

Progression of SARS-COV-2 Infection in Patients Requiring Hospital Admission During the Second COVID-19 Pandemic Wave

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Abstract: Objective: Establish the characteristics and number of patients with a diagnosis of SARS-COV-2 who end up requiring hospital admission, and which of them require assistance in Intensive Care Units (ICU), and determine the time that passes from diagnosis to hospitalization. Compare our own health data between the different waves to see how the pandemic is evolving to manage healthcare resources. Methods: Retrospective observational epidemiological study of 517 COVID-19 patients, microbiologically confirmed, in a tertiary hospital, between June 1 and November 30, 2020. Results: The diagnosis of SARS-COV-2 infection was made by Reverse Transcription Polymerase Chain Reaction (RT-PCR) in 78% of the cases, and by Antigen (Ag) test in the rest. In patients who presented symptoms, an average of 3 days elapsed until diagnosis. In asymptomatic patients, the time from the positive test to the onset of symptoms was 8.4 days on average in the cases of screening and 1 day in the case of contact studies. The mean time from the onset of symptoms to hospital admission was 9 days, 15.3 days in the cases detected by screening and 7.8 days in contact studies. The average hospital stay was 10 days and there was an overall mortality of 13%. 10% of the positive patients needed intensive care, where the average stay was 21 days, the median age was 61 years, and the mortality was 21%. Conclusions: A high percentage of patients diagnosed with SARS-COV-2 infection in Primary Care will require hospitalization (70% according to our study). This information is essential to anticipate the need for hospital resources and the time frame in which they will be needed.

Keywords: COVID-19, Hospitalization, Pandemics

1. Introduction

Some viruses in the coronavirus family are responsible for zoonotic infections, which can be transmitted from animals to humans, as in the case of the new coronavirus SARS-COV-2 [1]. The disease caused by SARS-COV-2, called COVID-19, was first detected in Wuhan (Hubei province, China), at the end of December 2019, when the Municipal Health Commission reported a group of 27 cases of pneumonia [2], initially of unknown etiology, whose causative agent was identified on January 7, 2020 [3].

Since then, the number of cases of this disease has grown

exponentially, spreading outside the borders of China, until the World Health Organization (WHO) declared a global pandemic on March 11, 2020 [4]. As at December 31, 2020, 81,159,096 cases of SARS-COV-2 infection have been reported worldwide, 25,361,223 in Europe and 1,928,265 in Spain [5].

During the first wave, in Spain, 43% of the reported cases required hospital admission, 3.9% admission to the intensive care unit (ICU) and 8.2% died [6]. The province of Salamanca, belonging to the community of Castile and Leon, was one of the Spanish regions most affected by COVID-19 during the first months of the pandemic [7]. In December

2020, the incidence due to onset of symptoms in the last 14 days in Salamanca was 106.8 cases per 100,000 inhabitants [5], which indicate that more than half of the cases are asymptomatic when the microbiological diagnosis is made, but who later develop the disease.

One of the characteristics of this disease, which has been seen as the pandemic evolves, is the high percentage of asymptomatic patients, but with the capacity to transmit the disease, as well as the variability of the severity of symptoms in symptomatic patients. It is important to know what percentage are those who subsequently develop symptoms, their severity, and the time it takes for them to appear, to make a forecast of the need for health resources. As diagnostic capacity has increased thanks to the improvement of diagnostic test of active COVID-19 infection, it appears that there is an increase in mild cases and a decrease in case fatality (as the denominator increases). The course of the disease is apparently more benign, with a higher proportion of asymptomatic cases, so the percentage of hospitalizations in the second wave is lower. With data from August, 3.7% of the cases required hospital admission, and 0.3% admission to the ICU [8].

To date, there are few studies that clearly describe the evolution of the disease [9], so it is important to select criteria that allow identifying those patients who require more strict follow-up and early detection of the need for higher-level healthcare, as well as the period of time that such monitoring must be carried out. Establishing the phases and duration of the disease is one of the challenges that have been posed, and for this reason it is interesting to publish reports of the cases in different areas, which help to better understand the course and epidemiology of COVID-19 [10]. The present study aimed to assess the magnitude of patients who, being initially asymptomatic or with few symptoms, later required hospitalization, as well as to estimate the time that elapsed between the diagnosis and the need for higher-level care and the possible factors associated with this situation during the second wave of the COVID-19 pandemic.

2. Materials and Methods

2.1. Case Definition

A retrospective observational epidemiological study was carried out of patients hospitalized in the CAUSA between June 1, 2020 and November 30, 2020, with a positive diagnostic test of active COVID-19 infection, either a molecular detection of SARS-COV-2 (RT-PCR), or of Ag SARS-COV-2, of all ages and both sexes.

A differentiation was made between a serious case, like any patient requiring hospital admission, and a critical case, one who has spent some day in any of the beds assigned to Intensive Care, including extended ICUs (expansion of ICUs due to the need for beds during the pandemic).

2.2. Data Sources

Since the beginning of the pandemic, the Salamanca University Assistance Complex (CAUSA) established a surveillance system for COVID-19, complementary to the Autonomous Community Surveillance System (SIVIE) and the National Epidemiological Surveillance Network (RENAVE) to guarantee immediate control and isolation of cases, bed management and follow-up of contacts. For this, the Microbiology Service sends an alert via email when a positive case is detected by RT-PCR SARS-COV-2 or SARS-COV-2 2nd generation antigen, with the data, requesting service and location of the patient, so that the result is available almost immediately.

An Excel database was designed with hospitalized patients (filiation data, sex, age, date of onset of symptoms, date of diagnosis, date of admission, location and date of discharge or death) that was updated daily.

The study was expanded with the following variables: origin of request for the first positive diagnostic test of active COVID-19 infection, reason for request (close contact, compatible symptoms, screening study), date of onset of symptoms, admission to ICU (yes / no), days of ICU admission, from a residential center (yes / no), nosocomial case (yes / no).

Some data collected from patients admitted during the first wave to the same hospital were compared. So that we could assess the differences between the two waves and thus improve the health forecast.

2.3. Methods

Data analysis was performed with the SPSS 25.0 statistical package. For the quantitative variables, means and standard deviation (SD) were calculated, and Student T-Test was used to compare these variables. For the qualitative variables, percentages were calculated and the comparison was made using chi-square.

3. Results

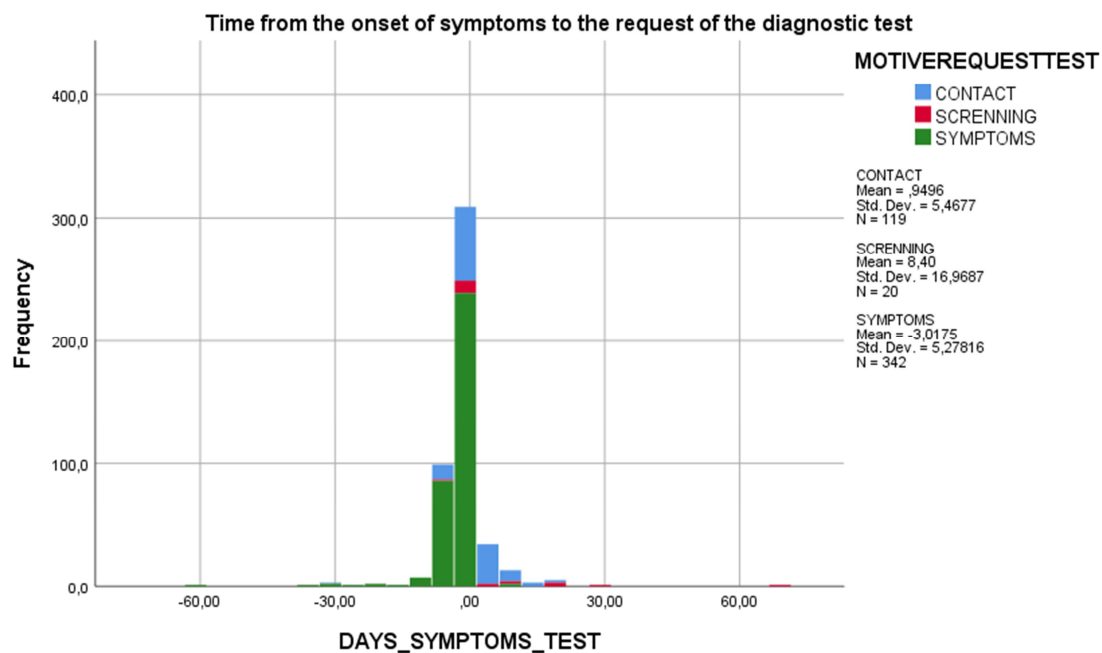
Between June 1 and November 30, 2020, a total of 517 hospitalizations of patients with a positive diagnostic test for active COVID-19 infection occurred in our center, a third-level referral hospital, of which 288 (55.7%) were men and 229 (44.3%) were women, with no statistically significant difference based on sex. The diagnosis was made by Ag test in 21.7% of the cases (112) and by RT-PCR in the rest of the patients (405), which represented 78.3%. In all cases in which RT-PCR was performed after the Ag test, it was positive. The mean age of the admitted patients was 69 years (SD 17.2), and a median age of 71 years (range 88 years, minimum 12 and maximum 101). 45 patients (8.7%) of the total admitted to this second wave came from Residences for the elderly. These data are presented in Table 1.

Table 1. Hospitalized patients from 06/01/2020 to 11/30/2020 according to origin and reason for the first positive SARS-COV-2 test.

| | Positive Ag Test | Positive RT-PCR | Total |
|--------------------------|------------------|-----------------|----------------|
| Primary Care | 93 | 265 | 358 (69.2%) |
| Contact | 15 | 98 | 113 |
| Symptom | 77 | 156 | 233 |
| Screening | 1 | 11 | 12 |
| Emergencies | 13 | 83 | 96 (18.6%) |
| Contact | 0 | 2 | 2 |
| Symptom | 12 | 70 | 82 |
| Screening | 1 | 11 | 12 |
| Hospitalization | 0 | 24 | 24 (4.6%) |
| Screening upon admission | -- | 12 | 12 |
| Contact | -- | 1 | 1 |
| Symptom | -- | 11 | 11 |
| Preventive Medicine | 0 | 4 | (2 nosocomial) |
| Screening | -- | 4 | 4 (0.7%) |
| Residences | 3 | 24 | 4 |
| Contact | 2 | 12 | 27 (5.2%) |
| Symptom | 1 | 12 | 14 |
| Private Sanity | 3 | 5 | 13 |
| Contact | -- | 1 | 8 (1.5%) |
| Symptom | 3 | 4 | 1 |
| Total | 112 (21.7%) | 405 (78.3%) | 7 |

Figure 1 describes the time between the appearance of symptoms and the positive diagnostic test, depending on the reason why the diagnostic test for active SARS-COV-2 infection was performed, with symptoms compatible with COVID-19 disease in 67.1% of cases, both in Primary Care

as in Hospital Emergencies; In 25.3% it was requested because it was close contact with confirmed cases, and in the rest for screening prior to surgery, other medical procedures, or pre-admission, who later developed severe symptoms that required hospital admission.

**Figure 1.** Evolution between symptoms and positive diagnostic tests.

The mean time that elapsed between the onset of symptoms and the request for the diagnostic test was 1.6 days (SD 6.8). Depending on the reason for requesting the test, this mean time was -0.95 days (SD 5.5) in close contacts, 3 days (SD 5.3) in patients who presented symptoms and -8.4 days (SD 17) in the patients who underwent screening.

Figure 2 shows the mean time from the onset of symptoms

to hospital admission of 9 days (SD 6.9). When the reason for request was a contact with a positive case, the mean time from the onset of symptoms to admission was 6.7 days (SD 5.3); of 9.8 days (SD 7) when the reason for consultation was the appearance of symptoms, and 8.3 days (SD 9.6) among the patients subjected to screening, which indicates that the symptoms appear after the positive test.

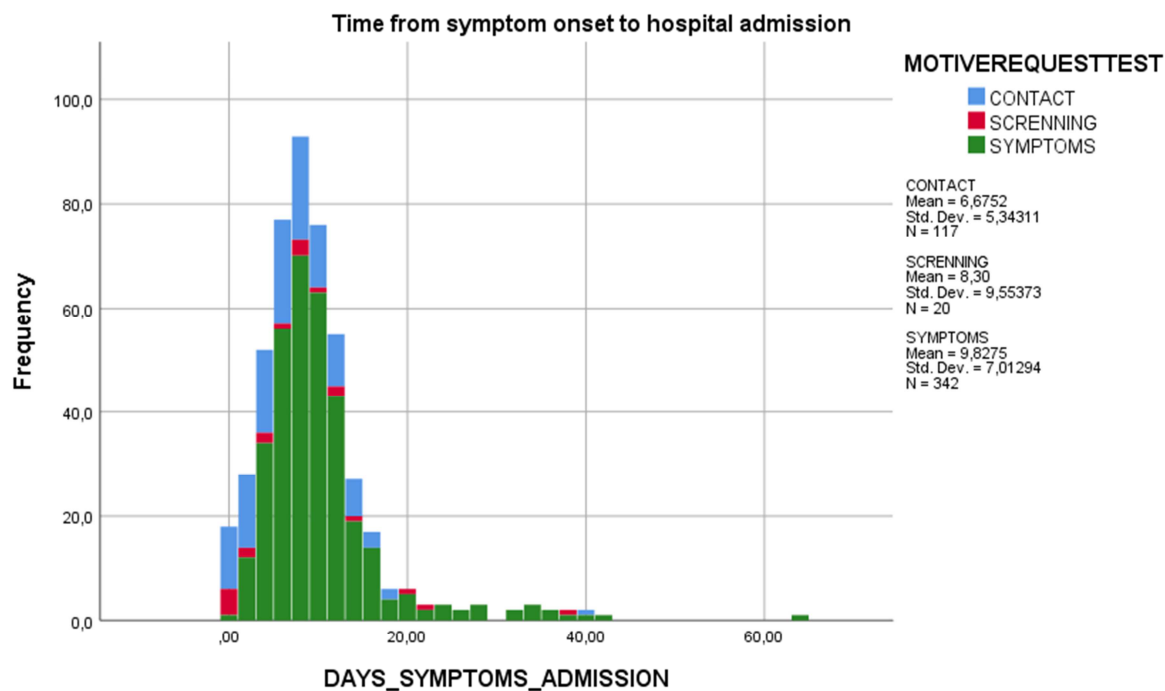


Figure 2. Evolution between symptoms and hospitalization.

Figure 3 shows the mean time that elapsed from diagnosis with a positive diagnostic test to admission, which was 7.8 days (SD 6.9); 7.8 days with an SD 4.7 among those who were in close contact with a case; 7 days with a SD 5.9 among symptomatic patients and 15.3 days with a SD 14 in those detected by screening.

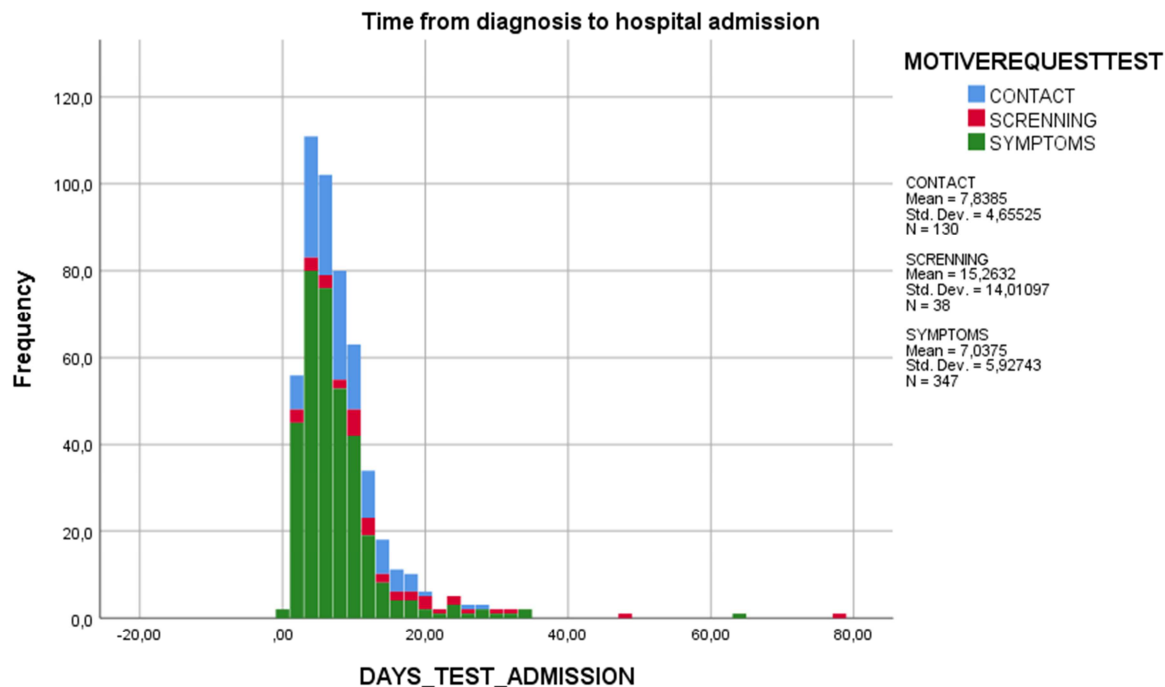


Figure 3. Evolution between positivity of diagnostic tests and hospitalization.

The overall mean stay was 10.5 days (SD 8.1 days), with a maximum of 63 days (although there are patients hospitalized at the end of the study), with no statistically significant difference between patients who recovered and were given

hospital discharge and those who died during hospitalization (10.6 and 9.8 days, respectively).

Of all admissions, 52 (10%) were admitted to the Intensive Care Unit, with a mean stay in the ICU of 21.4 days (SD 14),

of which only 3 came from Residence. Among them, 34 were men, representing 11.8% of all admitted men (34/288), and 18 women, who represented 7.9% of all admitted women (18/229), although the difference it was not statistically significant. The mean age of the patients admitted to the ICU was 60.8 years (SD 14.2), while in non-critical patients it was 70 years (SD 17.3), with a statistically significant difference.

Overall mortality was 13.2% (68/517), and in ICU 21.2% (11/52), while in patients who were not admitted to critical care units, mortality was 12.3%, without finding statistically significant differences. The mean age of the discharged patients was 66.7 years, while the mean age of the deceased patients was 83.8 years, with a statistically significant difference. By sex, 10% of the women admitted (23/229) and 15.6% of the men (45/288) died. The difference in mortality by sex was not statistically significant. The mean time elapsed between the onset of symptoms and the admission of deceased patients was 9.4 days (SD 7.9).

In the first wave (March to May 2020), 1,196 patients were admitted to our hospital, of which 510 (42.6%) were women and 686 (57.4%) were men. The mean age was 73 years (SD 16). 246 (20.6%) were previously institutionalized patients. The mean hospitalization stay was 14 days (SD 13). 110 patients (9.3%) were admitted to one of the Intensive Care Units, with a mean stay in it of 16 days. A total of 406 patients (33.9%) died, with an average age among the deceased of 82 years (SD 10).

Table 2. COVID-19 patients with critical illness (admission to ICU) from 06/01/2020 to 11/30/2020.

| | Total | Statistical significance |
|------------------|----------------------|--------------------------|
| Average stay | | |
| No ICU (serious) | 9.3 days (SD 6.1) | p < 0.000 |
| ICU (critical) | 21.4 days (SD 14) | p > 0.05 (N. S) |
| Exitus (68) | 9.8 days (SD 10) | |
| No exitus | 10.6 days (SD 7.8) | p < 0.000 |
| Mean age | | p < 0.000 |
| No ICU (serious) | 69.9 years (SD 17.3) | |
| ICU (critical) | 60.8 years (SD 14.2) | p > 0.05 (N. S) |
| Exitus (68) | 83.8 years (SD 10.4) | |
| No exitus | 66.7 years (SD 17) | p > 0.05 (N. S) |
| Exitus (n) % | 68/517 (13.2%) | |
| No ICU (serious) | 57/465 (12.3%) | p < 0.000 |
| ICU (critical) | 11/52 (21.2%) | p > 0.05 (N. S) |
| Sex | | |
| Men in ICU | 34/288 (11.8%) | p < 0.000 |
| Women in ICU | 18/229 (7.9%) | p < 0.000 |

4. Discussion

One of the key points for controlling the transmission of the COVID-19 pandemic is the early detection of all compatible cases, including asymptomatic cases detected by contact studies or screening in risk situations, for which it is necessary to increase the ability to perform diagnostic tests. But this in turn is associated with the proper management of the cases detected, being necessary to know the burden that it will entail for the different levels of care, distinguishing between cases that only require follow-up by Primary Care and cases that require hospitalization and for how long, and

estimate what percentage of initially mild cases get worse and in what period of time, to adapt the management of health resources to the evolution of the pandemic. Therefore, it is important to publicize the information available in the different areas of our territory, since it is a still unknown disease in many aspects and the data are highly variable depending on the country or continent where we are.

In our study, important differences have been observed in the evolution of the pandemic and characteristics of the cases in the first and second waves. Thus, when comparing our own data, they are consistent with studies published in Spain [11], where we see that the percentage of deaths in hospitalized patients in the first wave was much higher (33.9% versus 13.2%). Also, a study carried out in 30 Spanish ICUs during the first wave [12] shows that mortality in hospitalized patients ranges between 18% and 31%. However, the percentage of patients who required admission to the ICU is similar between the first and second waves, although the mean stay in the ICU is longer in the second stage (21 days in the second wave versus 16 days in the first wave), in contrast to the mean stay in the hospital ward, which is lower (10.5 days compared to 14.4 days at the beginning). These figures lead to the need for a greater number of intensive care resources.

Another indicator of interest for the adequacy of resources in the management of the pandemic is the percentage of patients initially asymptomatic or with mild symptoms (69.2% had been diagnosed in Primary Care) that evolve to more serious conditions and that will require hospitalization [11, 13].

There are studies that analyze the time elapsed between the different events, such as the time between the onset of symptoms and the first contact with the health system (2 days with IQR of 1-4 days), or the time between the onset of symptoms and the onset of severe symptoms (1 week according to published data; 9 days in our study), or until death (2-8 weeks), but it is not reflected if this first contact is at the level of Primary Care or Hospital, or if this first contact has led to or subsequent hospital admission. Regarding the chain of transmission, the median incubation period has been established at 5.1 days (95% CI 4.5 to 5.8), and at 11.7 days (95% CI 9.7 to 14, 2) 95% of symptomatic cases have already developed symptoms. According to the RENAVE report [8], the median number of days between the onset of symptoms and diagnosis is 3 days (interquartile range 1-5) in Castile and Leon, but the time elapsed between the diagnoses or the onset of symptoms is not available until hospital admission, or until admission to critical care units.

Different studies have published the risk factors for mortality in hospitalized patients or ICU patients, but few studies have evaluated the risk of hospitalization in initially mild patients or the time that elapses from the SARS-COV-2 infection to the need for entry. For this reason, it should be noted the role played by asymptomatic people who a priori have no reason to think that they are infected, such as patients who undergo a SARS-COV-2 RT-PCR by screening study and who subsequently require a health resource advanced such as hospitalization, which represented 3.9% of

admissions in our study [12, 14].

The data disclosed so far establish the mean time from the onset of symptoms to recovery at 2 weeks when the disease has been mild and from 3 to 6 weeks when it has been severe or critical. The time between the onset of symptoms and the onset of severe symptoms, such as hypoxemia, is one week, and 2-8 weeks until death occurs [15, 16]. In our study, it is observed that the mean time from the onset of symptoms to hospital admission is 9 days, somewhat higher than the published data, and the mean time from admission to death is almost 10 days, while according to published reports ranges from 2 to 8 weeks [17]. These data are of great interest since they allow an estimate to be made of the moment in which the care pressure of hospital admission will increase (or decrease), assessing the epidemiological situation in the community, and anticipating an increase in the demand for hospital care from the increase at the population level. Likewise, they allow estimating the percentage of admitted patients who may require ICU care and making a forecast of the need for beds in critical care units, which has meant a significant change from the first to the second wave.

Our data and information collection system in real time will help to better understand the evolution of the disease and support the management of resources, which must be adapted to the specific situation of each area.

5. Conclusions

Around 70% of patients diagnosed with SARS-COV-2 infection in Primary Care will require hospitalization.

10% of patients with a positive test against SARS-COV-2 who require hospitalization, end up being admitted to ICU.

The mean stay in the Critical Care Unit is longer in the second wave thereby increasing the need for complex healthcare resources.

On the other hand, the mean number of days of hospitalization was lower in the patients who were admitted to non-critical units in the second wave compared to the first wave, partially alleviating the care pressure.

The longest time from the onset of symptoms to hospital admission appears when the reason for request was the appearance of symptoms, being also the cases with the longest mean time of admission.

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