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Incidence and clinical outcomes of ventilator-associated events in Russian tertiary care settings: an analysis of electronic health records

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Abstract

Objective This research aimed to evaluate the epidemiological and clinical characteristics of ventilator-associated events (VAE) using the CDC framework in a tertiary hospital in Moscow, Russia.

Results In this cohort study, we analyzed electronic health records from 407 mechanically ventilated adults who were admitted to the Kommunarka Moscow Multipurpose Clinical Center between September 2022 and December 2023. We identified a total of 35 VAE, resulting in an incidence rate of 8.39 (95% confidence interval, 5.84 to 11.67) events per 1,000 ventilator-days. The presence of VAE was associated with higher ICU mortality by day 30 from the start of mechanical ventilation (adjusted hazard ratio, 1.58; 95% confidence interval, 1.01 to 2.48), particularly in patients with infection-related ventilator-associated complications (adjusted hazard ratio, 2.09; 95% confidence interval, 1.17 to 3.74). The median durations of mechanical ventilation and ICU length of stay were comparable between patients with VAE and those without. Implementing surveillance measures and developing tailored preventive strategies for VAE may be beneficial in similar healthcare settings to improve outcomes for mechanically ventilated patients.

Keywords Ventilator-associated event, Mechanical ventilation, Epidemiology, Infection-related complication, Ventilator-associated pneumonia, Intensive care

Introduction

Surveillance for complications related to mechanical ventilation (MV) has historically focused on ventilator-associated pneumonia (VAP) [1, 2]. However, variations in VAP criteria interpretation among practitioners can lead to subjective reporting and hinder the development of preventive measures [2–4].

The ventilator-associated events (VAE) framework [5] was introduced in 2013 by the Centers for Disease Control and Prevention (CDC) to detect complications that may result in severe nosocomial respiratory deterioration in ventilated patients. The ventilator-associated condition

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(VAC), the first tier of VAE, captures cases of persistent hypoxemia without definitive signs of infection. The subsequent tiers, infection-related ventilator-associated complications (IVAC) and possible ventilator-associated pneumonia (PVAP), may indicate the presence of an infection process and pneumonia, respectively [5, 6].

The largest studies on VAE have been conducted in North America [7], East Asia [8], and Western Europe

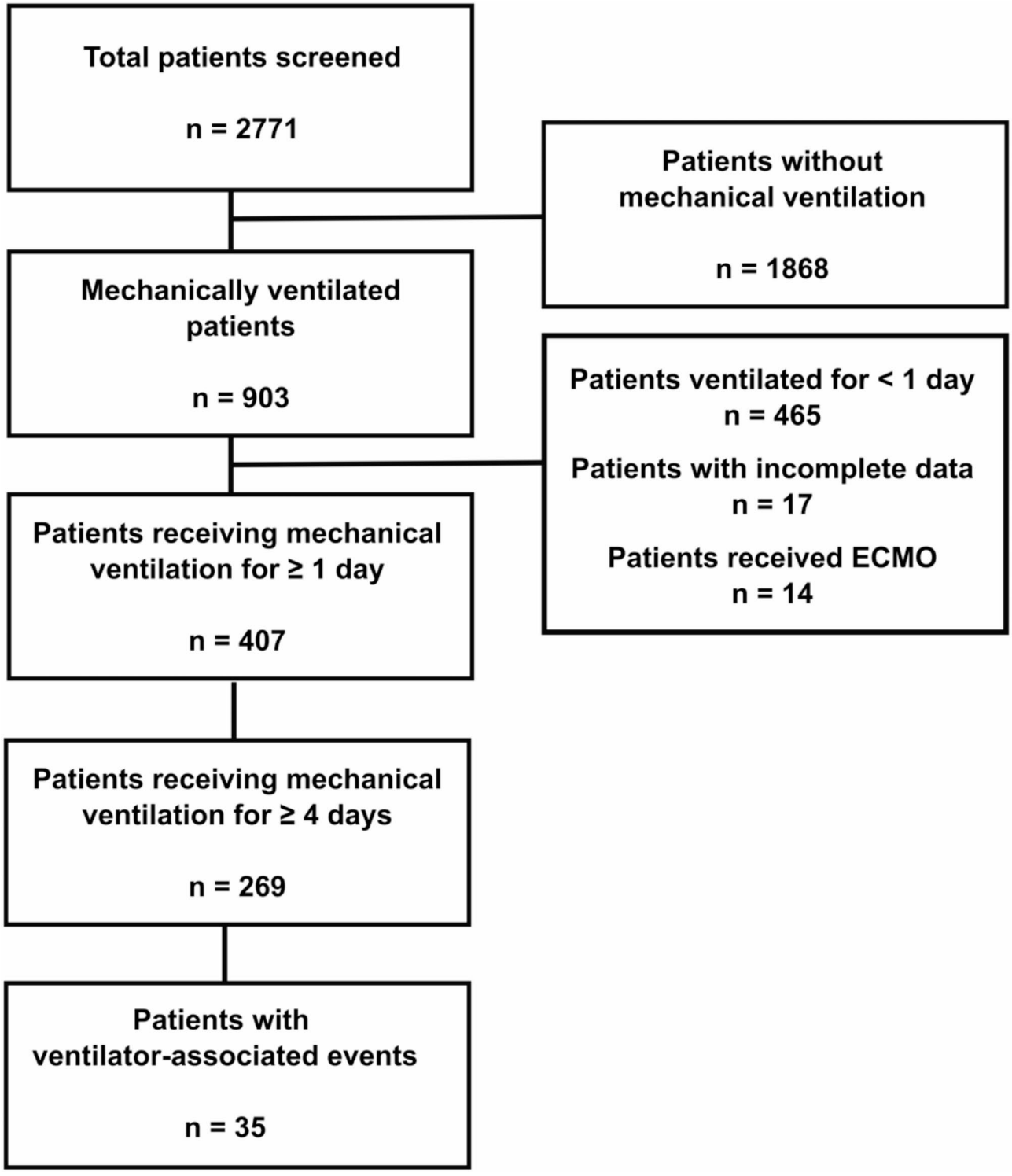

Fig. 1 Flow chart of the study

Table 1 Characteristics of patients ventilated for ≥ 4 consecutive days

Characteristic	Overall, *N* = 269	VAE-plus, *N* = 35	VAE-minus, *N* = 234
Age, mean (SD)	64 (17)	62 (17)	64 (17)
Sex, male	147 (55%)	18 (51%)	129 (55%)
Primary pathology			
Neoplasms or hematological diseases	72 (26.8%)	7 (20.0%)	65 (27.8%)
Diseases of the circulatory system	65 (24.2%)	8 (22.9%)	57 (24.3%)
Diseases of the respiratory system	35 (13.0%)	6 (17.1%)	29 (12.4%)
Diseases of the digestive system	33 (12.2%)	5 (14.3%)	28 (12.0%)
Injury, poisoning and external causes	26 (9.7%)	4 (11.4%)	22 (9.4%)
Other	38 (14.1%)	5 (14.3%)	33 (14.1%)
Comorbidities			
Congestive heart failure	106 (39.4%)	8 (22.9%)	98 (41.9%)
Localized tumor	60 (22.3%)	10 (28.6%)	50 (21.4%)
Metastatic cancer	35 (13.0%)	6 (17.1%)	29 (12.4%)
Hematological malignancy	30 (11.2%)	6 (17.1%)	24 (10.3%)
COPD	23 (8.6%)	3 (8.6%)	20 (8.5%)
Clinical scores and events at ICU admission			
SOFA, median (IQR)	7.0 (4.0, 9.0)	9.0 (4.0, 10.0)	7.0 (4.0, 9.0)
CCI, median (IQR)	6.0 (3.0, 9.0)	6.0 (2.0, 8.0)	6.0 (3.0, 9.0)
Major surgery	128 (47.6%)	21 (60%)	107 (45.7%)
Primary reason for MV initiation			
Respiratory failure	113 (42.0%)	10 (28.6%)	103 (44.0%)
Neurological deterioration	84 (31.2%)	14 (40.0%)	70 (29.9%)
General anesthesia	52 (19.3%)	11 (31.4%)	41 (17.5%)
CPR	20 (7.5%)	-	20 (8.5%)

Abbreviations: VAE, ventilator-associated event; SD, standard deviation; IQR, interquartile range; SOFA, Sequential Organ Failure Assessment score; CCI, Charlson Comorbidity Index; COPD, chronic pulmonary obstructive disease; CPR, cardiopulmonary resuscitation; N, number

Categories: VAE-plus, patients who developed VAE; VAE-minus, patients who did not develop VAE

[9], with many indicating the possible association of VAE with poor clinical outcomes.

Data on VAE from many countries are limited or absent, leading to unclear implications for surveillance in those regions [10].

The aim of this study was to assess key epidemiological and clinical characteristics of VAE using the CDC framework in a tertiary hospital in Moscow, Russia. We sought to derive insights to inform MV policies in similar healthcare settings.

Methods

Study design and settings

In this observational study, we utilized an electronic health record (EHR) database from the Kommunarka Moscow Multi-Purpose Clinical Center (Kommunarka MMCC), a high-volume tertiary hospital in Moscow, Russia. Kommunarka MMCC provides both urgent and elective medical services to the Troitsky and Novomoskovsky districts, which together have a population of approximately 700,000. Furthermore, it is one of the key hospitals in the city, offering specialized oncological and hematological care to patients from other districts of Moscow and various regions of Russia.

We constructed a retrospective cohort of patients admitted to two intensive care units (ICU) at Kommunarka MMCC from September 1, 2022, to December 31, 2023. Eligible patients were those who underwent mechanical ventilation (MV) for at least one day. Exclusion criteria were as follows: (1) age under 18; (2) incomplete MV parameter data; and (3) use of extracorporeal membrane oxygenation (ECMO).

Data source

Daily MV-related and laboratory data necessary for identifying VAE were extracted from ICU EHR database. Additionally, patient characteristics were gathered, which included demographic information, details on primary pathology, chronic comorbidities, surgical interventions, the Sequential Organ Failure Assessment (SOFA) score, and the Charlson Comorbidity Index (CCI) recorded upon ICU admission. The primary pathology and chronic comorbidities were identified by referencing the International Classification of Diseases, 10th edition (ICD-10) [11].

Daily MV parameters, including positive end-expiratory pressure (PEEP) and fraction of inspired oxygen (FiO_2), were independently assessed by two physicians

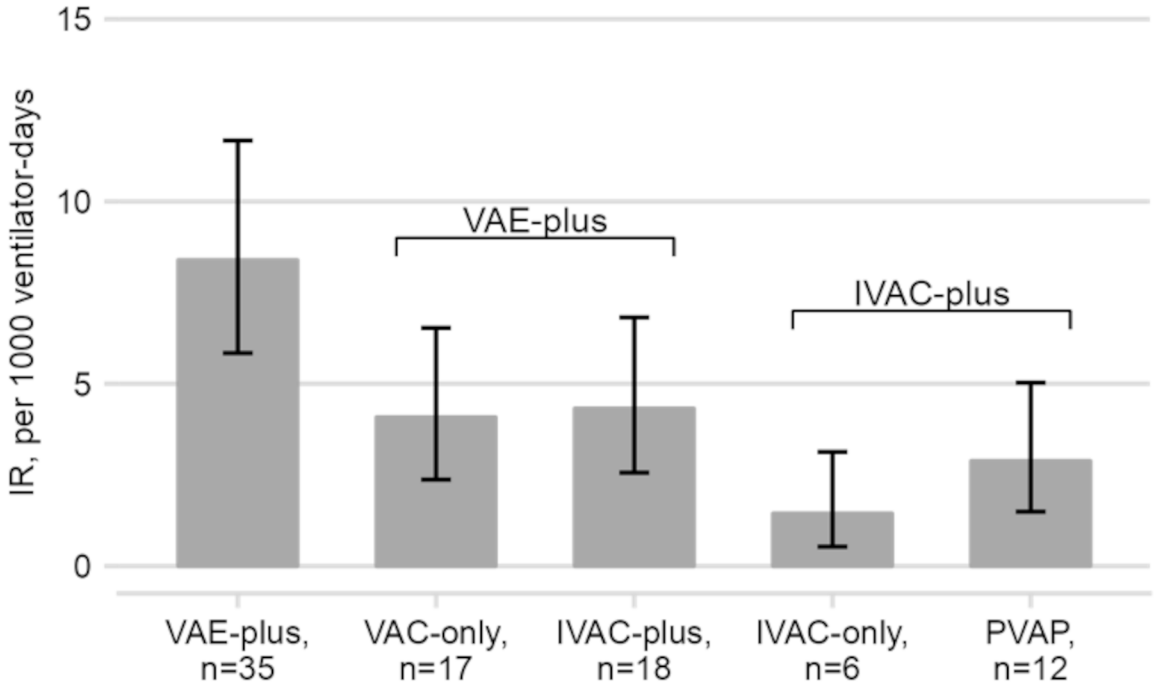

Fig. 2 Incidence rates of VAE and VAE tiers. Incidence rates (columns) are represented as number of events per 1000 ventilator days. Error bars represent 95% confidence intervals. Abbreviations: VAE, ventilator-associated event; VAC, ventilator-associated condition; IVAC, infection-related ventilator-associated complication; PVAP, possible ventilator-associated pneumonia; IR, incidence rate. Categories: VAE-plus, patients with VAE; VAC-only, patients with VAC and without criteria of subsequent tiers; IVAC-plus, patients with IVAC criteria (including patients with PVAP); IVAC-only, patients with IVAC and without PVAP criteria; PVAP, patients with PVAP criteria

(SV and IK) to confirm they met VAE criteria. We employed a custom R script to apply the VAC criteria through retrieved daily MV parameters, followed by a manual review of electronic health records for further VAE classification. Disagreements were resolved through discussion with a third investigator (NM).

Table 2 Incidence rates of VAE and its tiers, stratified by patients' profile

VAE tier	Incidence rate, by 1000 ventilator days (with 95% CI)	
	Surgical patients	Medical patients
VAE, overall	9.28 (5.75, 14.20)	7.32 (4.00, 12.30)
VAC-only	4.87 (2.43, 8.70)	3.14 (1.15, 6.84)
IVAC-plus	4.42 (2.12, 8.13)	4.19 (1.81, 8.25)
IVAC-only	1.77 (0.48, 4.53)	1.05 (0.13, 3.78)
PVAP	2.65 (0.97, 5.78)	3.14 (1.15, 6.84)

Abbreviations: VAE, ventilator-associated event; VAC, ventilator-associated condition; IVAC, infection-related ventilator-associated complication; PVAP, possible ventilator-associated pneumonia; IR, incidence rate; CI, confidence interval. Categories: VAE-minus, patients who did not develop VAE; VAE-plus, patients with VAE; VAC-only, patients with VAC and without criteria of subsequent tiers; IVAC-plus, patients with IVAC criteria (including patients with PVAP); IVAC-only, patients with IVAC patients with IVAC but not meeting PVAP criteria; PVAP, patients with PVAP criteria

Definitions

According to CDC criteria [5], VAE were identified and classified into three tiers.

VAC is defined by an increase in FiO_2 of ≥ 20% or PEEP of ≥ 3 cm H_2O, sustained for at least two consecutive days after two days of stable levels.

IVAC requires meeting VAC criteria and signs of infection, indicated by new antibiotics within two days of VAC onset and abnormal white blood cell counts (≤ 4,000 or ≥ 12,000 cells/mm^3) or abnormal body temperature (< 36 °C or > 38 °C).

PVAP builds on IVAC by requiring evidence of pneumonia, such as positive cultures from the lower respiratory tract.

Outcomes

The primary outcome was the incidence rate of VAE and its tiers. Secondary outcomes included ICU mortality,

Table 3 Characteristics of different VAE tiers

Characteristic	Overall	VAC-only	IVAC-plus	IVAC-only	PVAP
Time to event from MV start, days					
Median (IQR)	4.0 (4.0, 9.0)	4.0 (4.0, 7.0)	5.5 (4.0, 8.8)	5.0 (4.0, 14.3)	5.5 (3.8, 8.3)
Possible non-infectious reasons for VAC-only events, n (%)					
Atelectasis	7 (41.3%)	7 (41.3%)	-	-	-
ARDS	3 (17.6%)	3 (17.6%)	-	-	-
Other	3 (17.6%)	3 (17.6%)	-	-	-
Not identified	4 (23.5%)	4 (23.5%)	-	-	-
IVAC-related antimicrobials, n (%)					
Polymyxins	10 (55.6%)	-	10 (55.6%)	2 (33.3%)	8 (66.6%)
Carbapenems	4 (22.2%)	-	4 (22.2%)	2 (33.3%)	2 (16.7%)
Other	4 (22.2%)	-	4 (22.2%)	2 (33.3%)	2 (16.7%)
PVAP-related agents, n (%)					
A. baumannii	6 (50.0%)	-	6 (50.0%)	-	6 (50.0%)
K. pneumoniae	3 (25.0%)	-	3 (25.0%)	-	3 (25.0%)
C. striatum	3 (25.0%)	-	3 (25.0%)	-	3 (25.0%)
P. aeruginosa	1 (8.3%)	-	1 (8.3%)	-	1 (8.3%)
Other	5 (41.6%)	-	5 (41.6%)	-	5 (41.6%)

Abbreviations: ARDS, acute respiratory distress syndrome; VAE, ventilator-associated event; VAC, ventilator-associated condition; IVAC, infection-related ventilator-associated complication; PVAP, possible ventilator-associated pneumonia; IQR, interquartile range. Categories: VAC-only, patients with VAC and without criteria of subsequent tiers; IVAC-plus, patients with IVAC criteria (including patients with PVAP); IVAC-only, patients with IVAC but not meeting PVAP criteria; PVAP, patients with PVAP criteria

MV duration, and ICU length of stay (LOS). All endpoints were evaluated by day 30 after MV initiation.

Statistical analysis

The calculation of the incidence rate followed CDC guidelines [5], dividing the number of VAE episodes by the total number of ventilator days from all included patients during the follow-up period, then multiplying by 1,000. We employed the Poisson distribution to compute 95% confidence intervals (CIs) for the incidence rates. Rates were stratified based on patient profiles.

We selected patients who were ventilated for ≥ 4 consecutive days for evaluating secondary outcomes, as this meets the VAE minimum period of two days of stability followed by at least two days of respiratory decline. By using this four-day threshold, we aimed to minimize bias that could arise from including patients with shorter MV durations when comparing outcomes between those with and without VAE. Among VAE-plus patients, secondary outcomes were evaluated for VAC-only and IVAC-plus events, representing two important subcategories within the framework that account for suggested non-infectious and infectious complications, respectively.

Descriptive statistics were used to summarize characteristics of patients, with continuous variables expressed as medians with interquartile ranges (IQR), and categorical variables reported as frequencies and percentages.

To evaluate the association between VAE and ICU mortality, we used the Cox proportional hazards model with VAE as a time-dependent covariate. A multivariable model was created, incorporating baseline parameters like SOFA and comorbidities at ICU admission as fixed covariates to adjust for confounders. Adjusted hazard ratios (HR) for mortality, along with 95% CI, were calculated. Similar analyses were performed for VAC-only (individuals with VAE not meeting IVAC criteria) and IVAC-plus (those meeting IVAC criteria, including PVAP) cases.

The median number of days on MV and ICU LOS were compared using the Wilcoxon test.

Statistical significance was determined at a p-value of less than 0.05.

Data preparation and all statistical analyses were conducted using R, version 4.3.2 [12, 13].

Results

Study sample

Final analysis included 407 patients, totaling 4,171 ventilator days. Among them, 269 patients were eligible for VAE evaluation (Fig. 1).

Patient characteristics

The mean age of patients was 64 years, and 55% were male, with no substantial demographic differences between patients with and without VAE. Detailed conditions and indications for MV are provided in Table 1.

The cohort demonstrated a high level of comorbidity and illness severity at ICU admission, with a median CCI of 6.0 and a SOFA score of 7.0. The presence of solid tumors or hematological malignancies was notable,

Table 4 Clinical outcomes of patients ventilated for ≥ 4 consecutive days, by day 30 from MV initiation

Outcome	VAE-minus	VAE-plus	VAC-only	IVAC-plus
ICU mortality				
Crude, n (%)	140 (59.8%)	23 (65.7%)	9 (52.9%)	14 (77.7%)
HR (95% CI)[a]	-	1.76 (1.13, 2.74)	1.38 (0.77, 2.49)	2.37 (1.37, 4.11)
aHR (95% CI)[b] for multivariate model:				
VAE	-	1.58* (1.01, 2.48)	1.35 (0.75, 2.45)	2.09* (1.17, 3.74)
SOFA	-	1.08* (1.02, 1.18)	1.08* (1.03, 1.14)	1.08* (1.03, 1.13)
Hematological malignancy	-	1.78* (1.22, 1.78)	1.85* (1.17, 2.93)	1.46 (0.93, 2.30)
Metastatic cancer		2.18* (1.62, 2.78)	1.89* (1.24, 2.89)	1.79* (1.18, 2.71)
MV length				
Days, median (IQR)	11 (6,24)	13 (6,18)	12(6,25)	14 (6,18)
p-value[c]	-	0.8	0.9	0.6
ICU length of stay				
Days, median (IQR)	15 (8,27)	14 (9,21)	13 (9,24)	15 (9,20)
p-value[c]	-	0.6	0.4	0.7

[a]Compared to VAE-minus patients, univariate Cox regression

[b]Compared to VAE-minus patients, multivariate Cox regression

[c]Compared to VAE-minus patients, Wilcoxon test, p-value

*p-value less than 0.05, multivariate Cox regression

Abbreviations: MV, mechanical ventilation; ICU, intensive care unit; VAE, ventilator-associated event; VAC, ventilator-associated condition; IVAC, infection-related ventilator-associated complication; IQR, interquartile range; HR, hazard ratio; aHR, hazard ratio, adjusted for confounder variables at ICU admission; CI, confidence interval, SOFA, Sequential Organ Failure Assessment score. Categories: VAE-minus, patients who did not develop VAE; VAE-plus, all patients with VAE; VAC-only, patients with VAC and without criteria of subsequent tiers; IVAC-plus, patients with IVAC criteria (including patients with possible ventilator-associated pneumonia); PVAP, patients with PVAP criteria

affecting approximately half of patients with VAE and around 40% of those without. Approximately half of the patients underwent major surgery corresponding to the start of their MV episode.

Rates and characteristics of VAE

A total of 35 VAE were identified, resulting in an overall rate of 8.39 (95% CI, 5.84 to 11.67) events per 1,000 ventilator-days. Of these, 17 events were categorized as VAC-only, while 18 were classified as IVAC-plus, including 12 cases of PVAP (Fig. 2).

Surgical patients exhibited higher incidence of VAE compared to medical patients across almost all tiers (Table 2).

The median time to VAE from the initiation of MV was four days. IVAC were primarily linked to the use of polymyxins, while Acinetobacter baumannii was the most commonly isolated pathogen in PVAP. The most frequent non-infectious cause of VAC was atelectasis. We were unable to identify a clear possible reason in four VAC cases (Table 3).

Secondary outcomes

Presence of VAE was associated with higher ICU mortality in multivariate analysis, comparing VAE-plus and VAE-minus patients (65.7% vs. 59.8%; adjusted HR, 1.58; 95% CI, 1.01 to 2.48). Patients with IVAC demonstrated the highest mortality within the cohort in comparison to patients without VAE (77.7% vs. 59.8%; adjusted HR, 2.09; 95% CI, 1.17 to 3.74). The median durations of MV and ICU LOS in VAE-plus patients were similar to VAE-minus group.

A detailed comparison of secondary outcomes is provided in Table 4.

Discussion

Key findings

To our knowledge, this study represents the first exploration of the VAE framework in Russia. The incidence of VAE in our cohort aligns with largest international reports. Most events occurred early in the MV course, and patients with VAE had higher ICU mortality by day 30.

Incidence of VAE

The observed incidence of VAE aligns with findings from large studies in the USA [7], China [8], and France [14], indicating similar epidemiological features.

Variations in published VAE rates may stem from different methodologies, particularly in calculating ventilator days. For instance, a study on neurocritically ill patients [15] calculated both the number of VAEs and

ventilator days based on patients on mechanical ventilation (MV) for at least three days. Similarly, a multicenter study in Europe and Australia used this approach [9]. In contrast, two Japanese studies applied different criteria, selecting MV episodes lasting a minimum of two [16] or four consecutive days [17].

In our study, all ventilator days from patients ventilated for at least one calendar day were included in the rate denominator, aligning closely with CDC VAE guidelines [5].

Key characteristics of VAE

The majority of VAE in our study occurred within the first week of MV. Previous research also indicates that the risk of developing a VAE peaks during this period [6]. This may reflect several factors following tracheal intubation, including compromised lung mechanics, increased risk of microaspiration, and invasive manipulations during the initial phase of MV [18].

The increased incidence of VAE in surgical patients is consistent with prior research and may be related to perioperative factors such as altered lung mechanics, aggressive fluid management, limited mobility, and blood transfusions [1, 19].

The substantial proportion of IVAC is relevant to those published, suggesting that nosocomial infection may be the major contributor of respiratory deterioration in critically ill, especially those who require MV [1, 6]. This may result from factors such as immunosuppression, the necessity for invasive procedures, and the development of antimicrobial resistance resulting from exposure to broad-spectrum antibiotics.

Clinical outcomes

The presence of VAE was associated with increased mortality in the ICU by day 30 from the start of MV. While most previous studies have reported similar associations [1, 6], our research demonstrated a notably high crude mortality rate within the cohort. Additionally, we found no differences in the MV duration and the ICU LOS between patients with VAE and those without, which contrasts with results reported in the majority of other reports. This may stem from the high comorbidity burden and severe illness profile of our patients, influenced by the hospital's involvement in emergency care and its focus on oncology. One-third of our cohort had hematological or oncological diagnoses, potentially complicating outcomes due to issues like immunosuppression, organ dysfunction, and poor performance status [20, 21].

Prior research also indicates worse outcomes for mechanically ventilated patients with multiple comorbidities. For instance, in a cohort study of COVID-19 patients on MV in the USA, lower median CCI was associated with higher survival rates [22]. Additionally, an observational study from South Korea reported that the mortality for patients on prolonged MV with a CCI of 5 or greater was 54.2% [23], which is close to our findings.

In the analysis within VAE tiers, IVAC-plus individuals exhibited the highest mortality in our cohort. The predominant prevalence of Acinetobacter baumannii in patients with PVAP, along with the primary use of polymyxins and carbapenems as antibiotics in this subgroup, suggests a possible link between IVAC and gram-negative sepsis, which may contribute elevated mortality [24].

Possible implications for practice

Implementing tailored VAE prevention strategies that consider specific patient characteristics and factors in different healthcare settings may be beneficial [1, 6]. Our study found that most VAE cases were linked to nosocomial infections from gram-negative bacteria, indicating the potential value of infection control programs. In contrast, the majority of non-infectious VACs occurred in patients after major surgeries, highlighting the relevance of strategies aimed on reducing postoperative respiratory complications [19]. These may include optimizing fluid management, early rehabilitation, and improving ventilation during the perioperative period [25]. Since most events happen within the first week of invasive respiratory support, this period seems crucial for implementing preventive measures.

Limitations

First, being a single-center study restricts its external validity.

Second, we did not have hourly PEEP and FiO_2 data, as desirable according to CDC criteria. These parameters were recorded in the EHR database with approximately four entries per patient per day; however, the VAE guidelines allow for less frequent monitoring than hourly checks [5].

Third, the reliability of the EHR data concerning MV parameters in our study depended on precise data entry by physicians. Acquiring this information directly from ventilators in future studies can enhance data accuracy.

Fourth, our study may be underpowered to conclusively determine its impact on clinical outcomes, as these were secondary endpoints and should be viewed as exploratory.

Lastly, our follow-up was limited to 30 days post-MV initiation, which, although capturing most incident VAE cases, restricts the assessment of long-term outcomes.

Conclusions

VAE epidemiological features in our study are consistent with international data. Possible association of VAE with increased ICU mortality indicates a potential benefit

from surveillance and development of tailored preventive strategies in similar healthcare settings.

Abbreviations

ARDS	Acute Respiratory Distress Syndrome
CDC	Centers for Disease Control and Prevention
CCI	Charlson Comorbidity Index
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
EHR	Electronic Health Records
ECMO	Extracorporeal Membrane Oxygenation
FiO_2	Fraction of Inspired Oxygen
HR	Hazard Ratio
ICD-10	International Classification of Diseases, 10th edition
ICU	Intensive Care Unit
IR	Incidence Rate
IVAC	Infection-Related Ventilator-Associated Complication
LOS	Length of Stay
MV	Mechanical Ventilation
PEEP	Positive End-Expiratory Pressure
PVAP	Possible Ventilator-Associated Pneumonia
SD	Standard Deviation
SOFA	Sequential Organ Failure Assessment
SQL	Structured Query Language
VAC	Ventilator-Associated Condition
VAE	Ventilator-Associated Event

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Author contributions
All authors contributed to the study conception and design; Data acquisition and analysis: S.V and I.K.; Writing – original draft preparation: S.V; Writing – review and editing: D.S, S.V., N.M., D.P and I.K; Resources: N.M. and D.P.; Supervision: S.V. and D.S; All authors read and approved the final manuscript.

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Data availability
The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request. Data are located in controlled access data storage at Kommunarka MMCC.

Declarations

Ethics approval and consent to participate
This research was conducted in accordance with the principles set forth in the Declaration of Helsinki. The study protocol received approval from the ethical committee of Kommunarka MMCC (protocol №6, dated September 24, 2024). Due to the retrospective nature of data collection, informed consent from individual participants was waved. Anonymization was utilized to ensure the confidentiality of all subjects involved.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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