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TITLE: Authors' Reply: Starting beta-blockers during exacerbations of COPD

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MAIN TEXT:

We thank Hancox and colleagues for their interest in our recently published paper (1). Our study of beta-blockers started during admission with acute exacerbation of COPD (AECOPD) demonstrated that these drugs appeared to be well-tolerated (1)**.** In contrast , the feasibility study reported by Chang, Hancox and colleagues highlighted these authors' difficulties in recruiting for a prospective study of beta-blockers commenced in a similar context (2)**.**

Although we acknowledge the limitations of our retrospective study, our detailed review of 36 patients in whom beta-blockers were initiated during AECOPD [see Table 1, online supplement; (1)] found they were generally safe. Our study included patients with severe airflow obstruction, as well as those with significant bronchodilator response. It is reassuring that respiratory adverse effects were not prevalent in either our own study or in the prospective study of Chang et al (2). Unfortunately, given our study was a retrospective audit, we were unable to assess the long-term tolerability of beta-blockers in this cohort. Collection of such information in prospective trials will be critical to determining the utility of commencing beta-blockers in patients with COPD.

We concur with the opinion of Hancox and colleagues that cardioselective beta-blockers should not be withheld in patients with COPD and clear cardiac indications for their use, and our data suggest continuation of beta-blockers in patients admitted with respiratory illness is appropriate. We recently highlighted the prevailing perception among clinicians that beta-blockers are contraindicated in COPD through our finding that only 44.8% of patients with AECOPD and clear cardiac indications for beta-blocker therapy were found to be receiving beta-blockers (3). Unpublished data from this same cohort of 1,071 patients with AECOPD demonstrated significant rates of in-hospital cardiovascular events, including atrial fibrillation with rapid ventricular response (100 patients, 9.3%) and acute coronary syndrome (43 patients, 4.0%) occurring in the total cohort. Furthermore, our data suggest a statistically significant increase in rates of atrial fibrillation with rapid ventricular response following the cessation of beta-blockers during admission compared to those in whom they were continued throughout the hospital admission (see Table 1).

To further address these issues, we are conducting a prospective study of the safety and tolerability of initiating beta-blockers during AECOPD in patients with clear cardiac indications (4). While beta-blocker use is associated with reduced rates of AECOPD in numerous observational studies, it is unclear if this is due to a direct effect on COPD or due to improved medical management of concomitant cardiac disease (5, 6). Our study will include only patients with indications for beta-blocker use for which mortality benefit is unequivocal. It remains to be seen whether feasibility and tolerability mirror or differ from those reported by Chang et al, and we look forward to presenting these results.

REFERENCES:

1. Neef P, Burrell L, McDonald C, Irving L, Johnson D, Steinfort D. Commencement of cardioselective beta-blockers during hospitalisation for acute exacerbations of chronic obstructive pulmonary disease. Internal Medicine Journal. 2017;47(9):1043-50.

2. Chang C, Wong C, Beckert L, Shafuddin E, Beasley R, Young R, et al. β- blockers in exacerbations of COPD: feasibility of a randomised controlled trial. ERJ Open Res. 2017;3(1).
3. Neef P, McDonald C, Burrell L, Irving L, Johnson D, Steinfort D. Beta-blockers are under-prescribed in patients with chronic obstructive pulmonary disease and co-morbid cardiac disease. Internal Medicine Journal. 2016;48(11):1336-40.
4. ANZCTR. (Registration currently being processed, this will be updated in the pre-publication proof). 2017.
5. Bhatt S, Wells J, Kinney G, Washko Jr G, Budoff M, Kim Y, et al. B-Blockers are associated with a reduction in COPD Exacerbations. Thorax. 2016;71(1):8-14.
6. Du Q, Sun Y, Ding N, Lu L, Chen Y. Beta-Blockers Reduced the Risk of Mortality and Exacerbation in Patients with COPD: A Meta-Analysis of Observational Studies. PLOS ONE. 2014;9(11).

TABLES:

Table 1: Univariate analysis of risk of cardiovascular events following cessation of beta-blocker therapy compared to those in whom it was continued throughout admission

	Beta-blockers ceased	**Beta-blockers continued**	**Odds ratio (95% Confidence Interval)**	**p-value**
Atrial fibrillation with rapid ventricular response	10/23	13/253	14.2 (5.24-38.4)	<0.001
Acute coronary syndrome	0/23	9/253	0	0.62