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ORIGINAL RESEARCH CONTRIBUTION

Normalization of Vital Signs Does Not Reduce the Probability of Acute Pulmonary Embolism in Symptomatic Emergency Department Patients

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Abstract

Objectives: In a patient with symptoms of pulmonary embolism (PE), the presence of an elevated pulse, respiratory rate, shock index, or decreased pulse oximetry increases pretest probability of PE. The objective of this study was to evaluate if normalization of an initially abnormal vital sign can be used as evidence to lower the suspicion for PE.

Methods: This was a prospective, noninterventional, single-center study of diagnostic accuracy conducted on adults presenting to an academic emergency department (ED), with at least one predefined symptom or sign of PE and one risk factor for PE. Clinical data, including the first four sets of vital signs, were recorded while the patient was in the ED. All patients underwent computed tomography pulmonary angiography (CTPA) and had 45-day follow-up as criterion standards. Diagnostic accuracy of each vital sign (pulse rate, respiratory rate, shock index, pulse oximetry) at each time was examined by the area under the receiver operating characteristic curve (AUC).

Results: A total of 192 were enrolled, including 35 (18%) with PE. All patients had vital signs at triage, and 174 (91%), 135 (70%), and 106 (55%) had second to fourth sets of vital signs obtained, respectively. The initial pulse oximetry reading had the highest AUC (0.63, 95% confidence interval [CI] = 0.50 to 0.76) for predicting PE, and no other vital sign at any point had an AUC over 0.60. Among patients with an abnormal pulse rate, respiratory rate, shock index, or pulse oximetry at triage that subsequently normalized, the prevalences of PE were 18, 14, 19, and 33%, respectively.

Conclusions: Clinicians should not use the observation of normalized vital signs as a reason to forego objective testing for symptomatic patients with a risk factor for PE.

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Assessment of patients with suspected pulmonary embolism (PE) in the emergency department (ED) usually occurs over several hours. During this time, clinicians receive new information and update existing data that they use to formulate their gestalt impression as to whether the patient has PE or not. In contrast, objective decision rules operate in a static point in time. The heart rate, respiratory rate, pulse oximetry, blood pressure, and the derived variable, the shock index (pulse rate/systolic blood pressure), are variably incorporated into published objective decision rules.[1–4] Most clinicians probably consider vital signs as part of their gestalt process to formulate an initial pretest probability for PE. Gestalt decision-making is critical to PE diagnosis, because a clinician will not use a decision rule, a D-dimer, or any other diagnostic test for PE unless he or she has enough internal belief that the patient might have PE to launch an investigation.

The premise of this work derives from clinical observations of the authors, which has suggested that clinicians commonly use changes in vital signs to change or

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justify their belief in determining whether a workup for PE is warranted or not. To our knowledge, no data have been published to examine this question. As a practical example, some clinicians may judge that a patient with atypical chest pain and an initial heart rate of 101 beats/min may warrant testing with a D-dimer. However, if the same physician were aware that the patient's pulse rate decreased to 66 beats/min an hour later, in the absence of medication, the clinician may not order a D-dimer. This paradigm embodies the hypothesis of this report. Here, we test if normalization of vital signs in the ED is associated with a significant change in the observed outcome probability of PE in symptomatic patients being evaluated for suspected PE.

METHODS

Study Design

This was a prospective, single-center study of diagnostic accuracy intended to assess the relative value of multiple vital sign predictor variables for PE. The enrollment methods for this study were identical to those of a previously published study.[5] This study was approved by the Carolinas Healthcare System Institutional Review Board A. All included patients provided written informed consent.

Study Setting and Population

The study was conducted at Carolinas Medical Center (Charlotte, NC), an academic, urban teaching hospital. All patients had a computed tomography pulmonary angiography (CTPA) scan performed as part of standard care. A qualified research associate collected and recorded all data variables using standards consistent with those required by the U.S. Food and Drug Administration (FDA).

Inclusion criteria required that the enroller confirm from source documentation that patients were >17 years of age and had at least one of eight predefined signs of PE or at least one of seven predefined symptoms of PE and at least one of 21 predefined risk factors for PE. These have been previously described.[6] Patients were excluded if they were unlikely to provide follow-up (imprisonment, homelessness, no telephone, history of noncompliance) or if they were pregnant, hemodynamically unstable, intubated, or unable to breathe through their mouth; had fibrinolytic treatment within 48 hours of enrollment; had PE diagnosed within the previous 6 months and were on anticoagulation; or had known active tuberculosis.

Study Protocol

Patients were enrolled in the ED from 7 AM until 11 PM, 6 days per week. Patients were identified by research associates by surveying the electronic tracking system for any CTPA scan ordered from the ED. All data were collected prospectively at the point of care by trained research associates, as opposed to reviewing medical charts at a later time. General demographic information, as well as clinical characteristics and past medical history elements, were abstracted into a preformed written 17-page template.

Computed tomography pulmonary angiography images were obtained as part of standard care on 64-slice multidetector equipment with ≤2.5 mm collimation. Intravenous contrast media was given to all patients according to local protocol using a computer-controlled mechanized timing injector in all cases. Images were obtained using energy, pitch, and rotation settings as required for the patient's body habitus. All patients had reconstructions that included transverse, coronal, and sagittal views, which were interpreted by a board-certified radiologist with fellowship training in body scanning. Radiologists interpreted a CTPA scan as positive for acute PE based on a clearly evident filling defect in the presence of adequate pulmonary vascular opacification, requiring >250 Hounsfield units measured in the main pulmonary artery. All patients also had CT venography performed and interpreted as previously described.[7]

Vital signs were recorded as part of standard care. This protocol did not mandate any change in the frequency or method of vital sign acquisition. Vital signs were obtained by a qualified medical provider, usually a nursing assistant or a registered nurse. Pulse measurements were obtained from the plethysmogram waveform of the pulse oximeter; pulse oximetry was obtained with the patient breathing room air with an FDA-cleared commercial device at triage, but we did not remove oxygen for subsequent vital signs; blood pressure was measured with cuff sphygmomanometry using the automated oscillometric stepped cuff deflation method; respiratory rate was counted by visual observation over 20 to 30 seconds; and body temperature was assessed with a digital sublingual thermometer. Research associates transferred the vital sign values recorded by the qualified medical personnel from the medical record to the research case report form. All patients were under the care of a board-certified emergency physician, but in some cases the primary care giver was a resident physician or a midlevel provider. In previous work, we have found the answer to the subjective element of the Well's criteria taken alone has similar diagnostic splitting accuracy to asking a clinician's gestalt estimate of the probability of PE being low.[8] Accordingly, at the time of informed consent, research coordinators approached the primary clinician in charge of ordering the CTPA and asked the clinician to answer the question ''Do you believe the patient has an alternative diagnosis that is more likely than PE?'' If the clinician answered yes, the coordinator asked what the diagnosis was and recorded the answer as a free text entry into the data collection template. The protocol did not assess for changes in clinician's perception of pretest probability estimate over time. Case report forms were audited against source documents by an independent monitoring firm.

Follow-up occurred at 45 and 90 days after enrollment and included telephone questionnaire and structured review of the medical record. Study duration was the index visit with follow-up through 90 days. Follow-up was targeted to determine any deaths, any adverse clinical events in general, and any imaging or diagnosis of new PE or deep vein thrombosis (DVT).

Data Analysis

The aim of this study was to measure the change in diagnostic accuracy of vital signs measured at different times. This was done by examining the graphical plots of vital signs and their diagnostic accuracy by assessing the area under the receiver operating characteristic curve (AUC) for each vital sign at each point, graphical plots of the means, and tabular report of the prevalence of PE associated with normal values for each vital sign. The sample size was estimated at $N = 190$ assuming a prevalence of PE of 15% to reliably reduce the Delong standard error for the AUC to <0.10, computed using the Wilcoxon method for individual vital signs (Stats Direct v 2.7.8, Cheshire, England).

RESULTS

Enrollment occurred from May 31, 2007, until March 3, 2008. Figure 1 shows the flow diagram of patients who were screened, consented, and completed the study. The median time between the triage vital sign set and the CTPA order was 66 minutes (first to third quartile = 4 to 120 minutes) and the median time from CTPA order to informed consent was 121 minutes (first to third quartiles = 66 to 201 minutes). Table 1 presents demographic features and the frequency of inclusion criteria for the 192 patients comprising the study population. During the 9-month period of enrollment, 687 patients, representing approximately 1.4% of all adults cared for in our ED, underwent a CTPA scan, and of these, 192 (28%) were enrolled in this study, of whom 35 had a CTPA interpreted as positive for acute PE. All 35 were treated initially with systemic heparin, followed by oral anticoagulation with warfarin sodium. Eight of the 35 also had concomitant DVT diagnosed, with ultrasound confirmation. No patient in the study had an isolated DVT without PE. On 90-day follow-up, no patient with a negative CTPA had a new PE, but one was diagnosed with DVT. At the time of patient enrollment, clinicians estimated that an alternative diagnosis was more likely than PE in 109 of 192 (57%) of patients. The most frequent alternative diagnoses named by clinicians were exacerbation of chronic lung diseases ($n = 16$), pulmonary infection ($n = 12$), chest wall pain ($n = 11$), and a variety of other conditions ($n = 11$). Clinicians were unable or unwilling to name their alternative diagnosis in 59 patients (54%).

The second, third, and fourth sets of vital signs were obtained from 174 (91%), 135 (70%), and 106 (55%) patients. The frequency and timing of repeated vital signs for PE+ patients were 89, 77, and 49%, measured at median times of 2:20, 4:16, and 5:42. Among PE– patients, frequencies of repeated vital signs were 92, 70, and 58%, measured 2:32, 4:00, and 5:10 after triage. Sixty-two patients (33%) received supplemental oxygen at some point in the ED, including 14 (40%) who were

Table 1
Summary of Demographic and Risk Factor Data

Feature	Mean or *n*	±SD or % of 192
Height (inches), mean	66	±4
Weight (pounds), mean	184	±46
Age (years), mean	54	±16
Borg score, mean	3	±3
Male	72	37
Female	118	61
Hispanic	8	4
American Indian	7	4
Black or African American	85	44
White	98	51
New onset dyspnea	120	63
Syncope	7	4
Dyspnea worse than usual	22	12
Chest pain	72	37
Hemoptysis	9	5
Cough	73	38
Unilateral limb swelling	15	8
Previous surgery	22	12
Bed rest >72 hours	16	8
Heart failure	19	10
Estrogen use	15	8
Recent trauma	1	1
Thrombophilia	1	1
Active malignancy	34	18
Prior DVT or PE	31	16
Active connective tissue disease	7	4
Pregnant or post partum	2	1
Indwelling catheter	16	8
Body mass index >36	36	19
Beta blockade use	2	1

DVT = deep vein thrombosis; PE = pulmonary embolism.

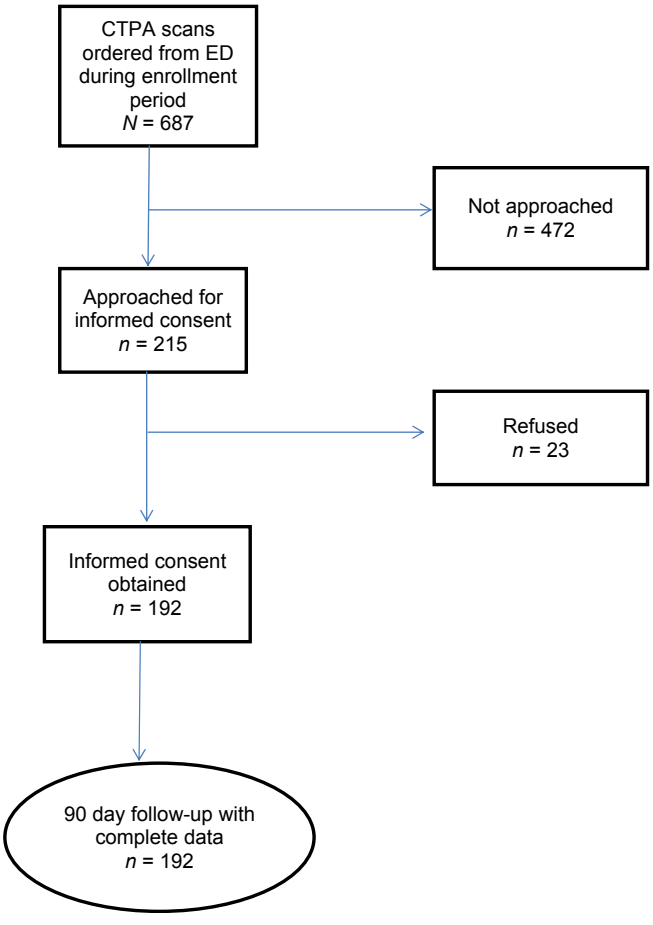

Figure 1. Flow diagram of patient enrollment. CTPA = computed tomography pulmonary angiography.

Table 2
Comparison of Mean Values of Vital Signs and Their Overall Diagnostic Accuracy at Four Measured Time Points

	Triage (N = 192)		Second (n = 174)				
Variable	Mean	±SD or 95% CI	Mean	±SD or 95% CI	% change vs. triage	±SD or 95% CI	Mean
Pulse rate (beats/min)							
PE+	94	23	88	22	−6%	16	85
PE−	90	21	87	20	−4%	16	86
AUC	0.53	0.42–0.63	0.51	0.40–0.63	0.57	0.44–0.69	0.51
Respiratory rate (breaths/min)							
PE+	19.6	4.5	19.5	21.6	−1%	27	21.6
PE−	20.7	4.0	20.2	6.2	4%	33	21.4
AUC	0.61	0.47–0.74	0.55	0.43–0.67	0.54	0.43–0.66	0.51
SaO_2							
PE+	96.4	2.8	96.6	4.0	0.3%	5.0	97.2
PE−	97.3	3.1	97.4	3.0	0.6%	3.8	96.8
AUC	0.63	0.50–0.76	0.59	0.47–0.71	0.53	0.41–0.65	0.52
Shock index							
PE+	0.73	0.26	0.71	0.24	0%	21	0.69
PE−	0.67	0.20	0.68	0.23	2%	19	0.68
AUC	0.55	0.44–0.65	0.53	0.42–0.64	0.51	0.39–0.64	0.52

AUC = area under the receiver operating characteristic curve; PE = pulmonary embolism.

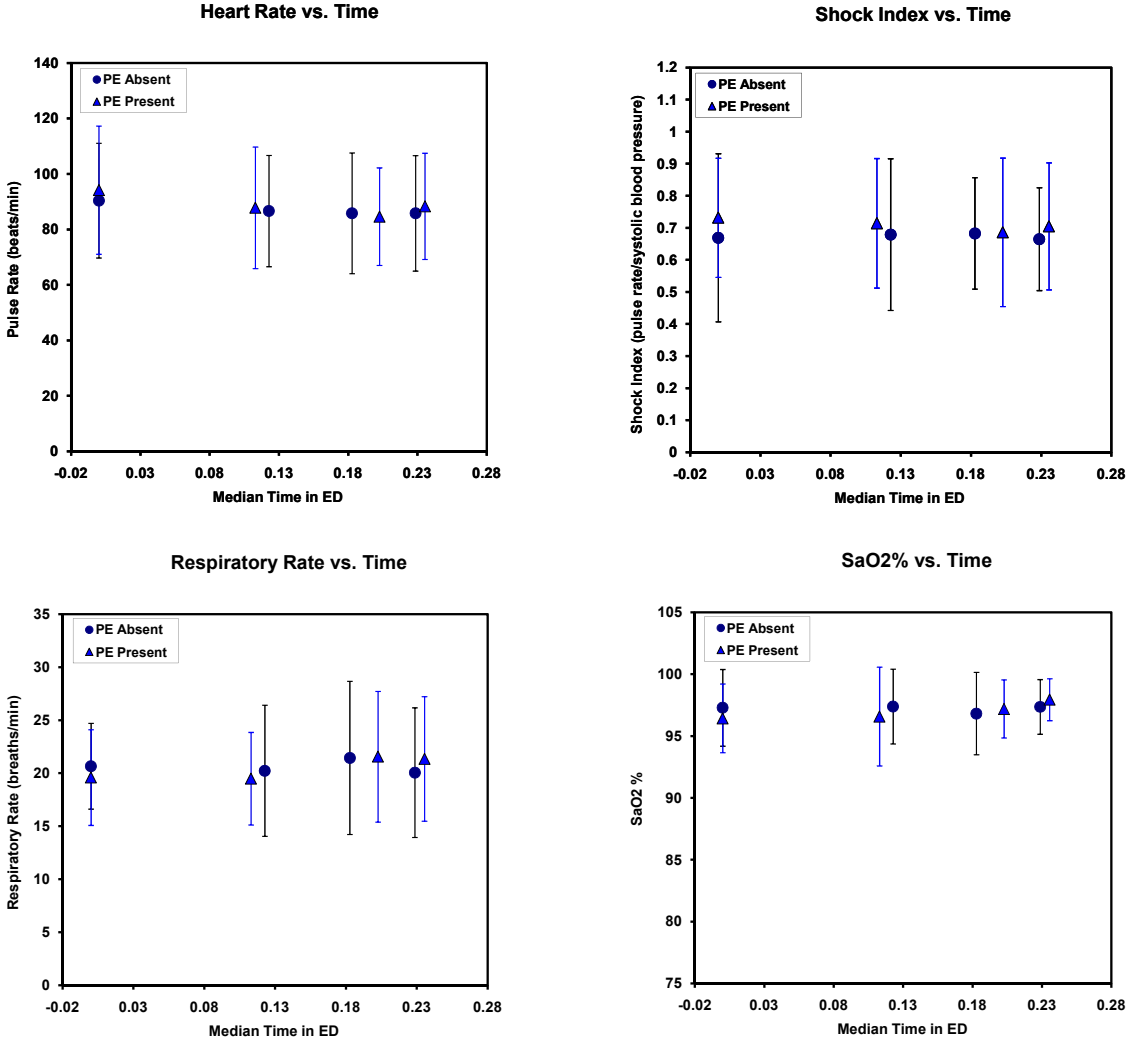

Figure 2. Plots of each vital sign over time (data are shown as means ± SDs). PE = pulmonary embolism.

Third (n = 135)			Fourth (n = 106)			
SD or 95% CI	% change vs. triage	±SD or 95% CI	Mean	±SD or 95% CI	% change vs. triage	±SD or 95% CI
18	−10%	16%	88	19	−10%	15%
22	−4%	18%	86	21	−4%	18%
0.40–0.62	0.59	0.44–0.73	0.55	0.40–0.70	0.57	0.41–0.74
6.2	5%	32%	21.4	5.9	−1%	34%
7.2	15%	43%	20.1	6.1	16%	39%
0.38–0.64	0.6	0.48–0.72	0.56	0.40–0.72	0.6	0.49–0.78
2.3	0.7%	3.4%	97.9	1.7	2.0%	3.0%
3.3	0.3%	4.0%	97.4	2.2	0.4%	3.7%
0.40–0.64	0.54	0.42–0.67	0.56	0.42–0.71	0.66	0.52–0.80
0.17	−5%	22%	0.70	0.16	−8%	23%
0.20	4%	27%	0.66	0.19	2%	23%
0.41–0.64	0.59	0.44–0.74	0.59	0.44–0.73	0.58	0.39–0.77

PE+ and 48 (30.5%) who were PE− (95% confidence interval [CI] for difference of 9.5% = −7% to 21%). Regarding the timing of the vital signs relative to diagnosis, the median time to CTPA completion was 1.3 hours (first to third quartiles = −1.0 to 4.0 hours) after the second set of vital signs was completed. We did not record the time when the radiologist's interpretation was posted or when the emergency physician became aware of the CTPA results. Table 2 presents the main findings of the report, including the pulse rate, respiratory rate, SaO_2%, shock index made at triage, and the subsequent values recorded for the next three measurements. Temperature is omitted because all 192 temperature measurements were normal at triage. Table 2 also presents the percentage change in each repeated vital sign relative to the first set of vital signs obtained in triage. The AUC for the receiver operating characteristic curve with associated 95% CIs is given for each variable and for the change in each variable. The only predictor parameter that showed a lower limit 95% CI over 0.50 (which would indicate better performance than random assignment) was the change in the fourth measured SaO_2%. The AUC values for all vital signs demonstrated consistent lack of significant diagnostic discriminative value across repeated measurements. Moreover, the percentage change in vital signs were similar between PE+ and PE− patients. For example, the pulse rate decreased by a mean (± standard deviation [SD]) of 6% (SD ± 16%) in PE+ patients and 4% (SD ± 16%) in PE− patients from triage to the first repeated vital sign set.

Figures 2A–2D plot of the mean vital sign values across the four measurements. These data suggest no clinically important difference between the mean vital sign values measured at any time point for patients with PE+ versus PE−.

Table 3 shows the number of PE+ and PE− patients, and the prevalence of PE when the vital signs were normal, using conventional cutoffs. The prevalence of PE among patients with normal vital signs did not change appreciably across repeated measurements. The data in the last column of Table 3 show that prevalence of PE did not change appreciably in patients who had abnormal vital signs at triage that normalized at any time.

DISCUSSION

This study documents that the prevalence of PE does not change appreciably among patients with an initial abnormal vital sign that then becomes normal. The probability of PE was not reduced based on normalization of any vital sign individually or all vital signs taken together. The AUC data from the receiver operating characteristic curve show that the ability of the vital signs to discriminate between the presence or absence of PE is not significantly better than random assignment at any time point. We believe that this is the first study to quantitatively examine this concept.

Vital signs are central to the clinical examination of patients with symptoms and signs suggestive of PE. Vital signs allow an estimation of pathophysiologic derangement for a broad variety of diseases that are commonly considered in the differential diagnosis for this subset of patients. The cost and risk of vital sign measurements are negligible and their availability is widespread. Accordingly, clinicians rely heavily upon the static and dynamic values of vital signs to assess need for further testing and treatment. In this context, the clinical importance of this study was its failure to support the hypothesis that the probability of PE decreases in patients with initially abnormal vital signs that subsequently become normalized.

Decision rules for PE, such as the PE rule-out criteria rule, incorporate vital sign data as criteria in the decision-making process. This particular rule requires the use of the most abnormal pulse oximetry and

Table 3
Prevalence of PE in Patients With Normal Vital Signs Measured at Four Time Points

	Triage			Second			Third			Fourth			Normalized at any time*		
Normal value	PE+	PE−	Prevalence (%)	PE+	PE−	Prevalence (%)	PE+	PE−	Prevalence (%)	PE+	PE−	Prevalence (%)	PE+	PE−	Prevalence (%)
Total†	35	157	23	31	143	22	27	108	25	17	89	19	N/A		
Pulse rate (beats/min) < 100‡	23	103	18	23	104	18	21	81	21	21	81	21	8	36	18
Respiratory rate (breaths/min) < 19	18	54	25	18	66	21	11	35	24	8	35	19	13	78	14
SaO_2 > 94%	29	124	19	28	118	19	24	86	22	16	74	18	6	25	19
Shock index < 0.8	24	120	17	23	100	19	18	80	18	11	67	14	6	12	33
All normal§	10	33	23	11	44	20	9	29	24	4	28	13	2	10	17

*Patients with vital signs that were abnormal at triage but then recorded as normal at least once during the next three measurements.
†Number of patients who had vital signs measured at triage (35 PE+ and 157 PE−, 192 total) and a second (174), third (135), and fourth (106) time.
‡Number of patients with normal vital signs, e.g., at triage 23 PE+ and 103 PE− had a pulse rate <100 beats/min.
§Number who had at least one vital sign abnormal at triage but then all subsequent vital signs were normal.
N/A = not applicable; PE = pulmonary embolism; SaO_2 = oxygen saturation.

pulse rate for interpreting the rule. This study builds on that concept by suggesting that the use of the most abnormal vital sign in gestalt decision making provides the most reliable data for accurate assessment.

LIMITATIONS

This study enrolled patients with one or more predefined signs or symptoms and one or more risk factors of PE and had a CTPA scan ordered or completed. Thus, our sample does not include a lower-risk population for whom clinicians might have correctly used ''normalization of vital signs'' as a criterion to decide not to order a CTPA and correctly discharged patients. This could have produced incorporation bias that excluded disease-negative patients and therefore would have primarily reduced the specificity of normalized vital signs, which would have created a bias toward overdepressing the AUCs values in Table 2 and overinflating the prevalences in Table 3. We did not record data to assess if and to what degree the vital sign data affected the beliefs of clinicians regarding the probability of PE. The timing, frequency, and method of performing vital signs were determined only by local standard care, as opposed to a protocol. It is possible that changes in vital signs observed in a larger sample of repeated measurements could have yielded better diagnostic utility. We did not record the administration of medications in the ED that might have affected vital signs. We are confident that all patients were breathing room air for the initial vital sign measurements. Per written protocol, all pulse oximetry measurements were supposed to be taken with the patient breathing room air. However, clinical experience suggests that this policy was not strictly followed, and we did not monitor for these deviations. Thus some later pulse oximetry readings were influenced by supplemental oxygen.

CONCLUSIONS

These data do not support the practice of using the observation that a patient's vital sign that was abnormal at triage but later is found to be normal as rationale to lower the pretest probability of pulmonary embolism in ED patients with a sign or symptom and risk factor for pulmonary embolism.

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