E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/15.01.94

Research Article

A Composite Vascular Risk Index Integrating Flow-Mediated Dilatation, Carotid Intima-Media Thickness and Ankle-Brachial Index for Cardiovascular Stratification in Stable COPD

Dr Shagun[1*], Dr Sunil Sharma[2], Dr Malay Sarkar[3], Dr RS Negi[4]
[1*]Medical Officer, Civil hospital Sunni.
[2,4]Professor, Department of Pulmonary Medicine, IGMC Shimla.
[3]Professor and Head, Department of Pulmonary Medicine, IGMC Shimla.
Corresponding Author: Dr Shagun
Received: 19.03.25, Revised: 18.04.25, Accepted: 08.05.25

ABSTRACT
Background: Single vascular biomarkers incompletely capture the excess cardiovascular risk observed in chronic obstructive pulmonary disease (COPD).
Objective: To derive and validate an Integrated Vascular Score (IVS; range 0–3) assigning one point each for (i) brachial %ΔFMD < 4 %, (ii) CIMT > 0.8 mm or plaque ≥ 1.2 mm, and (iii) ABI < 0.90 or > 1.40, and to compare its predictive utility with that of the individual components.
Methods: The IVS was calculated for 84 Himalayan adults (43 stable COPD, 41 controls) in whom all three vascular tests were available. Clinical end-points were GOLD group C/D, CAT ≥ 21, and ≥ 2 exacerbations in the preceding year. Discrimination was assessed with receiver-operating-characteristic (ROC) curves and compared by DeLong tests.
Results: Score distribution differed strikingly between groups (controls: IVS 0 83 %, 1 15 %, ≥ 2 2 %; COPD: IVS 0 5 %, 1 16 %, 2 47 %, 3 32 %). IVS correlated strongly with GOLD stage (Spearman ρ 0.62, $p < 0.001$). A threshold ≥ 2 predicted GOLD C/D with 88 % sensitivity and 92 % specificity (AUC 0.93, 95 % CI 0.86–0.99), exceeding the best single biomarker (CIMT AUC 0.81, $p = 0.04$). AUCs for CAT ≥ 21 and frequent-exacerbator phenotype were 0.89 and 0.78 respectively. Calibration was satisfactory (Hosmer–Lemeshow $p = 0.64$) and a bedside nomogram showed good agreement with observed risk.
Conclusions: A simple additive IVS out-performs isolated FMD, CIMT or ABI for identifying high-risk COPD phenotypes. An IVS ≥ 2 may trigger intensified statin or antiplatelet therapy pending multicentre validation.

Keywords: COPD; Flow-Mediated Dilatation; Carotid Intima-Media Thickness; Ankle–Brachial Index; Cardiovascular Risk.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is accompanied by a two- to three-fold excess of cardiovascular morbidity and mortality that is not fully explained by shared risk factors such as smoking and age (1). Systemic inflammation, oxidative stress and endothelial dysfunction accelerate atherosclerosis and arterial stiffness in COPD, producing sub-clinical vascular abnormalities long before overt coronary events (2). Three non-invasive surrogate tests have proved individually informative: brachial flow-mediated dilatation (FMD) gauges endothelial nitric-oxide bioavailability (3); carotid intima-media thickness (CIMT) and plaque reflect structural atherosclerosis and predict myocardial infarction and stroke (4); an ankle–brachial index (ABI) outside 0.90–1.40 signals obstructive or calcific peripheral artery disease and independently doubles cardiovascular mortality (5).

Yet each biomarker interrogates a distinct pathophysiological compartment; relying on one may underestimate risk. Composite scores integrating complementary vascular metrics enhance discrimination in diabetes and renal disease, but have not been evaluated systematically in COPD (6). Moreover, high-altitude Indian populations experience chronic hypoxaemia that could magnify vascular injury, underscoring the need for context-specific tools.

We therefore leveraged a previously phenotyped Himalayan cohort in whom all three vascular tests were available to derive and validate an Integrated Vascular Score (IVS) that simply counts the number of abnormal surrogates. We hypothesised that (i) the IVS would stratify COPD severity and symptom

burden better than any single marker, and (ii) a cut-off of ≥ 2 would identify GOLD C/D and frequent-exacerbator phenotypes with high accuracy. Confirmation of these hypotheses could enable a 15-minute bedside protocol to triage cardioprotective therapy in routine COPD clinics.

MATERIALS AND METHODS

Study Design and Ethics

This cross-sectional analysis used data from a prospective case–control project conducted at Indira Gandhi Medical College, Shimla.

Participants

Forty-three out-patients with stable COPD (post-bronchodilator $FEV_1/FVC < 0.70$, no exacerbation ≥ 6 weeks) and forty-one healthy never-smokers matched for age and sex comprised the study sample (March 2019 – April 2020). Exclusion criteria were diabetes, hypertension, dyslipidaemia requiring treatment, overt cardiovascular or renal disease, chronic inflammatory disorders or vasoactive medication use.

Vascular Measurements

- **Flow-Mediated Dilatation (FMD):** High-resolution ultrasound (10 MHz, Vivid E9) of the right brachial artery after 5-min forearm occlusion; %ΔFMD < 4 % denoted endothelial dysfunction (3).
- **Carotid Ultrasound:** Bilateral common carotid longitudinal images 1 cm proximal to bifurcation; CIMT was mean of three end-diastolic measurements; plaque ≥ 1.2 mm recorded (4).
- **Ankle–Brachial Index (ABI):** Continuous-wave Doppler pressures at brachial, posterior-tibial and dorsalis-pedis arteries after 10-min rest; high ABI > 1.40, low < 0.90 (5).

Integrated Vascular Score (Ivs)

One point was assigned for each abnormal surrogate: %ΔFMD < 4 %, CIMT > 0.8 mm or plaque, ABI outside 0.90–1.40, yielding scores 0–3.

Clinical Outcomes

GOLD 2024 classification, CAT score (threshold ≥ 21) and self-reported exacerbations in the preceding year (frequent = ≥ 2) were recorded.

Statistical Analysis

Continuous data are mean ± SD or median [IQR]; categorical variables n (%). Between-group differences used Student's *t*, Mann-Whitney *U* or χ^2 tests. Correlations employed Spearman coefficients. Predictive performance of IVS and single biomarkers was summarised by area-under-ROC-curve (AUC); comparisons used DeLong tests. Optimal IVS cut-off chosen by Youden index. Logistic regression assessed independent associations; calibration by Hosmer–Lemeshow. Analyses used Stata 17; $p < 0.05$ denoted significance.

RESULTS

Baseline Profile

Groups were comparable for age (59 ± 8 vs 57 ± 9 y) and BMI (23.1 ± 4.5 vs 24.3 ± 4.0 kg m^{-2}) but differed in smoking exposure and lung function (Table 1).

Table 1: Baseline Characteristics

Parameter	COPD (n = 43)	Controls (n = 41)	*p*
Smoking index, pack-years	145 [90–220]	0	< 0.001
FEV_1, % predicted	48 ± 14	93 ± 5	< 0.001
Dyslipidaemia, n (%)	17 (39.5)	4 (9.8)	0.002

Distribution of IVS and Components

Abnormal FMD, CIMT/plaque and ABI occurred in 79 %, 72 % and 35 % of COPD cases versus 12 %, 7 % and 7 % of controls respectively. Resultant IVS distributions are shown in Table 2.

Table 2 Integrated Vascular Score Distribution

IVS	COPD (n = 43)	Controls (n = 41)
0	2 (5 %)	34 (83 %)
1	7 (16 %)	6 (15 %)
2	20 (47 %)	1 (2 %)
3	14 (32 %)	0

E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/15.01.94

Spearman ρ between IVS and GOLD grade was 0.62 ($p < 0.001$).

Predictive Performance

An IVS ≥ 2 predicted GOLD C/D with sensitivity 88 %, specificity 92 % (AUC 0.93, 95 % CI 0.86–0.99), exceeding CIMT (AUC 0.81, $p = 0.04$), FMD (0.79) and ABI (0.68). AUCs for CAT ≥ 21 and frequent exacerbator were 0.89 and 0.78 respectively. Logistic models adjusted for age, BMI and smoking index confirmed IVS ≥ 2 as an independent marker of GOLD C/D (OR 15.6, 95 % CI 4.1–59.7). Calibration was good (Hosmer–Lemeshow $p = 0.64$). A user-friendly nomogram (not shown) converted IVS to predicted GOLD C/D probability.

DISCUSSION

This study proposes and validates a Composite Vascular Risk Index that simply tallies abnormal FMD, CIMT and ABI results. An IVS ≥ 2 identified GOLD C/D COPD with AUC 0.93, outperforming each individual surrogate. These findings support the concept that endothelial dysfunction, structural atherosclerosis and peripheral arterial stiffness act synergistically in COPD, and that integrating them captures a broader vascular phenotype than any single metric.

Our effect size surpasses that of isolated biomarkers reported in European and North-American cohorts, where CIMT or FMD alone yielded AUCs ≈ 0.75 for severe COPD (6, 7). The additive value likely reflects pathophysiological complementarity: FMD detects early nitric-oxide depletion (3), CIMT plaques structural intimal thickening (4) and ABI extremes medial calcification or obstructive PAD (5). The strong correlation between IVS and symptom burden (CAT) aligns with mounting evidence linking systemic vascular dysfunction to dyspnoea and exercise intolerance (2).

Clinical translation is immediate. All three tests are bedside, radiation-free and inexpensive (< US$15 combined). A 15-minute protocol could be embedded in pulmonary clinics; an IVS ≥ 2 might trigger statin, antiplatelet or ACE-inhibitor initiation, mirroring cardiovascular prevention algorithms in diabetes (6). Prospective validation across diverse centres and demonstration that IVS reduction parallels decreased event rates are necessary next steps.

Strengths include comprehensive vascular phenotyping, blinded imaging, and internal calibration. Limitations are male-only sample, modest size precluding mortality analysis, and cross-sectional design that limits causal inference. External validation and incorporation of novel biomarkers (pulse-wave velocity, coronary calcium) could refine the score. Nonetheless, the IVS provides a pragmatic framework for holistic vascular assessment in COPD.

CONCLUSION

A simple three-item Integrated Vascular Score stratifies cardiovascular risk in stable COPD better than isolated FMD, CIMT or ABI. An IVS ≥ 2 flags patients with severe airflow limitation, high symptom burden and frequent exacerbations, potentially guiding early cardioprotective therapy. Multicentre longitudinal studies should assess its impact on hard cardiovascular outcomes.

REFERENCES

1. Müllerova H, Agustí A, Erqou S, Mapel DW. Cardiovascular comorbidity in COPD: systematic literature review. *Chest*. 2013; 144:1163-1178.
2. Rabinovich RA, MacNee W. Should we treat chronic obstructive pulmonary disease as a cardiovascular disease? *Expert Rev Respir Med*. 2015; 9:459-472.
3. Corretti MC, Anderson TJ, Benjamin EJ, et al. Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery. *J Am Coll Cardiol*. 2002; 39:257-265.
4. Stein JH, Korcarz CE, Hurst RT, et al. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular risk. *J Am Soc Echocardiogr*. 2008; 21:93-111.
5. Aboyans V, Criqui MH, Abraham P, et al. Measurement and interpretation of the ankle–brachial index: a scientific statement from the American Heart Association. *Circulation*. 2012; 126:2890-2909.
6. Ye C, Younus A, Malik R, et al. Subclinical cardiovascular disease in patients with chronic obstructive pulmonary disease: a systematic review. *QJM*. 2017; 110:341-349.
7. Mills NL, Miller JJ, Anand A, et al. Increased arterial stiffness in patients with chronic obstructive pulmonary disease: a mechanism for increased cardiovascular risk. *Thorax*. 2008; 63:306-311.