logistic regression analysis. Source: Authors.

**Table 2** – Sociodemographic and clinical findings in the group with Severe Symptoms (without the depression domain) and non-severe symptoms on ESAS (N = 93).

| Variables                       | Severe ESAS<br>(n = 48 ) | Non -severe ESAS<br>(n = 45 ) | p value* | OR (95%CI)*           |
|---------------------------------|--------------------------|-------------------------------|----------|-----------------------|
| Age in Years, Mean ± SD         | 50.96 ± 20.63            | 55.40 ± 15.28                 | .242     | -                     |
| Female gender, n(%)             | 22 (55)                  | 18 (45)                       | .570     | -                     |
| Religion – very important, n(%) | 30 ( 45.5)               | 36 (54.5)                     | .906     | -                     |
| Non-white ethnicity, n(%)       | 37 (52.9)                | 33 (37.1)                     | .536     | -                     |
| Married, n(%)                   | 25 (55.6)                | 20 (44.4)                     | .462     | -                     |
| Schooling ≤ 8 years, n(%)       | 31 (55.4)                | 25 (44.6)                     | .247     | -                     |
| Self-reported Depression, n(%)  | 12 (75)                  | 4 (25)                        | .048     | 3.417 (1.012 -11.537) |
| CCI , Mean ± SD                 | 3.13 ± 2,73              | 2.89 ± 2.09                   | .639     | -                     |
| Non-infectious Diagnosis, n(%)  | 23 (45.1)                | 28 (54.9)                     | .167     | 0.559 (0.244 – 1.277) |
| LOS ≤ 30 days, n(%)             | 33 (45.8)                | 39 (54.2)                     | .044     | 0.338 (0.118 - 0.971) |

CCI: Charlson Comorbidity Index; LOS: Hospital Length of Stay . Severe ESAS=presence of a score of 7 points or more in at least one of the domains. \*Bivariate logistic regression analysis. Source: Authors.

Finally, in Table 3, the final model of multiple logistic regression revealed depression as the only factor associated (p= 0.02; OR =4.30 (95%CI 1.21-15.24)) with ESAS ≥ 7 in one domain or more. In addition, the final multiple logistic regression model also showed depression as the only factor associated (p = 0.04; OR =3.41 (95%CI 1.01-11.53)) with ESAS ≥ 7 (without the depression domain) in one domain or more.

**Table 3** – Multiple logistic regression models of factors associated with severe ESAS and with severe ESAS without the depression domain.

| Severe ESAS                               |         |                          |
|---|---------|--------------------------|
|   | P value | OR (95% CI)              |
| Self-reported Depression                  | 0.02    | 4.30 (95% CI 1.21-15.24) |
| Severe ESAS without the depression domain |         |                          |
|   | P value | OR (95% CI)              |
| Self-reported Depression                  | 0.04    | 3.41 (95% CI 1.01-11.53) |

Severe ESAS = presence of a score of 7 points or more in at least one of the domains. Source: Authors.

#### 4. Discussion

To the best of our knowledge, this is the first Brazilian study evaluating factors independently associated with severe ESAS and with severe ESAS without the depression domain. In addition, we showed that self-reported depression is the only associated factor. Thus, a clinical consequence of this fact is that physicians should evaluate symptoms, especially in inpatients with self-reported depression, because they have a higher probability (3 to 4-fold higher) of suffering severe symptoms and, consequently, need a more urgent approach based on symptom control.

However, we should not forget that more than 50% of inpatients had severe symptoms according to the severe ESAS and severe ESAS without the depression domain. Thus, at the appropriate time, it is also important that all the hospitalized patients should be evaluated regarding their symptoms. The literature shows that symptom control (evaluated by ESAS) is an actual problem in hospitalized patients, even around the time of hospital discharge (Borkenhagen et al., 2018; Pollack et al., 2017). Moreover, these symptoms measured around the time of hospital discharge may predict (better than classical instruments, such as the Charlson Comorbidity Index) 30-day hospital readmission or emergency department visit. Interestingly, it might be very necessary to control these symptoms for up to 30 days after hospital discharge (Pollack et al., 2017).

Regarding the sociodemographic and clinical characteristics of our patients, they are similar to other studies. This fact corroborates the possible external validation of our results. The age, (female) gender and (married) marital status were similar to other studies, including ones performed in Brazil (Roldi et al., 2016; Osorio et al., 2012; Nagaviroj et al., 2017). As for depression, its prevalence was similar to that in other studies evaluating hospitalized adults, also including one performed in Brazil (Mendonça et al., 2016; Pantilat et al., 2012).

Considering specifically the association between depression and symptom burden, it deserves to be discussed in a more detailed manner. Some studies have mentioned that the presence and intensity of symptoms could be or not related to ESAS evaluation. One showed that the symptoms are not related to depression or anxiety, except when they are related to the pain domain in the ESAS. Moreover, the intensity of symptoms in depressed patients is better assessed by the HADS (Hospital Anxiety and Depression Scale) scale when compared to ESAS regarding the drowsiness domain. There are no significant differences in the association between depression and ESAS domains such as pain, nausea, lack of appetite, tiredness, and dyspnea. However, this study does not mention the association of the evaluation of the presence of symptoms by ESAS and depressive mood (Teunissen et al., 2007). The symptom burden measured by ESAS is significantly higher in patients with depressive disorders as shown in our study and seen in previous reports, which demonstrates that the symptom burden

interferes with the psychological state of the hospitalized patient and leads to a decrease in the patient's quality of life. The presence and intensity of these symptoms is a predictor of depression in hospitalized patients (Liu et al.,2017).

Falk et al (Falk et al.,2016), in a cross-sectional study, reported on the data collected on a single random day after patient admission. They showed that there were statistical differences between the analyzed data regardless of the period of data acquisition, the format of the questions and/or answers and whether the study was retrospective or prospective. Hammond et al (Hammond et al.,2017) used convenience sampling according to the dynamics of each service where the research was carried out. Although this type of study hinders the external validation of its results, it does not invalidate them. Thus, our study, through the random application of ESAS after the third day of hospitalization, showed a high burden of severe symptoms in patients with signs of self-reported depression. Moreover, despite the wide application of ESAS in cancer patients under palliative care, it can also be used in internal medicine ward patients with severe diseases and poor prognosis, corroborating the study by Sigurdardottir (Sigurdardottir & Hayben,2008). Patients with a high symptom burden, whether oncological or not, should receive palliative care to improve their quality of life, as well as their caregivers' and their families'.

Our study has some limitations. First, it has a cross-sectional design, and consequently we cannot establish causality between depression and severe ESAS. Second, the patients were included in this study regardless of their hospital LOS. However, this fact occurred in other studies involving hospitalized patients (Falk et al.,2016). In fact, it may be seen as a strength, considering that our result suggest that self-reported depression is a marker of severe ESAS, regardless of hospital LOS.

## 5. Conclusion

The prevalence of severe symptoms (one or more ESAS domains with a score of 7 points or more) in hospitalized patients is high and is associated with self-reported depression. Consequently, patients with high severe symptom burden should be evaluated as a priority because of the greater likelihood of development depressive symptoms.

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