Mean pulmonary arterial pressure over cardiac output slope for risk stratification in patients with unexplained dyspnea: The Math Matters

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Background: The mean pulmonary artery pressure corrected for cardiac output (mPAP/CO), measured using exercise echocardiography and calculated as the mPAP/CO slope, has improved risk stratification in various populations. However, the prognostic value and reproducibility of simpler methods remain uncertain.

Purpose: To evaluate whether the methodology employed to calculate the non-invasive mPAP/CO relationship affects prognostic accuracy and measurement consistency.

Methods: This secondary analysis of a multicenter cohort study included patients with unexplained dyspnea who underwent exercise echocardiography. The mPAP was derived from the colloid-enhanced peak tricuspid regurgitation velocity using the Chemla formula. CO was calculated by multiplying heart rate by stroke volume, determined from the velocity time integral of the left ventricular outflow tract. The mPAP and CO were measured at rest, intermediate, and peak effort. The mPAP/CO relationship was calculated using six methods: (1) 3-point linear regression, (2) 2-point slope (rest to peak), (3) 2-point slope (rest to intermediate), (4) single-point mPAP/CO at rest, (5) single-point mPAP/CO at intermediate effort and (6) single-point mPAP/CO at peak effort. The primary outcome was a composite of all-cause mortality or heart failure hospitalization. Prognostic performance was evaluated using Receiver Operating Characteristic (ROC) curves, with area under the curve (AUC) comparisons conducted using the DeLong test to assess differences between calculation methods. Reproducibility was assessed by three independent observers using intraclass correlation coefficients (ICC) with 95% confidence intervals.

Results: Among 2538 exercise echocardiograms (January 2016-March 2023), 2278 were analyzed (age 62±15 years, 53% women) The patients' characteristics are shown in Figure 1. Over a median follow-up of 19 (11-36) months, the overall event rate was 6.0%. Single-value at peak effort (AUC: 0.715) performed better than 3-point slope, 2-point slope (rest to peak), and single-value at rest (p<0.05 for comparisons), with no difference with single-value at intermediate effort (Figure 2A). ICC for single values demonstrated good reproducibility (ICC between 0.841 – 0.873), while ICC for multipoint methods was poor to moderate (ICC between 0.394-0.556) (Figure 2B).

Conclusion: For risk stratification in unexplained dyspnea, single-point mPAP/CO ratios at peak and intermediate effort show at least similar prognostic value to more complex multipoint methods. Due to significantly better reproducibility, they are attractive and reliable alternatives to the currently used multipoint mPAP/CO slope in clinical and research practice.

Figure 1. Patient characteristics

Number of patients	2278
Demographics	
Age (years)	63±15
Female, n (%)	1218 (53)
Systolic blood pressure (mmHg)	138±22
Diastolic blood pressure (mmHg)	80±14
Body Mass Index (kg.m^{-2})	27±6
Hypertension, n (%)	1028 (45)
Diabetes, n (%)	275 (12)
Atrial Fibrillation history, n (%)	406 (18)
Biomarker	
NT-proBNP (ng.L^{-1})	296±620
Echocardiography	
LAVi (mL.m^{-2})	22±14
E/A at rest	1.7±0.8
E/e' at rest	10.6±4.6
TRG (mmHg) at rest	22.6±5.9

Figure 2. A) ROC curves for each calculation method. B) Interrater variability by intraclass correlation coefficient (ICC)