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Original Research

Sedation Practices of Mechanically Ventilated Patients During Critical Care Transport

Matthew A. Roginski, MD, MPH [1,2,*], Matthew C. Carroll, MD [1], Micah L. Trautwein, BS [2], Evan D. Watkins, BS, NRP [2], Alyson M. Esteves, PharmD, BCPS, BCCP [1]

[1] Dartmouth-Hitchcock Medical Center, Lebanon, NH
[2] Dartmouth Geisel School of Medicine, Hanover, NH

A B S T R A C T

Objective: Mechanically ventilated patients who receive deep levels of sedation have high mortality rates, longer lengths of stay, and longer duration of mechanical ventilation in the intensive care unit. Prior literature demonstrated a high frequency of deep sedation across all levels of care. Benzodiazepines have been attributed to similar morbidity and mortality findings.

Methods: This study was a descriptive retrospective review of mechanically ventilated adult critical care transport patients from January 1, 2019, to March 11, 2020. Our primary outcome was the percentage of patients who were deeply sedated at handoff to the receiving facility. Deep sedation was defined as a Richmond Agitation Sedation Scale of −3 to −5. Our secondary outcomes were the percentage of patients who received benzodiazepines; the number of unplanned extubations, crew injuries, and unsafe patient care situations; and the incidence of ventilator dyssynchrony.

Results: Five hundred fifty-three mechanically ventilated patients were transported. Ninety-three patients were excluded because they received paralytics during transport. Four hundred sixty patients were included in the analysis, 422 (91.7%) of whom were deeply sedated. Benzodiazepines were administered to 141 patients (30.6%). There were no differences observed in the secondary outcomes.

Conclusion: Deep sedation and benzodiazepine administration were frequent during critical care transport of mechanically ventilated patients.

Prior literature has estimated that unintentional oversedation occurs in 40% to 60% of intensive care unit (ICU) patients.[1] Current critical care guidelines for the sedation of mechanically ventilated patients advise targeting light levels of sedation. Although there is no universally accepted definition of light sedation, most of the published literature has defined it as a Richmond Agitation Sedation Scale (RASS) of −2 to 1.[2] Recent literature continues to highlight the relationship between deep levels of sedation and increases in mortality, ICU length of stay, and duration of mechanical ventilation.[3-6] Compared with other continuous sedative medications, benzodiazepines are more frequently associated with deep levels of sedation, increased rates of delirium, and increased ICU and hospital length of stay.[2] Current guidelines recommend alternative sedatives including propofol or dexmedetomidine over benzodiazepines because of these risks.[2] Furthermore, analagosedation or analgesia-first sedation has been correlated with reductions in deep levels of sedation, shorter durations of mechanical ventilation, and decreased exposure to sedative agents, making this strategy a favorable sedation approach in critically ill patients.[7,8]

Similarly, emergency department (ED) literature has demonstrated a high frequency of deep sedation in critically ill patients. Deep sedation in this setting has also demonstrated impacts on long-term outcomes including mortality, cognitive deficits, and ICU and hospital length of stay.[7,9] This literature has also highlighted therapeutic inertia, which influences ICU sedative medication selection and continuation of deep levels of sedation beyond initial ED management.[7,9] Recently, transport literature has similarly demonstrated a high frequency of deep levels of sedation, with most occurrences related to benzodiazepine use and/or paralytic use during transport.[10,11] One single-center study showed that deep levels of

*Address for correspondence: Matthew A. Roginski, MD, MPH, Department of Emergency Medicine, One Medical Center Drive, Lebanon, NH 03756.
E-mail address: Matthew.A.Roginski@hitchcock.org (M.A. Roginski).

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sedation during transport lead to increases in hospital length of stay.[11] Minimal data in critical care transport literature exist at this time related to sedation trends, best practices, or therapeutic inertia to the ICU setting. The objectives of this study were to assess the frequency of deep sedation in intubated and mechanically ventilated adult critical care transport patients; evaluate benzodiazepine use; and determine the frequency of unintentional extubations, crew or patient injuries, and unsafe situations.

Methods

Study Design

This was a descriptive retrospective cohort of mechanically ventilated patients ≥ 18 years of age from January 1, 2019, to March 11, 2020, who received invasive positive-pressure ventilation through an endotracheal tube or supraglottic airway. Patients who received paralytics during transport were excluded from the analysis. Transport was performed using a helicopter or ground service based at an academic medical center and a second helicopter based at an airport approximately 80 miles away. The critical care transport team consisted of a nurse and paramedic crew. This study was approved by the organization's institutional review board. Our primary outcome was the percentage of patients who were deeply sedated (defined as RASS of −3 to −5) at handoff to the receiving facility. Our secondary outcomes were the percentage of patients who received benzodiazepines; the number of unplanned extubations, crew injuries, and unsafe patient care situations; and the incidence of ventilator dyssynchrony. There was not a strict definition of ventilator dyssynchrony used in this descriptive cohort. Patients were categorized as having medications administered for ventilator dyssynchrony if supported by the transport narrative. A subgroup analysis was performed on patients who were intubated for a neurologic injury or cardiac arrest.

Data Collected

Data abstraction was performed by chart review of team transport forms. Contact time was defined as the elapsed time between crew arrival at the patient's bedside to the documented handoff time at the receiving hospital unit. Level of consciousness was assessed using the Glasgow Coma Scale, and sedation levels were measured with the RASS. Deep sedation was defined as an RASS of −3 to −5, and light sedation was defined as an RASS of 1 to −2.

Indications for mechanical ventilation were classified into the categories of trauma, cardiac arrest, chronic obstructive pulmonary disease, asthma, congestive heart failure/pulmonary edema, neurologic, sepsis, and other. Traumatic brain injury was classified as a traumatic rather than neurologic indication for mechanical ventilation. Medications were recorded if they were given by the transport crew. Medications given before arrival were not captured. For medication infusions, the last documented infusion rate was recorded and extrapolated for the total contact time. For patients without a documented weight, the mean cohort weight was used for weight-based infusions.

Transport narratives were reviewed by an investigator to determine the occurrence of adverse events during the course of care provided by the transport team. Unplanned extubation and patient or crewmember injury are mandatory documentation fields and recorded on every transport of mechanically ventilated patients. The use of analgesia or sedation boluses for unsafe situations and ventilator dyssynchrony were interpreted by an investigator after reading the transport narratives. Study data were collected and managed using REDCap (Research Electronic Data Capture; Vanderbilt University, Nashville, TN).

Statistical Analysis

Statistical analysis was performed using STATA IC/16 (StataCorp, College Station, TX). The groups were compared using summary statistics. Continuous variables were presented as mean values with standard deviations or medians with interquartile ranges as appropriate. Categoric variables were presented as counts with percentages. Analysis was conducted using the Student *t*-test, Wilcoxon rank sum test, and Pearson chi-square test or Fisher exact test for categoric variables as appropriate. One-way analysis of variance was used to compare the total amounts of medications received among patients who were intubated for neurologic, cardiac, and all other reasons. For analysis of variance results that were found to be significant, the Tukey post hoc test was performed. $P < .05$ was considered statistically significant.

Results

Five hundred fifty-three patients were intubated and mechanically ventilated during transport. Ninety-three patients were excluded from the analysis because they received paralytics during the transport. A description of patients who received paralytics is provided in Supplemental Appendix 1. A total of 460 patients were included in the analysis (Fig. 1). Three hundred fifty-six patients (77.4%) were transported by rotor wing. Four hundred forty-one patients (95.9%) were interfacility transports. One patient had a supraglottic airway, and all others were endotracheally intubated. The mean contact time was 88.4 ± 78.8 minutes. Table 1 displays a description of indications for intubation. Four hundred twenty-two (91.7%) patients were deeply sedated. Of the deeply sedated patients, the initial RASS was −3.9 ± 1.7, and the final RASS was −4.5 ± 0.7. Of the lightly sedated, the initial RASS was −1.2 ± 2, and the final RASS was −0.7 ± 1.2. Figure 2 displays a histogram of the initial and final RASS scores.

Patients frequently received boluses of opiates and sedatives. Fentanyl boluses were the most frequently administered (86.9%). Of the continuous infusions administered, propofol was the most frequent (66.1%). The total quantity of bolus and infusion doses was not statistically significantly different between the deep and light sedation groups (Table 2). The mean fentanyl bolus dose administered during transport was 210.7 ± 119.5 μg, and the median fentanyl infusion rate was 200 μg/h (interquartile range = 200-300 μg/h). The mean midazolam bolus dose was 4.1 ± 2.7 mg, and the median midazolam infusion rate was 4.5 mg/h (IQR 3-6.5 mg/h). Ketamine and lorazepam were infrequently administered. The mean propofol bolus dose administered was 41.3 ± 27.8 mg, and the mean infusion rate was 39.1 ± 21.3 μg/kg/min.

A total of 141 (30.6%) of the included patients received benzodiazepines during transport (boluses or infusions). This was most frequently in the form of midazolam boluses (29.8%). Compared with all other indications for intubation, patients intubated for neurologic injury and cardiac arrest received less fentanyl and the same amount of midazolam. Post−cardiac arrest patients received a higher quantity

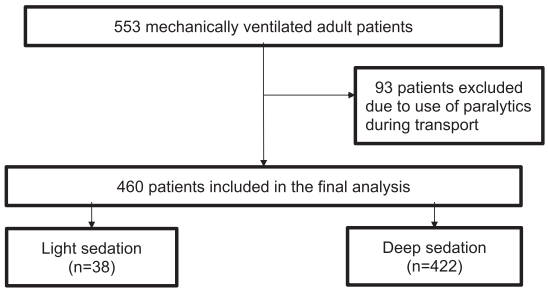

Figure 1. Study Participants.

Table 1
Baseline Characteristics

Characteristic	All (N = 460)	Deep Sedation (n = 422)	Light Sedation (n = 38)	*P* Value
Age (y), mean ± SD	57.8 ± 17.8	57.6 ± 17.7	59.4 ± 19.4	.55
Male sex, n (%)	265 (57.7)	245 (58.1)	20 (54.1)	.73
Method				
Rotor wing, n (%)	356 (77.4)	333 (78.9)	23 (60.5)	.01
Ground, n (%)	104 (22.6)	89 (21.1)	15 (39.5)	
Transportation type				
Interfacility transfer, n (%)	441 (95.9)	405 (96.0)	36 (94.7)	.71
Scene call, n (%)	19 (4.1)	17 (4.0)	2 (5.3)	
Contact time (min), mean ± SD	88.4 ± 78.8	88 ± 80.1	92.6 ± 63	.73
Reason for intubation				
Asthma, n (%)	5 (1.1)	5 (1.2)	0	.006
COPD, no. (%)	28 (6.1)	23 (5.5)	5 (13.2)	
Pulmonary edema/CHF, n (%)	24 (5.2)	20 (4.7)	4 (10.5)	
Neurologic injury, n (%)	136 (29.6)	129 (30.6)	7 (18.4)	
Other, n (%)	79 (17.2)	67 (15.9)	12 (31.6)	
Sepsis, n (%)	55 (12)	55 (13)	0	
Trauma, n (%)	76 (16.5)	70 (16.6)	6 (15.8)	
Cardiac arrest, n (%)	57 (12.4)	53 (12.6)	4 (10.5)	
Tidal volume (mL), mean ± SD	464.1 ± 66.5	465.2 ± 66.0	450.9 ± 71.7	.22
PEEP (cm H_2O), mean ± SD	6.3 ± 2.8	6.3 ± 2.8	5.9 ± 2.6	.41
Total IV fluids (mL), mean ± SD	249.8 ± 371.5	253.3 ± 383.2	211.9 ± 199.4	.53
Vasopressors used, n (%)	181 (40)	170 (40.8)	11 (31.4)	.37
Blood administered, n (%)	33 (7.2)	29 (8.9)	4 (10.5)	.34
Final SBP (mm Hg), mean ± SD	116.8 ± 20.9	117.0 ± 20.8	114.0 ± 22.2	.4
Final DBP (mm Hg), mean ± SD	70.7 ± 13.4	71.0 ±13.6	67.6 ± 11	.14
Initial RASS, mean ± SD	−3.6 ± 1.9	−3.9 ± 1.7	−1.2 ± 2	<.001
Final RASS, mean ± SD	−4.1 ± 1.3	−4.5 ± 0.7	−0.7 ± 1.2	<.001

CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; DBP = diastolic blood pressure; PEEP = positive end-expiratory pressure; RASS = Richmond Agitation Sedation Scale; SBP = systolic blood pressure; SD = standard deviation.

Table 2
Quantities of Medications Administered During Critical Care Transport

Medication Information	All (N = 460)	Deep Sedation (n = 422)	Light Sedation (n = 38)	*P* Value
Bolus dosing				
Fentanyl, n (%)	399 (86.9)	365 (86.7)	34 (89.5)	.8
Bolus total (μg), mean ± SD	210.7 ± 119.5	207.7 ± 118.2	243.4 ± 130.2	.1
Number of boluses, mean ± SD	3.4 ± 1.6	3.4 ± 1.6	3.7± 1.6	.34
Midazolam, n (%)	136 (29.8)	121 (28.9)	15 (39.5)	.2
Bolus total (mg), mean ± SD	4.1 ± 2.7	4.1 ± 2.5	4.7± 3.4	.38
Number of boluses, mean ± SD	3.1 ± 1.6	3.0 ± 1.5	3.6 ± 2.2	.15
Lorazepam, n (%)	3 (0.7)	2 (0.5)	1 (2.8)	.22
Bolus total (mg), median (IQR)	2 (2-4)	3 (2-4)	2 (0)	.5
Number of boluses, median (IQR)	2 (1-2)	1.5 (1-2)	2 (0)	.5
Propofol, n (%)	16 (3.5)	14 (3.4)	2 (5.3)	.64
Bolus total (mg), mean ± SD	41.3 ± 27.8	39.3 ± 25.9	55 ± 49.5	.47
Number of boluses, mean ± SD	1.7 ± 1	1.7 ± 1.1	1.5 ± 0.7	.79
Ketamine, n (%)	11 (2.4)	9 (2.2)	2 (5.3)	.64
Bolus total (mg), mean ± SD	148.2 ± 131.1	136.7 ± 134.7	200 ± 141.4	.56
Number of boluses, mean ± SD	2.5 ± 1.3	2.4 ± 1.4	2.5 ± 0.7	.96
Continuous infusions				
Fentanyl, n (%)	3 (0.65)	1 (0.24)	2 (5.26)	.02
Fentanyl infusion (μg/h), median (IQR)	200 (200-300)	200	250 (200-300)	1.00
Propofol, n (%)	304 (66.1)	281 (66.59)	23 (60.53)	.48
Propofol infusion (μg/kg/min), mean ± SD	39.1 ± 21.3	38.6 ± 21.2	44.6 ± 22	.2
Midazolam, n (%)	4 (0.87)	3 (0.71)	1 (2.63)	.29
Midazolam infusion (mg/h), median (IQR)	4.5 (3-6.5)	5 (2-8)	4	1.00
Ketamine, n (%)	7 (1.52)	5 (1.18)	2 (5.26)	.11
Ketamine infusions (mg/kg/h), median (IQR)	1.2 (0.6-10)	1.2 (0.9-10)	0.9 (0.6-1.2)	.43

IQR = interquartile range; SD = standard deviation.
All infusion rates represent the infusion rate at the end of transport.

of propofol compared with all other patients including neurologic injury (Table 3).

As seen in Table 4, no patients were unintentionally extubated in either group, and no crewmembers were injured. Three patients had an unsafe patient care situation for which additional sedation was given. Ten patients had ventilator dyssynchrony reported. These safety outcomes did not statistically differ despite deep or light sedation.

Table 3
Quantities of Medications Administered to Neurologic Injury and Cardiac Arrest Patients

	All (N = 460)	Neurologic (n = 136)	Cardiac Arrest (n = 57)	All Others (n = 267)	*P* Value
Fentanyl administration					
Total (μg), mean ± SD	213.5 ± 129.7	184.6 ± 90.2	192.4 ± 110.4	232.6 ± 146.5	.002
Total in deep sedation (μg), mean ± SD	207.7 ± 118.1	181.4 ± 88.2	198.1 ± 111.1	224.5 ± 131	.005
Total in light sedation (μg), mean ± SD	276.2 ± 211.8	260 ± 114	116.7 ± 46.4	297.7 ± 230.5	.38
Midazolam administration					
Total (mg), mean ± SD	4.3 ± 3	3.8 ± 3.5	4.2 ± 2.2	4.6 ± 3	.47
Total in deep sedation (mg), mean ± SD	4.2 ± 2.8	3.6 ± 3.3	4.2 ± 2.3	4.4 ± 2.7	.43
Total in light sedation (mg), mean ± SD	5.6 ± 4.3	6 ± 6.1	4	5.6 ± 4.3	.93
Lorazepam administration					
Total (mg), mean ± SD	2.7 ± 1.2	—	—	2.7 ± 1.2	—
Total in deep sedation (mg), mean ± SD	2	—	—	2	—
Total in light sedation (mg), mean ± SD	3 ± 1.4	—	—	3 ± 1.4	—
Propofol administration					
Total (mg), mean ± SD	289 ± 252.3	240.4 ± 185.4	391.1 ± 460.3	308.3 ± 253.7	.02
Total in deep sedation (mg), mean ± SD	286.1 ± 252	235.5 ± 182.4	411.2 ± 465.1	305.3 ± 252.9	.008
Total in light sedation (mg), mean ± SD	324.5 ± 258.2	343.3 ± 239.1	30.3	336.3 ± 267.8	.53
Ketamine administration					
Total (mg), median (IQR)	162 (72.8-331.2)	—	1,265.8	123.6 (65.5-300)	—
Total in deep sedation (mg), median (IQR)	199.3 (80-300)	—	1,265.8	162 (70-290)	—
Total in light sedation (mg), median (IQR)	100 (65.5-362.3)	—	—	100 (65.5-362.3)	—

IQR = interquartile range; SD = standard deviation.
Totals represent total medication quantity received during transport (bolus + infusion quantities).

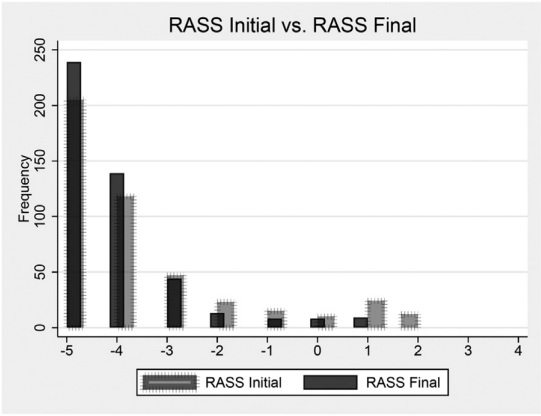

Figure 2. A histogram of the initial and final RASS scores.

Discussion

Deep sedation was observed in 91.7% of our cohort. Benzodiazepines were used in 30.6% of patient transports and likely contributed to the deep levels of sedation observed. Patients who were deeply sedated upon crew arrival had a deepening of their sedation during transport. This trend was not observed in the patients who were lightly sedated upon crew arrival. Regardless of initial level of sedation, patients received the same quantity of sedation throughout their transport. In prior literature, definitions of deep sedation and study methodology differed, however our study demonstrated high frequency of deep sedation during transport which is consistent with prior results in transport and in the ED.[9-11]

In our cohort, post–cardiac arrest patients and those who were neurologically injured were deeply sedated. Although this may represent underlying brain dysfunction and an indication for intubation, these patients received a similar quantity of sedation compared with all others. Specifically in post–cardiac arrest patients, early drug exposure, deep levels of sedation, and benzodiazepine use can interfere with neurologic examination and prognostication in the ICU. Current guidelines recommend limiting long-acting sedatives and benzodiazepine use.[12-14] Neurologically injured patients represent a heterogeneous group of pathologies, some of which include benzodiazepines as the standard of care (ie, seizures). Despite this, the Emergency Neurological Life Support guidelines recommend optimization of light sedation (RASS of 0 to −2) by using the lowest effective sedative dose possible, with the preference being propofol.[15,16] Deviations from light sedation should be intentional and representative of individual patient needs.

Despite the evolving literature on the negative impacts of deep levels of sedation and benzodiazepine exposure, there continues to be a high prevalence of these trends in clinical practice across critical care transport, ED, and ICU. The reasons for this are multifactorial. Although our study was not designed to answer this question, we hypothesize that this is a frequent observation in critical care transport because of environment complexity, task burden, therapeutic inertia, and the present bias when weighing short- and long-term risks of sedation. In our cohort, there was a mean patient contact time of 88 minutes, which encompasses many operational, patient, and safety tasks that need to be completed. Albeit a short time, critical care transport may offer an early opportunity to align with

Table 4
Secondary Outcomes

Outcome	All (N = 460)	Deep Sedation (n = 422)	Light Sedation (n = 38)	*P* Value
Unplanned extubation, n (%)	0	0	0	1.00
Crew injury, n (%)	0	0	0	1.00
Unsafe patient care situation, n (%)	3 (0.7)	2 (0.5)	1 (2.6)	.23
Ventilator dyssynchrony, n (%)	10 (2.2)	8 (1.9)	2 (5.3)	.2

guideline-directed therapy and be viewed as a part of the continuum of critical care regardless of patient location.

It is unclear if a change in sedation depth during a short period of transport would have an impact on long-term outcomes given patient comorbidities and system factors. These trends of deep sedation are likely a result of choices in the dynamic early phase of a critically ill patient's care. The short- and long-term risks of deep sedation should be weighed against potential benefits of light levels of sedation. The risks and benefits will likely change based on the environment, with more risks being inherently present in the transport realm. Risk considerations should include self-extubation, managing anxiety in a chaotic environment, crew safety, awareness with paralysis, morbidity, delirium, and mortality.[7,9,17] The goal of providing the right level of sedation to the right patient at the right time can be very challenging. Furthering the understanding surrounding sedation practices during critical care transport including the level of sedation, medication selection, and quantities provided as well as further influential factors based on patient populations served can begin to allow us to further optimize care in the transport environment, thus impacting short- and long-term outcomes. Based on the therapeutic inertia seen in the ED literature, it is likely that improvements in the transport realm will further improve the care of critically ill patients.[17] Future directions of study should include the minimization of benzodiazepine exposure, optimization of the time in light sedation, incorporation of sedation assessments during handoff, and establishment of best practices surrounding deep sedation in transport.

Limitations

This study was a single-center descriptive retrospective chart review that may have an impact on generalizability. Additionally, our cohort represents a large percentage (95.9%) of interfacility transports. We did not specifically capture details surrounding referring facility size, availability of critical care services, or time spent at the referring facility. These factors may have impacted the initial sedation depth and treatment decisions. Medication doses displayed were extrapolated from the final infusion rates upon arrival to the destination; therefore, these rates may not be representative of titration adjustments based on patient condition. Similarly, for patients without a documented weight, the mean cohort weight of 83 kg was used to calculate the total drug exposure. Short- and long-term outcomes were not captured in this study; therefore, it is unknown how sedation practices during transport impacted morbidity and mortality.

RASS scoring, as displayed in Supplemental Appendix 1, highlights a number of uncertainties. The mean initial RASS score in paralyzed patients was −2.6, and the mean final RASS score was −4.5. It is notable that this was a lighter level of sedation observed in our nonparalyzed cohort. It is unclear whether these RASS scores are representative of sedation levels surrounding paralysis. This scoring highlights concerns of patient assessments in relation to RASS score definitions, interrater reliability of RASS scoring, and appropriate sedation depth before and during paralytic administration (target RASS of −5).[18]

Conclusion

Deep sedation was observed in 91.7% of mechanically ventilated patients during critical care transport. Benzodiazepines were administered to 30.6% of the patients during transport. Despite sedation depth, there was no difference in the quantity of medications administered. These findings highlight an opportunity for a practice change directed at decreasing the frequency of deep sedation and benzodiazepine administration.

CRediT Author Statement

Matthew A. Roginski: Conceptualization, methodology, formal analysis, data curation, writing – review & editing, visualization, supervision, project administration. **Matthew C. Carroll:** Methodology, formal analysis, data curation, writing – original draft. **Micah L. Trautwein:** Methodology, formal analysis, data curation, writing – original draft. **Evan D. Watkins:** Methodology, formal analysis, data curation, writing – original draft. **Alyson M. Esteves:** Conceptualization, methodology, formal analysis, data curation, writing – review & editing, visualization, supervision, project administration.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amj.2023.05.002.

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