

## Appendix 3. Characteristics of the analyzed studies.

Author and publication year	Castagna O. et al. 2008[1]	Pecci R. et al. 2012[2]	Chen W. et al. 2015[3]	Pizarro C. et al. 2016[4]	Houben-Wilke S. et al. 2017[5]	Crisafulli E. et al. 2017[6]	Tuleta I. et al. 2017[7]
<b>Publication title</b>	Peripheral arterial disease: an underestimated aetiology of exercise intolerance in chronic obstructive pulmonary disease patients	Peripheral arterial disease in patients with chronic obstructive pulmonary disease	Is asymptomatic peripheral arterial disease associated with walking endurance in patients with COPD?	Lower extremity and carotid artery disease in COPD	Peripheral Artery Disease and Its Clinical Relevance in Patients with Chronic Obstructive Pulmonary Disease in the COPD and Systemic Consequences–Comorbidities Network Study	Asymptomatic peripheral artery disease can limit maximal exercise capacity in chronic obstructive pulmonary disease patients regardless of airflow obstruction and lung hyperinflation	High prevalence of COPD in atherosclerosis patients
<b>Publication type</b>	article	article	article	article	article	article	article
<b>Journal title</b>	European Journal of Cardiovascular Prevention and Rehabilitation	International Angiology	International Journal of COPD	European Respiratory Journal Open research	American Journal of Respiratory and Critical Care Medicine	European Journal of Preventive Cardiology	International Journal of COPD
<b>Study type</b>	cross sectional study	cross sectional study	cross sectional study	cross sectional study	cross sectional study	cross sectional study	cross sectional study
<b>Study aims</b>	- to assess the prevalence of peripheral arterial disease and its implications for exercise limitation in COPD patients	- to determine the prevalence of PAD in a population of patients with COPD - to investigate the relationship between PAD and lung disease severity	- to investigate the association between asymptomatic PAD and walking endurance, measured by the 6MWT in COPD patients - to analyze which factors were associated with the distance achieved on the 6MWT	- to determine the linkage between PAD and COPD	- to assess the prevalence of PAD in COPD compared with distinct control groups - to study the association between PAD and functional capacity as well as health status	- to evaluate in COPD patients the impact of asymptomatic/silent PAD on maximal exercise capacity - to search for predictors of PAD	- to determine the prevalence of COPD in patients with cerebral and/or peripheral artery disease - to assess factors associated with the presence of COPD
<b>Inclusion criteria</b>	- COPD patients from Toulon's hospital clinically stable with the absence of respiratory exacerbation within 2 months before the study - healthy control individuals	- patients with COPD	- COPD patients who volunteered to undergo ABI measurements and the 6MWT enrolled in the CMPICO study[8]	- patients aged ≥18 years receiving treatment for spirometrically and clinically confirmed COPD - nonCOPD control smokers	- patients aged ≥40 years having a diagnosis of COPD or symptoms of chronic bronchitis	- adult COPD patients having a former or current smoking history of at least 10 pack-years and in a cardio-respiratory stable condition for at least six weeks previous the enrolment	- confirmation of atherosclerotic cerebral and/or PAD in duplex sonography and the ability of the patient to conduct properly breathing maneuvers during body plethysmography.
<b>Exclusion criteria</b>	- taking medications that were prone to interfere with the tests	NR	- obvious symptoms of PAD - not current or former smokers with at least a 10-pack-year history - history of bronchial asthma and other structural lung diseases	- previously diagnosed LEAD and carotid artery disease (including cerebrovascular disorders) - acute exacerbated COPD at the time of evaluation	- patients with missing ABI or lung function data - unclassified patients - patients with alpha1 deficiency	- concomitant respiratory disease other than COPD, such as asthma or bronchiectasis - chronic respiratory failure needing long-term oxygen therapy - any signs or symptoms potentially attributable to a PAD	- restrictive pattern defined as total lung capacity < 80% of a predicted value
<b>Geographical location</b>	France	Spain	Taiwan	Germany	Germany	Italy	Germany
<b>Recruitment population</b>	COPD patients hospitalized in Toulon's hospital	COPD patients admitted consecutively in the Internal Medicine Department	COPD patients at the outpatient department of the Division of Pulmonary and Critical Care Medicine	patients receiving treatment at the Department of Pneumology and non COPD smokers	patients referred to the study by pulmonologists and general practitioners	COPD out-patients of Lung Function Unit	hospitalized patients and out-patients with confirmed atherosclerotic cerebral and/or peripheral artery disease
<b>Recruited population size</b>	224	246	200	129	2088	47	166
<b>PAD population size</b>	123	84	17	86	184	24	125
<b>COPD population size</b>	151	246	200	107	2088	47	36*
<b>PAD diagnostic criteria</b>	ABI	ABI	ABI	ABI	ABI	ABI	ABI
<b>COPD diagnostic criteria</b>	GOLD	GOLD	GOLD	GOLD	GOLD	GOLD	GOLD
<b>PAD stage</b>	NA	NA	NA	NA	NA	NA	F I 72.0% F IIa 10.4% F IIb 15.2% F III 0.8% F IV 1.6%
<b>COPD stage</b>	NR	GOLD I 2.4% II 48.0% III 41.1% IV 8.5%	GOLD I 14% II 48% III 31% IV 7%	GOLD A 5.6% B 48.6% C 3.7% D 42.1%	GOLD I 9.4% II 42.5% III 37.5% IV 10.5%	NR	NA
<b>Age of patients in PAD group [years±SD]</b>	NR	71.9±10.6	71.9±9	NR	68.5±7	68.7±8.4	NR
<b>Age of patients in COPD group [years±SD]</b>	67±3.1	70.2±11.0	70.9±8.9	64.6±10.4	65.3±8.2	68.3±7.1	72.4±8.6*
<b>Number of PAD patients among COPD patients (%)</b>	123 (81.5)	84 (34.1)	17 (8.5)	86 (80.4)	184 (8.8)	24 (51.1)	NA
<b>Number of COPD patients among PAD patients</b>	NA	NA	NA	NA	NA	NA	34 (27.2)
<b>Number of smoking patients (%)</b>	-- COPD group: - current or former 151 (100) -- PAD group - current or former - NR	-- COPD group: - current 57 (23.2) - former 134 (54.5) -- PAD group: - current 19 (22.6) - former 58 (69.0)	-- COPD group: - current 94 (47.0) - former 106 (53.0) -- PAD group: - current 8 (47.1) - former 9 (52.9)	-- COPD group: - current 22 (20.6) - former 80 (74.8) -- PAD group: - current - NR - former - NR	-- COPD group: - current 550 (26.3) - former 1424 (68.2) -- PAD group: - current 64 (34.8) - former 116 (63.0)	-- COPD group: - current 12 (25.5) - former 35 (74.5) -- PAD group: - current 8 (33.3) - former 16 (66.7)	-- COPD group*: - current 3 (8.3) - former 23 (63.9) -- PAD group: - current - NR - former - NR
<b>Remarks</b>	non-smokers excluded		symptomatic PAD patients and not current or former smokers with at least a 10-pack-year history excluded			symptomatic PAD patients and non-smokers excluded	patients with total lung capacity < 80% of a predicted value excluded

COPD, chronic obstructive pulmonary disease; PAD, peripheral arterial disease; 6MWT, six minute walk test; ABI, ankle-brachial index; CMPICO, Case Management Program and Integrated Care for Patients with COPD; GOLD, global initiative for chronic obstructive lung disease<sup>8</sup>; GOLD I-IV or A-D, global initiative for chronic obstructive lung disease classification<sup>8</sup>; NA, not applicable; NR, not reported; F, Fontaine classification<sup>9</sup>; \* in the group of patients with cerebral and/or peripheral artery disease

### **Appendix 3. references**

- [1] Castagna O, Boussuges A, Nussbaum E, et al. Peripheral arterial disease: an underestimated aetiology of exercise intolerance in chronic obstructive pulmonary disease patients. *Eur. J. Cardiovasc. Prev. Rehabil.* 2008;15:270–277.
- [2] Pecci R, De La Fuente Aguado J, Sanjurjo Rivo AB, et al. Peripheral arterial disease in patients with chronic obstructive pulmonary disease. *Int. Angiol.* 2012;31:444–453.
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- [4] Pizarro C, Linnhoff F, van Essen F, et al. Lower extremity and carotid artery disease in COPD. *ERJ open Res.* 2016;2.
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- [8] Lin M-S, Hsu K-Y, Chen Y-J, et al. Prevalence and risk factors of asymptomatic peripheral arterial disease in patients with COPD in Taiwan. *PLoS One.* 2013;8:e64714.