

Respiratory Drive and Survival in Comatose Out-of-Hospital Post-Cardiac Arrest Patients

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Purpose: This study aimed to explore alterations in respiratory drive in comatose patients after out-of-hospital cardiac arrest (OHCA) and their association with survival outcomes.

Patients and Methods: A prospective cohort study was conducted on comatose patients with OHCA who were admitted between October 2022 and October 2024. Patients were followed until their discharge from the hospital and subsequently categorized into survivors and non-survivors. Respiratory drive was evaluated using P0.1, representing the airway occlusion pressure measured within the first 100 ms of inspiration, as displayed on the ventilator. Measurements were collected together with additional parameters at 24, 48, and 72 h following admission.

Results: The analysis involved 30 patients, with an in-hospital mortality rate of 53.3%. Over the 72-h observation period, P0.1 values were greater in survivors than in non-survivors; however, this difference was not statistically significant. During the first 24 h, survivors demonstrated significantly lower tidal volumes per predicted body weight ($P = 0.034$). P0.1 values ranging from 1.5 to 3.5 cmH₂O in the initial 24 h were independently associated with reduced in-hospital mortality (adjusted OR 0.043, 95% CI 0.003–0.588, $P = 0.018$).

Conclusion: A trend toward elevated P0.1 levels in survivors was observed. P0.1 values within the range of 1.5–3.5 cmH₂O during the first 24 h were linked to a lower mortality rate. These results indicate that P0.1 could be utilized as a prognostic indicator for comatose patients following OHCA.

Plain Language Summary: This study explored how changes in respiratory drive relate to survival in unconscious patients after a cardiac arrest outside the hospital. Respiratory drive was assessed using P0.1, which measures the effort to take a breath, at 24, 48, and 72 hours after admission. The results showed that survivors tended to have higher P0.1 levels than non-survivors. Notably, patients with P0.1 values between 1.5 and 3.5 cmH₂O in the first 24 hours were more likely to survive. These findings suggest that P0.1 could be a useful tool for predicting outcomes in critically ill patients.

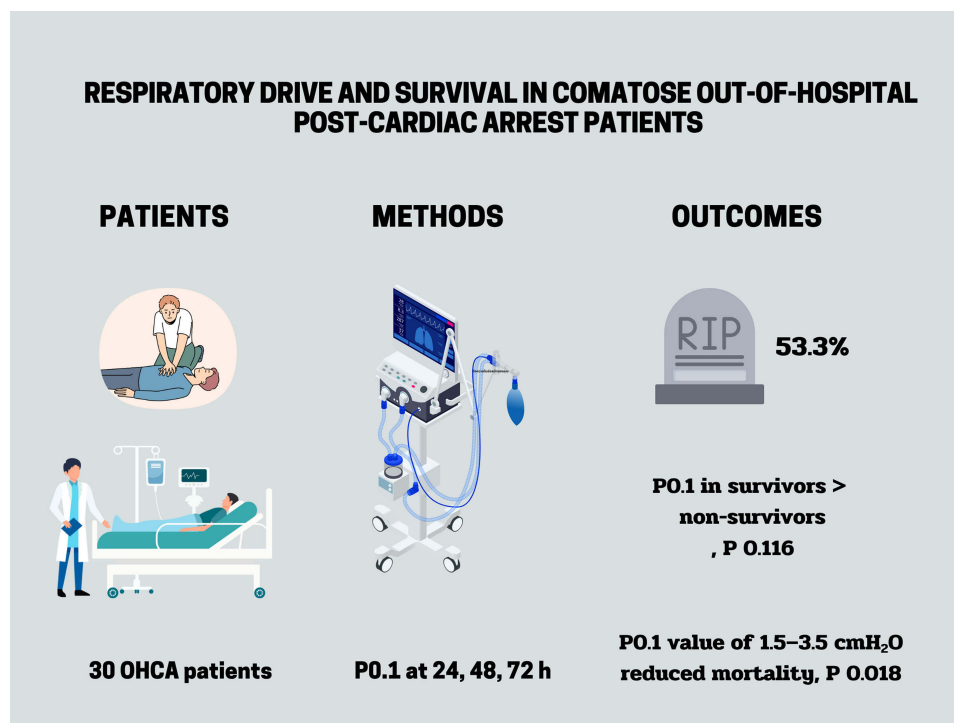
Keywords: respiratory drive, post-arrest, airway occlusion pressure, ventilation, survival

Introduction

Out-of-hospital cardiac arrest (OHCA) is a life-threatening medical emergency that requires rapid and efficient resuscitation. Evidence strongly supports the role of a multidisciplinary team in providing thorough post-resuscitation care after the return of spontaneous circulation (ROSC).¹ Despite advancements in treatment protocols, mortality rates remain elevated, and the majority of patients are discharged with unfavorable neurological outcomes.²

OHCA survivors frequently develop multiple organ failure resulting from ischemia-reperfusion injury, a condition collectively termed post-cardiac arrest syndrome (PCAS). This syndrome considerably impacts mortality rates.³ PCAS progresses through distinct phases, with the early and intermediate phases, spanning up to 72 h after ROSC,⁴ representing a critical period for intensive care monitoring and intervention. Previous studies have largely concentrated on the pathophysiology of PCAS with respect to the heart and brain, leaving the respiratory system relatively underexplored.

Graphical Abstract



Current guidelines emphasize general respiratory care measures, such as maintaining normal carbon dioxide levels and oxygen saturation levels above 94%.¹ Emerging evidence has begun to shed light on the potential role of respiratory dynamics in post-cardiac arrest outcomes. A study involving unconscious OHCA patients who underwent mechanical ventilation and temperature management in the first 72 h identified respiratory rate and driving pressure as key predictors of 6-month mortality.⁵ Similarly, animal models of post-cardiac arrest have demonstrated an elevated respiratory drive but reduced tidal volumes compared to non-arrested controls.⁶ This suggests that a mismatch between respiratory drive and ventilation, referred to as ventilation-drive coupling, potentially contributes to alveolar injury.

Modern ventilators can automatically evaluate the respiratory drive using measurements such as P0.1, which reflects the airway pressure recorded during the first 100 ms of an end-expiratory occlusion. P0.1 is considered a reliable metric because of its independence from respiratory mechanics and its minimal influence on patient responses during brief occlusions. For patients with critical illness, a P0.1 range of 1.5–3.5 cmH₂O is generally considered acceptable.⁷ However, the optimal range of P0.1 in patients following OHCA remains unclear, and its potential utility as a prognostic tool in this population remains unclear. This study aimed to investigate respiratory drive variations in comatose patients following OHCA and to examine their association with survival.

Materials and Methods

Study Design

This prospective cohort study included patients with OHCA admitted to Songklanagarind Hospital between October 2022 and October 2024. Enrollment was conducted within 24 h of hospital admission, and participants were followed up until discharge.

Adults aged 18 years or older diagnosed with OHCA and achieving ROSC for at least 20 min were included. Eligibility required unconsciousness with a Glasgow Coma Scale (GCS) score below 8 and admission to the medical intensive care unit (MICU) or cardiac care unit (CCU) within 24 h of ROSC. Additionally, patients were required to be on a ventilator capable of measuring P0.1 and were expected to require mechanical ventilation for over 24 h.

The following patients were excluded: terminally ill patients receiving palliative care, individuals on extracorporeal membrane oxygenation, pregnant patients, and those in a pre-cardiac arrest vegetative state or coma.

This research acquired approval from the Ethics Committee, Faculty of Medicine, Prince of Songkla University (REC 65–310-14-4) and adhered to the guidelines established in the Declaration of Helsinki. Informed consent was provided by the patient's nearest relative or designated individual promptly and subsequently by the patient upon regaining capacity. This study was registered in the Thai Clinical Trials Registry (TCTR20221010003).

Setting

Songklanagarind Hospital is an 850-bed tertiary referral center in Thailand. It includes a 12-bed MICU and 6-bed CCU staffed by 5 full-time intensivists and 4 cardiac interventionists available throughout the week. Patients who experienced cardiac arrest were treated following local policy guidelines, which aligned with the American Heart Association 2020 recommendations.¹ For comatose patients, targeted temperature management (TTM) was implemented based on physician discretion. Coronary angiography (CAG) and percutaneous coronary intervention (PCI) were performed by cardiac interventionists when considered clinically appropriate. Neuroprognostication utilizes a multimodal approach, with brain-death declarations made by a team of neurologists.

Data Collection

Electronic medical records provided information on baseline clinical variables, including sex, age, height, weight, underlying diseases, admission date, etiology of cardiac arrest, no-flow time, cardiopulmonary resuscitation (CPR) duration (from documented start to stop times), time to ROSC, and initial cardiac rhythm. If no height record was available in the medical chart, the height was estimated from the photograph of the patient's Thai national identity card, which includes a height scale. The predicted body weight (PBW) was then calculated using the standard formula: $50 + 0.91 \times (\text{height in centimeters} - 152.4)$ for males and $45.5 + 0.91 \times (\text{height in centimeters} - 152.4)$ for females.⁸ The height used for PBW calculation was primarily obtained from medical records; when unavailable, height from the identity card was used as an alternative.

Physiological and laboratory parameters were documented to compute the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, utilizing the worst values recorded within the initial 24 h following admission.⁹ Additional data included vital signs, respiratory and ventilator parameters, arterial blood gas results, sedation, and continuous neuromuscular blocking agent (NMBA) use, Richmond Agitation Sedation Scale (RASS), GCS at 24, 48, and 72 h post-admission, and the Cerebral Performance Category (CPC) score at the time of hospital discharge. Circulatory shock was defined as a systolic blood pressure < 90 mmHg for at least 30 min or the need for supportive measures to maintain a systolic pressure ≥ 90 mmHg, accompanied by signs of end-organ hypoperfusion, such as cool extremities, urine output < 30 mL/h, and a heart rate > 60 beats/min.¹⁰ The RASS, ranging from +4 (combative) to -5 (unarousable), assigns a score of 0 for patients who are alert and calm.¹¹ For patients on mechanical ventilation, a GCS verbal score of 1 is assigned.¹² The CPC scale ranges from 1, indicating good cerebral performance, to 5, representing brain death.¹³

P0.1 values and respiratory parameters, including arterial blood gas measurements, were obtained 24, 48, and 72 h post-admission, with a permissible variation of up to 3 h. P0.1 was measured with a Dräger Evita XL ventilator (Dräger Medical, Lübeck, Germany) through an automated maneuver performed four times at 1-min intervals, and the average value was calculated.¹⁴ At the time of measurement, all patients received full ventilatory support in either pressure-controlled or volume-controlled mode. The ratio of minute ventilation (VE) to P0.1 was used to evaluate the ventilation-drive coupling.^{15,16}

Primary Outcome

The primary outcome was the in-hospital mortality rate. Non-survivors were classified by the cause of death into one of the following categories: withdrawal of care attributed to neurological status, withdrawal of care due to comorbid conditions, refractory hemodynamic shock, refractory respiratory failure, or sudden cardiac death.¹⁷

Statistical Analyses

In a study by Rittayamai et al,¹⁸ the mean P0.1 value for critically ill patients, including those who had experienced cardiac arrest, was 2.6 ± 1.7 cmH₂O. For non-survivors, P0.1 value was estimated to be 1 cmH₂O lower than the reported mean

value of 2.6 cmH₂O, resulting in an estimated P0.1 of 1.6 cmH₂O. This estimation, along with a standard deviation of 1.70, alpha level of 0.05, and statistical power of 80%, indicated that a sample size of 23 was required to test the population mean.¹⁹ To account for a potential 30% dropout rate, the adjusted sample size was calculated to be 30 participants.

The Shapiro–Wilk test was used to assess the normality of the continuous data. Continuous variables are reported as medians with interquartile ranges (IQR), and the Mann–Whitney *U*-test was used for comparisons. Categorical variables are summarized as frequencies and percentages, and comparisons were performed using Fisher’s exact test. Repeated measurements over time were analyzed using generalized estimating equations.

The odds ratio of in-hospital mortality for P0.1 values considered acceptable in mechanically ventilated patients—which were 1.5–3.5 cmH₂O at 24, 48, and 72 h—was assessed using univariable logistic regression. Multivariable analysis was adjusted for established survival predictors, including witnessed arrest, bystander CPR, shockable rhythms, and prehospital ROSC.²⁰

The association between P0.1 and variables such as VE, tidal volume, compliance, and RASS over time were analyzed using linear mixed models. Variance explained by fixed effects was measured through Marginal R², while Conditional R² captured the combined contribution of fixed and random effects.^{21,22} A significance level of $P < 0.05$ was applied to all statistical analyses. Data were analyzed using STATA version 16 (StataCorp LP, College Station, TX, USA).

Results

Among 59 post-cardiac arrest patients, 29 were excluded, and 30 patients were prospectively evaluated (Figure 1). Of the 16 patients who died, the causes of death included withdrawal of care due to neurological status (8/16, 50%), withdrawal of care due to comorbid conditions (3/16, 18.8%), refractory respiratory failure (2/16, 12.5%), sudden cardiac death (2/16, 12.5%), and refractory hemodynamic shock (1/16, 6.2%).

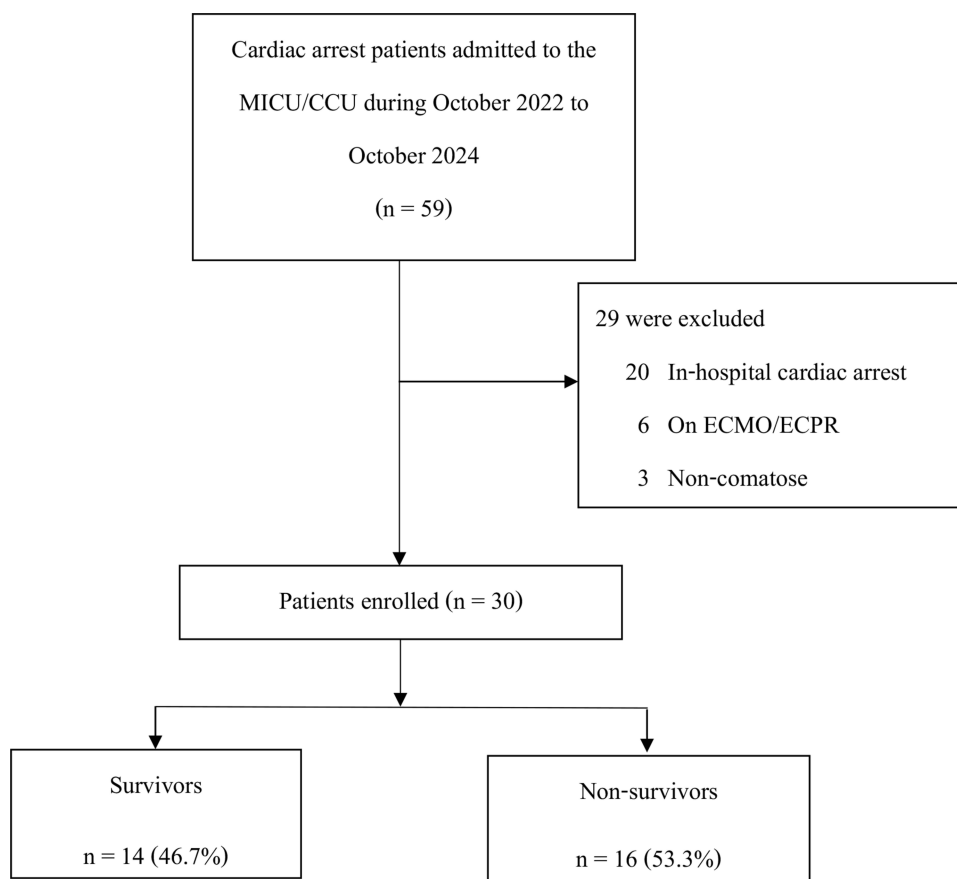


Figure 1 Patients enrolled in the study.

Abbreviations: CCU, cardiac care unit; ECMO, extracorporeal membrane oxygenation; ECPR, extracorporeal cardiopulmonary resuscitation; MICU, medical intensive care unit.

The baseline characteristics of patients, categorized by their survival status at hospital discharge, are presented in Table 1. Most patients were male (80%), with a median age of 61 years. While 86.7% experienced witnessed arrest, only 53.3% received bystander CPR. The most common initial cardiac rhythm was shockable rhythm. The median no-flow time was 12 min. Most surviving patients had poor neurological outcomes at discharge, with a median CPC score of 4.

Table 1 Baseline Characteristics of the Patients

Variables	Total (N = 30)	Survivors (n = 14)	Non-Survivors (n = 16)	P value
Male, %	24 (80)	13 (92.9)	11 (68.8)	0.175
Age, years	61 (53–76)	61 (52–73)	61 (53–78)	0.558
Comorbidities				
Hypertension	14 (46.7)	6 (42.9)	8 (50)	0.730
Diabetes mellitus	5 (16.7)	3 (21.4)	2 (12.5)	0.642
CKD	7 (23.3)	2 (14.3)	5 (31.25)	0.399
Witness arrest	26 (86.7)	13 (91.9)	13 (81.3)	0.602
Bystander CPR	16 (53.3)	9 (64.3)	7 (43.8)	0.299
Location of arrest				
Public	17 (56.7)	9 (64.3)	8 (50)	0.484
Home	13 (43.3)	5 (35.7)	8 (50)	0.484
Initial rhythm				
VF/VT	15 (50)	9 (64.3)	6 (37.5)	0.272
PEA	4 (13.3)	2 (14.3)	2 (12.5)	1.000
Asystole	11 (36.7)	3 (21.4)	8 (50)	0.142
Etiology				
Presumed cardiac cause	20 (66.7)	11 (78.6)	9 (56.2)	0.260
Non-cardiac cause	10 (33.3)	3 (21.4)	7 (43.8)	0.260
No flow time, min	12 (6–23)	10 (4–16)	12 (8–27)	0.258
CPR duration, min	20 (8–24)	15 (7–25)	20 (12–24)	0.629
Time to ROSC, min	30 (18–47)	28 (15–40)	33 (24–48)	0.160
Pre-hospital ROSC	6 (20)	1 (7.1)	5 (31.2)	0.175
APACHE II	25 (22–30)	25 (22–30)	23 (23–31)	0.796
GCS	3 (3–3)	3 (3–4)	3 (3–3)	0.585
Circulatory shock	22 (73.3)	10 (71.4)	12 (75)	1.000
TTM	9 (30)	6 (42.9)	3 (18.8)	0.236
CAG	13 (43.3)	8 (57.1)	5 (31.2)	0.269
PCI	7 (23.3)	5 (35.7)	2 (12.5)	0.204
Sedation used	26 (86.7)	12 (85.7)	14 (87.5)	1.000

(Continued)

Table 1 (Continued).

Variables	Total (N = 30)	Survivors (n = 14)	Non-Survivors (n = 16)	P value
Continuous NMB used	8 (26.7)	4 (28.6)	4 (25)	1.000
ICU LOS, days	7 (3–8)	7 (3–9)	7 (4–8)	0.613
Hospital LOS, days	7 (5–10)	8 (4–20)	7 (5–10)	0.585
CPC	5 (4–5)	4 (1–4)	5 (5–5)	<0.001

Note: Data are presented as median (interquartile range) or n (%).

Abbreviations: APACHE II, acute physiology and chronic health evaluation II; CAG, coronary angiography; CKD, chronic kidney disease; CPC, cerebral performance categories; CPR, cardiopulmonary resuscitation; GCS, Glasgow coma scales; ICU, intensive care unit; LOS, length of stay; NMB, neuromuscular blockade; PCI, percutaneous coronary intervention; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; TTM, targeted temperature management; VF, ventricular fibrillation; VT, ventricular tachycardia.

Regarding respiratory drive and ventilator parameters, the P0.1 values in the survival group were higher than those in the non-survival group (1.34 vs 0.56, 1.63 vs 0.16, and 1.28 vs 0.93 cmH₂O), but these differences did not achieve statistical significance (Table 2 and Figure 2). The tidal volume per predicted body weight was significantly lower in the

Table 2 Comparison of Respiratory Drive, Respiratory Parameters, and Sedation Depth Between Survivors and Non-Survivors Over a 72-h Period

Variables	Survivors		Non-Survivors		P value
	n	Median (IQR)	n	Median (IQR)	
P0.1, cm H₂O					0.116 ^a
24 h	14	1.34 (0.40–2.00)	16	0.56 (0.08–1.20)	0.415
48 h	13	1.63 (0.08–1.68)	14	0.16 (0.08–1.18)	0.379
72 h	9	1.28 (0–2.63)	13	0.93 (0.23–1.4)	0.644
TV/PBW, mL/kg					0.061 ^a
24 h	14	6.98 (6.23–8.02)	16	8.23 (7.20–8.84)	0.034
48 h	13	7.86 (6.47–8.43)	14	8.07 (7.75–9.98)	0.131
72 h	9	8.17 (7.40–8.75)	13	7.79 (6.90–8.08)	0.431
V_E, L/min					0.353 ^a
24 h	14	8.00 (5.70–8.55)	16	7.19 (6.94–7.85)	0.417
48 h	13	9.15 (6.10–9.40)	14	7.63 (6.90–9.40)	0.511
72 h	9	9.00 (6.20–9.10)	13	6.83 (5.27–8.09)	0.180
V_E/P0.1, L/min/cm H₂O					0.069 ^a
24 h	11	4.56 (2.84–10.25)	13	10.43 (4.06–23.83)	0.207
48 h	10	5.33 (3.67–10.07)	11	8.95 (5.60–55.89)	0.282
72 h	6	3.25 (2.36–7.06)	11	6.91 (2.77–16.00)	0.216

(Continued)

Table 2 (Continued).

Variables	Survivors		Non-Survivors		P value
	n	Median (IQR)	n	Median (IQR)	
HCO_3^- , mEq/L					0.382 ^a
24 h	14	22.90 (21.20–26.10)	16	23.15 (21.45–24.60)	0.992
48 h	14	23.35 (21.70–27.60)	14	25.05 (20.00–26.20)	0.743
72 h	11	26.2 (21.00–30.30)	13	25.20 (23.00–26.80)	0.340
pH					0.404 ^a
24 h	14	7.40 (7.37–7.46)	16	7.42 (7.37–7.45)	0.976
48 h	14	7.40 (7.32–7.47)	14	7.42 (7.40–7.46)	0.405
72 h	11	7.45 (7.34–7.51)	13	7.43 (7.39–7.44)	0.598
RASS					0.193 ^a
24 h	14	−5 (−5 to −5)	16	−5 (−5 to −3)	0.585
48 h	14	−5 (−5 to 0)	14	−5 (−5 to −4)	0.687
72 h	11	−5 (−5 to 0)	13	−5 (−5 to −4)	0.389

Note: ^aP values based on generalized estimation equation analysis, independent Data are presented as median (interquartile range) Sample size (n) varied across time points. For survivors, this was due to patients being extubated or ventilator data being unavailable following discharge or transfer. For non-survivors, the variation was due to death. Additionally, for the $\text{V}_E/\text{P}0.1$ parameter, no data were available when $\text{P}0.1 = 0$.

Abbreviations: HCO_3^- , bicarbonate; $\text{P}0.1$, airway occlusion pressure at 100 ms; PBW, predicted body weight; RASS, the Richmond Agitation Sedation Scale; TV, tidal volume; V_E , minute ventilation;

survival group during the first 24 h after admission ($P = 0.034$). Ventilation-drive coupling ($\text{VE}/\text{P}0.1$) was generally lower in the survival group than in the non-survival group, although this difference was not statistically significant (Table 2).

To evaluate the relationship between $\text{P}0.1$ values and mortality, patients with $\text{P}0.1$ values of 1.5–3.5 cmH_2O were analyzed. Measurements taken 24 h post-admission revealed an independent association with reduced in-hospital mortality (adjusted OR 0.043, 95% CI, 0.003–0.588; $P = 0.018$) (Table 3). When plotting $\text{P}0.1$ values over time for the survival and non-survival groups, patients in the survival group predominantly had $\text{P}0.1$ values within the range of 1.5–3.5 cmH_2O . In contrast, patients in the non-survival group mostly had values below 1.5 cmH_2O , falling outside the acceptable range (Figure 3).

Linear mixed model analysis showed no statistically significant associations between $\text{P}0.1$ and VE , tidal volume, lung compliance, or RASS over time (Table 4). These findings indicated that changes in $\text{P}0.1$ were not strongly correlated with these parameters during the study period.

Discussion

This study investigated the alteration of the respiratory drive, particularly $\text{P}0.1$, in comatose patients with OHCA and its correlation with sedation levels, ventilation parameters, and patient outcomes. The findings revealed a trend toward higher $\text{P}0.1$ values in survivors than in non-survivors. Additionally, survivors had significantly lower tidal volumes per predicted body weight than non-survivors. Notably, $\text{P}0.1$ levels within the optimum range of 1.5–3.5 cmH_2O were significantly associated with reduced in-hospital mortality.

To the best of our knowledge, this study is the first to investigate the respiratory drive and its association with outcomes in post-cardiac arrest patients. $\text{P}0.1$ serves as a reliable, non-invasive indicator of respiratory drive, reflecting

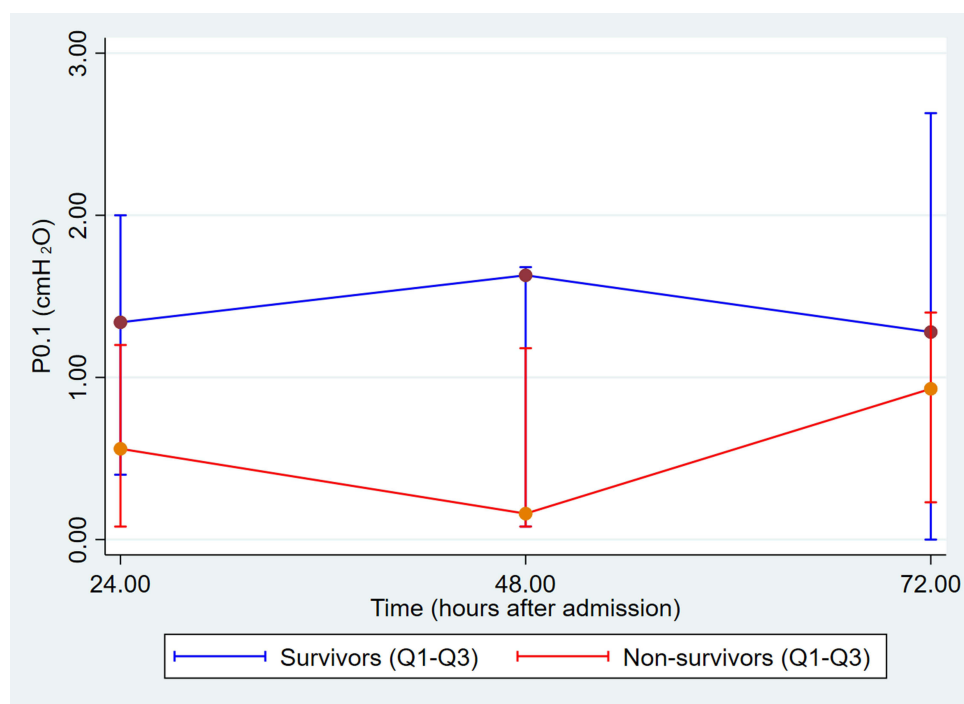


Figure 2 P0.1 trend in the survival and non-survival groups during the 72-h period post-admission.

Abbreviations: Q, quartile.

the neural effort involved in breathing. Previous studies have identified a normal range of 1.5–3.5 cmH₂O for P0.1 in mechanically ventilated critically ill patients, with deviations indicating abnormal respiratory drive.²³ Our study supports these findings by demonstrating an association between P0.1 values within this range and reduced in-hospital mortality, underscoring its potential as a prognostic tool in this patient population.

The concept of ventilation–drive coupling, which examines the relationship between respiratory drive and delivered ventilation, holds particular significance in critically ill patients. Post-cardiac arrest patients frequently exhibit a mismatch between the signals from the respiratory center and the mechanical ventilation administered, resulting in suboptimal ventilation strategies. For instance, animal studies, such as the porcine model by Yang et al,⁶ have shown that post-arrest animals require a higher respiratory drive to achieve the same level of ventilation as their non-arrested counterparts. This uncoupling can contribute to alveolar injury and adverse outcomes. In our study, the survivors

Table 3 Odds Ratio of in-Hospital Mortality for P0.1 Values (1.5–3.5 cmH₂O)

P0.1 in the Range of 1.5–3.5 cm H ₂ O	Odds Ratio (95% Confidence Interval)		Adjusted P value
	Unadjusted	Adjusted ^a	
At 24 h	0.067 (0.007–0.651)	0.043 (0.003–0.588)	0.018
At 48 h	0.190 (0.031–1.177)	–	–
At 72 h	0.577 (0.104–3.186)	–	–

Note: ^a Adjusted with witnessed arrest, bystander CPR, shockable rhythms, and prehospital ROSC.

Abbreviations: CPR, cardiopulmonary resuscitation; P0.1, airway occlusion pressure at 100 ms; ROSC, return of spontaneous circulation.

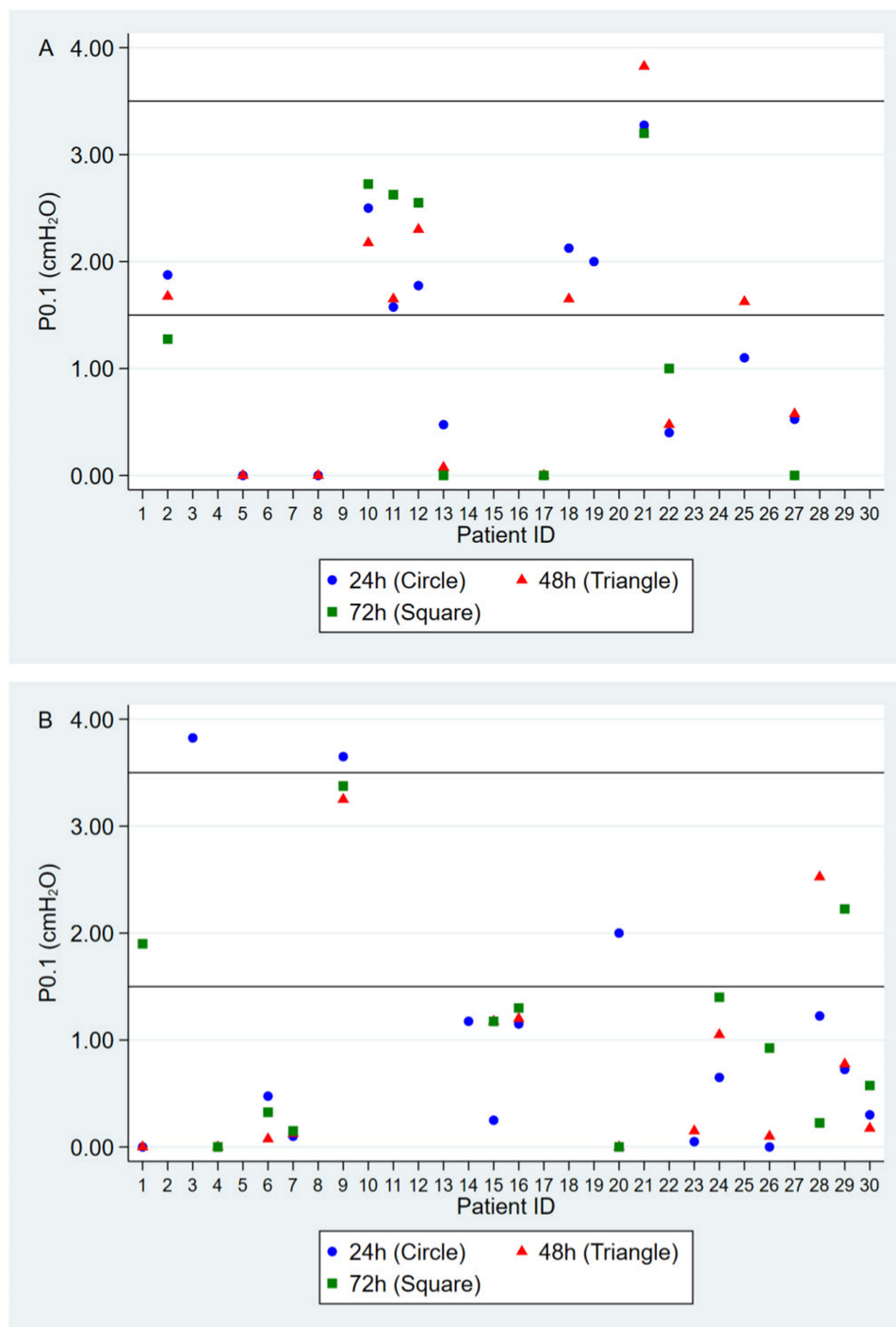


Figure 3 P0.1 values for surviving patients (A) and non-surviving patients (B).

demonstrated higher P0.1 values, reflecting a stronger respiratory drive, although the differences were not statistically significant. This discrepancy might stem from variations in the study techniques and settings. Nonetheless, the observed trend suggests that robust respiratory effort may be beneficial in the post-arrest setting.

The lower tidal volumes observed in survivors, relative to the predicted body weight, align with the principles of lung-protective ventilation aimed at reducing ventilator-induced lung injury. This strategy, commonly used to manage acute respiratory distress syndrome, may also benefit post-cardiac arrest patients. By limiting tidal volumes, the risks of

Table 4 Linear Mixed Model Association Between P0.1 and Ventilatory Parameters Over Time

Model Covariates	Marginal r^2	Conditional r^2	Variable of Interest	β (95% CI)	P value
V_E + time	1.924%	1.971%	V _E	-0.031 (-0.144 to 0.082)	0.594
TV + time	1.600%	1.609%	TV	-0.100 (-0.212 to 0.012)	0.081
Compliance + time	1.945%	1.991%	Compliance	-0.005 (-0.019 to 0.008)	0.461
RASS + time	1.901%	1.852%	RASS	0.056 (-0.054 to 0.167)	0.314

Abbreviations: P0.1, airway occlusion pressure at 100 ms; RASS, the Richmond Agitation Sedation Scale; TV, tidal volume; V_E, minute ventilation.

barotrauma and volutrauma can be minimized, potentially reducing mortality.^{24,25} Our findings suggest that survivors may have received more effective lung-protective ventilation, as evidenced by their lower tidal volumes. Therefore, P0.1 could serve as a critical metric for optimizing ventilator settings by ensuring that respiratory drive is adequately supported without over- or under-assisting the patient's respiratory efforts, thereby improving outcomes.

This study also critically examined the relationship between sedation levels, as assessed by the RASS and P0.1. Most patients were deeply sedated, with RASS scores between -5 and -4, indicating unresponsiveness. Despite this, we observed higher P0.1 values among survivors, suggesting a stronger respiratory drive, even under deep sedation. This finding is consistent with previous research conducted by Dzierba et al,²⁶ which demonstrated minimal influence of deep sedation on P0.1 in critically ill patients. The lack of a statistically significant association between RASS scores and P0.1 in our study highlights the reliability of P0.1 as a measure of respiratory drive, even in deeply sedated patients.

The interaction between sedation and the respiratory drive is complex. While deep sedation can suppress spontaneous respiratory effort, P0.1 captures the neural drive to breathe, which may persist despite sedation. In our study, the higher P0.1 values observed in survivors may indicate better overall physiological recovery, particularly in the brainstem, which regulates autonomic breathing functions. This observation may explain why survivors exhibited a higher respiratory drive than non-survivors, even though their sedation levels were similar to those of non-survivors. It is also plausible that elevated respiratory drive reflects a compensatory response to underlying respiratory or metabolic derangements.²⁷ These findings suggest that P0.1 serves as a reliable prognostic tool independent of sedation depth, offering important insights into a patient's respiratory status and recovery potential.

In addition to sedation, the use of NMBAs may also influence the interpretation of P0.1. P0.1 reflects neural respiratory drive and requires intact neuromuscular transmission for accurate measurement. Continuous infusion of NMBAs, commonly used in post-cardiac arrest patients to suppress shivering during targeted temperature management and manage ventilator asynchrony, can reduce inspiratory muscle activity and may eventually lead to low or absent P0.1 values despite preserved central respiratory drive.¹⁴ Therefore, caution is warranted when interpreting low P0.1 values in patients receiving neuromuscular blockade.

We explored various ventilatory parameters, including V_E, lung compliance, and tidal volume, to evaluate their relationships with P0.1. Although no statistically significant associations were identified, the findings suggested that P0.1 remained relatively independent of respiratory mechanics. This independence can be attributed to three factors: (1) P0.1 was assessed at end-expiratory lung volume, making the airway pressure drop unaffected by lung or chest wall recoil; (2) maneuver was performed without airflow, eliminating the influence of flow resistance on the measurement; and (3) lung volume was preserved during occlusion, minimizing the impact of vagal volume-related reflexes and the force-velocity relationships of respiratory muscles.¹⁴

Various ventilatory parameters, such as driving pressure, respiratory rate, and mechanical power, have been studied in relation to outcomes in post-cardiac arrest patients.²⁸ Among these parameters, mechanical power has emerged as a particularly noteworthy metric, as it integrates multiple aspects of ventilator-induced stress. Mechanical power has been associated with clinical outcomes in post-cardiac arrest populations; however, its calculation requires specific inputs, such as driving pressure and respiratory rate, and its clinical interpretation can be complex. To date, no randomized controlled trials have established a definitive cutoff value for mechanical power in this specific patient group.²⁸

The characteristics of our patients also reflect the typical cardiac arrest population in Thailand. Although 86.7% of arrests were witnessed, only 53.3% of patients received bystander CPR, which is consistent with previous national surveys.²⁹ Interestingly, the proportion of patients with prehospital ROSC was lower in the survival group (7.1%) than in the non-survival group (31.2%). While this finding appears to contradict the established literature,²⁰ it likely reflects a selection bias and the limitations of our small sample size. Additionally, differences in the quality and timeliness of pre-hospital emergency care in our setting may have contributed to this unexpected finding.

This study has some limitations. First, this was a single-center observational study with a limited sample size, which restricted its ability to establish causal inferences. Although advanced methods such as marginal structural models³⁰ may help address time-varying confounding in future research, our sample size was insufficient for causal modeling. Second, most post-arrest patients experienced prolonged no-flow times, with approximately 53% receiving bystander CPR, both of which could potentially influence neurological outcomes. Third, our focus was exclusively on patients with OHCA; the applicability of P0.1 in in-hospital cardiac arrest warrants further exploration, as these cases differ in characteristics and prognosis. Fourth, approximately one-quarter of patients received neuromuscular blockade, which may suppress inspiratory effort and lead to falsely low P0.1 values. Lastly, while we used P0.1, measured automatically by a specific ventilator, studies suggest that measurements from different machines are interchangeable.³¹

Conclusion

This study indicated a trend of higher respiratory drive in survivors than in non-survivors. A P0.1 value between 1.5 and 3.5 cmH₂O within the first 24 h was independently linked to reduced mortality. Survivors also demonstrated lower tidal volumes than non-survivors did. Given its simple measurement, P0.1 may serve as a neuroprognostic tool in patients following cardiac arrest. Further studies are needed to confirm these findings.

Data Sharing Statement

The data used to support the findings of this study are available from the corresponding author upon request.

Ethics Approval and Consent to Participate

This research was authorized by the Human Ethics Committee, Faculty of Medicine, Prince of Songkhla University, and was carried out in line with the Declaration of Helsinki (REC 65-310-14-4). Informed consent was provided by the patient's nearest relative or designated individual promptly and subsequently from the patient upon regaining capacity.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

References

1. Panchal AR, Bartos JA, Cabañas JG, et al. Part 3: adult basic and advanced life support: 2020 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2020;142(16_suppl_2):S366–s468. doi:10.1161/cir.0000000000000916
2. Virani SS, Alonso A, Benjamin EJ, et al. Heart disease and stroke statistics-2020 update: a report from the American Heart Association. *Circulation*. 2020;141(9):e139–e596. doi:10.1161/cir.0000000000000757
3. Lazzarin T, Tonon CR, Martins D, et al. Post-cardiac arrest: mechanisms, management, and future perspectives. *J Clin Med*. 2022;12(1):259. doi:10.3390/jcm12010259
4. Nolan JP, Neumar RW, Adrie C, et al. Post-cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication. A scientific statement from the International Liaison Committee on Resuscitation; the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Clinical Cardiology; the Council on Stroke. *Resuscitation*. 2008;79(3):350–379. doi:10.1016/j.resuscitation.2008.09.017
5. Robba C, Badenes R, Battaglini D, et al. Ventilatory settings in the initial 72 h and their association with outcome in out-of-hospital cardiac arrest patients: a preplanned secondary analysis of the targeted hypothermia versus targeted normothermia after out-of-hospital cardiac arrest (TTM2) trial. *Intensive Care Med*. 2022;48(8):1024–1038. doi:10.1007/s00134-022-06756-4
6. Yang Z, Zheng H, Lin L, et al. Alterations in respiratory mechanics and neural respiratory drive after restoration of spontaneous circulation in a porcine model subjected to different downtimes of cardiac arrest. *J Am Heart Assoc*. 2019;8(19):e012441. doi:10.1161/jaha.119.012441
7. Telias I, Junhasavasdikul D, Rittayamai N, et al. Airway occlusion pressure as an estimate of respiratory drive and inspiratory effort during assisted ventilation. *Am J Respir Crit Care Med*. 2020;201(9):1086–1098. doi:10.1164/rccm.201907-1425OC
8. Brower RG, Matthay MA, et al. Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med*. 2000;342(18):1301–1308. doi:10.1056/nejm200005043421801.
9. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med*. 1985;13(10):818–829. doi:10.1097/00003246-198510000-00009
10. Dankiewicz J, Cronberg T, Lilja G, et al. Hypothermia versus normothermia after out-of-hospital cardiac arrest. *N Engl J Med*. 2021;384(24):2283–2294. doi:10.1056/NEJMoa2100591
11. Ely EW, Truman B, Shintani A, et al. Monitoring sedation status over time in ICU patients: reliability and validity of the Richmond Agitation-Sedation Scale (RASS). *JAMA*. 2003;289(22):2983–2991. doi:10.1001/jama.289.22.2983
12. Knox DB, Lanspa MJ, Pratt CM, Kuttler KG, Jones JP, Brown SM. Glasgow coma scale score dominates the association between admission sequential organ failure assessment score and 30-day mortality in a mixed intensive care unit population. *J Crit Care*. 2014;29(5):780–785. doi:10.1016/j.jcrc.2014.05.009
13. Jacobs I, Nadkarni V, Bahr J, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the utstein templates for resuscitation registries: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, Interamerican Heart Foundation, Resuscitation Council of Southern Africa). *Resuscitation*. 2004;63(3):233–249. doi:10.1016/j.resuscitation.2004.09.008
14. Jonkman AH, de Vries HJ, Heunks LMA, de Vries LMA. Physiology of the respiratory drive in ICU patients: implications for diagnosis and treatment. *Crit Care*. 2020;24(1):104. doi:10.1186/s13054-020-2776-z
15. Scott GC, Burki NK. The relationship of resting ventilation to mouth occlusion pressure. An index of resting respiratory function. *Chest*. 1990;98(4):900–906. doi:10.1378/chest.98.4.900
16. Ninaber MK, Hamersma W, Schuerwegh A, Stolk J. Increased respiratory drive relates to severity of dyspnea in systemic sclerosis. *BMC Pulm Med*. 2014;14:57. doi:10.1186/1471-2466-14-57
17. Witten L, Gardner R, Holmberg MJ, et al. Reasons for death in patients successfully resuscitated from out-of-hospital and in-hospital cardiac arrest. *Resuscitation*. 2019;136:93–99. doi:10.1016/j.resuscitation.2019.01.031
18. Rittayamai N, Beloncle F, Goligher EC, et al. Effect of inspiratory synchronization during pressure-controlled ventilation on lung distension and inspiratory effort. *Ann Intensive Care*. 2017;7(1):100. doi:10.1186/s13613-017-0324-z
19. Ngamjaras C. n4Studies: sample size calculation for an epidemiological study on a smart device. *Siriraj Med J*. 2016;68(3):160–170.
20. Sasson C, Rogers M, Dahl J, Kellermann AL. Predictors of survival from out-of-hospital cardiac arrest: a systematic review and meta-analysis. *Circ Cardiovasc Qual Outcomes*. 2010;3(1):63–81. doi:10.1161/circoutcomes.109.889576
21. Nakagawa S, Schielzeth H, O'Hara RB. A general and simple method for obtaining R² from generalized linear mixed-effects models. *Methods Ecol Evol*. 2013;4(2):133–142. doi:10.1111/j.2041-210x.2012.00261.x
22. Nakagawa S, Johnson PCD, Schielzeth H. The coefficient of determination R² and intra-class correlation coefficient from generalized linear mixed-effects models revisited and expanded. *J R Soc Interface*. 2017;14(134):20170213. doi:10.1098/rsif.2017.0213
23. Le Marec J, Hajage D, Decavèle M, et al. High airway occlusion pressure is associated with dyspnea and increased mortality in critically ill mechanically ventilated patients. *Am J Respir Crit Care Med*. 2024;210(2):201–210. doi:10.1164/rccm.202308-1358OC
24. Battaglini D, Sottano M, Ball L, Robba C, Rocco PRM, Pelosi P. Ten golden rules for individualized mechanical ventilation in acute respiratory distress syndrome. *J Intensive Med*. 2021;1(1):42–51. doi:10.1016/j.jointm.2021.01.003
25. Nolan JP, Sandroni C, Böttiger BW, et al. European resuscitation council and European Society of intensive care medicine guidelines 2021: post-resuscitation care. *Intensive Care Med*. 2021;47(4):369–421. doi:10.1007/s00134-021-06368-4
26. Dzierba AL, Khalil AM, Derry KL, Madahar P, Beitler JR. Discordance between respiratory drive and sedation depth in critically ill patients receiving mechanical ventilation. *Crit Care Med*. 2021;49(12):2090–2101. doi:10.1097/ccm.0000000000005113

27. Vaporidi K, Akoumianaki E, Telias I, Goligher EC, Brochard L, Georgopoulos D. Respiratory drive in critically ill patients. Pathophysiology and clinical implications. *Am J Respir Crit Care Med*. 2020;201(1):20–32. doi:10.1164/rccm.201903-0596SO
28. Battaglini D, Pelosi P, Robba C. Ten rules for optimizing ventilatory settings and targets in post-cardiac arrest patients. *Crit Care*. 2022;26(1):390. doi:10.1186/s13054-022-04268-7
29. Sirikul W, Piankusol C, Wittayachamnankul B, et al. A retrospective multi-centre cohort study: pre-hospital survival factors of out-of-hospital cardiac arrest (OHCA) patients in Thailand. *Resusc Plus*. 2022;9:100196. doi:10.1016/j.resplu.2021.100196
30. Zhang Z, Jin P, Feng M, et al. Causal inference with marginal structural modeling for longitudinal data in laparoscopic surgery: a technical note. *Laparosc Endosc Robot Surg*. 2022;5(4):146–152. doi:10.1016/j.lers.2022.10.002
31. Beloncle F, Piquilloud L, Olivier P-Y, et al. Accuracy of P0.1 measurements performed by ICU ventilators: a bench study. *Ann Intens Care*. 2019;9(1):104. doi:10.1186/s13613-019-0576-x

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