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## Assessment of Anxiety and Depression in Hospitalized Patients with Severe Covid-19 Pneumonia

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### ABSTRACT

Anxiety and depression are highly prevalent psychiatric disorders among patients admitted for organic causes. To determine whether patients hospitalized with severe COVID-19 pneumonia present symptoms of anxiety and/or depression that are directly proportional to their clinical course. A longitudinal, prospective, observational study was conducted in the High Specialty and Advanced Medicine Building of the UANL University Hospital. Spanish-speaking patients of both sexes, aged 18 and over, diagnosed with severe COVID-19 pneumonia, were surveyed from September 2020 to January 2021. Sociodemographic data were obtained, including age, sex, comorbidities, occupation, education, marital status, national origin and religion, length of stay, and oxygen requirements. These data were collected directly from the patient or the most recent information from the patient's medical record. Anxiety and depression symptoms were assessed on the day of admission using the Hospital Anxiety and Depression Scale (HADS). Results: 57 patients hospitalized with COVID-19 pneumonia were followed during their hospital stay, until discharge, or until the patient required invasive mechanical ventilation. The mean age of the patients was 57.8 years. Upon admission, 29.8% of the patients presented symptoms suggestive of anxiety, and 7% presented clinically significant anxiety morbidity. In comparison, 8.8% of the patients presented symptoms suggestive of depression and 3.5% clinically indicative of comorbid depression. At the last evaluation in our study of patients, up to 12% presented anxiety symptoms (2% clinically morbid) and 2% significant depression morbidity. The trend toward depression and anxiety decreased over time and was highest in the first days of hospitalization. We found no association between these symptoms and having been intubated at any point during their stay. The median length of stay was 7 (4-10) days, and most were admitted with low-flow oxygen therapy (78.9%). Furthermore, we found a low to very low correlation between length of hospital stay, oxygen saturation, and oxygen volume with HADS scores for anxiety and depression. The prevalence of comorbid depression and anxiety was higher in the first days of hospital stay and was not related to patient clinical data, hospital stay, or receipt of invasive mechanical ventilation during their stay.

**Keywords:** COVID-19, Anxiety, Depression, Hospital Care

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## INTRODUCTION

Anxiety can occur in anyone, either temporarily or chronically; it can produce aggressive reactions that result in increased stress (1, 2). During an anesthetic-surgical procedure, the patient may experience psychological and physical discomfort arising from the sensation of immediate danger and is characterized by diffuse fear that can range from restlessness to panic. It can be a constitutional characteristic of the individual's personality. (3)

Anxiety defined as a transient emotional condition, consists of feelings of tension, apprehension, nervousness, fear, and heightened activity of the autonomic nervous system.

(1). Anxiety fulfills an adaptive function and is considered a habitual reaction to environmental demands. However, it sometimes tends to exceed one's capacities and lead to a lack of control in the face of a situation, either due to its intensity, difficulty in handling, or even a lack of internal resources that allow one to expand one's repertoire of reactions, which leads to inadequate management of coping strategies. (4, 5)

"On January 10, 2020, the WHO published a comprehensive technical guidance online with recommendations for all countries on detecting cases, conducting laboratory testing, and managing potential cases." (6)

The World Health Organization (WHO) declared the coronavirus disease 2019 (COVID-19) outbreak a public health emergency of international concern on January 30, 2020.

The most common initial symptoms of coronavirus disease 2019 (COVID-19) are fever, cough, fatigue, anorexia, myalgia, and diarrhea. Dyspnea is the most common symptom of severe illness and is often accompanied by hypoxemia. A striking feature of COVID-19 is the rapid progression of respiratory failure shortly after the onset of dyspnea and hypoxemia. The Diagnosis of COVID-19 can be established based on a clinical history and the detection of SARS-CoV-2 RNA in respiratory secretions. A chest X-ray should be performed, commonly showing bilateral consolidations or ground-glass opacities. For epidemiological purposes, severe COVID-19 in adults is defined as dyspnea, a respiratory rate of 30 or more breaths per minute, a blood oxygen saturation of 93% or less, a ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen ( $P_{aO_2}:F_{iO_2}$ ) of less than 300 mm Hg, or infiltration into more than 50% of the lung field within 24 to 48 hours of symptom onset. (7)

Previous research has shown that epidemic outbreaks inflict a broad and profound psychological impact on individuals. In the general population, at the individual level, it can precipitate the development of new psychiatric symptoms in people without mental illness, aggravate the condition in those with preexisting mental illness, and cause distress in caregivers of affected individuals. (8)

During epidemics, significant psychiatric morbidities have been found, ranging from symptoms of depression, anxiety, panic attacks, somatic symptoms, and post-traumatic stress disorder (PTSD) to even delirium, psychosis, and suicide, (8,9,10) which have been associated with younger age and increased self-blame. (11)

A high prevalence of psychological stress has been reported with long quarantine periods, associated with an increased prevalence of PTSD symptoms, which correlated with depressive symptoms. (12)

Quarantine and isolation of those suspected of contracting or carrying the virus can lead to mental health problems; these situations are known to be associated with acute stress disorder, depression and PTSD, insomnia, irritability, anger, and emotional exhaustion. (13)

In a study of 1,210 Chinese residents in the two weeks following the COVID-19 epidemic in China, Wang found that 53.8% of respondents rated the psychological impact of the outbreak as moderate or severe; 16.5% reported moderate to severe depressive symptoms; 28.8% reported moderate to severe anxiety symptoms; and 8.1% reported moderate to severe stress levels. Women reported higher levels of anxiety, depression, and stress (14) related to previous epidemiological studies that women are at greater risk for depression (15) attributed to their unique biology and socioeconomic factors. (16)

Given the high prevalence of anxiety and depression in patients admitted to hospital medical wards, it is necessary to assess these psychiatric disorders in patients hospitalized with COVID-19 and pneumonia, given the nature of this disease.

Previous investigations used the Hospital Anxiety and Depression Scale (HADS). with excellent outcomes in hospitalized patients (17)

**Objective:** To determine whether hospitalized patients with severe COVID-19 pneumonia present symptoms of anxiety and/or depression directly proportional to their clinical course.

## MATERIALS AND METHOD:

This is a prospective, analytical cohort study that lasted five months. It was conducted at a tertiary-level High Specialty and Advanced Medicine hospital at the UANL, where patients diagnosed with severe COVID-19 pneumonia were selected from September 2020 to January 2021. The survey staff followed institutional and WHO-recommended protection protocols.

### Inclusion Criteria:

1. Age over 18 years of age, regardless of gender.
2. Hospitalized patients with SARS-CoV-2 positive status (COVID-19 Diagnosis) with severe pneumonia.
3. Native Spanish speaker.
4. Alert and conscious patient who can communicate.

**Exclusion Criteria:**

1. Patients who do not wish to participate.
2. Cognitive or intellectual disability.
3. Diagnosis of dementia.
4. On invasive or noninvasive mechanical ventilation.
5. Previous Diagnosis of depression or anxiety.
6. Current medication with antidepressants or anxiolytics.
7. Patients with deafness or blindness or difficulty seeing or hearing.

**Elimination criteria:**

1. Having to withdraw from the study (transfer) during their stay or while completing any surveys.
2. Incomplete surveys.
3. Death after recruitment.

Measurements: Sociodemographic data were obtained, including age, sex, comorbidities, occupation, education, marital status, origin and religion, length of stay, and oxygen requirements, which were collected from the patient's medical record and the most recent information available to the patient.

Anxiety and depression symptoms were assessed on the day of admission using the Hospital Anxiety and Depression Scale (HADS).

This self-report questionnaire evaluates 14 categories of emotional symptoms of anxiety and depression that can be used in inpatients and outpatients. The scores on this questionnaire are interpreted as follows:

- Greater than 11: indicative of morbidity;
- 8-10 points: borderline;
- Less than 7 points: absence of significant morbidity.

**Follow-up:** Anxiety and depression symptoms were measured again every 48 hours after admission until the day of discharge or, if necessary, when invasive mechanical ventilation was required. Oxygen requirements were also collected for each measurement to compare clinical progress with symptoms of anxiety and depression.

Patients with anxiety and/or depression scores greater than eight were followed up with a mental status assessment 1 month after discharge from the family medicine clinic. If symptoms of anxiety and/or depression persisted, they were referred to a psychiatrist for appropriate treatment.

Data were captured in an Excel database.

**Statistical analysis:**

The study data were captured and validated using the Windows SPSS version 25 statistical package. Data were described using measures of central tendency and dispersion: mean and standard deviation for parametric variables and median and interquartile range for nonparametric variables, according to their distribution, using the Kolmogorov-Smirnov test. Qualitative variables were described using frequencies and percentages. Changes in the HADS score (primary outcome) were assessed using Student's t-test for related samples or Wilcoxon's test. Sociodemographic variables were compared using the chi-square test or Fisher's exact test, and a Pearson correlation analysis was performed to identify the degree of association between HADS scores and saturation oxygen and length of hospital stay. A P value < 0.05 and a 95% confidence interval were considered statistically significant. The IBM SPSS version 25 statistical package was used for data analysis, which had been previously captured using MS Excel software.

A sample size calculation was performed using a formula for estimating a proportion in a finite population estimated at 300, With a 50% prevalence of patients diagnosed with COVID-19 (SARS-CoV-2 infection) with symptoms of anxiety and/or depression, with a precision of 10%, a one-sided alpha of 0.05, and a power of 95%, at least 56 patients are required.

The patients gave verbal informed consent to participate in the study, and a written informed consent form was not completed, as the institutional Research Ethics Committee waived it.

The required procedures follow ethical standards, the General Health Law on Health Research Regulations, the Declaration of Helsinki of 1975, as amended in 1989, and current international codes and standards of good clinical research practice.

## RESULTS AND DISCUSSION

Sixty-one patients were surveyed, of whom four were eliminated for not meeting the inclusion criteria. Fifty-seven patients hospitalized with COVID-19 pneumonia in the High Specialty and Advanced Medicine Department of the University Hospital were included. 26 (47.3%) were men and 31 (54.4%) were women, with a mean age of 57.8 years. 33.3% had a university education, and 38.6% had a secondary education. The majority were married (63.2%), retired (29.8%), employed (26.3%), home-based (26.3%), and Catholic (80.7%) (Table 1).

The main comorbidities identified in the patients were type 2 diabetes mellitus (45.6%), obesity (43.9%), and high blood pressure (33.3%) (Table 2).

**Table 1: Patients' sociodemographic characteristics**

<b>Gender</b>		<b>Religion</b>		<b>Marital status</b>	
Male	26 (47.3%)	Catholic	46 (80 %)	Single	2 (3.5%)
Female	31 (54.4%)	Christian	7 (12.3%)	Married	36 (63.2%)
Age	57.8 ( $\pm$ 10.9)	Jehovah's W.	2 (3.5%)	Divorced	7 (12.3%)
>65 yrs	(38.6%)	Atheist	2 (3.5%)	Widowed	7 (12.3%)
<b>Profession</b>		<b>Type of Health Insurance</b>		<b>Schooling</b>	
Household	15 (26.3%)	Government insured	2 (3.5%)	Elementary	9 (15.8%)
Employed	15 (26.3%)	University Insur.	41 (71.9%)	Secondary	13 (22.8%)
Professional	8 (14%)	Municipal Insur.	8 (14%)	High School	5 (8.8%)
Retired	17 (29.8%)	Private Insurance	1 (1.8%)	Technical	11 (19.3%)
Technician	1 (1.8%)	No Insurance	5 (8.8%)	University	19 (33.3%)

**Table 2: Patients Comorbidities**

<b>Comorbidities</b>	<b>n</b>	<b>%</b>
Diabetes mellitus	26	(45.6%)
High blood pressure	19	(33.3%)
Obesity	25	(43.9%)
Osteoarthritis	2	(3.5%)
Hypothyroidism	3	(5.3%)
Benign prostatic hyperplasia	3	(5.3%)
Heart disease	2	(3.5%)
Rheumatoid arthritis	1	(1.8%)
Stroke sequelae	1	(1.8%)
Liver cirrhosis	1	(1.8%)
Chronic kidney disease	1	(1.8%)
Ankylosing spondylitis	1	(1.8%)
Fibromyalgia	1	(1.8%)
Dyslipidemia	1	(1.8%)
Migraine	1	(1.8%)
Osteoporosis	1	(1.8%)
HIV	1	(1.8%)
Asthma	1	(1.8%)
Sjögren's syndrome	1	(1.8%)
Myelomeningocele	1	(1.8%)

12.3% of patients met the criteria for evidence of low family poverty. Two-thirds of patients lived with their spouse and/or children (66.7%), and most earned three or more minimum wages within full family income (96.5%). Most had no children who were financially dependent on their income (71.9%), and currently lived in mildly crowded conditions, with one or two people in the home (96.5%)

Upon admission, most patients required low-flow oxygen therapy (n = 45, 78.9%), and one-fifth (n = 12) (21.1%) required high-flow therapy. One-fifth of patients also required invasive mechanical ventilation (n = 11) (19.3%). Patients were discontinued from the study when they required invasive mechanical ventilation or were discharged, at which point

follow-up ended, and they were discharged from the study. Patients' median length of stay was 7 (4-10) days.

At admission, 4 (7%) patients were identified with anxiety-related morbidity and 13 (22.8%) with borderline symptoms associated with a probable diagnosis of anxiety. Additionally, 2 (3.5%) were identified with depressive morbidity and 3 (5.3%) with borderline symptoms of probable depression. At discharge from our study, of the 50 patients who completed the assessment, 1 (2%) had anxiety-related morbidity, 5 (10%) had borderline symptoms of anxiety, and 1 (2%) had depressive morbidity, with no additional patients with borderline symptoms of probable depression (Table 3).

We observed that symptoms of anxiety (Table 4) and depression (Table 5) decreased as the assessment days progressed in our study. By day 6 of the follow-up, no patient assessed presented anxiety morbidity, and by day 9, no patient presented depressive morbidity.

**Table 3: Assessment of anxiety and depression symptoms using the HADS instrument at admission and discharge.**

Variable	n	%	Variable	n	%
<b>Hospital admission</b>	57		<b>Hospital discharge</b>	50	
<i>Level of anxiety</i>			<i>Level of anxiety</i>		
Absence of significant morbidity	40 (70.2%)		Absence of significant morbidity	44 (88%)	
Borderline	13 (22.8%)		Borderline	5 (10%)	
Indicative of morbidity	4 (7%)		Indicative of morbidity	1 (2%)	
<i>Level of depression</i>			<i>Level of depression</i>		
Absence of significant morbidity	52 (91.2%)		Absence of significant morbidity	49 (98%)	
Borderline	3 (5.3%)		Borderline	0 (0%)	
Indicative of morbidity	2 (3.5%)		Indicative of morbidity	1 (2%)	

**Table 4: Prevalence of anxiety symptoms during patient follow-up.**

<b>Anxiety</b>				
<b>Hospital confinement day</b>	<b>n</b>	<b>Absence of significant morbidity</b>	<b>Borderline</b>	<b>Indicative of morbidity</b>
Day 1	57	40(70%)	13(23%)	4 (7%)
Day 2	50	44(88%)	5 (10%)	1 (2%)
Day 3	2	2(100%)	0 (0%)	0 (0%)
Day 4	6	6(100%)	0 (0%)	0 (0%)
Day 5	40	37(92%)	1 (2.5%)	2 (5%)
Day 6	2	2(100%)	0 (0%)	0 (0%)
Day 7	1	1(100%)	0 (0%)	0 (0%)
Day 8	25	19(76%)	6 (24%)	0 (0%)
Day 9	2	1 (50%)	1 (50%)	0 (0%)
Day 10	7	7(100%)	0 (0%)	0 (0%)
Day 11	7	6 (85%)	1 (14%)	0 (0%)
Day 12	2	1 (50%)	1(50%)	0 (0%)
Day 13	0	0 (0%)	0 (0%)	0 (0%)
Day 14	3	3 (100)	0 (0%)	0(0%)

**Table 5: Prevalence of depressive symptoms during patient follow-up.**

<b>Depression</b>				
<b>Hospital confinement day</b>	<b>n</b>	<b>Absence of significant morbidity</b>	<b>Borderline</b>	<b>Indicative of morbidity</b>
Day 1	57	52 (91%)	3 (5.3%)	2 (3%)
Day 2	50	42 (84%)	6 (12%)	2 (4%)
Day 3	2	2 (100%)	0 (0%)	0 (0%)
Day 4	6	6 (100%)	0 (0%)	0 (0%)
Day 5	40	36 (90%)	2 (5%)	2 (5%)
Day 6	2	2 (100%)	0 (0%)	0 (0%)
Day 7	1	1 (100%)	0 (0%)	0 (0%)
Day 8	25	21 (84%)	3 (12%)	1 (4%)
Day 9	2	2 (100%)	0 (0%)	0 (0%)
Day 10	7	7 (100%)	0 (0%)	0 (0%)
Day 11	7	7 (100%)	0 (0%)	0 (0%)
Day 12	2	2 (100%)	0 (0%)	0 (0%)
Day 13	0	0 (0%)	0 (0%)	0 (0%)
Day 14	3	3 (100%)	0 (0%)	0 (0%)

We did not find an association between the presence of symptoms of depression or anxiety at admission and having received invasive mechanical ventilation (being intubated) at any point during their stay ( $P > 0.05$ )

The first day of admission was chosen for this comparison because it was the day the assessment was accurately known for all patients, with no loss to follow-up. (Table 6).

Furthermore, we observed a low to very low correlation between the HADS anxiety or depression score and the patient's length of stay, oxygen saturation at the time of the survey, and the volume of oxygen they were receiving (Table 7).

**Table 6: Association of anxiety and depression upon admission with invasive mechanical ventilation during hospital admission (first day).**

<b>Variable</b>	<b>Intubated</b>	<b>Non-intubated</b>	<b>p</b>
Anxiety on admission	2 (20%)	2 (4.3%)	0.138
Depression on admission	1 (10%)	1 (2.1%)	0.323

**Table 7: Correlation between the HADS scores with hospital stay, oxygen saturation, and volume of oxygen received.**

<b>Spearman's RHO</b>	<b>HADS Anxiety</b>	<b>p</b>	<b>HADS Depression</b>	<b>p</b>
Days of hospitalization	-0.133	0.057	-0.092	0.191
Oxygen saturation (%)	-0.011	0.879	-0.049	0.05
O2 (L/min)	0.227	0.001	0.26	0.001

## DISCUSSION

COVID-19 is a highly infectious and pathogenic disease that has established itself as a global pandemic. The previous SARS outbreak was catastrophic for people's mental health, and during that epidemic, infected medical workers and survivors showed high levels of stress, manifested as depression and anxiety. (18, 19)

The COVID-19 pandemic has also had a significant impact on the general population. In Poland, a high average level of post-traumatic stress was found as a result of the COVID-19 pandemic, with at least the minimum level occurring in all surveyed people. There was also a high incidence of depression (48.00%), anxiety (39.29%), and stress (54.86) (20). Even patients with mental disorders had more serious symptoms related to their mental health and suicidal ideation. (21)

Patients with suspected or confirmed COVID-19 exhibited higher levels of psychological stress, higher depression scores, and lower quality of life (22), and in Wuhan, according to Bo et al., the initial epicenter of the pandemic in China and worldwide, the prevalence of post-traumatic stress symptoms associated with COVID-19 was as high as 96.2%. (23)

During the COVID-19 pandemic, new health and preventive measures emerged in hospitals and health centers, as well as in public places, avoiding crowded places and limiting family visits, in addition to the enormous attention of health institutions to care for a considerable number of patients, which limited the interaction between patients and doctors during their stay, returning patients to a more isolated environment and with an enormous psychosocial impact.

In our study, 57 patients who were hospitalized with COVID-19 pneumonia and met our inclusion criteria were followed during their hospital stay, until discharge, or when the patient required invasive mechanical ventilation, making patient assessment difficult. Most patients presented risk comorbidities for COVID-19 severity, such as diabetes mellitus, arterial hypertension, and obesity. These comorbidities have been highly recognized as factors of disease severity, hospitalization, use of invasive mechanical ventilation, and mortality in patients, and a considerable percentage of the population suffers from these problems, which has made the disease have a significant impact on populations around the world (40) (24). Therefore, it was unsurprising to have identified one-third to one-half of the population with these comorbidities, as in our study. At admission, 29.8% of patients presented symptoms suggestive of anxiety, and 7% presented clinically significant anxiety morbidity, while 8.8% of patients presented symptoms suggestive of depression and 3.5% clinically indicative of comorbid depression.

At the final evaluation of our study, up to 12% of patients presented anxiety symptoms (2% clinically morbid) and 2% significant morbidity from depression. We observed that the trend

toward depression and suggestive anxiety decreased over time and was more significant in the first few days of hospitalization. It could be due to the patient's tendency to improve or a sense of well-being from receiving health care that could support their quality of life, as some patients suggested during the interview.

Xueyi et al. used the same instrument to evaluate associated factors of depression and anxiety symptoms in patients hospitalized with COVID-19 in Wuhan, China, finding that patients with a similar age to that reported in our study presented higher levels of depression and anxiety than the rest of the population and that those with a stay of more than 14 days had a higher risk of depression symptoms. (25) However, in our study, it was not possible to evaluate this effect because the median hospital stay of the patients in our study at the time of the evaluation was half of these days, in addition to the fact that there is the possibility that patients with greater severity who required a more extended hospital stay could develop psychopathology, however, their evaluation within our study for the reasons previously stated. Similar to our study, they did not find an association between the level of dyspnea and the symptoms of depression and anxiety. (25).

In our study, dyspnea was evaluated through the patients' oxygen levels and the degree of oxygen saturation in their blood, and the findings were similar to those of these Chinese authors. Similar to our work, Sun et al. observed that negative psychological symptoms predominated in the early stages of hospitalization. As the days progressed, there was a shift to a mixture of negative and positive emotions. (26)

In our work, we observed this similarity through a decrease in the prevalence of suggestive depression and anxiety symptoms in patients assessed day by day. However, Parker et al. observed contradictory results in a study conducted with a patient sample similar to ours. They found that 36% of patients presented elevated anxiety symptoms and 29% depression symptoms upon admission. At a 2-week follow-up, 9% had increased anxiety symptoms and 20% had increased depression symptoms, while 25% presented symptoms of mild to moderate acute stress disorder. (27) However, this could be related to the patient's environment in New York, which became an epicenter of the disease in the United States, where there was a great need for patient care and could have influenced patient psychology and a longer follow-up compared to our work. Furthermore, contrary to our work, Kong et al. observed that oxygen saturation, as well as other factors such as gender, age, and social support, were associated with anxiety levels in individuals, while social support, family infection with the SARS-CoV-2 virus, and age were related to depression. (28)

Reports of anxiety, depression, and perceived stress in hospitalized patients, despite our report, denote the enormous need to provide psychological support to patients and social support to improve their hospital stay and prevent symptoms after hospitalization. (29)

Post-traumatic stress disorder, major depression, and anxiety, as well as other non-communicable conditions, are significantly associated with disability in patients and can be associated as predictors of more significant inflammation during their illness and after discharge. (30)

Perceived discrimination against patients with COVID-19 has been linked as one of the main predictors of mental illness after discharge. (31) It is important to carry out early maneuvers to improve biopsychosocial health conditions during the hospitalization of patients with COVID-19 pneumonia and to carry out timely interventions to detect psychopathology associated with patients and their families after discharge and in their recovery. Despite the low prevalence of anxiety and depression in our population and the fact that the prevalence decreased as the length of stay increased, identifying them remains important due to the enormous impact on patients' overall health and quality of life.

## CONCLUSION

Fifty-seven patients hospitalized with COVID-19 pneumonia were followed during their hospital stay, until discharge, or until the patient required invasive mechanical ventilation. Upon admission, 29.8% of patients presented symptoms suggestive of anxiety, and 7% presented clinically significant anxiety morbidity, while 8.8% of patients presented symptoms suggestive of depression and 3.5% clinically indicative of comorbid depression. At the last evaluation of our study patients, up to 12% presented anxiety symptoms (2% clinically morbid) and 2% significant depression morbidity. We observed that the trend toward depression and suggestive anxiety decreased over time in patients and was more significant in the first few days of hospitalization. We found no relationship between the manifestation of these symptoms and having been intubated at some point during hospitalization, despite having identified that a fifth of patients required such assistance. The median length of stay was 7 (4-10) days, and most were admitted with low-flow oxygen therapy (78.9%). Furthermore, we found a low or very low degree of correlation, suggesting that both psychological disorders measured by the HADS scale in the study population were independent of these factors assessed daily.

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