An algorithm for the management of chronic obstructive pulmonary disease patients in units of internal medicine

Ombretta Para,[1] Carmen Stabile,[2] Donato Cinquepalmi,[2] Maria Sandra Magnoni,[2*] Francesco Nasso,[3] Flavio Tangianu,[4] Mauro Silingardi,[5] Antonella Valerio,[6] Dario Manfellotto,[7] Francesco Dentali[8]

[1]Internal Medicine 1, Careggi Hospital, Florence; [2]GSK Medical Department, Verona; [3]Internal Medicine, Hospital of Polistena; [4]General Medicine 1, Medical Center, Ospedale di Circolo e Fondazione Macchi, ASST Sette Laghi, Varese; [5]Department of Medicine, Ospedale Maggiore, Bologna; [6]Research Department, FADOI Foundation, Milan; [7]Internal Medicine, Isola Tiberina Hospital, Gemelli Isola, Rome; [8]Department of Medicine and Surgery, University of Insubria, ASST dei Sette Laghi, Varese, Italy

*Present address: GSK Medical Affairs Department, Verona, Italy

Correspondence: Carmen Stabile, GSK Medical Department, Viale dell'Agricoltura 7, 37135, Verona, Italy
E-mail: carmen.x.stabile@gsk.com

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ABSTRACT

Patients with acute exacerbations of chronic obstructive pulmonary disease (COPD) are often hospitalized in internal medicine units (IMUs), and their management is challenging due to a multiplicity of factors affecting the outcome, such as correct patient classification, appropriate pharmacologic therapy, patient discharge, and follow-up. In this context, a standardized pathway (algorithm) for the management of these patients was designed and tested. Specifically, based on information collected through a survey on the management of COPD patients in IMUs, an initial version of an algorithm was designed by the scientific board and proposed to 45 IMUs for a 6-month period to evaluate its feasibility, usefulness, and critical issues. After this preliminary phase, a second version was released, which was again brought to the attention of the participating centers, leading to the final algorithm. The algorithm reports the steps for the management of patients with severe exacerbations of known or suspected COPD, namely: correct diagnosis, treatment of the acute phase, management of comorbidities, appropriate therapy at discharge, and planning of the follow-up. Focus is given to the shift from systemic therapy in the acute phase to early in-hospital inhalation triple therapy (inhaled corticosteroids/long-acting muscarinic antagonists/long-acting β agonists) and the need for education in the use of the inhaler. The algorithm was considered useful by most of the participating centers. The proposed algorithm is an agile and usable tool for managing the main steps of care of COPD patients in IMUs. The future goal is to make the model available to a wider audience of internists.

Introduction

In Italy, many patients with acute exacerbation of chronic obstructive pulmonary disease (COPD) refer to internal medicine units (IMUs), and their management may be challenging due to a multiplicity of factors affecting the outcome, such as patient classification and appropriate pharmacologic treatment on discharge and follow-up, as suggested by the results of a recent survey.[1]

In this context, the scientific board of the Federation of Associations of Hospital Doctors on Internal Medicine

(FADOI) Foundation developed a project aimed at optimizing and standardizing the management of hospitalized patients for known or suspected COPD exacerbation. FADOI Foundation and GSK contributed equally to the execution of this project.

Materials and Methods

Starting from the results of the survey carried out in 176 IMUs distributed throughout Italy,[1] the Scientific Board of the FADOI Foundation analyzed the critical points detected and wrote the first draft of the algorithm for the management of COPD patients in IMUs, with a sharing process carried out through various collegial meetings.

This document was proposed to 45 centers for a 6-month pilot phase of implementation to evaluate its feasibility, usefulness, and any critical issues.

After this phase of testing, a second version, which incorporated the modification proposals, was released and again brought to the attention of the participating centers, leading to the final version of the algorithm.

Results

The algorithm (Figure 1) is divided into three parts, relating to the acute management of patients hospitalized for COPD exacerbations, the assessment of patients hospitalized for COPD exacerbations at 30 days from discharge, and the management of COPD in an outpatient setting.

Management of patients hospitalized for chronic obstructive pulmonary disease exacerbations (acute phase)

As regards the acute phase, the management steps entail the definition of the patient's clinical status through the description of symptoms, the anamnesis and identification of risk factors, the assessment of comorbidities, the measurement of peripheral oxygen saturation, and the use of specific questionnaires to assess the impact or severity of symptoms [COPD Assessment Test (CAT) or Modified Medical Research Council (mMRC)].

After the acquisition of this information, the next step is the diagnostic framework, with all the first-level and second-level tests for the differential diagnosis with respect to other comorbidities, both pulmonary and cardiological, characterized by respiratory symptoms (*i.e.*, pulmonary embolism, that is found in about 20% of patients with COPD).

In the first level assessment, it is necessary to perform blood tests (blood count with eosinophil count), electrocardiogram, blood gas analysis, and chest X-ray.

The assessment of comorbidities relies on an accurate clinical history, physical examination, laboratory, and instrumental tests (echocardiography, brain natriuretic peptide (BNP) or NT-proBNP, D-dimer, sputum culture examination, Sars-CoV-2 testing, high resolution computed tomography/angio-computed tomography).

Treatment of the exacerbation in the acute phase should be guided by the severity of symptoms, presence of comorbidities, patient's response, and side effects.

The drugs administered are nebulized short-acting β_2-agonists+short-acting muscarinic antagonists+inhaled corticosteroids (ICS) in addition to systemic corticosteroids. Antibiotics are administered when signs of bacterial infection are present.

Oxygen therapy and ventilatory support (non-invasive or invasive) are fundamental to managing acute respiratory failure.

Some fundamental steps for the treatment of the patient are described in the algorithm, starting with the early in-hospital shift from aerosol and systemic therapy to triple therapy [long-acting β agonists (LABA)/long-acting muscarinic antagonists (LAMA)/ICS] administered by single inhaler, to conclude with the planning of a 30-day re-evaluation at discharge.

Assessment of patients hospitalized for chronic obstructive pulmonary disease exacerbations at 30 days from discharge

In the management of a patient discharged from the hospital for known or suspected COPD exacerbation, 30 days is an appropriate time frame for re-assessment. The basic steps entail the assessment of lung function by simple spirometry, symptoms with CAT and/or mMRC, inhalation technique, and risk/benefit profile of the therapy, with a possible confirmation of triple inhalation therapy (LABA/LAMA/ICS). The aim is to optimize the therapy to improve symptom control and reduce hospital readmissions.

Management of chronic obstructive pulmonary disease in an outpatient setting

The outpatient management of symptomatic patients who do not come from a direct hospitalization finds its pivotal step in the execution of spirometry, to confirm the presence of an obstructive syndrome. The therapy is based on the extent of the symptoms, the presence of comorbidities, and blood eosinophilia, varying from a single bronchodilator (LABA or LAMA) to the association between two drugs (LABA+LAMA or LABA+ICS), up to a triple combination therapy (LABA+LAMA+ICS) in patients with frequent exacerbations not controlled by dual combinations. Any de-escalation should be considered only in specific cases, depending on contraindications, appropriateness, and risk/benefit of the proposed therapy. For instance, a possible de-escalation of therapy could be a possible option in patients who do not benefit from the introduction of ICS, and in whom the indication was probably inappropriate, such as those with a history of relapsing pneumonia.

Discussion and Conclusions

The algorithm reports the steps for the management of patients with exacerbations of COPD hospitalized in IMUs, from the diagnosis to the treatment of the acute phase, from the management of comorbidities to the choice of the appropriate therapy at discharge and follow-up. In addition to the acute phase, the algorithm also entails the diagnostic-therapeutic management of outpatients who do not come from a direct hospitalization.

An important aspect highlighted in the model is the holistic and multidisciplinary approach for a correct assessment of comorbidities, including those underlying and not frankly

manifest, to optimize both the diagnostic and therapeutic path. It is known that some comorbidities are frequently found in patients with COPD, especially cardiovascular diseases, anxiety, depression, and osteoporosis. These can increase COPD mortality and morbidity.[2-4]

Focus is also given to hospital discharge, with the switch from the systemic or aerosol therapy used in the acute phase to the early in-hospital triple inhalation therapy (LABA/LAMA/ICS) and the need for proper education on the use of the inhaler.

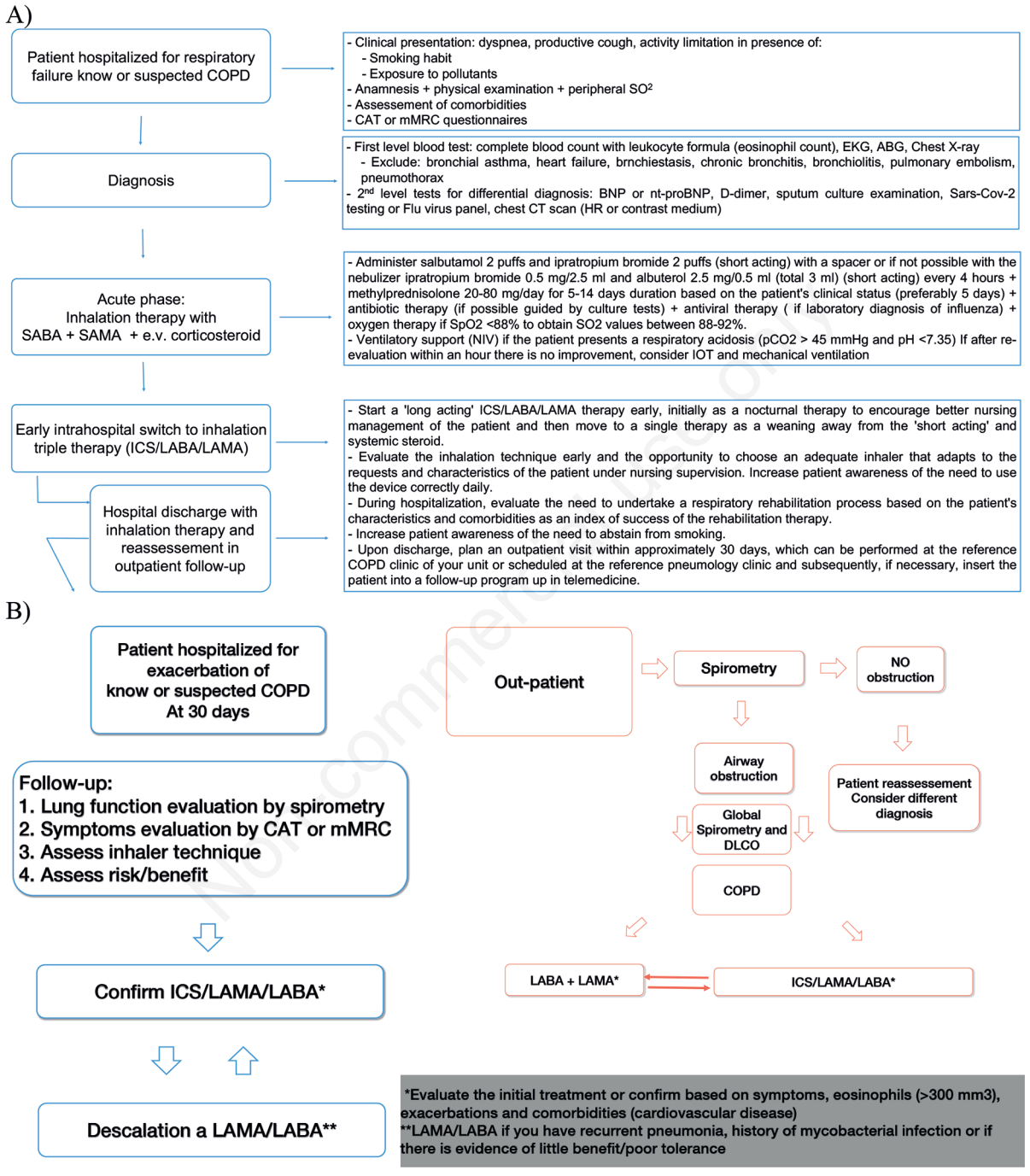

Figure 1. A) The algorithm for the management of the acute phase of chronic obstructive pulmonary disease (COPD) exacerbation in hospital settings; B) the algorithm for the management of COPD in outpatient settings. CAT, COPD Assessment Test; mMRC, Modified Medical Research Council; BNP, brain natriuretic peptide; CT, computed tomography; HR, high resolution; SABA, short-acting β2-agonists; SAMA, short-acting muscarinic antagonists; e.v., endovenous; ICS, inhaled corticosteroids; LABA, long-acting β agonists; LAMA, long-acting muscarinic antagonists; SpO2, peripheral capillary oxygen saturation; SO2, oxygen saturation; pCO2, partial pressure of carbon dioxide; NIV, non invasive ventilation; IOT, orotracheal intubation; DLCO, diffusing capacity of the lungs for carbon monoxide.

This highlights the concept that patient discharge and follow-up are key aspects of the healthcare *continuum*. Readmissions within a few days/weeks may suggest inadequate in-hospital care, inadequate hospital discharge, and/or poor cooperation between hospital and primary care providers. Since in the first weeks/months following an exacerbation-related hospitalization, the risk of readmission is high,[5,6] it is crucial for patients to receive an appropriate maintenance therapy at discharge, regardless of the incoming therapy (often inappropriate or obsolete, and unable to prevent this risk). In this light, the proposed algorithm underlines the importance of a standardized preventive approach.

To support this position, several data show the importance of a timely intervention with appropriate therapy to reduce the risk of exacerbations and hospital readmissions. An Italian population-based cohort study using linked health information systems that included 12,124 patients discharged after a COPD exacerbation and followed for an average of 2.4 years showed that the regular use in the follow-up of ICS in combination with long-term bronchodilators is associated with longer survival than occasional use of the combination or regular use of long-term bronchodilators without ICS.[7]

Randomized controlled trials and a network meta-analysis show that triple combination ICS/LABA/LAMA in a single inhaler are more effective in reducing the risk of exacerbations and improving lung function and quality of life than dual combinations with bronchodilators (LABA/LAMA).[8-12] In the IMPACT study, the largest of these trials (10,335 patients), the triple combination fluticasone furoate (FF)/ umeclidinium (UMEC)/ vilanterol (VI) was significantly more effective than LABA/LAMA in reducing exacerbations, including severe episodes with hospitalization, and all-cause mortality.[9] This latter result was corroborated by a recent *post-hoc* analysis showing that the triple therapy significantly lowered the risk of a composite cardiopulmonary adverse event *vs.* LABA/LAMA.[13]

There is limited real-world evidence to inform about the optimal timing of triple-therapy initiation.[14,15] A recent retrospective cohort study on 1904 patients showed that prompt initiation (within 30 days) of FF/UMEC/VI following a moderate or severe COPD exacerbation was associated with significantly lower rates (28%) of overall exacerbations and COPD-related healthcare costs compared with delayed initiation (after 30 days). The data are consistent with the results from two previous cohort studies.[14-16]

Based on all these findings, in exacerbating patients, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2023 guidelines prioritize the use of triple therapy ICS/LAMA/LABA in a single inhaler, even as initial treatment (not an approved indication for triple therapy in the European Union, where the Summary of Product Characteristics stipulates step up from dual therapy with ICS/LABA or LAMA/LABA), to provide the most benefit to these patients also in terms of reduced risk of mortality.[17] An additional recommendation for the use of ICS-containing regimens is to consider the eosinophil count, >300 cells/μL, to identify patients with a strong likelihood of treatment benefit.[17] On the other hand, since there is a continuous gradation of the preventive effect of ICS in patients with eosinophil values between 100 and 300 cells/μL, GOLD 2023 suggests the possibility of taking into consideration ICS-containing regimens at eosinophil values ≥100 cells/μL.

Considering that inhalation therapy is a cornerstone in COPD management, advances in inhaler technology and design are important to minimize the risk of misuse, favoring patient compliance. Thus, the 2023 GOLD Report, in addition to medication, recommends matching the inhaler with the patient's inhalation ability.

The health benefits of appropriate therapy at discharge and follow-up may result in a reduction in costs and a lowering of the financial burden for the National Health Services.[15] Along this line, the recommendation by the FADOI algorithm of re-assessing the patients during follow-up offers the opportunity to check the efficacy of the prescribed therapy, the patient's compliance, and the onset of any side effects.

It is well known that COPD subjects are often complex patients with comorbidities; for this reason, at discharge and follow-up, it is advisable to move towards a treatment that is as simple as possible (combination therapies, once daily dosing, ease to use inhalers) and to assess the risk/benefit profile.[9,18]

Finally, it is important to evaluate the need for respiratory rehabilitation from the perspective of a benefit for the resumption of the patient's daily activities.

In conclusion, the proposed algorithm is an agile and usable tool for the comprehensive care of COPD patients in internal medicine settings.

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