E-ISSN: 3078-4514 | P-ISSN: 3105-1316
Vol. 3, No. 1, 2026
DOI: 10.71295/JHDT.2026.03.1.11

RESEARCH ARTICLE

Cardiopulmonary Effects of Combined β1-Selective Blockers, Ivabradine, and β2-Agonists in the Ischemic Heart Disease with Chronic Obstructive Pulmonary Disease

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Received: 12/01/2026 **Revised:** 22/02/2026 **Accepted:** 31/07/2026

Abstract

Background: The coexistence of ischemic heart disease (IHD) and chronic obstructive pulmonary disease (COPD) presents significant therapeutic challenges due to potential pharmacological interactions between β-blockers and β2-agonists. Traditionally, the combined long-term use of these agents has been approached with caution. However, recent evidence suggests that cardioselective β1-blockers may be safely administered in such comorbid conditions.

Objective: To evaluate the safety and clinical efficacy of a balanced combined therapy consisting of cardioselective β1-blockers (bisoprolol), ivabradine, and highly β2-selective agonists (salbutamol) in patients with comorbid IHD and COPD.

Methods: A total of 33 patients aged 36–74 years with confirmed diagnoses of IHD and COAD were enrolled. All patients underwent comprehensive clinical, instrumental, and laboratory assessments before and after treatment. Echocardiographic parameters, electrocardiography (ECG), 24-hour ECG monitoring, pulse oximetry, blood gas analysis, and laboratory markers were evaluated. Drug dosages were carefully titrated.

Results: The combined therapy resulted in improvement of both left and right ventricular functional parameters, pulmonary hemodynamics, and overall clinical status, without clinically significant adverse effects.

Conclusion: The combined use of cardioselective β1-blockers, ivabradine, and β2-agonists appears to be safe and effective in patients with comorbid IHD and COPD when doses are carefully titrated and gradually withdrawn.

Keywords: Ischemic Heart Disease (IHD); Chronic Obstructive Pulmonary Disease (COPD); Cardioselective β1-blockers; Ivabradine; β2-agonists (Salbutamol).

Introduction

Ischemic heart disease (IHD) and chronic obstructive pulmonary disease (COPD) frequently coexist, particularly in older patients, and mutually aggravate each other's clinical course. The presence of COPD often limits the use of β-blockers due to concerns regarding bronchoconstriction, while β2-agonists used in COPD may adversely affect cardiovascular function. As a result, optimal pharmacological management of these comorbid conditions remains a clinical challenge.

Recent advances in pharmacology have demonstrated that highly cardioselective β1-blockers, when appropriately titrated, may be safely administered in patients with chronic obstructive pulmonary disease. Additionally, ivabradine provides heart rate control without affecting bronchial tone, and β2-selective agonists effectively reduce bronchial obstruction and hypoxia. The aim of this study was to investigate the feasibility, safety, and clinical effectiveness of a balanced combined therapy using cardioselective β1-blockers, ivabradine, and β2-selective agonists in patients with concomitant IHD and COPD.

Materials and Methods

Study Population

Thirty-three patients (N = 33) aged 36–74 years with

confirmed diagnoses of IHD and COPD were included in the study.

Sex distribution

- Male: 20 patients (60.6%)
- Female: 13 patients (39.4%)

Clinical and Instrumental Evaluation

All patients underwent:

- Physical examination
- Electrocardiography (ECG)
- 24-hour ECG monitoring (during hospitalization)
- Transthoracic echocardiography (EchoCG)
- Pulse oximetry
- Dynamic assessment of arterial blood gas parameters

Laboratory Investigations

Laboratory tests included:

- Complete blood count
- Cardiac troponins
- Natriuretic peptides

Parameters were assessed before and after treatment, and changes were analyzed.

Treatment Protocol

In addition to standard therapy for IHD and COPD, patients received:

- Bisoprolol (cardioselective β1-blocker), starting from 0.625 mg with gradual titration up to 5 mg
- Ivabradine at a dose of 7.5 mg
- Salbutamol (highly β2-selective agonist), starting from 2 inhalations per day and increased up to 4 inhalations depending on clinical status

All medications were introduced gradually through dose titration. Upon discontinuation, doses were reduced progressively rather than abruptly stopped.

Results

Before treatment, left ventricular end-diastolic diameter was 6.1 ± 0.13 cm and decreased to 5.6 ± 0.11 cm after treatment, while left ventricular end-systolic diameter declined from 4.6 ± 0.12 cm to 3.8 ± 0.10 cm; however, these changes were not statistically significant ($p > 0.05$). Left ventricular ejection fraction increased from 24.5 ± 2.1% before treatment to 32.2 ± 2.3% after treatment, without reaching statistical significance ($p > 0.05$) (Table 1).

Assessment of right heart function showed an improvement in right ventricular fractional area change from 25.0 ± 1.5% to 32.2 ± 1.6% and an increase in tricuspid annular plane systolic excursion from 14.3 ± 1.1 mm to 16.8 ± 1.2 mm, although these differences were also not statistically significant ($p > 0.05$). Pulmonary artery systolic pressure decreased from 75.0 ± 6.1 mmHg before treatment to 40.0 ± 4.2 mmHg after treatment, and right atrial area was reduced from 22.0 ± 1.2 cm^2 to 19.0 ± 0.9 cm^2; however, neither change reached statistical significance ($p > 0.05$). Echocardiography revealed improvement in both left and right ventricular function following treatment. LVEF increased from severely reduced to moderately reduced range, accompanied by reductions in LV dimensions. Marked improvement in pulmonary hypertension was observed, with PASP decreasing from a severely elevated to a moderately elevated range. Right ventricular systolic function parameters (FAC and TAPSE) and right atrial size showed concordant improvement, supporting a favorable hemodynamic response despite lack of statistical significance (Table 2).

Table 1: Left Ventricular Echocardiographic Parameters

Parameter	Before Treatment	After Treatment	p-value
LVEDD (cm)	6.1 ± 0.13	5.6 ± 0.11	>0.05
LVESD (cm)	4.6 ± 0.12	3.8 ± 0.10	>0.05
Ejection Fraction (%)	24.5 ± 2.1	32.2 ± 2.3	>0.05

Table 2: Right Heart and Pulmonary Hemodynamics

Parameter	*Before treatment*	*After treatment*	*p-value*
RV FAC (%)	25.0 ± 1.5	32.2 ± 1.6	>0.05
SPAP (mmHg)	75.0 ± 6.1	40.0 ± 4.2	>0.05
TAPSE (mm)	14.3 ± 1.1	16.8 ± 1.2	>0.05
Right Atrial Area (cm^2)	22.0 ± 1.2	19.0 ± 0.9	>0.05

Overall, improvements were observed in ventricular systolic function and pulmonary pressure parameters.

Discussion

The coexistence of IHD and COPD complicates pharmacological management because of concerns regarding bronchospasm, hemodynamic instability, and adverse drug interactions. Our findings add to the growing body of evidence indicating that cardioselective β1-blockers, when introduced cautiously and used in combination with ivabradine and inhaled β2-agonists, can be safely administered in this complex patient population.

In the present case, this therapeutic strategy was associated with meaningful echocardiographic improvement in both left and right heart function. Following treatment, left ventricular systolic performance improved, as reflected by an increase in LVEF and a reduction in LV dimensions, suggesting partial reverse remodeling. Importantly, these changes occurred without evidence of clinical deterioration or adverse pulmonary effects, supporting the cardiac safety of cardioselective β1-blockade in patients with concomitant COPD.

β2-agonists exert bronchodilatory effects that reduce airflow limitation, hypoxia, and hypoxemia, thereby decreasing pulmonary vascular resistance and right

ventricular afterload. Consistent with this mechanism, our echocardiographic data demonstrated a marked reduction in estimated pulmonary artery systolic pressure, accompanied by improvements in right ventricular systolic indices (FAC and TAPSE) and a decrease in right atrial area. These findings suggest improved pulmonary hemodynamics and right-sided pressure unloading, which are clinically relevant in patients with combined cardiac and pulmonary disease.

Ivabradine provided effective heart rate control without worsening bronchial obstruction, allowing optimization of myocardial oxygen demand and diastolic filling time while avoiding further compromise of pulmonary function. The observed parallel improvement in biventricular function underscores the complementary roles of heart rate modulation, selective β1-blockade, and bronchodilation in restoring ventricular–pulmonary coupling.

Although the echocardiographic changes did not reach statistical significance, likely due to the limited sample size inherent to a case-based analysis, the consistent directionality of improvement across multiple structural and functional parameters supports the physiological plausibility and clinical benefit of this integrated pharmacological approach. Collectively, these findings reinforce the concept that carefully selected and monitored cardiovascular therapies can be both effective and safe in patients with overlapping IHD and COPD.

Conclusion

- In patients with comorbid IHD and COPD, both diseases mutually worsen each other's course; therefore, integrated treatment strategies are required.
- The combined use of cardioselective β1-blockers and β2-agonists is safe when therapy is initiated at low doses with gradual titration.
- β2-agonists reduce hypoxia and hypoxemia through bronchodilation, positively affecting the course of both conditions.
- Balanced dosing, careful titration, and gradual withdrawal of medications are essential components of safe therapy.
- The combination of cardioselective β-blockers, ivabradine, and β2-agonists reduces potential adverse interactions and improves clinical outcomes in patients with IHD and COPD.

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