Hip Fracture Outcomes in Patients with COPD

Running title: Hip Fracture Outcome in COPD

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Word count: 1193

Key words: Chronic Obstructive Pulmonary Disease, COPD, Hip Fracture, Osteoporosis, mortality

Abstract

Hip fractures are common in patients with COPD and contemporary outcome data is needed. Patients admitted with a hip fracture to one acute trust (2010-2015) were assessed prospectively (UK National Hip Fracture Database audit) and mortality data collected. Of the 4020 patients, 16.2% had a recorded COPD diagnosis. Mortality was significantly greater in patients with COPD compared to non-COPD: 30-days (12.6% vs 7.8%) and 1-year (35.3% vs 25.3%), both $p<0.001$ and remained significant after adjustment (aOR at 1 year 1.44 95% CI 1.18 -1.76). There is further excess mortality following a hip fracture in those with COPD.

Word count: 97

Editor - Patients with chronic obstructive pulmonary disease (COPD) are at increased risk of osteoporosis[1] and hip fracture[2], with systematic assessment demonstrating osteoporosis in up to 32%[1]. Fracture is a composite of osteoporosis and other factors such as falling, also common in COPD[3]. Previously, worse outcomes have been demonstrated following hip fracture in patients with COPD. However, interpretation is limited due to data that is not contemporaneous[4,5], poorly generalizable[5], with limited follow up[6] or where confounders could not be comprehensively accounted for[4,6].

Using the National Hip Fracture Database (NHFD) dataset[7] and additional fields from the Nottingham centre, the objective of this study was to investigate short and longer-term outcomes following hip fracture in patients with COPD. Patients admitted with a hip fracture to Nottingham University Hospitals Trust are prospectively audited as part of the NHFD. All patients are managed within the local hip fracture pathway, based on national UK standards[8]. Permission to use the dataset was granted by the Trust's Clinical Quality Risk and Safety team, project number 17-267c. Admission co-morbidities (including COPD); length of stay; and mode of anaesthesia (regional (RA) or general (GA) anaesthesia) were collected as was chest infection (an audit term used for lower respiratory tract infection including pneumonia). The Nottingham Hip Fracture Score (NHFS)[9] was calculated where possible and mortality was collected via the Office for National Statistics. The records of patients presenting between 1/10/2010 and 1/10/2015 were retrieved. Exclusions were all those <50 years old and those presenting with bilateral or peri-prosthetic fractures.

Multivariate logistic regression was used to assess the association of COPD diagnosis with mortality following admission (30-day and 1-year) and post-operative complications. Co-variates (see table 1 and also "chest infection") were included if they altered the association

with COPD by 5% or more. There was minimal missing data in secondary variables (Table 1) and all subjects were included in the final analysis with complete age, gender, comorbidities, smoking and functional status. As a sensitivity analysis, the preceding 5-year period (1/10/05 - 30/09/10) was also analysed. A further analysis examining the association between anaesthetic modality and mortality, limited to patients with a diagnosis of COPD was conducted, using the same co-variates with the addition of operation type.

Of the total 4020 subjects, there were 651 (16.2%) cases with a recorded admission diagnosis of COPD, Table 1. There were more current smokers, more with polypharmacy and a greater use enteral steroids in those with COPD. 94 (14%) of patients with COPD were prescribed antiresorptive bone treatment on admission.

Both 30-day (12% vs 7.75%) and 1-year (35% vs 25%) mortality were greater in patients with COPD than those without. This remained significant after adjustment for confounding variables: adjusted odds ratio (aOR) of 1.69 (95%CI 1.28 to 2.23) and 1.44 (1.19 to 1.76) at 30-days and 1-year respectively. The aOR over the previous 5 years (3808 cases with similar demographics and admission characteristics) was similar, as was the crude mortality. Most patients (98.3%) were managed operatively, with no difference in type of operation across those with or without COPD. Of those that received an operation, anaesthetic mode differed: 38.7% of patients with COPD received a GA compared to 58.9% of those without COPD ($p<0.001$). Amongst those with COPD, after adjustment, no difference was noted in mortality with the use of RA compared to GA at 30 days (aOR 0.85, 95%CI 0.49 to 1.5, $p=0.561$), however at one-year, was lower in the RA group (aOR 0.61 95%CI 0.42 to 0.90, $p=0.012$). Length of stay was longer for COPD (median 15vs14 days, $p=0.018$). Of 3676 patients that survived to discharge, 48.7% were discharged on an antiresorptive medication.

Amongst patients with COPD, 22.7% developed a chest infection during their admission as compared to 10.9% of patients without COPD, (aOR 2.41 (95%CI 1.95 to 2.98, p <0.001). Chest infection was associated with an aOR of 2.1 (95%CI 1.3 to 2.2, p<0.001) and 2.3 (95%CI 1.8 to 2.8, p<0.001) for 30-day and 1-year mortality, respectively. When stratified for COPD diagnosis the association between chest infection and mortality became non-significant in the COPD group for both 30-days and 1-year.

We have demonstrated a marked increase in short- and medium-term mortality for patients with an admission diagnosis of COPD presenting with a hip fracture compared to those without COPD. Patients with COPD were at greater risk of a chest infection and few presented on bone antiresorptives at admission. Mortality risk for patients with COPD and hip fracture has been reported previously. Studies from America[5] and Denmark[4] have shown worse mortality in patients with COPD following hip fracture with up to 40% at 1-year where COPD was considered "severe"[5]. In both cases the mortality figures are limited to patients that received surgery, which may have excluded those that were less fit on presentation. The data reported are not contemporary, making direct comparison difficult, but demonstrate similar mortality suggesting there has been little improvement for those with COPD. The finding that the development of a chest infection was more common in patients with COPD is consistent with existing reports[5,10]. Previously, chest infection has been shown to be a determinant of mortality following hip fracture[10]. This finding was repeated in this study; however, chest infection was not significantly associated with mortality in those patients with COPD. This was an unexpected finding but may reflect limitations of the audit term "chest infection" used here.

Ongoing debate concerning the optimal mode of anaesthesia for patients with hip fracture ensues. In this cohort, fewer patients with COPD received a GA, potentially due to comorbid chest disease altering the risk benefit judgement about modality of anaesthesia. In previous studies, little, if any difference in mortality has been observed between the two modalities generally[11], however, RA has previously been associated with better mortality outcomes specifically in patients with COPD[5] and a similar finding was repeated here; although not apparent until the 1-year point. This temporal dissociation makes it difficult to attribute the mortality difference directly to the choice of anaesthetic[12]. Our data are inconclusive on this issue and ongoing randomised controlled trials (e.g. REGAIN[13]) may provide clarity.

The main limitations of this study were that data were drawn from a single site. COPD diagnosis was a record of the presence (or not) of COPD, based on presenting history and inpatient notes, without spirometric confirmation. No other COPD severity variables such as exacerbation frequency or patient related outcomes were available.

Given the substantial excess mortality associated with COPD, efforts to prevent hip fracture in this group deserve to be prioritised. Current NICE osteoporosis guidelines suggest assessing fracture risk in all patients with COPD[14], though this appears to be rarely recorded in practice using the Health Improvement Network database[15]. In this audit, only 14% of patients with COPD admitted with hip fracture were prescribed antiresorptives, seemingly low, although difficult to retrospectively calculate the correct proportion who should have been.

These results demonstrate the implications of this gap in delivering COPD care, which goes beyond antiresorptive treatment and includes management of co-morbid factors that

contribute to falls risk; as well as non-pharmacological interventions ranging from smoking cessation to dietary changes in order to improve bone health. A holistic approach is needed in the management of those with COPD.

Authors' contributions

LB analysed the dataset, wrote the first draft and revised subsequent versions of the manuscript; TM advised on the statistical analysis and contributed to revision of the manuscript; JN extracted and advised on the dataset and contributed to revision of the manuscript; RA contributed to revision of the manuscript; BO was involved with the original dataset, approval of the project and revision of the manuscript; IM was involved with the original dataset, advised on the statistical analysis and contributed to the revision of the manuscript; CB conceived the project, advised on the statistical analysis and revised all stages of the manuscript

Declaration of interests

LB, TM, JN, RA, BO, IM have no interests to declare. CB holds investigator sponsored study grants from Pfizer and GSK for COPD research studies, honoraria from Chiesi and has received consultancy fees from Boehringer Ingelheim.

Funding

This work was supported by the NIHR Nottingham BRC respiratory theme.

References:

1. Bolton CE, Ionescu AA, Shiels KM, et al. Associated loss of fat-free mass and bone mineral density in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2004;170(12):1286-1293.
2. Reyes C, Estrada P, Rogues X, et al. The impact of common co-morbidities (as measured using the Charlson index) on hip fracture risk in elderly men: a population-based cohort study. In. Vol 25.6. O*steoporos Int*2014:1751-1758.
3. Hakamy A, Bolton CE, Gibson JE, McKeever TM. Risk of fall in patients with COPD. *Thorax Published Online First: 21 March 2018.*DOI: 10.1136/thoraxjnl-2017-211008.
4. de Luise C, Brimacombe M, Pedersen L, Sørensen HT. Chronic obstructive pulmonary disease and mortality following hip fracture: a population-based cohort study. *Eur J Epidemiol* 2008;23(2):115-122.
5. Regan EA, Radcliff TA, Henderson WG, et al. Improving hip fractures outcomes for COPD patients. *Int J Chron Obstruct Pulmon Dis.* 2013;10(1):11-19.
6. Dodd A, Bulka C, Jahangir A, Mir H, Obremskey W, Sethi M. Predictors of 30-day mortality following hip/pelvis fractures. *Orthop Traumatol Surg Res.* 2016;102(6):707-710.
7. Royal College of Physicians. National Hip Fracture Database annual report 2017. London: RCP, 2017 https://www.nhfd.co.uk/.
8. National Institute of Health and Care Excellence (NICE). Hip fracture: management. NICE clinical guideline [CG124]. https://wwwniceorguk/guidance/cg124. June 2011.
9. Maxwell M, Moran C, Moppett I. Development and validation of a preoperative scoring system to predict 30 day mortality in patients undergoing hip fracture surgery. *Br J Anaesth.* 2008;101(4):511-517.
10. Roche J, Wenn RT, Sahota O, Moran CG. Effect of comorbidities and postoperative complications on mortality after hip fracture in elderly people: prospective observational cohort study. *BMJ.* 2005;331(7529):1374.
11. Waesberghe J, Stevanovic A, Rossaint R, Coburn M. General vs. neuraxial anaesthesia in hip fracture patients: a systematic review and meta-analysis. *BMC Anesthesiol.* 2017;17(1):87.
12. White S, Griffiths R, Moppett K. Type of anaesthesia for hip fracture surgery–the problems of trial design. *Anaesthesia.* 2012;67(6):574-578.
13. Neuman MD, Ellenberg SS, Sieber FE, Magaziner JS, Feng R, Carson JL. Regional versus General Anesthesia for Promoting Independence after Hip Fracture (REGAIN): protocol for a pragmatic, international multicentre trial. *BMJ open.* 2016;6(11):e013473.
14. National Institute for Health and Care Excellence. Osteoporosis: assessing the risk of fragility fracture, https://www.nice.org.uk/. 2012.
15. Akyea R, McKeever TM, Gibson J, Scullion J, Bolton CE. Osteoporosis and fracture risk in patients with Chronic Obstructive Pulmonary Disease (COPD): a UK based population-based cohort study (as abstract in world congress on osteoporosis, osteoarthritis and musculoskeletal disease). *Osteoporos Int.* 2018;26.

Legend of table

Table 1 Baseline admission characteristics of patients with and without COPD presenting with hip fracture between 1st October 2010 and 1st October 2015

Baseline admission characteristics	**Patients with COPD** N= 651	**Patients without COPD** N=3369	**p-value**
Age years median (IQR) Δ	82 (75-87)	84(77-89)	<0.001
Male sex n(%) Δ	215(33.0)	928(27.6)	0.005
Current smoking n(%) Δ	130(20.0)	328(9.7)	<0.001
Co-morbidities n(%) Δ			
Cardiovascular disease ł	437 (67.1)	2129 (63.2)	0.056
Stroke or TIA	103 (15.8)	504(14.0)	0.574
Diabetes	122 (18.7)	524(15.6)	0.043
Renal disease	83 (12.8)	431 (12.8)	0.976
Rheumatoid arthritis	31 (4.8)	104 (3.1)	0.030
Parkinson's disease	15 (2.3)	121 (3.6)	0.096
Malignancy	88 (13.5)	496 (14.7)	0.425
Four or more medications n(%) Δ	406(62.4)	1530(45.4)	<0.001
Enteral steroids n(%) Δ	70(10.8)	113(3.4)	<0.001
Admitted from own home n(%) Δ	477(73.3)	2475(73.5)	0.818
Fully independent of ADLs n(%) Δ	234(35.9)	1410 (41.9)	0.005
Walking independently n (%)	392(60.2)	2015(59.8)	0.670
Unknown	96 (14.8)	479 (14.2)	
AMTS ≤6 n(%) Δ	168(25.8)	1101(32.7)	0.002
Unknown	30(4.6)	119(3.5)	
Haemoglobin of ≤10 g/dL n(%)	68(10.4)	349(10.4)	0.797
Unknown n(%) Δ	2 (0.31)	17 (0.5)	
NHFS* of ≥6 (/10) n(%)	230 (35.3)	961 (28.5)	0.001
Unknown	31 (4.8)	135 (4.0)	
ASA grade of ≥4 n(%)	159(24.4)	402 (11.9)	<0.001
Unknown	122 (18.7)	727(21.6)	
Anti-resorptive treatment prior to admission n(%)	94(14.4)	375(11.1)	0.016
Type of fracture n(%)			0.78
Intracapsular	387(59.5)	2016(60.0)	
Intertrochanteric	219(33.6)	1083(32.2)	
Subtrochanteric	33(5.1)	201(6.0)	
Other (e.g. reverse oblique)	12(1.8)	63(1.9)	

ADLs, activities of daily living; NHFS, Nottingham hip fracture score, ASA, American Society of Anaesthesiologists; AMTS, Abbreviated Mental Test Score; TIA, Transient Ischaemic Attack

Δ Co-variates tested in multivariate logistic regression models assessing mortality and complications as outcomes

* Calculated from component parts on admission

Ł including hypertension