



Association Between Anemia Severity and Mechanical Ventilation Duration in Patients Admitted to the Intensive Observation Room at Dr. Soetomo General Hospital, Surabaya: A Retrospective Cohort Study

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DOI : 110.55497/majanestrcicar.v4i3.529

ABSTRACT

Introduction: Anemia may impair tissue oxygen delivery in critically ill patients, but its association with weaning and extubation outcomes remains unclear. This study examined the association between anemia severity and mechanical ventilation duration at Dr. Soetomo General Hospital, Surabaya.

Methods: This retrospective cohort study included 107 mechanically ventilated patients admitted from January to June 2022. Anemia severity was classified by hemoglobin levels on ICU admission day 1. Ventilation duration, from initiation to extubation or death, was categorized as <1, 1–3, 4–7, or >7 days. Analyses used Spearman's rank correlation and the Fisher–Freeman–Halton exact test with Monte Carlo estimation, including trauma-based subgroups. Exploratory survivor analyses included pairwise Mann–Whitney U tests with Holm adjustment.

Results: No significant correlation was found in the overall cohort ($p = 0.121$, $p = 0.213$; 95% BCa CI: -0.093 to 0.309), trauma subgroup ($p = 0.018$, $p = 0.883$; 95% BCa CI: -0.237 to 0.275), or non-trauma subgroup ($p = 0.304$, $p = 0.053$; 95% BCa CI: -0.007 to 0.550). Among 67 survivors, a significant positive correlation emerged ($p = 0.368$, $p = 0.002$; 95% BCa CI: 0.129 to 0.559). Ventilation duration differed significantly between mild and severe anemia (Holm-adjusted $p = 0.009$) and moderate and severe anemia ($p = 0.012$), but not mild and moderate anemia ($p = 0.104$).

Conclusion: No significant correlation was found in the overall cohort or trauma-based subgroups. The positive correlation among survivors should be interpreted cautiously due to potential selection bias. Further studies accounting for confounders are warranted.

Keywords: anemia, critical illness, hemoglobin, intensive care units, ventilator weaning



Hubungan antara Derajat Keparahan Anemia dan Durasi Ventilasi Mekanik pada Pasien yang Dirawat di Ruang Observasi Intensif RSUD Dr. Soetomo, Surabaya: Studi Kohort Retrospektif

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DOI : 110.55497/majanestcricar.v44i3.529

ABSTRAK

Pendahuluan: Anemia dapat mengganggu pengiriman oksigen ke jaringan pada pasien sakit kritis, tetapi hubungannya dengan penyapihan ventilasi mekanis dan ekstubasi belum jelas. Penelitian ini menganalisis hubungan derajat anemia dengan durasi ventilasi mekanis di RSUD Dr. Soetomo, Surabaya.

Metode: Penelitian kohort retrospektif ini melibatkan 107 pasien yang menerima ventilasi mekanis pada Januari–Juni 2022. Derajat anemia ditentukan berdasarkan kadar hemoglobin pada hari pertama masuk ICU. Durasi ventilasi mekanis hingga ekstubasi atau kematian dikategorikan menjadi <1, 1–3, 4–7, atau >7 hari. Analisis menggunakan korelasi Spearman dan uji eksak Fisher–Freeman–Halton dengan estimasi Monte Carlo, termasuk analisis berdasarkan status trauma. Analisis eksploratif pada pasien yang bertahan hidup menggunakan uji Mann–Whitney U dengan penyesuaian Holm.

Hasil: Tidak ditemukan korelasi bermakna pada keseluruhan kohort ($p = 0,121$; $p = 0,213$; IK 95% BCa: $-0,093$ hingga $0,309$), subkelompok trauma ($p = 0,018$; $p = 0,883$; IK 95% BCa: $-0,237$ hingga $0,275$), maupun nontrauma ($p = 0,304$; $p = 0,053$; IK 95% BCa: $-0,007$ hingga $0,550$). Pada 67 pasien yang bertahan hidup, ditemukan korelasi positif bermakna ($p = 0,368$; $p = 0,002$; IK 95% BCa: $0,129$ hingga $0,559$). Perbedaan durasi bermakna ditemukan antara anemia ringan dan berat (p terkoreksi Holm = $0,009$) serta anemia sedang dan berat ($p = 0,012$), tetapi tidak antara anemia ringan dan sedang ($p = 0,104$).

Simpulan: Tidak ditemukan korelasi bermakna pada keseluruhan kohort maupun subkelompok trauma. Korelasi positif pada pasien yang bertahan hidup perlu ditafsirkan hati-hati karena potensi bias seleksi. Penelitian lebih lanjut dengan mempertimbangkan faktor perancu diperlukan.

Kata kunci: anemia, hemoglobin, pasien kritis, penyapihan ventilator, unit perawatan intensif

INTRODUCTION

Anemia is a prevalent condition in critically ill patients in the intensive care unit (ICU).¹ Around 60% of ICU patients experience anemia.^{2,3} Severe anemia can reduce arterial oxygen content and compromise tissue oxygen delivery, potentially contributing to tissue hypoxia and organ dysfunction, particularly when compensatory mechanisms are insufficient to meet metabolic demands.⁴ Mechanical ventilation is one method for sustaining organ function in ICU patients.⁵ An epidemiological study in Southern Ethiopia found that approximately 70% of ICU patients required mechanical ventilation during treatment.⁶ Although mechanical ventilation may preserve lives, there is a considerable chance of complications, which can typically lead to an increase in morbidity and mortality.⁷ A recent systematic review highlighted ongoing debate regarding the association between hemoglobin levels and weaning or extubation outcomes.¹ Furthermore, to our knowledge, no studies investigating the relationship between hemoglobin levels and mechanical ventilation weaning have been conducted in Indonesia. Therefore, further research is warranted to determine whether anemia severity is associated with the duration of mechanical ventilation in the Indonesian clinical setting. This study aimed to investigate the association between anemia severity and mechanical ventilation duration among patients treated in the Intensive Observation Room at Dr. Soetomo General Hospital, Surabaya. The findings may contribute to the local evidence base and provide a foundation for future research.

METHODS

Ethical clearance for this research was granted by the Health Research Ethics Committee of Dr. Soetomo General Hospital, Surabaya, under approval ID 1449/LOE/301.4.2/IX/2023 (date 14 September 2023). The committee waived the requirement for informed consent because the study involved a retrospective review of medical records. Patient confidentiality was maintained by removing direct personal identifiers from the analytical dataset and restricting access to study data to authorized research personnel. The data were used exclusively for research purposes.

This retrospective cohort study used secondary data derived from patient medical records archived at the Dr. Soetomo General Hospital Medical Records Center. The study population consisted of patients who received mechanical ventilation in the Intensive Observation Room from January to June 2022. Total sampling was employed, including all patients who met the specified inclusion and exclusion criteria during the study period. No a priori sample-size calculation was performed because all eligible patients identified in the medical records during the study period were included. Eligible patients were aged 19 years or older and had complete medical records. Patients were excluded if they were not anemic on the first day of ICU admission, were pregnant, or had underlying respiratory diseases, as these conditions may affect respiratory function and complicate liberation from mechanical ventilation.⁸ Patients with malignancies, chronic kidney disease, inherited red blood cell disorders (sickle cell disease or thalassemia), or autoimmune diseases were also excluded. Of the 323 patients initially screened, 42 were excluded because they did not have anemia on the first day of ICU admission, and 40 were excluded because they were younger than 19 years. An additional 22 patients were excluded because of incomplete medical records, 19 because of pregnancy, 23 because of respiratory disorders, 18 because of malignancies, 31 because of chronic kidney disease, and 21 because of autoimmune diseases. No patients were excluded because of inherited red blood cell disorders. Each excluded patient was assigned a single primary reason for exclusion to avoid double-counting. The final study population comprised 107 patients who met the eligibility criteria. Subgroup analyses included 66 patients with trauma and 41 without trauma. Exploratory analyses restricted to survivors included 67 patients. The primary exposure variable was anemia severity, classified based on hemoglobin concentration according to the World Health Organization (WHO) criteria: mild (11.0–12.9 g/dL for males, 11.0–11.9 g/dL for females), moderate (8.0–10.9 g/dL), and severe (<8.0 g/dL).⁹ Hemoglobin concentration was determined using the first measurement recorded on the first day of ICU admission.

When multiple hemoglobin measurements were available on that day, only the first recorded result was used. Measurements were included regardless of whether blood transfusion or surgery had occurred before the hemoglobin assessment. The primary outcome was the duration of mechanical ventilation, defined as the total number of hours of ventilator support in the Intensive Observation Room. For patients who were not reintubated, the duration was calculated from the initiation of mechanical ventilation to extubation or death, whichever occurred first. For patients who underwent reintubation, the durations of all mechanical ventilation episodes were summed to determine the total duration. The calculated duration was subsequently categorized into four groups: <1 day, 1–3 days, 4–7 days, and >7 days. Additional variables included sex, age, body mass index (BMI), case type on admission, and extubation condition, which were analyzed as descriptive characteristics of the study population. Sex was classified as male or female, and age was categorized according to the Indonesian Ministry of Health criteria: adult (19–59 years) and older adult (≥ 60 years); only patients aged 19 years and above were included.¹⁰ BMI was categorized according to Centers for Disease Control and Prevention (CDC) standards as underweight (<18.5 kg/m²), normal (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), and obese (≥ 30.0 kg/m²).¹¹ Case type on admission was classified as trauma or non-trauma, with trauma defined as injuries caused by sudden physical forces (e.g., motor vehicle accidents, burns, drowning) and non-trauma as acute non-traumatic conditions, such as central nervous system, cardiovascular, or respiratory failure, and hypoglycemia.¹² The extubation condition was categorized as extubated, unplanned extubation, or deceased before extubation. All study variables were extracted from the medical records according to predefined operational definitions. The collected data were analyzed using SPSS Statistics (version 27.0.1.0; IBM Corp.). The association between anemia severity and categorized mechanical ventilation duration was assessed using the Fisher–Freeman–Halton exact test with Monte Carlo estimation because the expected cell frequencies violated the assumptions of the

chi-square test. Spearman's rank correlation was used to assess the direction and strength of the monotonic association between the two ordinal variables. Anemia severity was coded as mild (1), moderate (2), and severe (3), while mechanical ventilation duration was coded as <1 day (1), 1–3 days (2), 4–7 days (3), and >7 days (4). Exploratory subgroup analyses were performed according to trauma status (trauma and non-trauma) to examine whether the association between anemia severity and mechanical ventilation duration differed between these groups, given the potential differences in the underlying pathophysiology of anemia. The same statistical methods used in the overall analysis were applied to each subgroup. Additional exploratory analyses were performed among the 67 survivors to assess the association between anemia severity and categorized mechanical ventilation duration. Spearman's rank correlation and the Fisher–Freeman–Halton exact test were used for this analysis. Pairwise comparisons were also conducted to identify differences in the distribution of mechanical ventilation duration categories between anemia severity groups using the Mann–Whitney U test. The comparisons were performed between patients with mild and severe anemia, moderate and severe anemia, and mild and moderate anemia. The U statistic, standardized Z statistic, and Holm-adjusted p-value were reported for each comparison. Holm's procedure was used to control the family-wise error rate across the three comparisons. Patients with incomplete medical records were excluded before the analysis.

RESULTS

The distribution of characteristics of ventilated patients with anemia is presented in Table 1. Of the 107 patients, 68.2% belonged to the adult age group (19–59 years), and the majority had a normal BMI (18.5–24.9 kg/m²), accounting for 48 patients (44.8%). The male-to-female ratio was 1.6:1. Trauma-related cases upon admission were identified in 66 patients (61.7%). The most common severity of anemia was moderate anemia (8.0–10.9 g/dL), observed in 67.3% of the patients. A total of 70 patients (65.4%) had a history of blood transfusion during

hospitalization, and nearly all patients (93.5%) of patients did not experience reintubation, underwent surgical procedures. A total of 82.2% while 17.8% required reintubation.

Table 1. Distribution of patient characteristics

Variables	n	%
Age group (years)		
Adult (19-59)	73	68.2
Older adult (≥60)	34	31.8
Sex		
Male	66	61.7
Female	41	38.3
BMI		
Under-weight	5	4.7
Normal	48	44.8
Over-weight	43	40.2
Obese	9	8.4
No data	2	1.9
Case type upon admission		
Trauma	66	61.7
Non-trauma	41	38.3
Anemia severity		
Mild	23	21.5
Moderate	72	67.3
Severe	12	11.2
History of blood transfusion		
Yes	70	65.4
No	37	34.6
History of surgery		
Yes	100	93.5
No	7	6.5
History of reintubation		
No reintubation	88	82.2
Reintubation	19	17.8

BMI: Body Mass Index

The majority of patients (57.0%) were extubated, as shown in Table 2. Among patients who were not reintubated, extubation was the most common outcome (63.6%). In contrast, among patients who required reintubation, the majority (63.2%) were deceased.

Table 2. Distribution of extubation conditions

Extubation Conditions	No Reintubation		Reintubation	
	n	%	n	%
Extubated	56	63.6	5	26.3
Unplanned extubation	4	4.6	2	10.5
Deceased	28	31.8	12	63.2

Among all patients, ventilation for less than one day was the most common duration, occurring in 37 patients (Table 3). Among patients with mild anemia, the largest proportion (47.8%) required mechanical ventilation for less than one day. Among patients with moderate anemia, the largest proportion (37.5%) required ventilation for 1–3 days. In contrast, among patients with severe anemia, the largest proportion (41.7%) required ventilation for 4–7 days. However, the Fisher–Freeman–Halton exact test with Monte

Carlo estimation did not show a statistically significant association between anemia severity and categorized mechanical ventilation duration in the overall cohort ($p = 0.385$). Similarly, Spearman's rank correlation analysis showed no statistically significant association between anemia severity and mechanical ventilation duration in the overall study population (Spearman's $\rho = 0.121$, $p = 0.213$; 95% BCa CI: $-0.093 - 0.309$).

Table 3. Association between anemia severity and mechanical ventilation duration in all patients

Anemia Severity		Duration of Ventilator Use (days)				Total
		<1 (n=37)	1-3 (n=34)	4-7 (n=26)	>7 (n=10)	
Mild	n	11	5	6	1	23
	%	47.8	21.7	26.1	4.3	100.0
Moderate	n	22	27	15	8	72
	%	30.6	37.5	20.8	11.1	100.0
Severe	n	4	2	5	1	12
	%	33.3	16.7	41.7	8.3	100.00
Test		Statistic		p-value	95% BCa CI for Spearman's ρ	
Fisher–Freeman–Halton exact test (Monte Carlo)		6.205		0.385	-	
Spearman's rank correlation		$\rho=0.121$		0.213	$-0.093 - 0.309$	

In the trauma subgroup ($n = 66$), no statistically significant correlation was observed between anemia severity and categorized mechanical ventilation duration (Spearman's $\rho = 0.018$, $p = 0.883$, 95% BCa CI: $-0.237 - 0.275$; Table 4). In the non-trauma subgroup ($n = 41$), a positive correlation was observed between anemia severity and categorized mechanical ventilation duration, although the association did not reach statistical significance (Spearman's $\rho = 0.304$, $p = 0.053$, 95% BCa CI: $-0.007 - 0.550$; Table 5). Death before extubation terminates mechanical ventilation and represents a competing event when extubation is the outcome of interest. Of the 107 patients included in the study, 40 died (Table 2). Therefore, a secondary exploratory analysis was conducted among the remaining 67 survivors to further examine the association between anemia severity and categorized mechanical ventilation duration. The Fisher–

Freeman–Halton exact test with Monte Carlo estimation indicated a statistically significant association between anemia severity and categorized mechanical ventilation duration ($p = 0.031$; Table 6). Similarly, Spearman's rank correlation analysis showed a statistically significant positive monotonic correlation between anemia severity and mechanical ventilation duration (Spearman's $\rho = 0.368$, $p = 0.002$; 95% BCa CI: $0.129 - 0.559$; Table 6). However, only five survivors had severe anemia, limiting the precision of the subgroup estimates. Pairwise comparisons using the Mann–Whitney U test (Table 7) showed statistically significant differences in the distribution of categorized mechanical ventilation duration between patients with mild and severe anemia (Holm-adjusted $p = 0.009$) and between those with moderate and severe anemia (Holm-adjusted $p = 0.012$). No statistically significant difference

was observed between patients with mild and moderate anemia (Holm-adjusted $p = 0.104$). These survivor-only findings should be interpreted cautiously because conditioning on

survival may introduce selection bias, and the results may not be generalizable to the entire cohort.

Table 4. Association between anemia severity and mechanical ventilation duration among trauma subgroup

Anemia Severity		Duration of Ventilator Use (days)				Total
		<1 (n=28)	1-3 (n=25)	4-7 (n=11)	>7 (n=3)	
Mild	n	4	4	5	2	14
	%	28.6	28.6	35.7	7.1	100.0
Moderate	n	10	16	8	7	41
	%	24.4	39.0	19.5	17.1	100.0
Severe	n	4	1	5	1	11
	%	36.4	9.1	45.5	9.1	100.00
Test				Statistic	p-value	95% BCa CI for Spearman's ρ
Fisher–Freeman–Halton exact test				6.456	0.363	-
Spearman's rank correlation				$\rho=0.018$	0.883	-0.237 – 0.275

Table 5. Association between anemia severity and mechanical ventilation duration among non-trauma subgroup

Anemia Severity		Duration of Ventilator Use (days)				Total
		<1 (n=28)	1-3 (n=25)	4-7 (n=11)	>7 (n=3)	
Mild	n	7	1	1	0	9
	%	77.8	11.1	11.1	0.0	100.0
Moderate	n	12	11	7	1	31
	%	38.7	35.5	22.6	3.2	100.0
Severe	n	0	1	0	0	1
	%	0.0	100.0	0.0	0.0	100.00
Test				Statistic	p-value	95% BCa CI for Spearman's ρ
Fisher–Freeman–Halton exact test				8.117	0.289	-
Spearman's rank correlation				$\rho=0.304$	0.053	-0.007 – 0.550

Table 6. Association between anemia severity and mechanical ventilation duration among survivors

Anemia Severity		Duration of Ventilator Use (days)				Total
		<1 (n=28)	1-3 (n=25)	4-7 (n=11)	>7 (n=3)	
Mild	n	8	3	1	0	12
	%	66.7	25.0	8.3	0.0	100.0
Moderate	n	20	21	7	2	50
	%	40.0	42.0	14.0	4.0	100.0
Severe	n	0	1	3	1	5
	%	0.0	20.0	60.0	20.0	100.00
Test		Statistic		p-value	95% BCa CI for Spearman's ρ	
Fisher–Freeman–Halton exact test (Monte Carlo)		11.949		0.031	-	
Spearman's rank correlation		$\rho=0.368$		0.002	0.129–0.559	

Table 7. Results of Mann–Whitney U test for pairwise comparisons of ventilator duration across anemia severity groups among survivor

Comparison	n1 vs n2	U	Z	p-value	Holm-adjusted p
Mild vs Moderate	12 vs 50	216.0	-1.625	0.104	0.104
Mild vs Severe	12 vs 5	4.0	-2.934	0.003	0.009
Moderate vs Severe	50 vs 5	37.0	-2.934	0.006	0.012

DISCUSSION

Most patients in this study were aged 19–59 years, and trauma accounted for a substantial proportion of admissions (Table 1). This distribution may reflect the case mix of the Intensive Observation Room at Dr. Soetomo General Hospital. Moderate anemia was the most common anemia category, consistent with reports of anemia among critically ill patients in Jember, Indonesia.¹³ A significant proportion of patients underwent blood transfusions and surgical procedures. The need for blood transfusion has been associated with weaning failure and prolonged mechanical ventilation; however, this association may partly reflect greater underlying disease severity and persistent critical illness among transfused patients, rather than an independent effect of transfusion itself.¹⁴ Reintubation occurred in

17.8% of patients (Table 2), which is comparable to the approximately 15% incidence reported in a previous review.⁸ Most patients who required reintubation did not survive, consistent with evidence linking reintubation to increased mortality among critically ill patients.¹⁵ On the other hand, meta-analysis evidence found that at least one episode of unplanned extubation occurred in 6.6% of adult ICU patients receiving mechanical ventilation. Unplanned extubation commonly occurs through self-extubation and may lead to aspiration of gastric contents and respiratory tract injury, potentially increasing the risk of morbidity and mortality. Therefore, identification and monitoring of patients at risk of self-extubation is necessary.¹⁶ No statistically significant correlation was found between anemia severity and mechanical ventilation duration (Spearman's $\rho = 0.121$, $p = 0.213$; Table

3). Therefore, this study did not demonstrate a statistically significant monotonic association between anemia severity and mechanical ventilation duration in the overall cohort. Death before successful extubation may affect the observed duration of mechanical ventilation because it terminates ventilation without successful liberation from ventilatory support. Thus, death represents a competing event when considering time to successful extubation. The relatively short duration of mechanical ventilation observed in some patients with severe anemia may therefore reflect death before extubation rather than faster recovery. Intrauma patients, anemia may be related to acute blood loss, tissue injury, and trauma-induced coagulopathy, whereas anemia in critically ill non-trauma patients may reflect heterogeneous processes, including inflammation, impaired erythropoiesis, nutritional deficiencies, and blood loss associated with medical procedures. These differences may influence the clinical significance of anemia and its relationship with outcomes in critically ill patients.^{4,17} In the non-trauma subgroup, no statistically significant association was found between anemia severity and mechanical ventilation duration. This may reflect the multifactorial nature of critical illness, in which the relationship between anemia and clinical outcomes may vary according to the underlying disease and other clinical factors.^{4,18} A statistically significant positive correlation was observed between anemia severity and mechanical ventilation duration among survivors (Spearman's $\rho = 0.368$, $p = 0.002$, 95% BCa CI: 0.129 - 0.559; Table 6). However, this finding should be interpreted cautiously because restricting the analysis to survivors may introduce selection bias, potentially including collider bias. Furthermore, only five survivors had severe anemia, which may limit the reliability of the subgroup findings. A study conducted in the United States on patients undergoing prolonged mechanical ventilation identified hemoglobin levels as a significant predictor of successful ventilator weaning. Patients with higher hemoglobin levels were associated with successful liberation from mechanical ventilation (OR = 1.43; 95% CI: 1.01–2.03, $p = 0.04$).¹⁹ Pairwise comparison showed statistically

significant differences in categorized mechanical ventilation duration between patients with severe anemia and those with mild or moderate anemia (Table 7). These results indicate severe anemia (Hb <8 g/dL) as the main differentiator in the results of duration of ventilator use. Extended durations of ICU and overall hospital stay have been reported in connection with more severe anemia at the time of admission among patients in critical condition.^{2,20} Anemia has been linked to increased mortality, complications involving the cardiovascular system, and impaired oxygen delivery—factors that may prolong the need for assisted respiratory support. This concern is particularly relevant for patients with pre-existing cardiac conditions.²¹ This study has several limitations. First, the analysis was limited to bivariate methods and did not account for potential confounding factors, such as age, sex, BMI, surgical history, comorbidities, and illness severity. Future studies should consider multivariable analyses to better assess the association between anemia severity and mechanical ventilation duration. Second, although total sampling was employed, no a priori sample-size calculation was performed because all eligible patients identified during the study period were included. Consequently, the statistical power of the study was not established in advance. Furthermore, the distribution of patients across anemia severity categories was uneven, with very few patients classified as having severe anemia, particularly among survivors. These factors may have reduced the precision of the estimates and the ability to detect associations, warranting cautious interpretation of the findings. Third, death during mechanical ventilation may have influenced the observed ventilation duration, while restricting the analysis to survivors may have introduced selection bias. Fourth, although hemoglobin levels were assessed on the first day of ICU admission, subsequent changes in hemoglobin levels and anemia severity were not captured. Blood transfusions during hospitalization may also have affected hemoglobin levels and clinical outcomes. Finally, residual confounding from unmeasured or unadjusted clinical factors may have influenced the observed associations. Therefore, the findings should be interpreted

cautiously and should not be considered evidence of a causal relationship between anemia severity and mechanical ventilation duration.

CONCLUSIONS

No statistically significant correlation was observed between anemia severity and mechanical ventilation duration in the overall cohort or in the trauma and non-trauma subgroups. However, a secondary analysis restricted to survivors revealed a statistically significant positive correlation between anemia severity and mechanical ventilation duration. These secondary findings should be interpreted with caution because restricting the analysis to survivors may introduce selection bias. Further research accounting for potential confounding factors is needed to clarify the association between anemia severity and mechanical ventilation duration.

CONFLICT OF INTEREST

No statistically significant correlation was The authors declare no conflict of interest.

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