Usefulness of Oximetry Paradoxus to Diagnose Cardiac Tamponade

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Although echocardiography is usually diagnostic of cardiac tamponade, it may not be readily available at the point-of-care. We sought to develop and validate a measurement of respirophasic variation in the amplitude of pulse oximetry plethysmographic waveforms as a diagnostic tool for cardiac tamponade. Pulse oximetry plethysmographic waveforms were recorded, and the ratio of maximum-to-minimum measured amplitude of these waveforms from one respiratory cycle was calculated by blinded observers. Ratios from 3 consecutive respiratory cycles were then averaged to derive an "oximetry paradoxus" ratio. Cardiac tamponade was independently confirmed or excluded according to a "blinded" objective interpretation of echocardiography or right heart catheterization. Seventy four subjects were enrolled (51% men; mean age 54 ± 15 years); 19 of whom had cardiac tamponade. Oximetry paradoxus area under the curve for diagnosis of cardiac tamponade was 0.90 (95% confidence interval, 0.84 to 0.97); its diagnostic performance was superior to sphygmomanometer-measured pulsus paradoxus (area under the curve difference = 0.16, p = 0.022). In a derivation cohort (n = 37; tamponade, 9 cases), 3 diagnostic oximetry paradoxus thresholds were identified and validated in an independent validation cohort (n = 37; tamponade, 10 cases): 1.2 (100% sensitivity, 44% specificity), 1.5 (80% sensitivity, 81% specificity), and 1.7 (80% sensitivity, 89% specificity). Furthermore, oximetry paradoxus was significantly reduced after draining pericardial fluid. In conclusion, we defined and validated oximetry paradoxus as a simple and ubiquitous point-of-care test to diagnose cardiac tamponade using respirophasic changes in pulse plethysmography waveforms. This test can aid in identifying patients with cardiac tamponade, thus expediting confirmatory testing and life-saving treatment. **(Am J Cardiol 2019;123:498−506)**

Pericardial tamponade is a life-threatening condition caused by a pathologic fluid accumulation in the pericardial space, leading to increased intrapericardial pressure, compression of cardiac chambers, and eventual hemodynamic collapse. Arriving to a rapid diagnosis is essential for timely drainage of the pericardial fluid to prevent or treat cardiovascular collapse. The clinical signs and symptoms of tamponade are nonspecific, but the diagnosis can be confirmed with echocardiography or right heart catheterization (RHC). Pulsus paradoxus, defined as excessive respiratory variation in the systolic blood pressure (≥10 mm Hg), is considered pathognomonic,[1,2] but it is difficult to measure by inexperienced clinicians. Pulse oximetry plethysmographic waveform is a product of capillary volume which is dependent on stroke volume and arterial blood pressure. The amplitude of the plethysmography waveform varies with the respiratory cycle in conditions such as cardiac tamponade, establishing a graphic representation of pulsus paradoxus commonly seen in severe asthma exacerbation and pericardial tamponade.[3,4] Respiratory variation in pulse oximetry plethysmographic waveforms have been suggested as a diagnostic tool in pericardial tamponade,[5] but has not been well validated. In this investigation, we sought to identify and validate critical thresholds of respiratory variations in the amplitude of pulse plethysmography waveform to be used as a tool in diagnosing cardiac tamponade.

Methods

A dual-center prospective study was conducted in sequential and separate Derivation and Validation Cohorts of patients with suspected or confirmed pericardial tamponade at the John H. Stroger, Jr. Hospital of Cook County (Chicago, Illinois) and Rush University Medical Center (Chicago, Illinois). Consenting patients underwent a pulse oximetry plethysmography recording and a transthoracic echocardiogram or RHC to confirm or rule-out pericardial tamponade. No written consent was obtained for pulse oximetry evaluation, being a standard of care. A Health Insurance Portability and Accountability Act (HIPAA) consent to collect personal health information was obtained. In critically ill or impaired patients who were unable to participate in the informed consent process, plethysmography tracings were collected and a proper consent to retain these data was obtained after clinical

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stabilization. The study was approved by the institutional review board in each participating institution.

Patients with suspected cardiac tamponade referred for cardiology consultation or echocardiography examination were recruited. Identical exclusion criteria were applied in both cohorts, these were as follows: (1) severe reactive airway disease with active wheezing[2]; (2) known pulmonary hypertension which can ameliorate tamponade physiology[6]; (3) acute pulmonary embolism, as it may mimic tamponade physiology[7]; (4) traumatic or postsurgical pericardial hematoma, since the hemodynamic characteristics and management of these conditions differ from medical tamponade.

Basic demographics, co-morbidities, cancer history, and laboratory values were collected. The confirmed or presumed cause of pericardial effusion was tabulated. Subjects were examined by a senior cardiology fellow for jugular venous distention and pulsus paradoxus.

A pulse oximetry sensor was placed on the patient's index finger and pulse plethysmography waveforms were recorded using a commercially available Passport 2—Datascope pulse oximetry device (Mindray, Shenzhen, China), shown in Figure 1. Pulse plethysmography waveforms from ≥5 respiratory cycles were printed on gridded paper immediately before or after confirming the presence or absence of pericardial tamponade. Subsequently, the waveforms were analyzed off-line by observers blinded to the patient's clinical, echocardiography, or RHC data (GI, MJS). To ensure complete blinding, waveforms from each center were analyzed by an investigator affiliated with the partner institution. The vertical amplitudes of plethysmography waveforms were measured (nadir to peak) and the ratio from of the maximum-to-minimum amplitude from one respiratory cycle was calculated. The ratio from 3 consecutive respiratory cycles were subsequently averaged and labeled as "*oximetry paradoxus*" (Ox-P). No decision or intervention was based on the assessment of pulse oximetry waveforms. The majority of patients who underwent clinically indicated pericardiocentesis or pericardial window had a repeat pulse plethysmography recording after pericardial fluid drainage. In order to demonstrate the reproducibility of Ox-P measurement, 2 observers (YG, CJB) independently measured Ox-P in 20 plethysmography recordings. Using 2-way mixed model, the absolute interclass correlation agreement between observers was 0.987

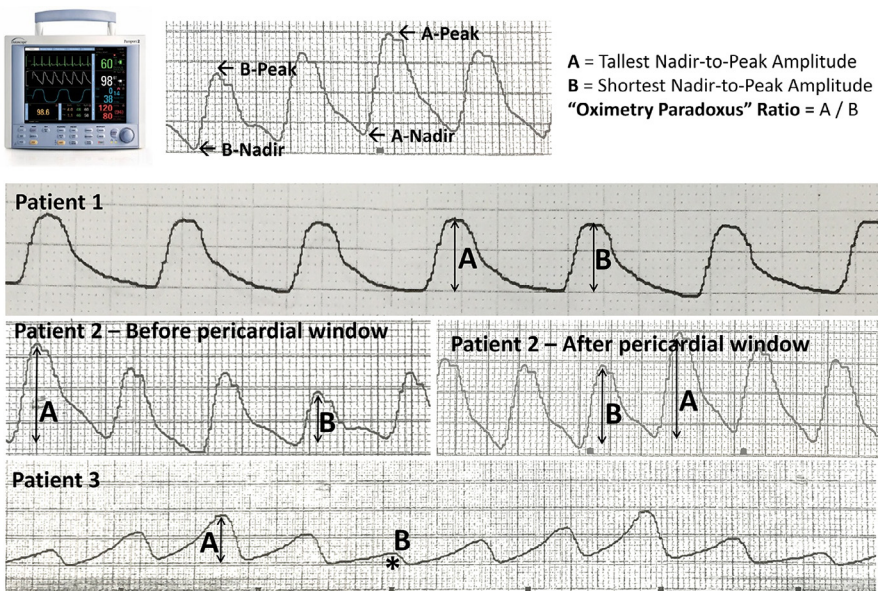

Figure 1. Pulse oximetry plathysmographic waveforms.

Top left: Image of cardiac monitor Datascope Passport 2 (Mindray; Shenzhen, China) used to record pulse oximetry plethysmographic waveform.

Top right: Depicts method of calculating "oximetry paradoxus" ratio: the vertical amplitude of the pulse oximetry waveform was measured nadir to peak. The ratio of the maximum (*A*) to minimum (*B*) amplitude within a 3 second interval was measured.

Patient 1. This was a 63-year-old with heart failure with preserved ejection fraction, diabetes mellitus, and chronic kidney disease who presented with dyspnea. Pulsus paradoxus, 6 mm Hg; oximetry paradoxus, A/B = 9 mm / 8 mm = 1.1; echocardiography, large pericardial effusion with no echocardiographic evidence of tamponade.

Patient 2. This was a 71-year-old with stage IV adenocarcinoma lung cancer who presented with dyspnea and chest pain. Pulsus paradoxus before treatment, 18 mm Hg; oximetry paradoxus before treatment, A/B = 15 mm / 8 mm = 1.9; Echocardiography, medium-sized circumferential pericardial effusion, mild right ventricular collapse (< 50% of the cardiac cycle), moderate right atrial collapse, and respirophasic changes in transmitral and tricuspid inflow velocities. The patient was diagnosed with cardiac tamponade and underwent a pericardial window procedure. Pulsus paradoxus after treatment, 8 mm Hg; oximetry paradoxus after treatment, A/B = 16 mm / 12 mm = 1.3. Echocardiography after treatment showed a small effusion with no signs of tamponade.

Patient 3. This was a 62-year-old with recent pericarditis, presented with dyspnea. Pulsus paradoxus, 45 mm Hg; oximetry Paradoxus, A/B = 8.5 mm / 3 mm = 2.83; Echocardiography showed a large, partially loculated pericardial effusion with marked right ventricular chamber collapse, diagnostic for cardiac tamponade.

(95% confidence interval [CI], 0.968 to 0.995), indicating excellent inter-rater agreement.

The diagnosis of tamponade was confirmed based on clinical, echocardiographic, or RHC findings. (1) Clinical Criteria: defined as hypotension (systolic blood pressure <100 mm Hg), tachycardia (heart rate ≥100/min), and pulsus paradoxus (≥10 mm Hg) or jugular venous distention, in association with echocardiographically proven pericardial effusion. (2) Echocardiographic Criteria: defined as echocardiographically proven pericardial effusion with one of the following criteria: (i) right ventricular collapse >50% of the cardiac cycle; (ii) excessive (≥25%) respiratory variation in early mitral inflow E-wave velocity (defined a priori), as measured by pulsed-wave Doppler at the tips of the mitral valve leaflets in diastole, and inferior vena cava dilatation (≥2.1 mm) with absent respirophasic variation (<10%) by M-mode echocardiography; (iii) right atrial collapse >50% of the cardiac cycle and inferior vena cava dilatation (≥2.1 mm) with absent respirophasic variation (<10%), as measured by M-mode echocardiography. Echocardiography interpretations were performed in a blinded fashion by cardiologists (BM, CJB) specialized in echocardiography. To ensure complete blinding, echocardiography studies from each institution were interpreted by an investigator affiliated with the other participating institution. (3) RHC: defined as equalization (≤5 mm Hg) of the right atrial pressure, right ventricular diastolic pressure, pulmonary arterial diastolic pressure, pulmonary capillary wedge pressure, and intrapericardial pressure in the presence of echocardiographically confirmed pericardial effusion. The size of the effusion was *semiquantitatively* determined by 2-dimensional (2D) echocardiography on the basis of the size of the echo-free space seen between the parietal and visceral pericardium at end-diastole: trivial (seen only in systole), small (<10 mm), moderate (10−20 mm), large (>20 mm), or very large (>25 mm).[8]

In the derivation cohort, a receiver operator characteristic (ROC) curve was used to determine the discriminatory capacity of Ox-P ratio, expressed as area under the curve (AUC) with CI. Based on the coordinates of the ROC curve, we determined *a priori* 2 desired Ox-P parameters: (1) ≥90% sensitivity threshold; (2) ≥80% specificity threshold. The diagnostic performance of each threshold was validated in the validation cohort using 2 × 2 contingency tables (test +/− versus disease +/−) to calculate sensitivity, specificity, positive predictive value, and negative predictive value.

Sample size was estimated based on findings reported in the case series by Stone et al.[5] From data reported in that study, we used pre-pericardiocentesis Ox-P values as "cases" (tamponade) and post-pericardiocentesis values as "controls". The calculated mean Ox-P values for cases and controls were 1.91 and 1.22, respectively, and the pooled standard deviations was 0.51. Assuming cases to controls enrollment ratio of 1:2, we calculated a minimum of 9 cases are needed in each cohort to detect a statistically significant difference in the mean Ox-P between tamponade cases and controls using 2-tailed independent samples *t* Test (power = 0.90, $\alpha = 0.05$). To allow for error, we targeted a sample size of 36 subjects in each cohort (12 cases and 24 controls).

The chi-square test was used to compare dichotomous variables. The 2-tailed independent-samples Student's *t* Test and the Wilcoxon test were used to compare normally-distributed and skewed continuous variables, respectively. The discriminatory capacities of various diagnostic parameters were compared using the AUC (C-statistic) and the chi-square test. The paired-samples 2-tailed *t* Test was used to compare Ox-P values pre- versus post-pericardial fluid drainage. The SPSS 23 (IBM - Armonk, New York) was used in data analysis, except for AUC comparisons which were performed using Stata 11 (StataCorp, LLC - College Station, Texas).

Results

In the period between January 2, 2013 and June 9, 2014, 74 subjects with suspected or diagnosed pericardial tamponade were enrolled. The baseline characteristics of the study subjects were summarized in Table 1. All 74 subjects underwent transthoracic echocardiography assessment and 13 underwent RHC. One subject did not have echocardiography images available for blinded evaluation, but did undergo RHC confirming cardiac tamponade. A total of 19 (26%) subjects had evidence for pericardial tamponade, 7 by echocardiography and RHC, 9 by echocardiography alone, and 3 by RHC alone. One subject satisfied the clinical and echocardiographic criteria. Table 2 summarizes the clinical and echocardiographic findings in patients with and without pericardial tamponade. Notably, patients with pericardial tamponade had lower mean systolic blood pressure, higher mean heart rate, and higher prevalence of pulsus paradoxus. Patients with tamponade were more likely to be selected for RHC. The median Ox-P ratio was 1.28. As shown in Table 2 and Figure 2, subjects with pericardial tamponade had statistically significant higher Ox-P ratios than those without evidence for tamponade (1.97 ± 0.64 vs 1.26 ± 0.24, $p < 0.001$).

As shown in Figure 3, Ox-P ratio had an excellent discriminatory capacity for pericardial tamponade (AUC 0.905; $p < 0.001$). There was a moderate correlation between Ox-P ratios and pulsus paradoxus values (Pearson's $r = 0.59$, $p < 0.001$) and between Ox-P ratios and mitral valve inflow respirophasic variation (Pearson's $r = 0.58$, $p < 0.001$). In 68 subjects who had pulsus paradoxus measurement, Ox-P ratio was associated with significantly greater discriminatory capacity than pulsus paradoxus ($p = 0.022$), providing an incremental AUC of 0.16 (Figure 3). Moreover, there was no statistically significant difference in the discriminatory capacity of Ox-P (AUC 0.90; CI 0.83 to 0.97) and the mitral inflow E-wave respirophasic changes (AUC 0.89; CI 0.82 to 0.97).

The derivation cohort consisted of 37 subjects, in whom 9 met study criteria for pericardial tamponade. As illustrated in Figure 3, Ox-P ratio was associated with an AUC of 0.90 for cardiac tamponade. Examination of the ROC curve coordinates yielded 2 Ox-P values meeting the *a priori* defined diagnostic

Table 1
Baseline characteristics of the patient population

Variables	All patients n = 74	Derivation cohort n = 37	Validation cohort n = 37	p Value
Age, years	54 ± 15	53 ± 14	54 ± 15	0.800
Female	36 (49%)	16 (43%)	20 (54%)	0.352
Institution				0.483
- JHSHCC	41 (55%)	22 (59%)	19 (51%)	
- RUMC	33 (45%)	15 (41%)	18 (49%)	
Medical history				
- Hypertension	39 (53%)	19 (51%)	17 (46%)	0.816
- Diabetes mellitus	20 (27%)	10 (27%)	10 (27%)	1.000
- Heart failure	25 (34%)	10 (27%)	15 (41%)	0.219
- Chronic kidney disease	15 (20%)	7 (19%)	8 (22%)	0.772
- Dialysis therapy	6 (8%)	2 (5%)	4 (11%)	0.394
- Hypothyroidism	6 (8%)	3 (8%)	3 (8%)	1.000
- Connective tissue disease	8 (11%)	5 (14%)	3 (8%)	0.454
- Pericarditis	3 (4%)	2 (5%)	1 (3%)	0.556
- Lung cancer	16 (22%)	8 (22%)	8 (22%)	1.000
- Breast cancer	4 (5%)	1 (3%)	3 (8%)	0.304
- Other cancers	15 (20%)	8 (22%)	7 (19%)	0.772
Presenting symptoms				
- Dyspnea	52 (70%)	26 (70%)	26 (70%)	1.000
- Fatigue	22 (30%)	9 (24%)	13 (35%)	0.309
- Chest pain	16 (22%)	10 (27%)	6 (16%)	0.259
- Dizziness	13 (18%)	5 (14%)	8 (22%)	0.359
- Edema	6 (8%)	1 (3%)	5 (14%)	0.088
- Syncope	1 (1%)	0 (0%)	1 (3%)	0.314
Suspected etiology				0.326
- Malignancy	29 (39%)	14 (38%)	15 (41%)	
- Idiopathic	10 (14%)	3 (8%)	7 (19%)	
- Uremia	10 (14%)	6 (16%)	4 (11%)	
- Connective tissue disease	8 (10%)	5 (14%)	3 (8%)	
- Heart failure	6 (8%)	2 (5%)	4 (11%)	
- Suspected viral	4 (5%)	3 (8%)	1 (3%)	
- Hypothyroidism	2 (3%)	0 (0%)	2 (5%)	
- Other	5 (7%)	4 (11%)	1 (3%)	
SBP (mm Hg)	129 ± 27	129 ± 29	128 ± 24	0.890
DBP (mm Hg)	76 ± 17	78 ± 18	74 ± 16	0.357
Heart rate (bpm)	96 ± 22	95 ± 20	97 ± 23	0.700
Respiratory rate (bcpm)	22 ± 5	21 ± 4	22 ± 6	0.458
Oxygen saturation (%)	96 ± 3	96 ± 4	97 ± 2	0.333
Pulsus paradoxus value (mm Hg)	10.3 ± 7.4	9.1 ± 8.1	11.5 ± 6.5	0.182
Pulsus paradoxus ≥10 mm Hg	33 (45%)	11 (30%)	22 (59%)	0.015
Jugular venous distention	15 (20%)	7 (19%)	8 (22%)	0.818
Creatinine (mg/dl)	1.8 ± 1.9	1.7 ± 1.7	2.0 ± 2.2	
Effusion size				0.325
- Trivial/small	5 (8%)	3 (8%)	2 (6%)	
- Moderate	23 (32%)	12 (32%)	11 (31%)	
- Large	24 (33%)	14 (38%)	10 (28%)	
- Very large	21 (29%)	8 (22%)	13 (36%)	
Tamponade present	19 (26%)	9 (24%)	10 (27%)	0.790
Tamponade confirmation method				
- Echocardiography	16/19 (84%)	8/9 (89%)	8/10 (80%)	0.596
- Right heart catheterization	10/53 (14%)	5/9 (56%)	5/10 (50%)	0.809
- Clinical	1/19 (5%)	0/9 (0%)	1/10 (10%)	0.330

bpm = beat per min; bcpm = breathing cycle per minute; DBP = diastolic blood pressure; SBP = systolic blood pressure.
Data presented as mean ± standard deviation or n (%).

performance; these were 1.24 (sensitivity ≥90%) and 1.48 (specificity ≥80%). We also identified a higher threshold of 1.74, as a potential higher specificity cutoff. For simplicity, these thresholds were rounded to the nearest 1 decimal place value.

The validation cohort consisted of 37 subjects, in whom 10 met the study criteria for cardiac tamponade. As illustrated in Figure 3, Ox-P ratio had an AUC of 0.90. Two-by-two contingency tables were constructed to validate each threshold identified in the derivation

Table 2
Baseline clinical and echocardiographic characteristics of patients with and without pericardial tamponade

Variables	All patients n = 74	Tamponade		p Value
		YES (n = 19)	NO (n = 55)	
Age, years	54 ± 15	52 ± 11	54 ± 16	0.666
Female	36 (49%)	10 (53%)	26 (47%)	0.687
Institution				0.064
- JHSHCC	41 (55%)	14 (74%)	27 (49%)	
- RUMC	33 (45%)	5 (26%)	28 (51%)	
Symptoms	67 (91%)	49 (89%)	18 (95%)	0.468
Malignant effusion	29 (39%)	12 (63%)	17 (31%)	0.013
Uremic effusion	10 (14%)	0 (0%)	10 (18%)	0.046
SBP (mm Hg)	129 ± 27	117 ± 17	133 ± 28	0.006
Heart rate (bpm)	96 ± 22	107 ± 20	92 ± 21	0.009
Respiratory rate (bcpm)	22 ± 5	23 ± 4	21 ± 5	0.283
O_2 saturation (%)	96 ± 3	96 ± 3	97 ± 3	0.488
Pulsus paradoxus value (mm Hg)	10.3 ± 7.4	15.8 ± 11.2	8.6 ± 4.7	0.023
Pulsus paradoxus >10 mm Hg	33 (49%)	13 (81%)	20 (38%)	0.003
Jugular venous distention	15 (21%)	5 (26%)	10 (19%)	0.469
Electrical alternans	8 (11%)	4 (21%)	4 (8%)	0.115
Creatinine (mg/dl)	1.8 ± 1.9	1.1 ± 1.0	2.1 ± 2.1	0.011
MV E velocity variation (%)	24 ± 11	36 ± 9	20 ± 9	< 0.001
MV E velocity variation >25%	29 (40%)	17 (94%)	12 (22%)	< 0.001
TV E velocity variation (%)	34 ± 12	38 ± 11	33 ± 12	0.134
TV E velocity variation >40%	15 (28%)	6 (43%)	9 (23%)	0.159
IVC diameter ≥2.1 cm	28 (38%)	13 (72%)	15 (27%)	0.001
Blunted (<10%) IVC collapse	24 (33%)	12 (67%)	12 (22%)	< 0.001
RHC performed	13 (18%)	11 (58%)	2 (4%)	< 0.001
Effusion size				< 0.001
- Trivial/small	5 (8%)	0 (0%)	5 (9%)	
- Moderate	23 (32%)	2 (11%)	21 (38%)	
- Large	24 (33%)	5 (28%)	19 (35%)	
- Very large	21 (29%)	11 (61%)	10 (18%)	
Oximetry paradoxus (Ox-P) ratio				< 0.001
- Mean ± SD	1.4 ± 0.50	1.97 ± 0.64	1.26 ± 0.24	
- Median (25th−75th percentile)	1.28 (1.12−1.56)	1.79 (1.49−1.79)	1.21 (1.08−1.33)	
- Range (min−max)	1.02−3.30	1.24−3.30	1.02−2.20	

bpm = beat per min; bcpm = breathing cycle per minute; E = early diastolic mitral or tricuspid inflow velocity by pulsed wave Doppler; IVC = inferior vena cava; JHSHCC = John H. Stroger, Jr. Hospital of Cook County; MV = mitral valve; RHC, right heart catheterization; RUMC = Rush University Medical Center; SBP = systolic blood pressure; SD = standard deviation; TV = tricuspid valve.

Data presented as mean ± standard deviation or n (%).

cohort. As shown in Table 3, Ox-P ≥1.2 was confirmed as a highly sensitive threshold, whereas ≥1.5 and ≥1.7 were confirmed as highly specific. The design of the study predated the 2013 American Society of Echocardiography clinical recommendations for cardiovascular imaging of patients with pericardial disease.[8] Thus, according to these guidelines, we performed additional sensitivity analyses using ≥30% (rather than 25%) as the threshold to define excessive respiratory variation in early mitral inflow velocity. In these analyses, Ox-P maintained similarly high discriminative capacity in diagnosing cardiac tamponade.

In all study subjects, 35 (47%) underwent percutaneous (n = 18) or surgically (n = 17) drainage of the pericardial fluid. The median fluid volume drained was 680 ml (25th to 75th percentile, 500 to 900 ml). Patients who underwent fluid drainage had lower blood pressure, faster heart rate, and faster respiration rate. Moreover, they had larger effusions and were more likely to have tamponade physiology (Table 4). In 22 subjects who had Ox-P measured after initial fluid drainage, the mean Ox-P decreased from a mean of 1.69 ± 0.61 pre-drainage to 1.35 ± 0.42 post-drainage (p <0.001), a mean decline of 0.34 ± 0.38 (Figure 4). In the 11 patients with tamponade, Ox-P decreased from 1.93 ± 0.70 pre-drainage to 1.52 ± 0.54 immediately post-drainage (p = 0.004).

Discussion

We prospectively derived and validated oximetry paradoxus as an objective and reproducible diagnostic test for cardiac tamponade. We identified an Ox-P of ≥1.2 to be highly sensitive for cardiac tamponade, thus a value <1.2 can effectively "rule-out" this life-threatening condition, particularly when the pretest likelihood is low. In contrast, an Ox-P ≥1.5 should raise suspicion of cardiac tamponade and trigger confirmatory testing. Our

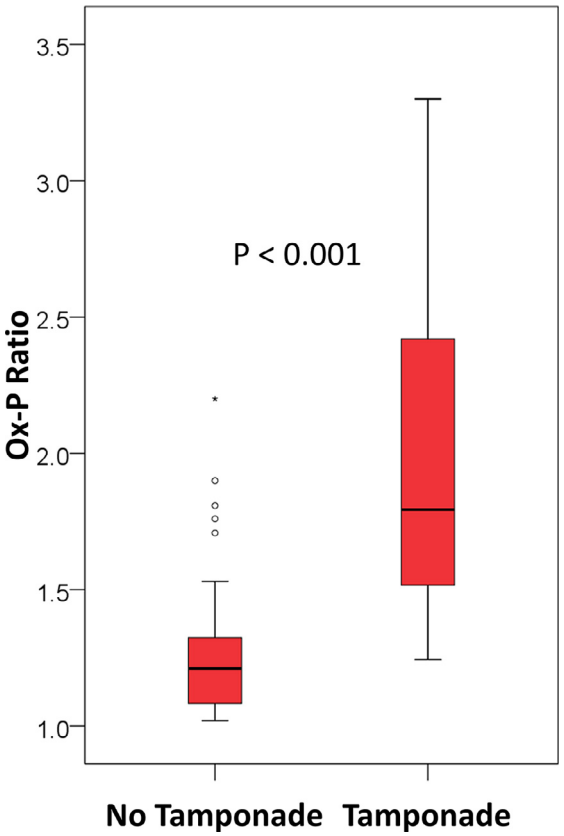

Figure 2. Oximetry paradoxus ratio in patients with and without cardiac tamponade.

investigation proposes "oximetry paradoxus" as a simple and ubiquitous diagnostic tool for cardiac tamponade.

Cardiac tamponade is a clinical diagnosis that manifests in a spectrum of hemodynamic derangements based on number of factors including: size of effusion, rate of accumulation, systemic and pulmonary pressure, and intravascular volume status. Acute tamponade presents with cardiogenic shock whereas in subacute tamponade hypotension is rather uncommon[9]; and many patients are hypertensive upon presentation.[10] Clinical diagnosis of subacute cardiac tamponade is therefore challenging. The clinical presentation is often vague with nonspecific symptoms, such as dyspnea and chest discomfort.[11] Physical exam findings are nonspecific either and may include hypotension, tachycardia, tachypnea, jugular venous distension, and peripheral edema.[12] Pulsus paradoxus, defined as the exaggerated decline in systolic blood pressure during inspiration ≥10 mm Hg, is more specific to cardiac tamponade.[2,12,13] Its prevalence in cardiac tamponade in the published literature varies from 12% to 75% (81% in our study).[14] Moreover, while often propagated as "pathognomonic", pulsus paradoxus have been reported in other conditions such as right ventricular infarction, severe hypovolemia, pulmonary embolism, obstructive lung disease, constrictive pericarditis, and pneumothorax, to name a few.[9] The "paradox" refers to the heart sounds being heard over the precordium when the radial pulse is not felt. In the normal state, during inspiration, more blood returns to the right heart and pools in the expanded pulmonary vasculature. Blood pooling in the pulmonary circulation decreases the blood return to the left heart, leading to a slight decrease in the systemic stroke volume and systolic blood pressure (<10 mm Hg) during inspiration. In cardiac tamponade, due to external constraint from pericardial pressure, the inspiratory increase in venous return cannot be accommodated by expansion of the right heart, but rather by shifting the interventricular septum to toward the left ventricle, decreasing left ventricular filling which further diminishes the stroke volume and systolic blood pressure. During the subsequent expiration, decreased systemic venous return to the right heart along with the return of the blood pooled in the pulmonary circulation to left heart lead to augmentation in systemic stroke volume and systolic blood pressure, thus exaggerating the respirophasic variation in systolic blood pressure to ≥10 mm Hg.[2] Pulsus paradoxus can be measured whereas deflating the sphygmomanometer cuff by calculating the difference in systolic blood pressure of when Korotkoff sounds are initially heard in expiration only to when those sounds are heard consistently in inspiration and expiration upon further cuff deflation. Measuring pulsus paradoxus requires significant clinical skills. In contrast, pulse oximetry is a standard element of the evaluation of acutely ill patients; thus, measuring Ox-P can be easily performed as part of a routine assessment of these patients. Our study demonstrated that Ox-P measurement is not only simple and reproducible, but also more accurate than pulsus paradoxus and as accurate as Doppler echocardiography. These findings establish the foundation for Ox-P as a powerful bedside tool in the assessment of patients with suspected cardiac tamponade. Moreover, Ox-P may be useful to monitor response to treatment as patients who underwent drainage had a significant decrease in Ox-P ratio. Notably, 4 subjects had their pericardial fluid drained but still had an oximetry paradox >1.5 (Figure 4). It is plausible that these patients had incomplete drainage or effusive-constrictive pathophysiology. In these cases, Ox-P assessment pre- and postdrainage may help raise these suspensions.

It is established that acute bronchospasm can cause respirophasic changes in systemic stroke volume manifesting as pulsus paradoxus and increased Ox-P ratio.[2] Hence, Ox-P values should be always interpreted in light of the clinical context. Moreover, pericardial fluid seen on point-of-care 2-Dechocardiography or enlarged cardiac silhouette on chest x-ray can point out to cardiac tamponade as an etiology for high Ox-P value, whereas lung exam and spirometry would clearly direct attention toward acute bronchospasm.

It is important to note that the Ox-P thresholds we derived from a specific commercially available device. However, since our Ox-P measurement is based on wave amplitude ratio rather than absolute values, it is expected for devices from other manufacturer to produce similar results, but this assumption should be validated.

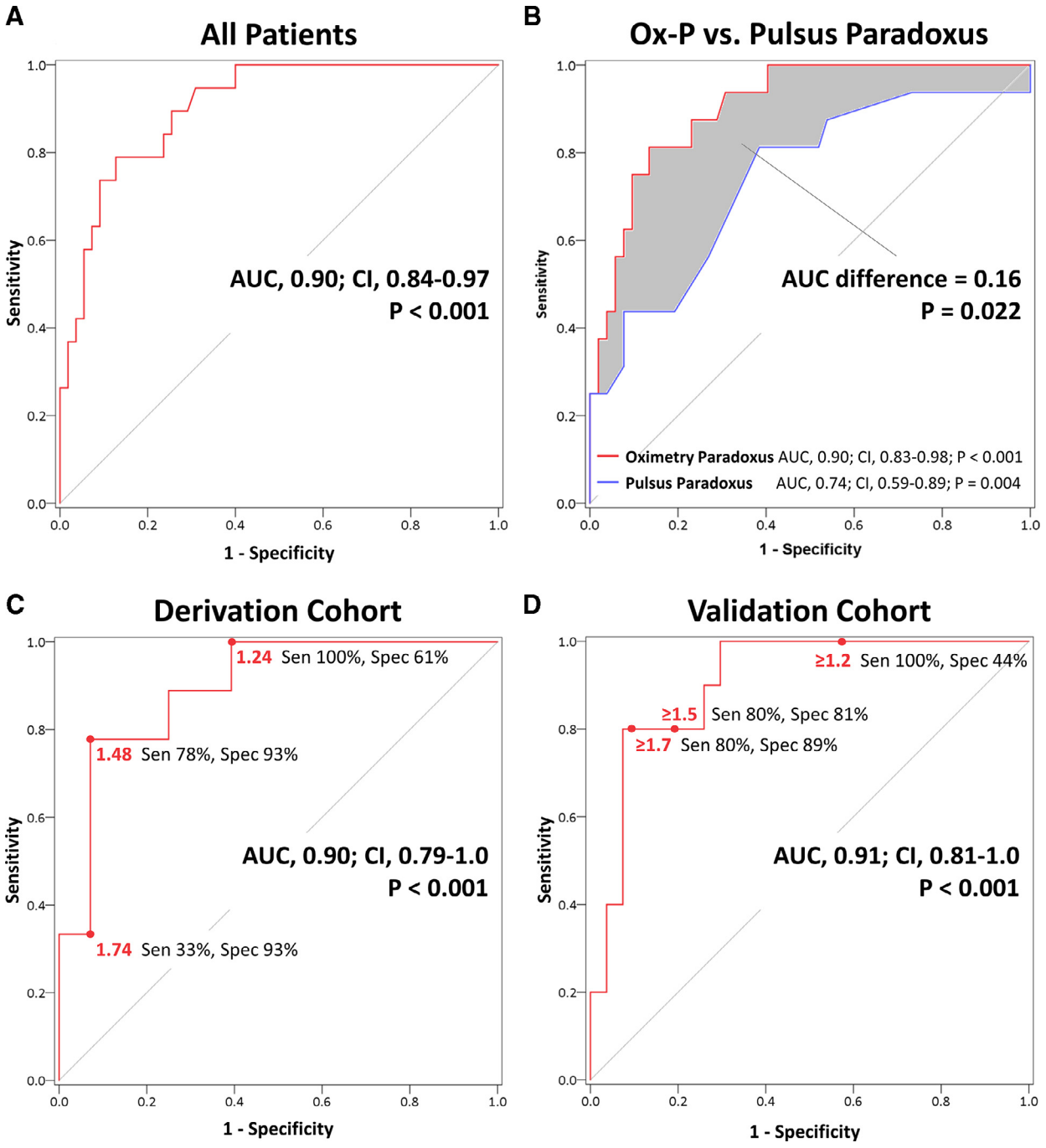

Figure 3. The discriminatory capacity of oximetry paradoxus.
The figure depicts receiver operator characteristic curves for oximetry paradosus (Ox-P) as a diagnostic tool for cardiac tamponade in all study subjects (*A*), compared with pulsus paradoxus (*B*), and in the derivation (*C*), and validation (*D*) cohorts.
AUC = area under the curve; CI = 95% confidence interval; Ox-P = oximetry paradoxus; Sen = sensitivity; Spec = Specificity.

In the future, the measurement of Ox-P can be automated using waveform analysis software embedded in the pulse oximetry equipment. Automatic warnings can be triggered when the Ox-P ratio exceeds a set threshold in order to alert healthcare providers to the possibility of cardiac tamponade.

The small sample size is an obvious limitation. This study exclusions (acute bronchospasm, pulmonary emboli, and pulmonary hypertension, etc.) may limit the applicability of the study findings. The clinical context, lung exam, chest X-ray, and 2D echocardiography can help differentiate between these distinct clinical entities. Similarly, the measurement and application of Ox-P in patients with frequent ectopy or in atrial fibrillation rhythm have not been defined in this study. Although Ox-P measurement was blinded, waveform tracing selection for

Table 3
Validation of Ox-P ration diagnostic thresholds

	Tamponade absent n = 27 (73)	Tamponade present n = 10 (27)	Diagnostic performance	
Threshold 1.2				
Ox-P ratio <1.2 n = 12 (32)	12 (44%)	0 (0%)	Sensitivity	100%
			Specificity	44%
			PPV	40%
Ox-P ratio ≥1.2 n = 25 (68)	15 (56%)	10 (100%)	NPV	100%
			Accuracy	59%
			p value	0.010
Threshold 1.5				
Ox-P ratio <1.5 n = 24 (65)	22 (81%)	2 (20%)	Sensitivity	80%
			Specificity	81%
			PPV	62%
Ox-P ratio ≥1.5 n = 13 (35)	5 (19%)	8 (80%)	NPV	81%
			Accuracy	81%
			p value	0.001
Threshold 1.7				
Ox-P ratio < 1.7 n = 26 (70)	24 (89%)	2 (20%)	Sensitivity	80%
			Specificity	89%
			PPV	73%
Ox-P ratio ≥1.7 n = 11 (30)	3 (11%)	8 (80%)	NPV	92%
			Accuracy	86%
			p value	<0.001

Two-by-two contingency table for E/e' ≥8.0 versus <8.0 test status and LAA thrombus status.
Data is presented as frequencies (%).
Sensitivity = 100%; Specificity = 41%; Positive Predictive Value = 10%; Negative Predictive Value = 100%; Positive Likelihood Ratio = 1.69.
Negative Likelihood Ratio = 0.

Table 4
Salient baseline characteristics on the basis of undergoing effusion drainage

	Effusion drained		
Variables	YES (n = 35)	NO (n = 39)	p Value
Age, years	52 ± 16	55 ± 14	0.365
Female	18 (51%)	18 (47%)	0.650
Tamponade present	18 (51%)	1 (3%)	<0.001
Institution			0.040
- JHSHCC	15 (43%)	26 (67%)	
- RUMC	20 (57%)	13 (33%)	
Symptoms	33 (94%)	34 (87%)	0.297
Malignant effusion	19 (54%)	10 (26%)	0.012
Uremic effusion	2 (6%)	8 (18%)	0.063
SBP (mm Hg)	120 ± 20	137 ± 29	0.006
Heart rate (bpm)	103 ± 20	90 ± 21	0.010
Respiratory rate (bcpm)	23 ± 6	20 ± 4	0.037
O_2 saturation (%)	96 ± 3	97 ± 3	0.532
Pulsus paradoxus >10 mm Hg	21 (64%)	12 (34%)	0.016
Jugular venous distention	10 (29%)	5 (13%)	0.103
MV E velocity variation >25%	21 (62%)	8 (21%)	<0.001
IVC diameter ≥2.1 cm	19 (56%)	19 (23%)	0.004
Blunted (<10%) IVC collapse	16 (47%)	8 (21%)	0.016
RHC performed	11 (31%)	2 (5%)	0.003
Effusion Size			<0.001
- Trivial/small	0 (0%)	5 (13%)	
- Moderate	7 (21%)	16 (41%)	
- Large	9 (26%)	15 (39%)	
- Very large	18 (53%)	3 (8%)	
Oximetry paradoxus (Ox-P) ratio			<0.001
- Mean ± SD	1.69 ± 0.60	1.22 ± 0.18	
- Median (25th−75th percentile)	1.52 (1.24−1.90)	1.21 (1.08−1.32)	
- Range (min−max)	1.02−3.30	1.02−1.77	

bpm = beat per min; bcpm = breathing cycle per minute; IVC = inferior vena cava; JHSHCC = John H. Stroger, Jr. Hospital of Cook County; MV = mitral valve; E = early diastolic mitral inflow velocity by pulsed wave Doppler; RUMC = Rush University Medical Center; RHC = right heart catheterization; SBP = systolic blood pressure; SD = standard deviation.
Data presented as mean ± standard deviation or n (%).

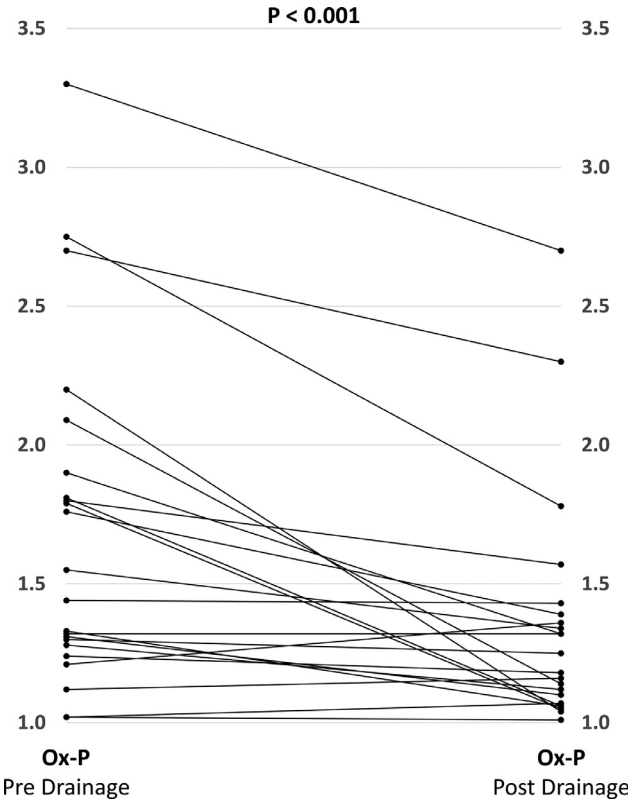

Figure 4. Oximetry paradoxus pre- and post drainage of pericardial fluid. Ox-P = oximetry paradoxus.

subsequent analyses may have been biased. Finally, not assessing the interobserver agreement in measurement of pulsus paradoxus and defining jugular venous distention is a minor limitation.

In conclusion, we defined and validated oximetry paradoxus as a simple and ubiquitous point-of-care test to screen for cardiac tamponade using respirophasic changes in the amplitude of pulse plethysmography waveforms. Identifying patients with likely cardiac tamponade using this method can trigger confirmatory testing and expedite the implementation of life-saving treatment.

Disclosures

The authors have no conflict of interest to report related to this manuscript.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at ttps://doi.org/10.1016/j.amjcard.2018.10.031.

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