Online Supplement

Aspiration and severe exacerbations in COPD: a prospective study

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Study design, patients, baseline and follow-up study measurements

Studies were conducted at Monash Lung and Sleep at Monash Medical Centre, a tertiary care hospital in Melbourne, Australia. Community-dwelling patients were identified from a hospital pulmonary function database (≥10 pack-year history of smoking, post-bronchodilator FEV₁/FVC≤0.7 and FEV₁<80% predicted [1]) and invited to participate. They had to have a diagnosis of COPD by a general practitioner or respiratory physician, stable lung disease in the preceding 12 weeks and had to be aged 40-80 years. Participation was restricted to those with no known neurological disease, no significant head or neck surgery impacting swallow, no abnormal cranial nerve function on examination, no history of head or neck cancer and no current smokers. Medication use and relevant health history information including comorbidities associated with COPD were obtained from patient history, hospital medical records and medical practitioners.

Measurements of spirometry, gas transfer, lung volumes by body plethysmography and exhaled nitric oxide (FE\textsubscript{NO}) (MGC Diagnostics Medisoft® and Aerocrine NIOX NO monitoring systems) were obtained as per American Thoracic Society and European
Respiratory Society guidelines [2-6]. Measurements were made at baseline and repeated after 6 months. Patients were instructed to withhold inhaled medications prior to assessments.

Transcutaneous oximetry (Nellcor™ PM10N, Covidien) was used to measure peripheral capillary oxygen saturation ($S_pO_2$). Readings were performed at rest and 5 minutes. Respiratory rate was recorded at rest and one minute after drinking.

The Airways Questionnaire 20 (AQ20), a short version of the St George’s Respiratory Questionnaire (SGRQ) [7], was used to evaluate quality of life. It is a validated measure of disease severity and healthcare utilization in COPD [8, 9] with scores $\geq$8 predictive of exacerbations [10]. The Eating Assessment Tool-10 (EAT-10) [11] identifies abnormal swallowing symptoms (score of $\geq$3) and higher scores (>9) may be predictive of increased risk of aspiration in COPD populations [12]. Patients completed the AQ20 and EAT-10 at baseline, 6 months and 12 months.

Baseline assessments of voice function employing auditory perceptual evaluation and a numerical rating scale (0 = no problem/disruption; 1 = mild disruption to voice production; 2 = moderate with frequent episodes; and 3 = severe voice disruption) were performed. The Oral Health Assessment Tool (OHAT), a valid screening instrument was administered at baseline to identify oral health issues in eight categories: lips, tongue, gums and tissues, saliva, natural teeth, dentures, oral cleanliness and dental pain [13]. Resting pH of unstimulated saliva was also measured as per manufacturer’s instructions (GC Australasia Dental) using pH reference $\geq$6.4 [14].
Table S1. Baseline characteristics of 10 patients who did not complete 12-month follow-up

| Patient characteristics (n=10)                  | Age (years, range) | Gender (M/F) | Body Mass Index (kg/m²) | FEV₁ (% predicted) | FEV₁/FVC ratio (%) | TLC (% predicted) | RV/TLC (%) | FEₙO₂ (ppb) | S₉O₂ (%) | Respiratory rate (breaths/min) | Comorbidities (n) |
|------------------------------------------------|--------------------|--------------|-------------------------|--------------------|--------------------|-------------------|-------------|-------------|----------|-------------------------------|-------------------|
| Age (years, range)                             | 71.0±11.5 (41.2-78.8) | 5/5          | 28.6±6.4                | 48.3±17.4          | 50.4±16.3          | 134.6±24.3       | 61.4±8.5    | 31.2±20.7   | 93.5±6.6  | 20.4±2.5                      | Cardiovascular disease 9 |
| Gender (M/F)                                   |                    |              |                        |                    |                    |                   |             |             |          |                               | Chronic kidney disease 0 |
| Body Mass Index (kg/m²)                        |                    |              |                        |                    |                    |                   |             |             |          |                               | Gastro-oesophageal reflux disease 4 |
| FEV₁ (% predicted)                             |                    |              |                        |                    |                    |                   |             |             |          |                               | Obstructive sleep apnoea 1 |
| FEV₁/FVC ratio (%)                             |                    |              |                        |                    |                    |                   |             |             |          |                               | Diabetes 0 |
| TLC (% predicted)                              |                    |              |                        |                    |                    |                   |             |             |          |                               | Anxiety-depression 3 |
| Medication (n)                                                                 |   |
|------------------------------------------------------------------------------|---|
| ICS/LABA only                                                                 | 4 |
| ICS/LABA/LAMA                                                                | 5 |
| Systemic corticosteroids (long term)                                         | 2 |
| Antibiotics (long term)                                                      | 0 |
| Oxygen therapy                                                               | 3 |
| Influenza vaccination                                                        | 3 |
| Pneumococcal vaccination                                                     | 2 |
| Antihypertensives                                                            | 8 |
| Antianxiety/Antidepressant                                                   | 4 |
| Angiotensin-converting enzyme inhibitors                                      | 1 |
| Reflux medications                                                           | 4 |
| AQ20 score                                                                  | 10.1±5.6 |
| AQ20 score >8 (n)                                                            | 6 |
| EAT-10 score                                                                 | 4.1±6.2 |
| OHAT score                                                                   | 2.0±2.4 |
| Resting saliva pH                                                            | 6.4±0.5 |

Data shown as mean ± SD unless otherwise indicated; LABA, long-acting beta agonists; LAMA, long-acting, muscarinic antagonist; ICS, inhaled corticosteroids; AQ20, Airways Questionnaire-20; EAT-10, Eating Assessment Tool; OHAT, Oral Health Assessment Tool.
### Table S2. Subgroup analyses of history and types of AECOPD associated with aspiration or no aspiration in 151 patients

| Study Description                                                                 | Aspiration not detected (n = 121) | Aspiration† detected (n = 30) | Odds Ratio (95% CI)       | P Value  |
|-----------------------------------------------------------------------------------|-----------------------------------|-------------------------------|---------------------------|----------|
| All exacerbations previous year ≥1; n (%)                                           | 42 (34.7)                         | 13 (43.3)                     | 1.44 (0.64-3.24)          | 0.402    |
| Hospital/ED exacerbations (severe) previous year ≥1; n (%)                        | 24 (19.8)                         | 11 (36.7)                     | 2.34 (0.98-5.57)          | 0.057    |
| All moderate/severe exacerbations current study; n (%)                            | 88 (72.7)                         | 24 (80)                       | 1.5 (0.56-4.00)           | 0.491    |
| Hospital/ED exacerbations current study; n (%)                                     | 22 (18.2)                         | 15 (50)                       | 4.5 (1.92-10.55)          | 0.001    |
| Hospital/ED exacerbations ≥2 current study; n (%)                                 | 13 (10.7)                         | 6 (20)                        | 2.08 (0.72-6.02)          | 0.216    |

†Aspiration score of 6-8 on the penetration-aspiration scale [15]; ED, Emergency Department; AECOPD, acute exacerbation of COPD
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