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Heart rate, a poor predictor of Pulmonary Embolism

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ABSTRACT

Objective

To determine if there is a significant difference in vital signs between patients with confirmed and excluded pulmonary embolism (PE) throughout their Emergency Department presentation.

Methods

We conducted a retrospective cohort study with patients presenting with suspected PE to Monash Health Emergency Departments between July 2014 and July 2019. Vital signs were compared between patients with confirmed or excluded PE as determined by imaging (CTPA or VQ). Vital signs were compared at three unique data points: initial, minimum, and maximum values.

Results

3549 patients met inclusion criteria, 922 with confirmed PE and 2627 with excluded PE based on CTPA or VQ. Patients with PE had significant elevations in mean respiratory rates, systolic blood pressures and reduced oxygen saturations compared to patients without PE. Heart rate was not significantly different at initial and maximum datapoints.

Conclusion

Vital signs were demonstrated to be poor predictors of acute PE. Receiver operating characteristic curve analysis suggests that heart rate has poor discriminative power. AUC values for heart rate were: 0.516 (initial), 0.549 (maximum) and 0.519 (minimum). Furthermore, 95% of patients with confirmed PE did not exceed heart

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rates of 100 BPM during presentation to Emergency. The utility of elevated heart rate and other vital signs in predicting PE were not substantiated in this study.

INTRODUCTION

A pulmonary embolism (PE) refers to a blockage in the lung's arterial network due to the migration of clot material [1, 2]. Although uncommon, with a reported incidence of 60 to 70 per 100,000, mortality rates can range from up to 1% for small PEs, and between 18 to 65% in massive PEs [1]. Patient with suspected PE report symptoms of dyspnoea, haemoptysis, and pleuritic chest pain. On examination, patients may also exhibit abnormal vital signs, such as tachycardia [3, 4], tachypnoea [5] and hypotension [5, 6]. 20 per cent of patients with suspected PE return positive diagnoses, hence, the diagnostic workflow for PE must employ safe, timely and primarily non-invasive methods [7].

Definitive investigations for PE may include a ventilation-perfusion scintigraphy (V/Q scan) or computed tomography pulmonary angiography (CTPA) [2]. To minimise inappropriate use, risk stratification tools are utilised to exclude PE in low-risk patients. These include the Wells' criteria, revised Geneva score (rGeneva) and PERC rule, all of which employ vital signs to stratify risk of PE [8, 11].

The Wells' criteria have been validated in numerous clinical settings to provide an estimated pre-test probability and risk stratification for PE – assisting clinicians in selecting appropriate investigations [10]. To establish pre-test probability, the Wells' criteria allocate points to clinical factors, such as tachycardia (>100 BPM) and evidence of deep vein thrombosis (DVT) [12]. The rGeneva similarly quantifies risk but enables a finer level of stratification by ascribing greater weight to heart rates (HR) exceeding 95 BPM, compared to 75-94 BPM. The PERC rule increases suspicion for PE in patients with HR greater than 100 BPM and oxygen saturations less than 95 per cent [8]. However, a meta-analysis demonstrated the inadeuacy of these scores in the final exclusion of PE [13].

Non-specific tachycardia in emergency department (ED) patients has reportedly led to false positive screening and unnecessary diagnostic tests [14, 15]. Despite associations between abnormal vital signs and PE, these derangements are unpredictable, transient, and may even normalise during an ED stay. Thus, for a theoretically accurate stratification of risk, vital signs need to be robust and persistent, suggesting potentially limited clinical utility.

Mortality rates in patients with confirmed PE can be estimated with the Pulmonary Embolism Severity Index (PESI) and BOVA score [16, 17]. These tools utilise vital signs to inform the necessity of inpatient management. The BOVA score utilises HR and systolic blood pressure (SBP), whilst the PESI utilises HR, SBP, respiratory rate (RR), temperature, and oxygen saturation [16, 17]. These scores also rely on the persistence of deranged vital signs, which suggests that they are a potentially inaccurate representation of a patient's evolving clinical state. Hence, appraising these scores against the stability and trend of a patient's vital signs is necessary.

The adoption of the D-dimer was thought to revolutionise the diagnostic approach for PE and reduce unnecessary diagnostic imaging. However, as the D-dimer has inherently low specificity and excellent sensitivity, there is potential for false positivity that has been criticised in the literature [18, 20]. There is an evolving body of research focused on advancing and optimising the diagnostic approach for PE, resulting in novel technologies, such as focused cardiac ultrasound. However, current practice continues to place significance on vital sign derangements, which could potentially impede development of novel clinical approaches [21].

The impact of PE on vital sign derangements are diverse and unpredictable, due to the marked variation of emboli size and obstructive location [22]. Smaller emboli may remain asymptomatic, while larger and more proximal emboli may result in striking changes to a patient's clinical state, with acute hypotension, tachycardia, and reduced saturation [3, 4, 22, 23]. Considering the heterogeneity of PE presentations, an evaluation of the clinical utility of vital signs is prudent.

METHODS

Population and study design

This retrospective cohort study included adults investigated for PE attending Monash Health EDs from July 2014 to July 2019. Monash Health is in south-east Melbourne, with approximately 230,000 annual presentations across several institutions. This study was approved by Monash Health and the Monash University Human Research and Ethics Committees (Ref: RES-19-0000-535Q).

Selection

Eligible cases were identified through Emergency medical records (Symphony, EMIS Health, Leeds, UK) by filtering for patients who were suspected and investigated for a PE between July 2014 to July 2019.

The rationale to perform confirmatory imaging with VQ or CTPA was based on risk stratification on clinical presentation, vital signs, and pertinent risk factors. Patients deemed low risk, as established by a PERC rule score of 0, did not undergo imaging. Patients deemed moderate risk, commonly had D-dimer levels measured, where normal levels did not necessitate imaging, and elevations were consequently investigated.

Patients deemed high risk all underwent confirmatory imaging to further investigate PE.

To supplement the study population, data was extracted from two datasets of patients presenting to Monash Health EDs between July 2014 to July 2019. The first dataset included patients with a provisional diagnosis of PE on presentation, who were then risk stratified and investigated with VQ or CTPA imaging if deemed appropriate. The second dataset of patients included those who underwent VQ scans to rule out a diagnosis of PE, where CTPA was contraindicated. Duplicate entries were collated. Patient were excluded if they did not undergo confirmatory imaging.

Data gathered during presentations included age, gender, presenting complaint, vital signs, provisional diagnosis, confirmed diagnosis, tests ordered and subsequent results. Reported vital signs included: HR, RR, SBP, oxygen saturation and temperature. Patients with confirmatory imaging (VQ scans or CTPA) and serum biomarkers (D dimer) were identified. Patient imaging was retrieved from Carestream (Carestream Radiography Software, Carestream Health, Inc, Rochester, NY).

Patients were excluded if any of the following criteria were applicable: incomplete or missing vital signs, repeat presentations for a previously diagnosed PE, self-discharge against medical advice without investigation, death prior to imaging, having PE diagnosed in a non-Monash Health hospital, or having a history of known chronic PE.

Following exclusion, eligible patients with a confirmed PE diagnosis via CTPA or VQ were compared to those with excluded PE.

This is summarised in **Figure 1**.

Statistical analysis

Observations that were recorded included: HR, SBP, RR, oxygen saturation and temperature. For each vital sign, the following datapoints were recorded: initial observations at presentation, the highest recorded observation, and the lowest recorded observation.

The Shapiro-Wilk test was employed, with any non-normal data logarithmically transformed. The difference in mean vital signs between patients with confirmed PE and excluded PE were analysed at the corresponding initial, maximum and minimum datapoints using the Mann-Whitney U Test. The difference in means between sex (Male or Female) and age (Age > 50 or Age < 50) groups were also conducted. A value of $p < 0.05$ was considered statistically significant.

An Area Under the Receiver Operating Characteristic curve (AUC-ROC) approach was utilised to appraise the discriminative power of the following observations: HR, BO, O2 saturation and RR.

Computational statistical analysis was completed using IBM® SPSS® Statistics (v27).

RESULTS

A total of 3,549 patients met inclusion criteria; 684 (19.27%) were diagnosed with PE through CTPA, and 238 (6.71%) were diagnosed through VQ scan. Patients with negative PE on confirmatory imaging formed the control group 2627 (74.02%). 272 (7.66%) patients had PE excluded on CTPA and 2355 (66.36%) were excluded on VQ scan.

Patients with confirmed PE had significantly higher mean HR than patients with excluded PE at the minimum data point: 73.80 (15.26) versus 71.04 (13.02), $p < 0.001$ **(Table 1, 2)**. The difference in means at maximum HR, 97.92 (19.43) versus 97.01 (18.46), $p = 0.153$, and initial HR, 92.95 (19.88) versus 92.06 (19.85), $p = 0.181$, were not significant **(Table 1, 2)**.

Mean SBP, RR and O2 saturations were all significantly different in patients with confirmed PE compared to those with excluded PE at initial, maximum, and minimum datapoints **(Table 2)**. Mean temperature was significantly different at maximum and minimum data points between the two groups **(Table 2)**.

Mean HR was significantly higher in female patients with confirmed PE compared to males at the minimum data point only **(Table 3)**. Mean temperature was significantly higher in female patients with confirmed PE compared to males at the initial, maximum, and minimum data points **(Table 3)**. Oxygen saturation was significantly higher in female patients with confirmed PE compared to males at maximum and minimum data points **(Table 3)**.

Mean HR was significantly lower in patients aged > 50 years with confirmed PE, compared to patients < 50 years at the initial and maximum data point **(Table 4)**. Mean SBP was significantly higher in patients aged > 50 years with confirmed PE, compared to patients < 50 years at the initial, maximum, and minimum data points **(Table 4)**. Mean RR was significantly higher in patients aged > 50 years with confirmed PE, compared to patients <50 years at the minimum data point **(Table 4)**. Mean oxygen saturation was significantly lower in patients aged > 50 years with confirmed PE, compared to patients <50 years at the initial, maximum, and minimum data points **(Table 4)**.

An Area Under the Receiver Operating Characteristic Curve (AUC-ROC) approach was employed to determine the discriminative power of HR, SBP, RR and oxygen saturation in predicting PE **(Figure 2) (Table 5)**.

The AUC for mean HR was 0.516 (initial), 0.549 (maximum) and 0.519 (minimum). The AUC for mean SBP was 0.568 (initial), 0.605 (maximum) and 0.569

(minimum). The AUC for mean RR was 0.339 (initial), 0.346 (maximum) and 0.313 (minimum). The AUC for mean oxygen saturation was 0.559 (initial), 0.598 (maximum) and 0.557 (minimum).

DISCUSSION

Our study demonstrates that HR is not statistically different at initial (p = 0.181) and maximum (p = 0.153) data points between patients with confirmed and excluded PE **(Table 1, 2)**. While the minimum data point was significantly different (p < 0.001) between groups, ROC analysis suggests that HR has poor discriminative power and predicts PE slightly better than chance, with AUC values of 0.516 (initial), 0.549 (maximum) and 0.519 (minimum) **(Table 5)**. Thus, while these differences between groups are statistically significant, they are not clinically useful. The effectiveness of other vital signs in predicting acute PE were also poor. The corresponding AUC values were: 0.568 (initial), 0.605 (maximum) and 0.569 (minimum) for SBP, 0.339 (initial), 0.346 (maximum) and 0.313 (minimum) for RR, and 0.559 (initial), 0.598 (maximum) and 0.557 (minimum) for oxygen saturation.

This study also determined that 95% of all patients with confirmed PE at Monash Health EDs have a maximum HR between the values of 96.64 and 99.19 BPM **(Table 1)**. This suggests that most patients in the study population with confirmed PE would not satisfy the HR component of the Wells', PERC, PESI and BOVA risk stratification tools **[8, 11, 16, 17]**. Furthermore, patients with confirmed PE that were >50 years of age had a significantly lower mean HR at initial, maximum, and minimum data points compared to patients <50 years of age **(Table 4)**. This may indicate that an increase in age of greater than 50 years further reduces the efficacy of HR in predicting acute PE.

Our study suggests that the use of HR >100 or >110 BPM, in several risk stratification tools does not reliably or strongly predict acute PE. In agreement with our findings, a cohort study by Meneveau et al. **[24]**, found that HR >100 BPM in patients with confirmed PE was not an independent predictor of adverse outcomes such as inpatient death, bleeding, or recurrent PE. Specifically, in all adverse events HR >100 BPM was found in 55% of patients, whilst in cases without adverse events, HR >100 BPM was found 42% of patients (p = 0.11) **[24]**. Similarly, Wicki et al. **[25]** found that patients with confirmed PE with HR >100 BPM compared to those with HR <100 BPM had no significant difference in adverse outcomes (p = 0.051). While our study suggests that higher cut offs are not predictive of PE, a study by Keller et al. **[26]**, found that a HR value of 86 BPM may acceptably predict right ventricular dysfunction in acute PE (AUC = 0.706).

This study has several strengths and limitations. The strengths include the large population size, multi-centre study design and age and sex subgroups. The main limitation is the retrospective and observational nature of our study and the inability to follow up patient outcomes. In our data collection process, our study design did not account for patients that were negative for PE by imaging, but subsequently died from misdiagnosed PE – this diagnostic outcome would benefit from analysis in future studies. Our study has the potential for measurement error in obtaining vital signs, due to variation in technique, equipment, and personnel.

CONCLUSION

Differences in vital signs between patients with confirmed and excluded PE were inconsistently significant and poor clinical predictors of acute pathology. This study suggests that the utilisation of elevations in HR of >100 and >110 BPM within risk stratification tools are potentially poor predictors of acute PE. Future investigations into lower HR thresholds, as well as considering age in risk stratification could prove to be beneficial in optimising the diagnosis and prediction of PE.

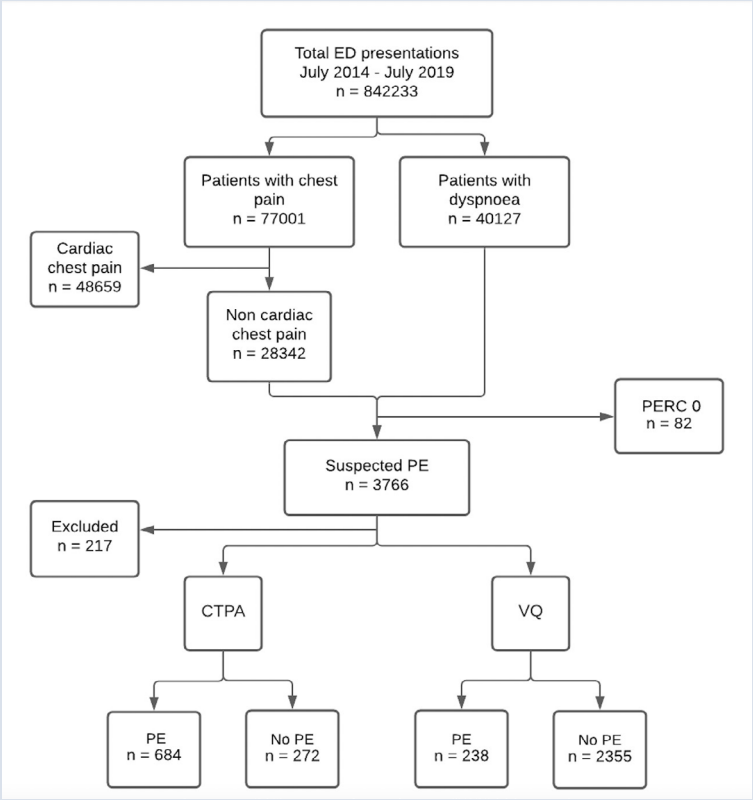

FIGURE 1 - Summary of ED presentations to Monash Health from July 2014 to July 2019 and subsequent study samples following exclusion.

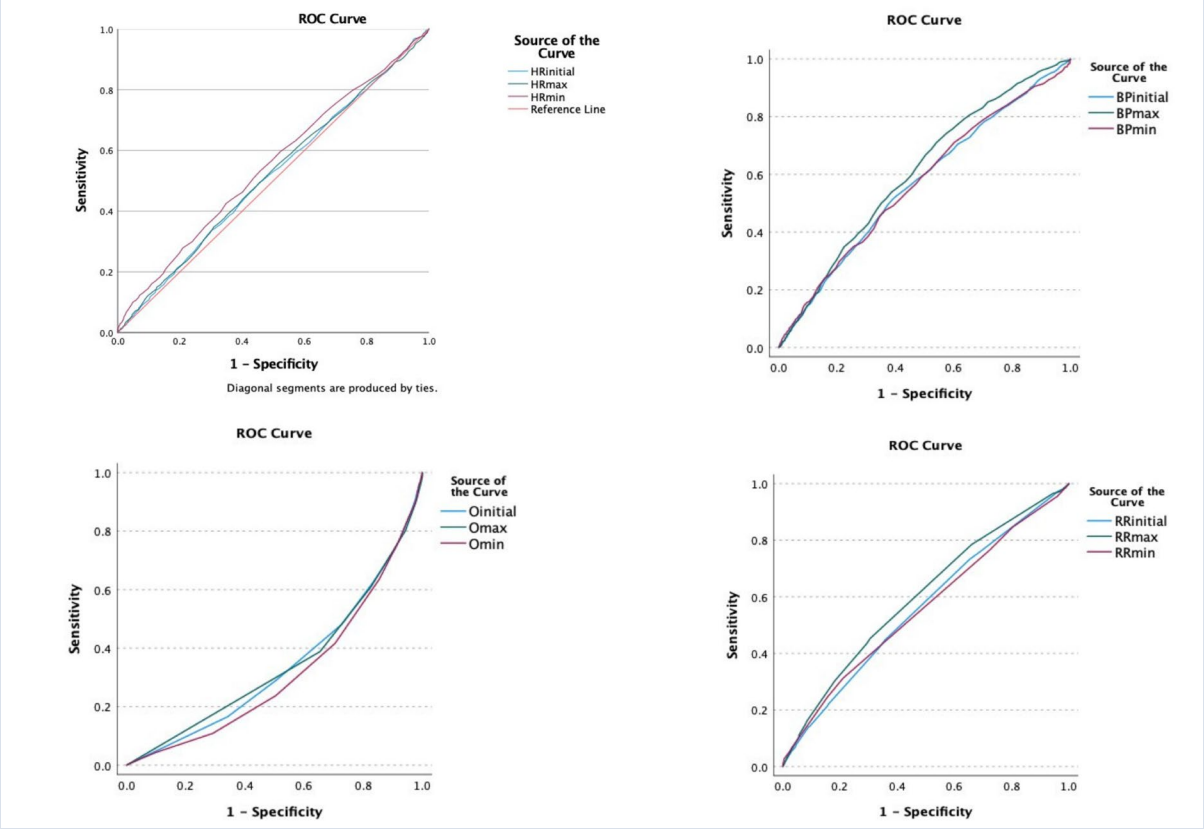

FIGURE 2 - Receiver Operating Characteristic curves for HR, SBP, RR and oxygen saturation.

TABLE 1 - Vital sign means (SD) at initial, maximum, and minimum datapoints in patients with confirmed or excluded PE

		Mean (SD) (95% Confidence interval)	
		Pulmonary embolism	*No pulmonary embolism*
Heart rate (Beats/min)	Initial	92.95 (19.88) (91.64 – 94.25)	92.06 (19.85) (91.28 – 92.85)
	Maximum	97.92 (19.43) (96.64 – 99.19)	97.01 (18.46) (96.28 – 97.74)
	Minimum	73.80 (15.26) (72.80 – 74.80)	71.04 (13.02) (70.52 – 71.55)
Respiratory rate (Breaths/min)	Initial	19.25 (3.40) (19.03 – 19.48)	18.61 (3.10) (18.49 – 18.73)
	Maximum	21.56 (3.43) (21.33 – 21.78)	20.51 (3.02) (20.39 – 20.63)
	Minimum	16.23 (2.02) (16.10 – 16.36)	15.87 (1.62) (15.80 – 15.93)
Systolic blood pressure (mmHg)	Initial	133.17 (20.41) (131.84 – 134.51)	128.80 (19.84) (128.01 – 129.58)
	Maximum	144.87 (19.68) (143.58 – 146.16)	138.24 (20.36) (137.43 – 139.04)
	Minimum	114.23 (16.95) (113.11 – 115.34)	110.45 (14.98) (109.86 – 111.04)
Oxygen saturation (%)	Initial	96.81 (2.94) (96.62 – 96.00)	98.20 (2.08) (98.12 – 98.28)
	Maximum	98.65 (1.53) (98.54 – 98.75)	99.41 (1.00) (99.37 – 99.45)
	Minimum	94.57 (3.17) (94.37 – 94.78)	96.23 (2.32) (96.13 – 96.32)
Temperature (Degrees Celsius)	Initial	36.60 (0.62) (36.56 – 36.64)	36.56 (0.60) (36.54 – 36.59)
	Maximum	36.99 (0.55) (36.95 – 37.02)	36.94 (0.54) (36.92 – 36.96)
	Minimum	36.06 (0.51) (36.02 – 36.09)	35.99 (0.45) (35.97 – 36.01)

TABLE 2 - Difference in means in patients with confirmed or excluded PE using Mann-Whitney U Test

		Mean Rank (PE; No PE)	p	Z
Heart rate (Beats/min)	Initial	1808.75; 1756.41	0.181	-1.337
	Maximum	1794.50; 1738.93	0.153	-1.430
	Minimum	1878.87; 1708.96	<0.001	-4.373
Respiratory rate (Breaths/min)	Initial	1942.19; 1699.67	<0.001	-6.201
	Maximum	2003.62; 1643.34	<0.001	-9.318
	Minimum	1920.82; 1671.44	<0.001	-6.454
Systolic blood pressure (mmHg)	Initial	1927.05; 1718.31	<0.001	-5.452
	Maximum	1997.49; 1661.00	<0.001	-8.883
	Minimum	1897.79; 1696.58	<0.001	-5.557
Oxygen saturation (%)	Initial	1346.20; 1924.88	<0.001	-15.082
	Maximum	1351.40; 1901.95	<0.001	-15.943
	Minimum	1273.35; 1929.10	<0.001	-17.068
Temperature (Degrees Celsius)	Initial	1797.37; 1727.53	0.073	-1.793
	Maximum	1766.35; 1658.25	0.004	-2.855
	Minimum	1773.42; 1655.69	0.002	-3.114

TABLE 3 - Difference in means in female patients with confirmed PE and male patients with confirmed PE using Mann-Whitney U Test

		Mean		p
		Female	Male	
Heart rate (Beats/min)	Initial	94.31	91.48	0.077
	Maximum	99.16	96.21	0.070
	Minimum	75.93	72.49	0.002
Respiratory rate (Breaths/min)	Initial	133.24	133.88	0.528
	Maximum	145.62	144.92	0.774
	Minimum	114.95	114.83	0.498
Systolic blood pressure (mmHg)	Initial	19.69	19.08	0.088
	Maximum	21.84	21.49	0.270
	Minimum	16.40	16.24	0.326
Oxygen saturation (%)	Initial	96.72	96.32	0.005
	Maximum	98.54	98.38	0.003
	Minimum	94.44	94.20	0.006
Temperature (Degrees Celsius)	Initial	36.65	36.57	0.020
	Maximum	37.02	36.95	0.012
	Minimum	36.13	36.01	<0.001

TABLE 4 - Difference in means in patients over 50 years old with confirmed and patients under 50 years old with confirmed PE using Mann-Whitney U Test

		Mean		p
		Age < 50 years	Age > 50 years	
Heart rate (Beats/min)	Initial	98.34	90.46	<0.001
	Maximum	102.89	95.22	<0.001
	Minimum	76.05	73.40	0.052
Respiratory rate (Breaths/min)	Initial	129.91	135.37	0.002
	Maximum	140.04	147.90	<0.001
	Minimum	111.51	116.55	<0.001
Systolic blood pressure (mmHg)	Initial	19.53	19.39	0.904
	Maximum	21.60	21.77	0.637
	Minimum	16.13	16.44	0.003
Oxygen saturation (%)	Initial	97.20	96.19	<0.001
	Maximum	98.83	98.29	<0.001
	Minimum	95.02	93.96	<0.001
Temperature (Degrees Celsius)	Initial	36.65	36.59	0.143
	Maximum	37.01	36.97	0.169
	Minimum	36.11	36.06	0.505

TABLE 5 - Area Under the Receiver Operating Characteristic curve for each test variable (HR, SBP, RR and oxygen saturation)

Test Result Variable(s)	Area
Heart rate	
Initial	0.516
Maximum	0.549
Minimum	0.519
Systolic blood pressure	
Initial	0.568
Maximum	0.605
Minimum	0.569
Respiratory rate	
Initial	0.339
Maximum	0.346
Minimum	0.313
Oxygen saturation	
Initial	0.559
Maximum	0.598
Minimum	0.557

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Author contributions

All authors contributed equally and validated the final version of record.

Declarations

Conflicts Of Interests

The Authors declare that there is no conflict of interest.

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Registration

No registration applicable.

Data availability statement

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

Ethical approval

This study was approved by Monash Health and the Monash University Human Research and Ethics Committees (Ref: RES-19-0000-535Q).

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