Epidemiological Profile and Complications of Patients on the Waiting List for Liver Transplantation

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Section editor: Ilka de Fátima Santana F Boin

ABSTRACT

Objective: To identify the epidemiological profile of candidates for liver transplantation and the complications that occurred up to the sixth month of admission to the waiting list. **Method:** Descriptive-exploratory study conducted in a liver transplant program located in a city in the interior of the state of São Paulo. Candidates aged ≥ 18 of both genders who entered the waiting list between January 1, 2018, and February 28, 2019, made up the study sample, totaling 51 patients. Data analysis was performed using descriptive statistics. **Results:** The average age of the participants was 52.7 years, most male (60.8%) with incomplete primary education (58.8%). Arterial hypertension was the most frequent comorbidity (51.4%). Most participants had blood type O (58.8%). The average Body Mass Index was 28.8 Kg/m² (overweight). Alcoholic cirrhosis was the most frequent indication for transplantation (31.4%). The average MELD score when joining the waiting list and six months later was 17.9 points. Class B of the Child-Pugh score had the highest frequency at the patient's admission and the first follow-up. Ascites were the most frequent complication (56.9%), followed by portal hypertension (52.9%) and hepatic encephalopathy (33.3%). At the end of the study, 29 patients remained on the waiting list (56.9%), ten patients were transplanted (19.6%), and 12 died (23.5%). **Conclusion:** As for the epidemiological profile, the study's results were in line with other studies, that is, participants with a predominance of male biological sex, most frequent age group of 50 to 59 years and low level of education. Concerning the identified complications, ascites were the most frequent. Among participants who did not remain on the waiting list, the number of deaths was more significant than the number of transplants performed, evidence that differs from other studies.

Descriptors: Liver transplant; Health Profile; Patient Assistance Team; Perioperative Nursing; Terminal Liver Disease; Liver diseases.

Perfil Epidemiológico e Complicações de Pacientes em Fila de Espera para Transplante de Fígado

RESUMO

Objetivo: Identificar o perfil epidemiológico de candidatos ao transplante de fígado e as complicações que ocorreram até o sexto mês do ingresso em lista de espera. **Método:** Estudo descritivo-exploratório, conduzido em programa de transplante de fígado, localizado em cidade do interior do estado de São Paulo. Os candidatos com idade ≥ 18 anos, de ambos os sexos, que ingressaram na lista de espera entre 1º de janeiro de 2018 até 28 de fevereiro de 2019 compuseram a amostra do estudo, totalizando 51 pacientes. A análise dos dados foi por meio de estatística descritiva. **Resultados:** A média de idade dos participantes foi 52,7 anos, sendo a maioria do sexo masculino (60,8%), com ensino fundamental incompleto (58,8%). A hipertensão arterial foi a comorbidade mais frequente (51,4%). A maioria dos participantes era do tipo sanguíneo O (58,8%). A média do Índice de Massa Corporal foi 28,8 Kg/m² (sobrepeso). A cirrose alcoólica foi a indicação para o transplante de frequência maior (31,4%). As médias do escore MELD no ingresso em lista de espera e seis meses após foram 17,9 pontos. A classe B do escore Child-Pugh foi a que obteve maior frequência tanto no ingresso do paciente quanto no primeiro retorno. A ascite foi a complicação mais frequente (56,9%), seguida da hipertensão portal (52,9%) e encefalopatia hepática (33,3%). Ao final do estudo, 29 pacientes permaneceram em lista de espera (56,9%), dez pacientes foram transplantados (19,6%) e 12 evoluíram para óbito (23,5%). **Conclusão:** Quanto ao perfil epidemiológico, os resultados do estudo demostraram consonância com outras pesquisas, ou seja, participantes com predomínio

do sexo biológico masculino, faixa etária mais frequente de 50 a 59 anos e nível de escolaridade baixo. Com relação às complicações identificadas, a ascite foi a mais frequente e, entre os participantes que não permaneceram em lista de espera, o número de óbitos foi maior que o de transplante realizado, evidências divergentes de outros estudos.

Descritores: Transplante de Fígado; Perfil de Saúde; Equipe de Assistência ao Paciente; Enfermagem Perioperatória; Doença Hepática Terminal; Hepatopatias.

INTRODUCTION

The liver is considered the largest solid organ in the human body. It regenerates itself and constantly works to maintain body homeostasis, having a weight reaching up to 2% of the body.[1] In addition to implications for other systems in the human body, the hepatic system stores blood, vitamins and iron; forms bile; metabolizes fats, hormones, proteins and chemical agents; and synthesizes blood clotting factors.[2]

Liver transplantation has advanced so that the survival rate in the first year after surgery is 85%, in addition to this procedure being performed with a living donor.[3] It is indicated for treating patients of all age groups, with irreversible chronic liver disease, in the absence of another therapeutic option.[4]

More than 10,000 liver transplants are performed worldwide each year.[5] Brazil, with the largest public system of organ transplants, is a world reference in performing transplants.[4] In addition, in 2021, it ranked fourth among the countries that most perform liver transplants, behind the United States, China and India.[6]

The liver transplant waiting list is organized using the Model for End-Stage Liver Disease (MELD) score, which scores 6 to 40 points. Laboratory tests are performed to determine the score, quantifying levels of creatinine, bilirubin and the International Normalised Ratio (evaluation of liver conditions in relation to the production of coagulation factors through the functions of prothrombin).[7] In Brazil, patients have a high mortality rate in the pre-transplant period due to the high MELD scores, varying between 20 and 38%. A patient with a high MELD score urgently needs the transplant due to the severity of the underlying disease; in addition, due to the growing demand, there are no organs to serve everyone, which increases the mortality rate of patients on the waiting list.[1,7] Thus, through the MELD score, patients in more severe conditions, therefore, at a higher risk of mortality, can be selected.[8]

Patients with end-stage liver disease on the waiting list for liver transplantation has different complications during the waiting period for surgery, such as ascites, hepatic encephalopathy, hepatorenal syndrome and spontaneous bacterial peritonitis.[3] Age can also contribute to complications. The worst evolutions are related to older patients, notably when associated with patients who developed diabetes mellitus or needed mechanical ventilation.[9]

It is essential to point out that in the pre-transplant period, when the patient is affected by complications, there is an increase in the MELD score, indicating the severity of the situation. Therefore, the patient with complications that lead to multisystem organ failure becomes too vulnerable to undergo transplantation, and its performance is contraindicated.[3]

Often, patients on the waiting list develop or recover from behaviors that tend to worsen the underlying disease, for example, drinking alcohol.[1] In this context, health professionals, especially nurses, considered a link between teams, must develop skills and competencies in view of the complexity of the procedure in its different stages (preoperative, intraoperative and postoperative period), so that, with mastery of all stages of the transplant, the assistance provided can prepare the patient for surgery, seeking the effectiveness of the therapy.[4,8]

Considering that the number of patients on the waiting list for liver transplantation is high, the health care provided by the multidisciplinary team requires constant management of the evolution of the candidate's condition, with emphasis on the work of the nursing team, which is present in the planning and implementation of care from the primary diagnosis to the indication for transplantation to the recovery of the patient after surgery. Thus, the investigation of the epidemiological profile offers subsidies for understanding the chronic condition of liver disease, as well as the needs of this population, contributing to the early identification of possible complications. The scarcity of studies in the literature on the issue is also highlighted. Thus, the research results can contribute to the scientific community and encourage new research.

OBJECTIVE

The study's objective was to identify the epidemiological profile of candidates for liver transplantation and the complications that occurred up to the sixth month of admission to the waiting list.

METHOD

The present is a descriptive-exploratory study. The research was conducted in a public General Hospital located in a municipality in the state of São Paulo, with a liver transplant program accredited by the National Transplant System.

The target population consisted of participants aged ≥ 18 years of both genders who entered the waiting list from January 1, 2018, to February 28, 2019.

This study is a subproject of a broad project investigating risk factors for mortality in liver transplant candidates on the waiting list. The final product of the comprehensive project was a doctoral thesis and two scientific initiation research (SI). It should be noted that the present study consists of the final product of the SI research. A single script was prepared for the collection of data from the subprojects. The data collection script was divided into three sections: 1) components of the epidemiological profile, 2) variables on the indication of liver transplantation, and 3) clinical variables on the waiting list.

The following information was collected to achieve the objective of the study: demographic characteristics (biological sex, age, education and state of origin) and clinical characteristics (diagnosis for liver transplantation, Body Mass Index, presence of chronic diseases, blood type and MELD, corrected MELD, and Child-Pugh scores). Such scores were collected when the patient entered the waiting list and at the first return visit (six months after the patient entered the waiting list). Complications were recorded at the first follow-up.

Data were collected from the hospital's electronic medical records in March and April 2021. Data was collected on complications related to the period from July 1, 2018, to June 30, 2019.

The information was collected on the REDCap[10] platform and exported to a Microsoft Excel spreadsheet. The presentation of the data was under the nature of the variables, and the qualitative variables were described by the frequency of distribution of the participants between the delimited categories, and the quantitative variables were evaluated in terms of position (mean) and dispersion (standard deviation). The Statistical Package Social Sciences software, was adopted for data analysis.

The Ethics Committee approved the broad project.

RESULTS

In the period defined for conducting the study, 83 entries were made on the waiting list. Of the total, 32 registrations were excluded, and 51 participants composed the sample of this research. The reasons for exclusion from the waiting list are as follows:

- Thirteen patients were removed by the multidisciplinary team for reasons not recorded in the electronic medical records;
- Nine joined the list for a second time;
- Five, the MELD score was more than 90 days old;
- Two patients diagnosed with acute fulminant hepatitis;
- One patient with expired MELD;
- One, removed without clinical conditions;
- One, due to suspension (> 365 days).

In Table 1, the demographic characterization of the sample is presented. Most participants were male, from the state of São Paulo. The mean age was 52.7 years, with the most frequent variation between 50 and 59 years. Regarding education, most participants had incomplete primary education, and only four participants had completed higher education.

Table 1. Distribution of candidates on the waiting list for liver transplantation, according to demographic data.

Variables	n (%)	Mean (SD)
Age		52,7 (12,3)
18 – 29 years old	5 (9,8)	
30 – 39 years old	1 (2,0)	
40 – 49 years old	7 (13,7)	
50 – 59 years old	20 (39,2)	
60 – and over	18 (35,3)	
Biological sex		
Female	20 (39,2)	
Male	31 (60,8)	
Education		
Elementary (incomplete)	30 (58,8)	
Elementary (complete)	4 (7,8)	
High School (incomplete)	2 (3,9)	
High School (complete)	9 (17,6)	
University/college (incomplete)	2 (3,9)	
University/college (complete)	4 (7,8)	
State of Origin		
São Paulo	45 (88,2)	
Minas Gerais	6 (11,8)	

SD: Standard deviation. Source: elaborated by authors

Alcoholic liver cirrhosis was more frequent as an indication for liver transplantation. Of the 51 participants, 37 had comorbidities, with high blood pressure being the most frequent, followed by diabetes mellitus (Table 2).

Table 2. Distribution of candidates on the waiting list for liver transplantation, according to main diagnosis and comorbidities.

Variables	n (%)
Main diagnosis for liver transplantation	
Viral liver cirrhosis	7 (13,7)
Alcoholic liver cirrhosis	16 (31,4)
Cryptogenic liver cirrhosis	15 (29,4)
NASH liver disease	2 (3,9)
Cholestatic liver cirrhosis	5 (9,8)
Other diseases	6 (11,8)
Comorbidities	
Arterial hypertension	19 (51,4)
Diabetes mellitus	18 (48,6)
Musculoskeletal disorder	3 (8,1)
Thyropathies	3 (8,1)
Chronic kidney disease	2 (5,4)
Abdominal wall hernia	2 (5,4)
Metabolic disorder	1 (2,7)

Source: elaborated by authors

The mean Body Mass Index of the sample was 28.8 Kg/m² (overweight), with the highest frequency being within the range of 25.0 – 29.9 Kg/m², also indicating overweight. As for blood type, most participants were type O. The mean MELD score was 17.9 points when joining the waiting list. Of the 17 patients with corrected MELD, only one had a score in the medical record (20 points). Of the remaining 16 patients, the data were not recorded in the medical records since, in this situation, there are ninety days for candidates to carry out the necessary tests to calculate the exception points. Regarding the Child-Pugh score, classification B had the highest frequency. It is essential to point out that there was a loss of one value of the score in question (Table 3).

Table 3. Distribution of candidates on the waiting list for liver transplantation, according to clinical data (admission).

Variables	n (%)	Mean (SD)
Body Mass Index (Kg/m²)		28,8 (5,9)
< 18.5 (underweight)	0	
18.5 - 24.9 (eutrophy)	15 (29,4)	
25.0 - 29.9 (overweight)	17 (33,3)	
30.0 - 34.9 (Class I obesity)	13 (25,5)	
35,0 – 39,9(Class II obesity)	2 (3,9)	
≥ 40 (Class III obesity)	4 (7,8)	
Blood type		
A	16 (31,4)	
AB	1 (2,0)	
B	4 (7,8)	
O	30 (58,8)	
MELD Score		17,9 (6,5)
Child-Pugh* Score		
A	7 (13,7)	
B	28 (54,9)	
C	15 (29,4)	

SD: Standard deviation.; MELD: Model for End-stage Liver Disease; *missing value to Child-Pugh. Source: elaborated by authors

Table 4 presents clinical data and complications of candidates for liver transplantation in the first return visit. Mean MELD and corrected MELD scores were 17.9 and 24.3 points, respectively. As for the Child-Pugh score, category B was also the one with the highest frequency.

Regarding the complications of liver transplant candidates on the waiting list, ascites were the most frequent, followed by portal hypertension.

As for the need for hemodialysis, only one patient was indicated for this therapy. In the sample, mean serum albumin was 3.1 g/dL, mean sodium was 137.3 mmol/L, and median platelet count was 66 platelets/mm³

Table 4. Distribution of candidates on the waiting list for liver transplantation, according to clinical data and complications related to a six-month waiting list.

Variables	n (%)	Mean (SD)	Median (range)
MELD[1]		17,9 (6,7)	
MELD corrected[2]		24,3 (4,5)	
Child-Pugh[3]			
A (5 – 6)	8 (15,7)		
B (7 – 9)	22 (43,1)		
C (10 – 14)	20 (39,2)		
Complications			
Ascites	29 (56,9)		
Portal hypertension	27 (52,9)		
Hepatic encephalopathy	17 (33,3)		
Gastroesophageal varices	16 (31,4)		
Infection[4]	11 (21,6)		
Hepatocellular carcinoma	9 (17,6)		
Digestive hemorrhage	9 (17,6)		
Kidney damage	8 (15,7)		
Anemia	6 (11,8)		
Pleural effusion	3 (5,9)		
Abdominal wall hernia	3 (5,9)		
Spontaneous bacterial peritonitis	3 (5,9)		
Hepatorenal syndrome	3 (5,9)		
Hepatic hydrothorax	1 (2,0)		
Portal vein thrombosis	1 (2,0)		
Hemodialysis	1 (2,0)		
Serum albumin (g/dL)5		3,1 (0,7)	
Sodium (mmol/L)[6]		137,3 (6,1)	
Platelets (platelets/mm³)[7]			66 (14 - 273)

SD: Standard deviation.; [1]MELD: Model for End-stage Liver Disease; [2]seven missing values of the corrected MELD score; [3]one missing value of the Child-Pugh score; [4]any type of infection except spontaneous bacterial peritonitis; [5]reference value of serum albumin: 3,5 – 4,7 g/dL; [6]sodium reference value: 36 – 145 mmol/L; [7]platelet reference value: 166–389 platelets/mm³. Source: elaborated by authors

Of the 51 participants, 24 (47%) were hospitalized, 19 exclusively in the ward, and five in the ICU and ward. Regarding the length of stay, most participants stayed from one to twenty days (n=21, 87.5%) (data not shown in the table).

At the end of the study, most patients remained on the waiting list (n=29, 56.9%).

Liver transplantation occurred in ten patients (19.6%). The death affected 12 individuals (23.5%) due to the following causes: septic shock – three, upper variceal digestive hemorrhage – two, grade 4 hepatic encephalopathy – one, not determined– six (out-of-hospital death without a record of the cause in the medical records).

DISCUSSION

There is evidence in the literature that men have a higher number of liver diseases in comparison to women. In a retrospective study conducted at the Organ Transplantation Unit of the Hospital Israelita Albert Einstein, in Brazil, in 2005, the results showed that, of the 35 participants selected for the survey, 22 were male (62.7%).[11] This data corroborates the results of the present study since most patients were male.

As for age, a literature review showed that advanced age (≥ 65 years) may be associated with increased risks of complications on the waiting list as the person becomes more vulnerable.[9] In this research, 35.3% of the participants (n=18) were older than sixty years.

Schooling is considered an important aspect in the construction of care planning for candidates for liver transplantation, as this data indicates the person's level of education, helping health professionals in the teaching-learning process of the necessary maintenance of the candidate on the waiting list. In this research, most participants did not complete elementary school. In a cross-sectional study conducted at the University of California (USA), 303 liver transplant recipients were included in the sample. In the analysis of socioeconomic and demographic factors, one of the results evidenced was that the higher the level of education, the better the evolution of individuals after transplantation.[12]

In a retrospective study conducted at the Liver Transplant Service at the Hospital de Clínicas of the Federal University of Paraná, 152 liver transplants were included in the sample; twenty of which were indicated for alcoholic cirrhosis, and 19 were male.[13]

These results corroborate data from a literature review, which pointed out that men are prone to higher alcohol consumption, increasing the risk of developing liver diseases.[14]

In another literature review, the authors indicated that patients diagnosed with cirrhosis have greater chances of complications and reduced life expectancy. In addition, ascites is a recurrent complication in patients with cirrhosis, often being the cause of hospitalization for these individuals.[15]

In a retrospective study carried out in Germany, with the participation of 481 adult patients on the waiting list for liver transplantation, the results showed that cardiovascular comorbidities were common among patients (n=225, 46.8%), with arterial hypertension being the most frequent (26%) and 115 patients (23.9%) had diabetes mellitus.[16]

Given the above, the data from the studies mentioned are in line with the results of this research; that is, the male gender was the most frequent; arterial hypertension and diabetes mellitus, the most common comorbidities; alcoholic cirrhosis was the leading diagnostic indicator for transplantation and ascites, the most frequent complication.

Concerning BMI, the sample mean was 28.81 Kg/m², indicating overweight. In a literature review, obesity is shown as a risk factor for liver transplantation. However, it cannot be considered a contraindication by itself but a risk factor for developing respiratory and infectious complications in the perioperative period. The management of patients with obesity is necessary through implementing preventive or control strategies by health professionals.[17] It is noteworthy that obesity does not necessarily increase the risk of mortality during surgery but increases the chance of developing thromboembolism, wall dehiscence and reduced life expectancy, as in other surgical procedures.[18]

A retrospective study carried out in Espírito Santo, Brazil, addressed the most frequent blood type in a sample of 244 patients on the waiting list for liver transplantation. The result of the research showed that 43.8% of the sample had blood type O, followed by A, with 41.8% of the sample.[19] While in another retrospective study carried out in São Paulo, Brazil, in which the theme was also addressed, using a sample of 24 people, 79% of the participants had blood type O, followed by type A, representing 17% of the participants.[20] Since blood type O is the most frequent in both studies, such data align with the present research's results.

The MELD score was adopted on the waiting list to improve organ allocation. Indicators of liver failure and predictors of mortality in people with chronic liver diseases could be considered; that is, there is also an assessment of the risk of death and not only the waiting time on the list. Thus, the higher the MELD score, the greater the risk of mortality to which the patient is exposed.[21] Generally, patients with a MELD score equal to or greater than 15 are indicated for the liver transplant waiting list.

In an integrative review carried out in Brazil, the objective was to analyze the knowledge produced about MELD and its relationship with survival after liver transplantation, with eight studies being included. The data indicated that the period on the waiting list increased the MELD, leading to an increase in the risk of complications during surgery.[22] Thus, managing patients on the waiting list must be carried out judiciously, contributing to the success of liver transplantation.[23] In the present study, the mean MELD scores at the patient's admission and the first follow-up were the same.

There is discussion in the literature on whether the Child-Pugh score predicts mortality or complications in candidates on the waiting list and whether the MELD score is a better independent predictor of mortality than the Child-Pugh score. The MELD score has advantages over the Child-Pugh score, especially when comparing populations. Still, regarding individual care, the Child-Pugh score indicates interesting results when combined with other clinical information.[24]

In a retrospective cohort study conducted in Germany, with the participation of 481 patients on the waiting list for liver transplantation, the results showed that ascites (n=256;53.2%) and encephalopathy (n=156;32 .4%) were the most frequent complications, arising from the last stages of liver disease.[16] These data corroborate the results of this research.

In a quasi-experimental study carried out in the state of São Paulo, 55 liver transplant candidates were included. The results showed that esophageal varices were present in 81.82% of the sample, ascites in 58.2% and hepatic encephalopathy in 50.9%.[3] In the present study, esophageal varices were identified in 31.4% of the sample (n=16).

In a cross-sectional study, also conducted in the state of São Paulo, the sample consisted of 103 candidates for liver transplantation. The results showed that the three main complications were esophageal varices in 59 patients (57.3%), ascites in 54 (52.4%) and portal hypertension in 49 (47.6%).[25]

In a retrospective cohort study conducted in the Netherlands, 327 patients on the waiting list for liver transplantation were included. The results indicated that 144 candidates had at least one infection. This situation may result in an increase in the period on the waiting list, with an average length of time on the list for those with infection being 381 days and for candidates without infection, 163 days. In addition, a total of 318 infections occurred, including cholangitis, spontaneous bacterial peritonitis and urinary tract infection, which had the following frequencies: 24%, 18% and 12%, respectively.[26] In the present study, 11 patients (21.6%) had an infection as a complication and spontaneous bacterial peritonitis was recorded separately, occurring in three patients (5.9%). The data presented justify the need to implement measures aimed at preventing and controlling infection by the multidisciplinary team.

In a systematic review with meta-analysis, the authors stated that renal failure should be considered a significant risk factor in the indication for liver transplantation in patients with end-stage liver disease. In pre and intraoperative periods, hemodialysis is an alternative treatment for establishing electrolyte balance.[27] In the present study, of the 51 patients, only one needed such therapy.

In a retrospective study conducted in the State of Ceará, 85 medical records of candidates for liver transplantation and/or transplanted patients were included from 2010 to 2014. The results showed that, while waiting for the transplant (preoperative), 10% of the patients had some complications that led to hospitalization. In addition, there was only one death among patients enrolled on the waiting list.[7] In the research under discussion, 24 patients (47.1%) were admitted to the ward, and five evolved with an ICU indication. Concerning death, of the 51 participants, 12 (23.5%) had this outcome.

In a retrospective cohort study conducted in Turkey, 266 candidates for liver transplantation were included. The results indicated that 119 (44.7%) underwent transplantation, 103 died (38.7%), 40 (15%) remained on the waiting list, and four patients had changes of position on the waiting list. The MELD score values of the patients who died were considerably high, while the preoperative MELD score values of those who underwent the transplant did not show consequences on the survival of these patients.[28] Comparing the mentioned data with the results of the present study, the percentages of deaths and patients who underwent transplantation were lower. In contrast, the percentage of patients who remained on the waiting list was higher.

CONCLUSION

As for the epidemiological profile, the results of the study were in line with other studies, that is, participants with a predominance of male biological sex, more frequent age group of 50 to 59 years and low level of education. Alcoholic cirrhosis was the most frequent indication for transplantation, and arterial hypertension was the most common comorbidity. Concerning the identified complications, ascites were the most frequent, and among participants who did not remain on the waiting list, the number of deaths was more significant than the number of transplants performed, evidence that differs from other studies.

Therefore, conducting the study generated a body of evidence on the epidemiological profile and identified complications of candidates for liver transplantation on the waiting list, which offers subsidies for decision-making by the multidisciplinary team for the planning and implementation of effective interventions directed toward the success of the surgery.

CONFLICT OF INTEREST

Nothing to declare.

AUTHOR'S CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Siqueira LR, Siqueira LR, Mendes KDS, Galvão CM; **Conception and design:** Siqueira LR, Siqueira LR, Mendes KDS, Galvão CM; **Data analysis and interpretation**: Siqueira LR, Siqueira LR, Mendes KDS, Galvão CM; **Writing:** Siqueira LR, Siqueira LR, Mendes KDS, Galvão CM; **Critical review:** Siqueira LR, Siqueira LR, Mendes KDS, Galvão CM; **Final approval:** Siqueira LR, Siqueira LR, Mendes KDS, Galvão CM.

DATA AVAILABILITY STATEMENT

All dataset were generated or analyzed in the current study.

FUNDING

ACKNOWLEDGEMENT

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