In their classic presentations, asthma and chronic obstructive pulmonary disease (COPD) are usually easy to diagnose. However, their high prevalence means they often co-exist, which can make diagnosis and treatment more challenging (Maselli et al, 2019).

The concept of asthma-COPD overlap syndrome (ACOS) was introduced in 2015 (Global Initiative for Asthma and Global Initiative for Chronic Obstructive Lung Disease, 2015). Two years later, it was re-described as asthma and COPD overlap (ACO) to prevent it from being seen as a single disease (Global Initiative for Asthma, 2017). According to GINA (2018), “ACO is characterised by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD. ACO is, therefore, identified in clinical practice by the features that it shares with both asthma and COPD”.

International studies have proposed a prevalence of ACO in the general population ranging from 0.9% (Matsumoto et al, 2015) to 11.1% (Sorino et al, 2016).

**Burden of ACO**

Compared with people who have COPD or asthma alone, those with ACO have been found to have an increased burden of disease. This includes:

- More symptoms (Llanos et al, 2018);
- Lower quality of life (Miravitlles et al, 2014);
- More hospitalisations (Kim et al, 2015);
- More comorbidities (Llanos et al, 2018);
- Increased mortality (Kumbhare and Strange, 2018);
- Higher healthcare costs (Kim et al, 2017);
- Greater prevalence of insomnia (Mindus et al, 2018);
- More exacerbations (Llanos et al, 2018).

**Misdiagnosis**

Health professionals in general practice will encounter patients with characteristics and symptoms of both asthma and COPD but, because of overlap between the two, patients can be misdiagnosed (Nissen et al, 2018). In a qualitative study to determine possible misdiagnosis in UK primary care, Nissen et al (2018) concluded that overdagnosis of asthma in people with COPD was
more likely than overdiagnosis of COPD in people with asthma. They proposed that this was because asthma was more liberally diagnosed than COPD as it was seen as a less severe disease and suggested careful use of electronic health records to help identify misdiagnosis and prevent incorrect management of people with asthma, COPD or ACO. They also observed that people were often diagnosed with asthma years before receiving a diagnosis of COPD, after which there was no further documentation relating to asthma – thereby casting doubt over the original asthma diagnosis.

Baarnes et al (2017) found a large number of people with a new COPD diagnosis could be classified as having ACO via opportunistic screening in general practice, suggesting primary care was pivotal in identifying those with overlap. GINA (2018) suggested appropriately trained primary care professionals can identify those who may have ACO, provide initial therapy and refer to specialist care as appropriate.

Table 1 lists the main characteristics of asthma and COPD, and offers guidance on when to consider a diagnosis of ACO.

**Table 1. Characteristics features of asthma and COPD**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset</td>
<td>Before age 20 years</td>
<td>After age 40 years</td>
</tr>
<tr>
<td>Pattern of symptoms</td>
<td>Variation over minutes, hours or days</td>
<td>Persistent despite treatment</td>
</tr>
<tr>
<td></td>
<td>Worse during the night or early morning</td>
<td>Good and bad days but symptoms and exertional dyspnoea always occur daily</td>
</tr>
<tr>
<td></td>
<td>Triggered by exercise, laughter, dust, exposure to allergens</td>
<td>Chronic cough and sputum preceded onset of dyspnoea, unrelated to triggers</td>
</tr>
<tr>
<td>Lung function</td>
<td>Record of variable airflow limitation (spirometry or peak flow)</td>
<td>Record of persistent airflow limitations (FEV1/FVC post-bronchodilator)</td>
</tr>
<tr>
<td>Lung function between symptoms</td>
<td>Normal</td>
<td>Abnormal</td>
</tr>
<tr>
<td>Past history/family history</td>
<td>Previous doctor diagnosis of asthma</td>
<td>Previous doctor diagnosis of COPD, chronic bronchitis or emphysema</td>
</tr>
<tr>
<td></td>
<td>Family history of asthma, and other allergic conditions (allergic rhinitis or eczema)</td>
<td>Heavy exposure to risk factor: tobacco smoke, biomass fuels</td>
</tr>
<tr>
<td>Time course</td>
<td>No worsening of symptoms over time; variation in symptoms seasonally or from year to year</td>
<td>Symptoms slowly worsen over time (progressive course over years)</td>
</tr>
<tr>
<td></td>
<td>May improve spontaneously or have an immediate response to bronchodilators or to ICS over weeks</td>
<td>Rapid-acting bronchodilator treatment provides only limited relief</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>Normal</td>
<td>Severe hyperinflation</td>
</tr>
</tbody>
</table>

Note: These features best distinguish between asthma and COPD. If a patient has three or more for either asthma or COPD, suggest that diagnosis; if there are a similar number for each, consider diagnosis of asthma COPD overlap.

ACO = asthma COPD overlap. FEV1 = forced expiratory volume in one second; FVC = forced vital capacity; ICS = inhaled corticosteroid

Source: Adapted from Global Initiative for Asthma and Global Initiative for Chronic Obstructive Lung Disease (2015)

Treatment

The treatment for asthma, COPD and ACO is summarised in Fig 1. Management of ACO has been based mainly on expert opinion (Maselli et al, 2019), as there have been no large-scale therapeutic trials for ACO and, owing to the overlap of their symptoms, people who have it have been intentionally excluded from therapeutic trials for asthma or COPD alone (Cosio et al, 2018; Sin, 2017). The heterogeneity of ACO also precludes a ‘one-size-fits-all’ approach – care and treatment of ACO needs to be individualised (Cosio et al, 2018; Cazzola and Rogliani, 2016).

A future shift is likely towards medicine that is predictive, preventative, personalised and participatory – described as the P4 approach for all disease (Vanfleteren et al, 2014). However, for airways diseases, some tests to identify disease biomarkers and therapies, such as those that are biologic, are currently only available in secondary or tertiary care; as such, professionals in general practice need guidance on how to diagnose and manage people with ACO, including timely referral to specialist colleagues to receive targeted treatments.

Treatment goals for ACO include:

- Reduced mortality;
- Relief of symptoms;
- Improved quality of life;
- Increased lung function;
- Enhanced exercise tolerance;
- Slowing of disease progression;
- Exacerbation prevention;
- Management of complications and comorbidities;
- Avoidance of adverse effects from therapy (Kondo and Tamaoki, 2018).

Along with pharmacological therapy, long-term management of ACO should include:

- Patient education;
- Pulmonary rehabilitation;
- Vaccination against influenza and pneumococcus;
- Nutritional support;
- Oxygen therapy (Kondo and Tamaoki, 2018);
- Smoking cessation;
- A self-management plan (GINA, 2018; Ohr et al, 2018).

Inhaled corticosteroid (ICS) therapy is the preferred initial treatment for ACO, because of the risk of severe worsening of symptoms associated with long-acting beta agonist (LABA) monotherapy in people with asthma (Medicines and Healthcare products Regulatory Agency, 2014). People who remain symptomatic, or have significant bronchodilator reversibility or airway hyper-responsiveness, may benefit from the addition of bronchodilators (Maselli et al, 2019). Deshpande
and Arnoldi (2017) found that 15% of people with ACO received suboptimal therapy, while Kondo and Tamaoki (2018) suggested that, given its severity, people with ACO be treated more rigorously than those with asthma or COPD alone.

People with ACO may require triple therapy with ICS, LABA and long-acting muscarinic antagonist (LAMA) therapy if they are still symptomatic or have frequent exacerbations, in spite of the initial therapy administered (GINA, 2018). It should be noted that triple therapy is currently licensed for COPD but not asthma; for people with ACO its use is also off licence, but supported by GINA’s (2018) guidance.

Exacerbations

There are no established guidelines for the treatment of ACO exacerbation, but Kondo and Tamaoki (2018) suggested using:

- Inhalation of short-acting beta agonist (SABA), as this is indicated in exacerbation of both asthma and COPD;
- Systemic corticosteroids if there is no response to SABA (40-50mg prednisolone if asthma features are most prevalent; 30-40mg prednisolone, if COPD features are most prevalent);
- Viral and bacterial infections are also implicated in exacerbations and, although many ACO exacerbations are not caused by bacterial infections, antibiotics may be warranted if there is sputum colour change and an increase in volume or thickness (Kondo and Tamaoki, 2018). Other factors that may need considering include:
  - Previous exacerbations;
  - Hospitalisations;
  - Sputum culture and susceptibility results;
  - Risk of resistance;
  - Risk of complications (Her Majesty’s Government, 2019).

A protocol for general practice

In our GP practice, we developed a protocol to identify people with possible ACO to ensure appropriate diagnosis and treatment. We conducted a computer search to identify patients with a diagnosis of both asthma and COPD in their notes. We then sent them an invitation for review, together with an asthma control test (ACT) (Schatz et al, 2006) and COPD assessment test (CAT) (Jones et al, 2009) that we used as validated questionnaires to assess disease control.

At the review, the clinician took the patient’s history and made an assessment. Further investigations (such as chest X-ray, electrocardiogram and blood tests) were arranged where clinically appropriate if:
  - Such investigations had not already been conducted for the patient;
  - The patient’s symptoms had changed;
  - Other comorbidities had to be ruled out – particularly in older people, who have more differential diagnoses, such as atrial fibrillation, bronchiectasis, heart failure, anaemia and sleep apnoea (Walsh et al, 2018).

A summary flowchart and spirometric measures table from GINA’s (2018) guidance were used to make the diagnosis, with specialist respiratory opinion sought as necessary.

Results after six months

Out of a practice population of 12,400, 46 people were identified with a diagnosis of both asthma and COPD. An audit six months later showed that 42 (91%) of these patients attended for review, of whom 40% (n=17) were found to have an incorrect diagnosis. Fifteen of these patients (88%) were diagnosed with COPD and removed from the asthma register, while two (12%) were diagnosed with asthma and removed from the COPD register. The remaining 60% (n=25) of patients attending for review had features consistent with ACO.

Of the 42 patients reviewed, 32 (76%) had their therapies changed to fit with prescribing guidance. Follow-up after 4-8 weeks showed all had improved ACT and CAT scores as a result of medication changes: ACT scores increased by an average of 6.5 and CAT scores reduced by an average of 11, demonstrating improved symptom control. Fourteen (33%) patients accepted a referral to pulmonary rehabilitation and three were referred to the specialist respiratory team (one urgently for suspected lung cancer).

Results after 12 months

Patients with ACO were invited back for review after 12 months. Qualitative data was also gathered by sending out with the review invitation letter a survey containing both questions and space for written comments. Of the 25 patients with symptoms consistent with ACO, six (24%) failed to attend for review despite two reminders being sent. Nineteen (76%) were reviewed; ACT and CAT scores were maintained or improved for 16 (84%) of these patients, and worsened for three (16%). One patient whose score had worsened was referred to specialist respiratory care and two had their therapies adjusted. Follow-up 4-6 weeks later showed both patients had responded positively to changes in therapy, with one achieving a 14-point increase in ACT score and 27-point decrease in CAT score, and the other a three-point increase in ACT score and a four-point decrease in CAT score. There was also a 50% reduction in exacerbations.
Box 1. Feedback from people with ACO after 12 months

“Since having a new inhaler, I find I am breathing better than I have for years.”

“Not used blue inhaler. Breathing normal. No coughing. More confident in the morning that I will have a good day. I can do any job without worry of anything going wrong. I used to take the old inhaler hit and miss, but the new medicine I take regularly as I know it works. I think it works as a barrier to stop me catching other people’s infections.”

“Positive impact on my life: I can do things I could not do before.”

“I managed to paint my daughter’s house all day – I wouldn’t have been able to before. Great improvement. Not used my blue inhaler since Dec 2018.”

“After an ACO review (my first review for some years) I was told my condition had worsened and I was prescribed a new inhaler. Within 10-14 days my irritating cough had almost gone and I had stopped using the emergency inhaler. I have now been on this new inhaler for 6-8 weeks and my energy levels are a lot better. Recently I had a week’s holiday in Yorkshire and found a change to the distances I can walk now without having any breathing problems.”

“I can now sleep, not too much out of breath, two puffs at night, two puffs in the morning and wow, I feel so much better. Never thought I would see the day that I could breathe a lot better – well, I can. I’m so happy.”

“Able to walk in the town without getting breathless. Better in cold weather. Not needed blue inhaler since starting the new medicine.”

ACO = asthma and chronic obstructive pulmonary disease overlap

for all patients reviewed. Feedback from the questionnaire was positive, with patients indicating improvements in symptoms and quality of life (Box 1).

In addition, through a re-run of computer searches, seven new patients were identified and seen with a diagnosis coded for both asthma and COPD. Therapies were changed for two, another two were removed from the asthma register and one was removed from both registers after being given an alternative diagnosis.

Conclusion

The protocol offers a structured approach for identifying, diagnosing and treating people with ACO in primary care. Results from our GP practice suggest it can improve symptom scores and the lives of people with ACO, although larger-scale trials are required. There is potential for it to be used more broadly in general practice to manage people with challenging clinical features of ACO, particularly in the interim period before biomarkers are rolled out in primary care. NT

References