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The additive value of echocardiographic pulmonary to left atrial global strain ratio in the diagnosis of pulmonary hypertension

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ABSTRACT

Background: The distinction between pre-capillary and post-capillary pulmonary hypertension (PH) is central to accurate diagnosis and appropriate therapy. We aimed to investigate the ability of the novel echocardiographic pulmonary to left atrial global strain ratio (ePLAGS) to distinguish pre-capillary from post-capillary PH and compare its discriminatory strength with the echocardiographic pulmonary to left atrial ratio (ePLAR).
Methods: Consecutive subjects with unexplained dyspnea or heart failure underwent echocardiography immediately followed by right heart catheterization. Subjects who did not satisfy the ESC/ERS criteria for PH, in atrial fibrillation or under pacemaker therapy, or with significant concomitant valvular disease were excluded. ePLAGS was calculated as peak tricuspid regurgitation velocity divided by left atrial global reservoir strain.
Results: One hundred and thirty PH subjects, as defined by right heart catheterization, were included in the analysis (pre-capillary: $n = 64$, post-capillary: $n = 66$). ePLAGS was lower in pre-capillary compared with post-capillary PH (0.19 ± 0.14 vs. 0.45 ± 0.58 m/s/%; $p = 0.02$) and significantly different between combined post- and pre-capillary PH (Cpc-PH) and isolated post-capillary PH (Ipc-PH) (0.62 ± 0.85 vs. 0.32 ± 0.19 m/s/%; $p = 0.04$). ePLAR was higher in pre-capillary as compared with post-capillary PH (0.37 ± 0.16 vs. 0.20 ± 0.08; $p < 0.001$) but did not differ between Ipc-PH and Cpc-PH. ePLAGS demonstrated stronger discriminating power than ePLAR to distinguish pre-capillary from post-capillary PH (AUC = 0.80 vs. 0.70). In the setting of post capillary PH, ePLAGS showed reasonable ability to distinguish Ipc-PH from Cpc-PH (AUC = 0.65). ePLAR, however, did not differentiate these two groups (AUC = 0.49; $p > 0.05$).
Conclusions: ePLAGS accurately differentiates pre-capillary from post-capillary PH and demonstrates higher diagnostic ability than ePLAR.

1. Introduction

Current guidelines classify pulmonary hypertension (PH) on a hemodynamic basis into pre-capillary and post-capillary PH [1]. These two groups vary considerably in pathophysiology, diagnosis and treatment. While the former is characterized by isolated pre-capillary alterations, the latter is a result of hydrostatic retro-transmission of elevated pulmonary venous pressures, often secondary to left-sided myocardial or valvular disorders. Despite distinct hemodynamic definitions, overlaps between these two PH phenotypes have been documented in multiple studies [2–4] often posing challenges to clinical decision making and appropriate therapeutic management [1,4–6].

Scali and colleagues recently introduced a new echocardiographic measure to differentiate pre-capillary from post-capillary PH. The echocardiographic pulmonary to left atrial ratio (ePLAR) was calculated by dividing tricuspid regurgitation peak velocity (TRV_{max}) by early mitral inflow velocity to early diastolic myocardial velocity (E/e′) and has been proposed by the authors as an analogous correlate for transpulmonary gradient (TPG) [7]. In their study, ePLAR demonstrated the ability to differentiate pre-capillary PH from post-capillary PH. Further, among post-capillary PH subjects, the ratio provided a modest capacity to distinguish isolated post-capillary PH (Ipc-PH) from those with combined post- and pre-capillary PH (Cpc-PH) [7].

Conceptualization of ePLAR was built on the rationale that E/e′ ratio can be considered a surrogate for true left ventricular (LV) filling pressure. However, multiple studies suggest that E/e′ might not reflect left atrial (LA) pressures in a robust manner, especially in chronic heart failure, a group that often presents with PH [8,9]. Recently, LA global strain (LA-GS) has been proposed as an echocardiographic surrogate of LV filling pressures [10], demonstrating superiority over the E/e′ ratio in patients with reduced LV performance [11,12].

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We aimed, therefore, to investigate the ability of a novel parameter, the echocardiographic pulmonary to LA global strain ratio (ePLAGS) – expressed as TRV_{max}/LA-GS – to differentiate pre-capillary PH from post-capillary PH. Further, we wished to compare the discriminatory ability of ePLAGSs with ePLAR to differentiate pre- and post-capillary PH, in addition to Ipc-PH and Cpc-PH.

2. Methods

2.1. Patient population

We included consecutive subjects referred for right heart catheterization (RHC) to the Karolinska University Hospital, Stockholm, Sweden during the period February 2014 till February 2018 for the assessment of unexplained dyspnea or heart failure. Subjects with acute coronary syndrome or cardiac surgery within a period of <1 year prior to the RHC, atrial fibrillation, pacemaker rhythm, significant concomitant valvular disease or severe (>grade 3) tricuspid regurgitation, poor image quality and those with invasive mean PA pressure (PAP_M) <25 mmHg [1] were excluded. Supplementary analysis was performed including patients with PAP_M <25 mmHg. The study conformed with the ethical guidelines laid down by the 1975 Declaration of Helsinki and was approved by the local ethics committee (DNR 2008/1695-31). All patients provided written informed consent.

2.2. Echocardiography

All patients underwent transthoracic echocardiography using a Vivid E9 ultrasound system (GE Ultrasound, Horten, Norway) equipped with a 2.5 MHz matrix array transducer in keeping with current guidelines [13]. 2D gray-scale images were acquired at 50–80 frames/s over 3 heart cycles. Images were subsequently exported and analyzed offline (EchoPAC PC, version 11.0.0.0 GE Ultrasound, Waukesha, Wisconsin) by a single experienced operator (AV) blinded to patient data. Left ventricular ejection fraction (EF) was measured using the Simpson's biplane method. Detailed assessment of the right heart was performed in keeping with recommendations [14]. TRV_{max} was measured employing continuous wave Doppler. LA-GS was assessed using speckle tracking echocardiography. LA endocardial border was traced carefully, excluding the LA appendage and pulmonary veins. Zero point was set at the onset of the QRS complex on the ECG. LA reservoir function was estimated by peak LA longitudinal strain during ventricular systole. LA-GS was calculated by averaging strain measurements between apical 4- and 2-chamber views. Early (E) and late (A) mitral flow velocities were recorded using a 5 mm pulsed Doppler (PW) sample volume, placed beyond the tips of the mitral valve in the LV. Early myocardial velocities were measured using pulse wave spectral tissue Doppler by placing a 5-mm sample volume over the septal and lateral mitral annulus. ePLAR was calculated as TRV_{max}/E/e′ as previously published [7]. ePLAGS was calculated as:

$$ePLAGS = \frac{TRV\ \ max\left(\frac{m}{s}\right)}{LA{-}GS\ (\%)}$$

2.3. Right heart catheterization

RHC was performed in all patients using a 6F Swan Ganz catheter employing jugular or femoral vein access within 1 h of their echocardiographic evaluation. Mean right atrial pressure (RAP_M), pulmonary artery systolic-, diastolic- (PAP_S, $PAP_{D)}$ and PAP_M, in addition to mean pulmonary arterial wedge pressure ($PAWP_M$) were obtained under fluoroscopic guidance after calibration with the zero-level set at the mid-thoracic line. Cardiac output (CO) was measured using the Fick's principle. Pulmonary vascular resistance (PVR) transpulmonary gradient (TPG) and diastolic pulmonary gradient (DPG) were calculated as $PVR = (PAP_M - PAWP_M)/CO$; $TPG = PAP_M - PAWP_M$ and $DPG = PAP_D - PAWP_M$. Oxygen consumption was measured breath-by-breath by dedicated gas analysis system. All pressure tracings were stored (WITT Series III, Witt Biomedical Corp., Melbourne, FL) and analyzed off-line.

2.4. Stratification of PH subjects

Subjects were classified as having reduced (<50%) or normal (≥50%) EF [13]. Post-capillary PH subjects were further stratified into Ipc-PH (DPG < 7 mmHg and/or PVR ≤ 3WU) and Cpc-PH (DPG ≥ 7 mmHg and/or PVR > 3WU) [1]. Additionally, all subjects were also stratified based on $PAWP_M$ as follows: Group I = ≤11 mmHg; Group II = 12–14 mmHg; Group III = 15–18 mmHg and Group IV = ≥19 mmHg.

2.5. Statistical methods

IBM SPSS statistics version 23.0 was employed for analysis. Normality was tested using the Shapiro-Wilk test. Continuous variables were expressed as mean ± SD or median and interquartile range and categorical variables as numbers and percentage. The paired Student's *t*-test or the Wilcoxon test was used for comparisons. Correlations were performed using the Pearson's 2-tailed test. A regression equation was derived for ePLAGS and agreement with invasive PVR was graphed using Bland-Altman plot. LA-GS and ePLAGS means were compared across $PAWP_M$ subgroups using one-way ANOVA. Receiver operator characteristics (ROC) analysis was performed to determine the discriminatory ability of ePLAR and ePLAGS to detect $PAWP_M$ >15 mmHg to distinguish pre- vs. post-capillary PH and DPG ≥7 and/or PVR >3WU to distinguish Ipc-PH from Cpc-PH in post-capillary PH. Tests were performed at 95% confidence intervals and a *p*-value ≤0.05 was considered statistically significant.

2.6. Feasibility and reproducibility

Measurements of E/e′ could be performed in all cases (100%) whereas the feasibility for LA-GS and TR-Vmax was 97% and 93%, respectively. Subjects were excluded from the analysis when measurements were not possible. Double measurements for LA-GS in 40 randomly selected subjects demonstrated a coefficient of variation of 10% with intra-class correlation coefficient 0.91 (95% CI = 0.73–0.96). Inter-observer variability together with test–retest reliability was tested in 29 individuals, who had undergone two consecutive examinations each, within 20 min, performed by two different examiners and then the two recordings analyzed again by two different readers on two different days. Test re-test analysis for the LA-GS yielded high reliability with a slightly higher coefficient of variation of 12.8%.

3. Results

3.1. Patient population

As shown in Fig. 1, of 356 patients that underwent both RHC and echocardiography investigations during the study period, 130 subjects were finally analyzed. Ninety-three subjects (71%) demonstrated normal EF. Of 130 subjects, 64 demonstrated pre-capillary PH and 66, post-capillary PH. Of the post-capillary PH subjects, 39 (59%) were classified as Ipc-PH and 27 (47%) as Cpc-PH. Forty nine percent of post-capillary PH subjects ($n = 33$) presented with reduced LVEF.

3.2. Baseline characteristics

Post-capillary PH subjects showcased higher plasma creatinine levels and higher prevalence of diabetes, hypertension and hypercholesteremia than subjects with pre-capillary PH (Table 1). PAP_M, TPG, DPG and PVR were higher among subjects with pre-capillary PH than those with post-capillary PH (Table 2). Further, subjects with pre-capillary PH demonstrated smaller end-diastolic LV volumes (LVEDV), smaller LA volumes, lower E/e′, higher LVEF and higher LA-GS as compared with post-capillary PH. ePLAR was higher in pre-capillary PH as compared with post-capillary PH subjects (0.37 ± 0.16 vs. 0.20 ± 0.08; $p < 0.001$) but did not differ between Ipc-PH and Cpc-PH ($p > 0.05$). Further, no differences in E/e′ or LA-GS were observed between Ipc-PH and Cpc-PH groups.

ePLAGS was lower in pre-capillary PH as compared with post-capillary PH (0.19 ± 0.14 vs. 0.45 ± 0.58; $p = 0.02$). Among Ipc-PH subjects, the novel ratio was even higher in Cpc-PH as compared with Ipc-PH (0.62 ± 0.85 vs. 0.32 ± 0.19; $p = 0.04$) (Table 2). ePLAGS was significantly different between groups even when patients with PAP_M <25 mmHg were included in the analysis (Table S1).

3.3. Relationship between echocardiographic and invasive metrics

ePLAGS was associated with PVR ($r = 0.28$; $p = 0.02$) and TPG ($r = 0.30$; $p = 0.01$) in post-capillary PH. Bland-Altman plots demonstrated reasonable agreement between ePLAGS and PVR (bias = 0; SD = 1.9WU) (Fig. S1). When subjects with normal EF were analyzed, ePLAGS continued to demonstrate significant association with PVR both in pre-capillary ($r = 0.40$; $p = 0.02$) and post-capillary PH ($r = 0.38$; $p = 0.03$). ePLAR, conversely, showed no associations with any of these variables.

In the total group, LA-GS demonstrated a stronger association with $PAWP_M$ ($r = -0.68$, $p < 0.001$) as compared with E/e′ ($r = 0.26$, $p = 0.03$). LA-GS was significantly associated with $PAWP_M$ both in the setting of normal ($r = -0.62$; $p < 0.01$) and reduced LVEF ($r = -0.44$; $p = 0.004$). E/e′ demonstrated a positive relationship with $PAWP_M$ in subjects with normal LVEF ($r = 0.29$; $p = 0.01$) but showcased no association in reduced LVEF ($p > 0.05$). Both LA-GS [F

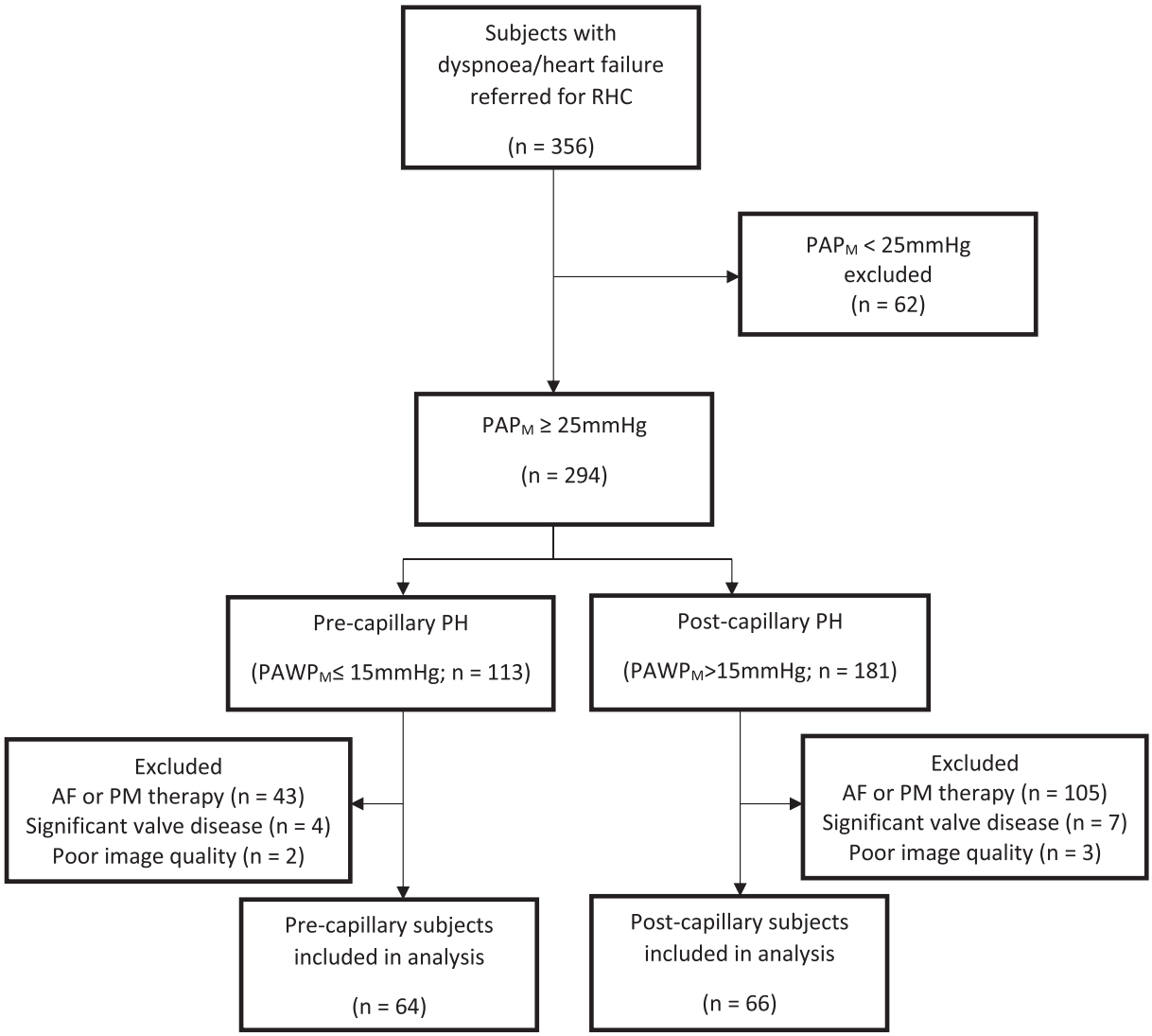

Fig. 1. Flowchart of study selection.

(3,120) = 35.9, $p < 0.001$] and ePLAGS [F (3,115) = 5.96, $p = 0.001$] were statistically different across $PAWP_M$ subgroups.

3.4. Diagnostic capability of ePLAGS

ePLAGS demonstrated a stronger ability to differentiate pre-capillary PH from post-capillary PH (AUC: 0.80, 95% CI: 0.72–0.89; $p < 0.001$) as compared with ePLAR (AUC: 0.70, 95% CI: 0.61–0.80; $p < 0.001$) (Fig. 2, Panel A & B). At an optimal cut-off limit of 0.24, ePLAGS yielded a sensitivity of 81% and specificity of 70% to distinguish pre-capillary PH from post-capillary PH. When subjects with normal EF were separately considered, ePLAGS continued to demonstrate a strong ability to distinguish PH subgroups in this subgroup (AUC: 0.73, 95% CI 0.61 to 0.85, $p < 0.001$). Further, ePLAGS demonstrated moderate ability to distinguish Ipc-PH from Cpc-PH among subjects with post-capillary PH (AUC: 0.65, 95% CI 0.52–0.79; $p = 0.05$). (Fig. 2, Panel C) ePLAR, however, did not show any significant diagnostic ability (Fig. 2, Panel D).

4. Discussion

In the present study, the novel ePLAGS ratio was able to differentiate pre-capillary PH from post-capillary PH and demonstrated greater diagnostic accuracy than ePLAR. Further, in the setting of post-capillary PH, ePLAGS retained modest ability to distinguish Ipc-PH from Cpc-PH, while ePLAR did not showcase discriminatory ability.

The recently proposed non-invasive ePLAR has demonstrated promising ability to distinguish between pre-capillary PH and post-capillary PH [7] in multiple clinical settings [15,16]. However, study limitations included a) the non-simultaneous acquisition of echocardiographic and RHC data which can lead to altered hemodynamic status and b) inclusion of subjects with atrial fibrillation and pacing therapy in the same cohort as those in sinus rhythm. We attempted to address these limitations in our study design by performing near-simultaneous studies, with RHC performed immediately (within 1 h) after echocardiography, and by including only patients with sinus rhythm.

In agreement with the findings of Scalia et al., ePLAR was significantly higher in pre-capillary PH compared with post-capillary PH in our cohort and demonstrated a strong differentiating capability. In contrast, ePLAR did not discriminate between Ipc-PH and Cpc-PH in the present group. ePLAGS, on the other hand, demonstrated significant diagnostic capability in this setting. Close to half of our subjects demonstrated reduced EF as compared to one in three in the previous investigator's patient group. The higher proportion of subjects with reduced EF in our post-capillary PH group coupled with the lack of association between E/e′ and LA pressures in the setting of reduced LVEF may offer a plausible explanation.

Table 1
Characteristics of patient population. Data presented as mean ± SD or number (%).

	Pre-capillary PH ($n = 64$)	Post-capillary PH ($n = 66$)	p-Value
Age (years)	55 ± 16	59 ± 17	0.18
Female gender	36 (53%)	29 (44%)	0.15
Medical history			
Diabetes	4 (6%)	17 (25%)	<0.01
Hypertension	17 (25%)	37 (56%)	<0.01
Hypercholesteremia	9 (13%)	19 (28%)	0.01
NYHA class			
I	7 (11%)	3 (4%)	
II	30 (47%)	16 (24%)	
III	21 (33%)	43 (65%)	
IV	6 (9%)	4 (6%)	
Clinical assessment			
Heart rate (bpm)	73 ± 12	72 ± 14	0.50
BSA (m^2)	1.87 ± 0.2	1.92 ± 0.2	0.06
BMI (kg/m^2)	25 ± 4	28 ± 6	0.04
Systolic blood pressure (mmHg)	118 ± 21	118 ± 27	0.98
Diastolic blood pressure (mmHg)	67 ± 10	65 ± 14	0.49
Laboratory			
Hemoglobin (g/L)	124 ± 24	130 ± 20	0.35
Creatinine (μmol/L)	84 ± 28	102 ± 24	0.004

IPAH, idiopathic pulmonary arterial hypertension; APAH-CTD, PH associated with connective tissue disease; CTEPH, chronic thromboembolic PH, PH-Lung, PH due to pulmonary fibrosis/chronic obstructive airway disease; NYHA, New York Heart Association; BSA, body surface area; BMI, body mass index.

Table 2
Invasive and echocardiographic data of patient population. Data shown as mean ± SD.

	Pre-capillary PH ($n = 64$)	Post-capillary PH ($n = 66$)	Ipc-PH ($n = 39$; PVR ≤ 3 and/or DPG < 7)	Cpc-PH ($n = 27$; PVR > 3 and/or DPG ≥ 7)
Right heart cath				
PAWP (mmHg)	8 ± 2	22 ± 6*	22 ± 6	22 ± 6
PAP_S (mmHg)	65 ± 16	55 ± 15*	49 ± 11	66 ± 16^
PAP_D (mmHg)	25 ± 10	22 ± 7	25 ± 8	21 ± 6
PAP_M (mmHg)	40 ± 11	36 ± 10*	33 ± 6	41 ± 10^
RAP (mmHg)	5 ± 3	10 ± 6*	10 ± 6	9 ± 6
PVR (WU)	7.3 ± 3.8	3.2 ± 2.0*	2.0 ± 0.6	5.2 ± 1.9^
DPG (mmHg)	17 ± 9	0.7 ± 6*	−0.8 ± 4.7	3.6 ± 7.5^
TPG (mmHg)	32 ± 10	14 ± 7*	10 ± 4	20 ± 8^
CO (L/min)	5.0 ± 1.8	4.9 ± 1.9	5.5 ± 1.9	3.9 ± 1.3^
Echocardiography				
EDV (ml)	91 ± 32	158 ± 77*	167 ± 77	145 ± 79
LVEF (%)	63 ± 10	49 ± 23*	46 ± 23	53 ± 22
RVIDd (mm)	44 ± 9	41 ± 7	42 ± 8	41 ± 6
RA area (cm^2)	21 ± 6	21 ± 8	22 ± 8	19 ± 7
TAPSE (mm)	18 ± 5	17 ± 6	17 ± 6	17 ± 5
TRV_{max} (m/s)	4.0 ± 0.8	3.3 ± 0.6*	3.1 ± 0.4	3.6 ± 0.6^
RVSP (mmHg)	64 ± 17	53 ± 18*	48 ± 12	64 ± 21^
LAVI (ml/m^2)	29 ± 12	46 ± 20*	45 ± 23	48 ± 16
LA-GS (%)	26 ± 10	12 ± 7*	12 ± 7	10 ± 7
E (cm/s)	71 ± 21	104 ± 35*	102 ± 36	107 ± 33
e′ (cm/s)	14 ± 8	6 ± 2*	6.4 ± 2.8	5.7 ± 1.9
E/e'_{sep}	13 ± 8	20 ± 11*	19 ± 12	21 ± 10
ePLAR (m/s)	0.37 ± 0.16	0.20 ± 0.08*	0.20 ± 0.09	0.20 ± 0.07
ePLAGS (m/s/%)	0.19 ± 0.14	0.45 ± 0.58*	0.32 ± 0.19	0.62 ± 0.85^

PH, pulmonary hypertension; Ipc-PH, isolated post-capillary pulmonary hypertension; Cpc-PH, combined post- and pre-capillary PH; PCWP, pulmonary capillary wedge pressure; PAPs, PAPd and PAPm, pulmonary artery systolic, diastolic and mean pressure; RAP, right atrial pressure; PVR, pulmonary vascular resistance; DPG, diastolic pulmonary gradient; TPG, transpulmonary gradient; CO, cardiac output; EDV, end diastolic volume; LVEF, left ventricular ejection fraction; RVIDd, right ventricular internal diameter during end-diastole; RA, right atrium; TAPSE, tricuspid annular plane systolic excursion; TRV_{max}, tricuspid regurgitation max velocity; RVSP, right ventricular systolic pressure; LAVI, left atrial volume index; LA-GS, left atrial global strain; E/e′, ratio between early transmitral and early myocardial diastolic velocity; sep, septal; ePLAR, echocardiographic pulmonary to left atrial ratio; ePLAGS, echocardiographic pulmonary to left atrial global strain ratio.
* $p < 0.05$ between pre-capillary and post-capillary PH.
^ $p < 0.05$ between Ipc-pH and Cpc-PH subgroups.

Although the E/e′ ratio has been widely adopted as an echocardiographic surrogate of LA pressure, its performance in the specific setting of left heart disease has been conflicting [8,17,18]. Mullens and colleagues suggest that the E/e′ ratio may not be reliable in the setting of large LV volumes, impaired cardiac indices and presence of resynchronization therapy seen in systolic heart failure [8]. They speculate that the higher grade of LV fibrosis and impaired output could restrict early diastolic mitral annular motion, making the relationship between inflow velocity and myocardial relaxation kinetics defective. In another study, Mitsutisho and colleagues suggest that E/e′ is reasonably accurate to assess PAWP in heart failure subjects with preserved LVEF but may not be accurate in the setting of reduced LVEF [18]. Forty-eight percent of our post-capillary PH group demonstrated reduced LV systolic function, suggesting that the accuracy of E/e′ to represent filling pressures may be limited in this cohort. This is strengthened by the observed lack of association between E/e′ and invasive $PAWP_M$ in the subjects with reduced LVEF.

In recent times, LA-GS has been proposed as an echocardiographic surrogate to represent the impact of LV filling pressures on atrial deformation [10]. The assessment of LA-GS by speckle-tracking echocardiography allows for a direct assessment of atrial myocardial deformation and is independent of Doppler-based limitations. LA reservoir strain has been shown to relate more closely to LVEDP as compared with other LA phasic strain measures and has emerged as an independent predictor of elevated filling pressures [19]. In a study including subjects with heart failure undergoing RHC and echocardiography, E/e′ demonstrated no correlation with $PAWP_M$, whereas there was a strong association with LA-GS yielding a high diagnostic accuracy for elevated $PAWP_M$ [12]. Similar results were shown by Cameli et al. who demonstrated a stronger relationship between LA-GS and filling pressures as compared with E/e′ in subjects with severely reduced LVEF [11]. In the present study, LA-GS demonstrated a strong association with $PAWP_M$, both in the setting of normal and reduced LVEF. Further, ePLAGS demonstrated a high discriminatory ability to distinguish both pre- and post-capillary PH as well as between Ipc-PH and Cpc-PH.

The presence of reduced LA-GS seen in our pre-capillary PH population as compared with published values from normal healthy populations [20] can be attributed to two plausible explanations. Firstly, strain is dependent on chamber loading. One can speculate that the presence of significant obstruction in the pulmonary capillary bed reduces inflow into the LA during the reservoir phase, thereby reducing LA-GS. We observed a modest inverse relationship between LA-GS and transpulmonary gradient in pre-capillary PH subjects which supports this hypothesis. Secondly, a recent study in subjects with severe pulmonary arterial hypertension demonstrates impaired LA-GS in the absence of LA enlargement [21] and suggests that this reflects subclinical diastolic dysfunction in this population. Our pre-capillary PH subjects demonstrated comparable LA-GS to this study and hence we speculate that low LA-GS may be owing to a combination of reduced preload and impaired relaxation. Further mechanistic studies are required to explore this in greater detail.

Limitations related to the assessment of LA-GS include current lack of standardization in image acquisition and vendor-dependency of strain measurements. In our study, strain analysis was performed by an experienced operator using a single software and additional studies may be necessary to assess reproducibility across different analysis platforms. Secondly, the absence of a healthy control group may be considered a limitation. Subsequent studies are needed to arrive at cut-off values for ePLAGS, both in healthy populations and in diagnosis-specific PH subgroups. Further, multiple sources of error related to the calculation of ePLAGS may be considered a limitation. It is to be reiterated that while this method offers promising value as a non-invasive aid in the triage

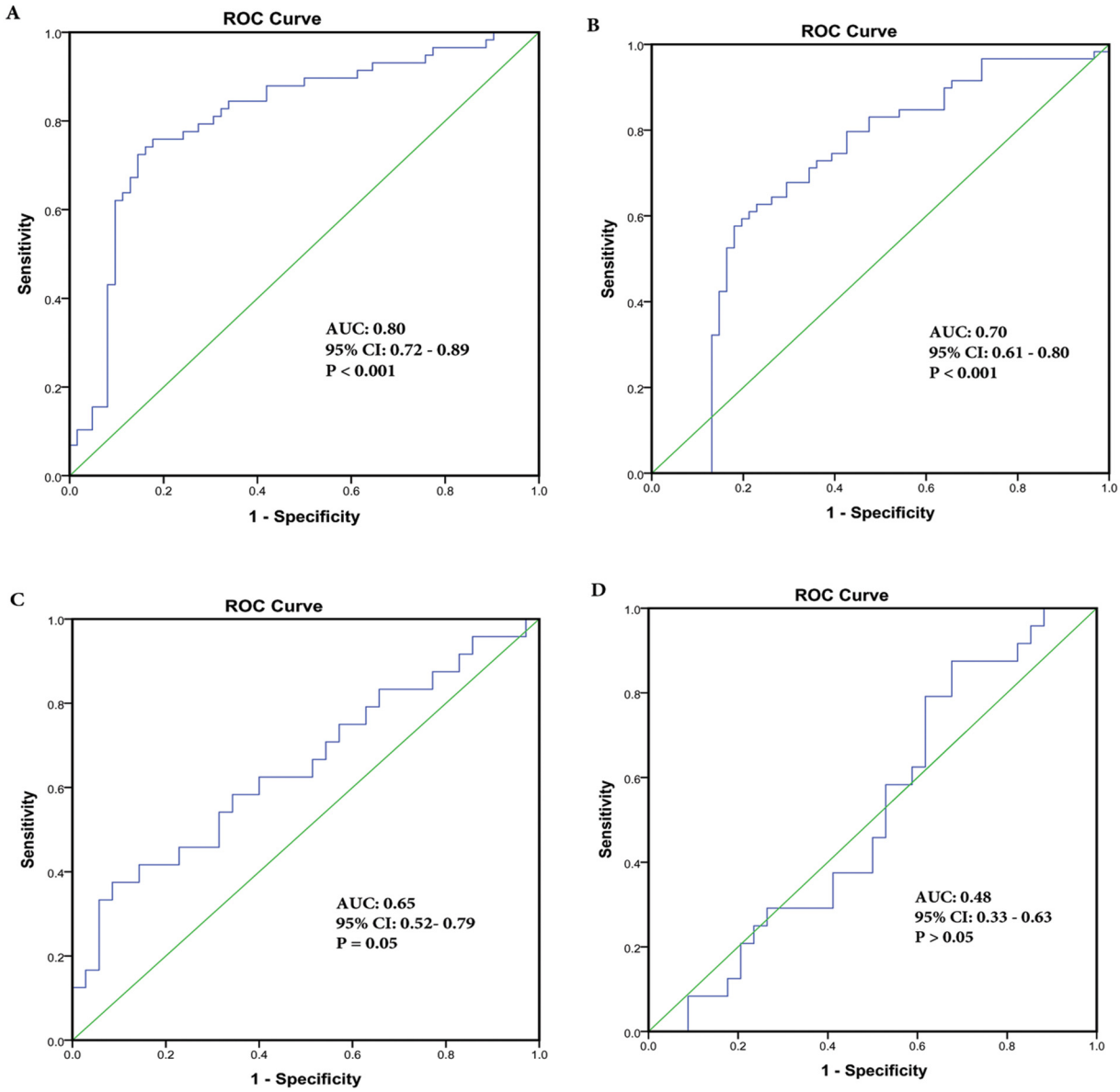

Fig. 2. ROC analysis which showcase the ability of A) ePLAGS to differentiate pre-capillary PH from post-capillary PH, B) ePLAR to differentiate pre-capillary PH from post capillary PH, C) ePLAGS to distinguish Ipc-PH from Cpc-PH, D) ePLAR to differentiate Ipc-PH from Cpc-PH.

of subjects to necessary care, it is currently not meant to be considered a potential substitute for benchmark RHC to distinguish PH groups. Finally, our post-capillary PH cohort included symptomatic subjects with a relatively high incidence of reduced LV performance, limiting the applicability of our results to less severe presentations.

5. Conclusion

The novel ePLAGS ratio distinguishes pre-capillary from post-capillary PH and demonstrates a stronger differentiating capability as compared to ePLAR. This non-invasive measure may be a useful adjunct to enhance non-invasive triage to comprehensive PH therapy.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.05.025.

Declaration of Competing Interest

None.

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