Chronic obstructive pulmonary disease in heart failure: influence on circulating biomarkers and outcome

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Background: Chronic obstructive pulmonary disease (COPD) is common in patients with chronic heart failure (CHF).

Purpose: We aimed to explore the impact of COPD on HF biomarkers (N-terminal fraction of pro-B-type natriuretic peptide [NT-proBNP], high-sensitivity troponin T [hs-TnT], and soluble suppression of tumorigenesis-2 [sST2]) and outcome.

Methods: Individual data from 14 cohorts of patients with stable chronic HF and NT-proBNP and hs-TnT values were analysed. Patients with known COPD status were evaluated.

Results: Patients (n=13,178) were aged 67 years (58–75), 75% males, and 76%, 11%, 13% with HF with reduced, mid-range, or preserved ejection fraction (HFrEF/HFmrEF/HFpEF), respectively. Patients with COPD were older than those without COPD (age 71 years [64–77] vs. 66 [57–75]; p<0.001), more frequently males (79% vs. 74%; p<0.001), had more often ischaemic HF (54% vs. 52%; p<0.001), and HFpEF (14% vs. 12%; p=0.011), but not HFpEF (12% vs. 11%; p=0.097). COPD patients had also more severe dyspnoea (44% in NYHA class III-IV vs. 31%; p<0.001), and slightly worse renal function (median estimated glomerular filtration rate [eGFR] 58 mL/min/1.73 m² [44–74] vs. 60 [46–67]; p<0.001). Patients with COPD had higher NT-proBNP (1501 ng/L [642–3333] vs. 1225 ng/L [476–2902]; p<0.001), hs-TnT (22 ng/L [13–38] vs. 17 ng/L [9–30]; p<0.001), and sST2 (30 ng/mL [22–45] vs. 29 [21–43]; p<0.001).

Over a median follow-up of 2.1 years (1.5–3.7, range 0–18 years), 3,865/12,489 patients (31%) died; among them, 2,443/12,450 (20%) died for cardiovascular causes; 3,373/12,469 patients (27%) were hospitalized for HF over 35 months (15–63, range 0–216 months). Patients with COPD had a significantly higher all-cause mortality, cardiovascular mortality, and worse survival free from HF hospitalization (all p<0.001; Figure). In a model including age, gender, ischaemic vs. non-ischaemic aetiology, eGFR, HFrEF/HFmrEF/HFpEF, and NYHA class III-IV, COPD retained independent prognostic significance from NT-proBNP for 1-year all-cause (p=0.009) and cardiovascular mortality (p=0.022), 5-year all-cause (p<0.001) and cardiovascular mortality (p=0.011) as well as 3- (p=0.033), 6- (p=0.019) and 12-month HF hospitalization (p=0.033). COPD lost its independent prognostic significance when hs-TnT and sST2 were included in the model.

Conclusions: COPD in HF is characterized by higher NT-proBNP, hs-TnT and sST2 levels. COPD adds prognostic significance over NT-proBNP alone, but not over the combination of NT-proBNP, hs-TnT, and sST2.

COPD	All-cause death					Cardiovascular death					HF hospitalization					
No	10,494	1,840	561	122	0	10,463	1,838	561	122	0	9,903	3,921	674	224	36	0
Yes	1,995	258	58	0	0	1,987	257	58	0	0	1,880	549	79	1	0	0