Clinical management practices of life-threatening asthma: an audit of practices in intensive care

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Asthma requiring management in the intensive care unit (ICU) is a serious but potentially reversible condition. Recent reviews of life threatening asthma (LTA) in Australia and New Zealand are more than 10 years old and lack detail on clinical management.[1] Although asthma prevalence is increasing, rates of presentation requiring ICU admission have been decreasing since the 1990s, despite an increasing severity of illness.[2-4] The need for mechanical ventilation is accepted as an indicator of LTA, with an associated mortality of 2.8%.[1,5]

Variation in both clinical practice guidelines and physician practices for asthma are well documented,[6,7] contributing to recurrent admissions, patient morbidity, costs of care, interval symptoms and mortality.[8] Currently, there are limited data examining these trends in adult LTA. Clinical audits allow current practices to be evaluated and provide insight into the efficacy of various treatments as well as drive further research. This study aims to elucidate contemporary physician practices and treatment modalities for LTA and to compare these practices with current guidelines.

Methodology

A multicentre retrospective cohort study was conducted using ICU and patient clinical charts from July 2010 to June 2013. All 15 ICUs in Queensland and the Northern Territory in Australia were invited to participate. Patients for inclusion were identified from local unit datasets of the Australia and New Zealand Intensive Care Society Centre for Outcome and Resource Evaluation database (ANZICS CORE), and eligible paediatric patients were identified from the Australian and New Zealand Paediatric Intensive Care (ANZPIC) registry, when a primary diagnosis of asthma was the primary reason for admission. Medical charts were audited using a written proforma to collect de-identified data. The data collected included patient demographics; Acute Physiology and Chronic Health Evaluation (APACHE) II score;[9] past clinical history of asthma, such as exacerbations, atopy, smoking history, outpatient management, intensive care pharmacological and mechanical ventilation management and discharge outcomes, including discharge destination; the presence of a documented asthma management plan; and follow-up arrangements. Children were defined as

ABSTRACT

Objective: Lack of management guidelines for life-threatening asthma (LTA) risks practice variation. This study aims to elucidate management practices of LTA in the intensive care unit (ICU).

Design: A retrospective cohort study.

Setting: Thirteen participating ICUs in Australia between July 2010 and June 2013.

Participants: Patients with the principal diagnosis of LTA.

Main outcome measures: Clinical history, ICU management, patient outcomes, ward education and discharge plans.

Results: Of the 270 (267 patients) ICU admissions, 69% were female, with a median age of 39 years (interquartile range [IQR], 26–53 years); 119 (44%) were current smokers; 89 patients (33%) previously required ICU admission, of whom 23 (25%) were intubated. The median ICU stay was 2 days (IQR, 2–4 days). Three patients (1%) died. Seventy-nine patients (29%) received non-invasive ventilation, with 11 (14%) needing subsequent invasive ventilation. Sixty-eight patients (25%) were intubated, with the majority of patients receiving volume cycled synchronised intermittent mechanical ventilation (n = 63; 93%). Drugs used included $ß_2$-agonist by intravenous infusion (n = 69; 26%), inhaled adrenaline (n = 15; 6%) or an adrenaline intravenous infusion (n = 23; 9%), inhaled anticholinergics (n = 238; 90%), systemic corticosteroids (n = 232; 88%), antibiotics (n = 126; 48%) and antivirals (n = 22; 8%). When suitable, 105 patients (n = 200; 53%) had an asthma management plan and 122 (n = 202; 60%) had asthma education upon hospital discharge. Myopathy was associated with hyperglycaemia requiring treatment (odds ratio [OR], 31.6; 95% CI, 2.1–474). Asthma education was more common under specialist thoracic medicine care (OR, 3.0; 95% CI, 1.61–5.54).

Conclusion: In LTA, practice variation is common, with opportunities to improve discharge management plans and asthma education.

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being aged less than 16 years at the time of admission. When there were multiple admissions for one patient during the study period, the details of the most severe episode (requiring invasive mechanical ventilation or with the longest length of ICU stay if not invasively ventilated) were used to record demographic data. Data from presentations were included in the study of clinical practice. It was not possible to identify patients presenting to different hospitals within the methodology of the blinded data collection. For non-invasive ventilation (NIV), the terms bilevel, BiPap and pressure support ventilation were combined as "B-PS" due to a common use of these terms interchangeably. Two units without a research assistant used an abbreviated survey form collecting information largely related to ICU management. Physiological data were collected from the ICU flowsheet. Management was compared with contemporary published guidelines for LTA, including the British Thoracic Society,[10] the National Heart, Lung, and Blood Institute *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma* (EPR-3)[11] and the Global Initiative for Asthma (GINA) guidelines.[12,13]

Table 1. Demographic characteristics of asthma admissions to the intensive care unit

Parameter	Asthma episodes *n* = 270
Total number of patients	267
Gender (female)	183/267 (69%)
Unit recruitment	
1	20 (7%)
2	21 (8%)
3	9 (3%)
4	35 (13%)
5	10 (4%)
6	21 (8%)
7	35 (13%)
8	34 (13%)
9	32 (12%)
10	15 (6%)
11	38 (14%)
Age (years), median (IQR)	39 (26–53)
Children (< 16 years)	8/267 (3%)
Onset asthma	
Child	101/267 (38%)
Adult (≥ 16 years)	66/267 (25%)
Unknown	100/267 (37%)
Smoking history	
Current smoker	119 (44%)
Lifelong non-smoker	59 (22%)
Previous smoker	49 (18%)
Unknown	43 (16%)
Current smoking use, pack years (*n* = 55), median (IQR) [range]	15 (5–20) [0.25–57]

(continued)

Sample sizing and statistical methods

For the time period of the study, it was estimated that 300 patients including children would be available for review. This would provide the potential to build a multivariate linear regression model from an anticipated 30 variables for asthma management predictors or outcomes.[14] Univariate data were described using median and interquartile range (IQR) and 95% confidence intervals (CI) unless otherwise specified. Actual data ranges were used to reflect the spread of a broad distribution when clinically relevant. Logistic models included variables in which associations in univariate analysis had $P \leq 0.2$ with goodness of fit and calibration assessed by the Hosmer–Lemeshow statistic and area under the receiver–operator curve, respectively. Analysis used Stata 15.1 statistical software (StataCorp, College Station, TX, USA).

Ethical considerations

Low risk ethics approval was granted from the Royal Brisbane and Women's Hospital Human Research Ethics Committee (HREC/13/QRBW/310). De-identified data were collected and stored using secure password-protected computer encryption.

Results

Study cohort

Over the 3-year study period, there were 270 ICU admissions, representing 267 patients. Demographic patient characteristics are summarised in Table 1. The majority of presentations were female (*n* = 183; 69%) with a median age of 39 years (IQR, 26–53 years), and there were only eight children (3%) included in the dataset. Most patients presented to hospital from their home (*n* = 205; 76%), with the source of ICU admission being the emergency department (*n* = 218; 81%) and 22 patients (8%) being admitted to the ICU from ward-based or specialised high dependency care.

There were 156 patients (58%) with one or more comorbid conditions, the most common being mood and psychiatric

Table 1. Demographic characteristics of asthma admissions to the intensive care unit *(continued)*

Parameter	Asthma episodes ***n*** = 270
Present packs per day (*n* = 74), median (IQR) [range]	0.75 (0.5–1) [0.07–3]
Previous smoking use, years ceased (*n* = 38), median (IQR) [range]	7 (0.25–40) [0.25–40]
Pack years (*n* = 21), median (IQR) [range]	15 (8–20) [2–70]
Previously known asthma triggers	
Allergen	55 (20%)
Upper respiratory tract infection	106 (39%)
Weather	47 (17%)
Exercise	17 (6%)
Other	19 (7%)
Unknown	65 (24%)
Comorbidities	
Diabetes mellitus	31/267 (12%)
Hypertension	47/267 (18%)
Ischaemic heart disease	10/267 (4%)
Congestive cardiac failure	4/267 (1%)
Gastro-oesophageal reflux	34/267 (13%)
Obstructive sleep apnoea	29/267 (11%)
Mood or psychiatric disorder	72/267 (27%)
Number of comorbidities	
0	111/267 (42%)
1	83/267 (31%)
2	40/267 (15%)
3	19/267 (7%)
4	8/267 (3%)
≥ 5	6/267 (2%)
Associates of asthma	
Rhinosinusitis or conjunctivitis	39/267 (15%)
Elevated IgE	19/267 (7%)
Atopic dermatitis/eczema	11/267 (4%)
Allergies	78/267 (29%)
Known +ve skin prick tests	10/267 (4%)
No associates	58/267 (22%)
Unknown	108/267 (40%)
Previous hospital admissions in the past 5 years	
0	104/216 (48%)
1	53/216 (25%)
2	17/216 (8%)
3	18/216 (8%)
4	9/216 (4%)
≥ 5	15/216 (7%)

IQR = interquartile range. +ve = positive.

disorders (*n* = 72; 27%). There was no history of atopy in 58 patients (22%). Only 59 patients (22%) had never smoked, while 119 (44%) were current smokers. There were 134 patients (50%) who had no previous asthma presentations. From the recorded 356 previous presentations for asthma in the cohort, 74 (27%) had two or more presentations. Of those patients with previous admissions, 89/356 (25%) required an ICU admission, with 23/89 (26%) needing intubation.

Information on usual maintenance therapy was available for 255 patients. Only a little over half the patients were receiving regular inhaled long-acting $ß_2$-agonists (*n* = 144; 56%) and inhaled corticosteroids (*n* = 151; 59%). Anticholinergics were used by 47 patients (18%), with systemic corticosteroids used regularly in 43 patients (17%). Emergency parenteral adrenaline prescription was only identified in three patients (1%). There was rescue therapy information recorded for 209 patients in the days before the acute hospital presentation. In contrast to the records of routine maintenance therapy, most patients were taking additional short-acting $ß_2$-agonists (SABA) (*n* = 191; 91%); however, only 64 patients (31%) were taking inhaled corticosteroids and 89 (43%) were receiving a systemic corticosteroid. Table S1 of the Appendix (online at cicm.org.au/Resources/Publications/Journal) summarises the relationship between maintenance therapy use and asthma control.

Acute asthma presentation

In the month before presentation, 61 patients (23%) had few or no symptoms, 58 (21%) were short of breath on two or fewer occasions a week, 44 (16%) were waking from sleep weekly or less frequently and 45 (17%) needed to use rescue medications less frequently than weekly. Overall, asthma symptoms were assessed as well controlled in only 52 patients (19%). The majority of presentations were precipitated by upper respiratory tract infections (*n* = 171; 63%, but 52 patients (19%) had no recognised precipitant. The details of the acute asthma presentations are summarised in Table S2 and Table S3 of the online Appendix.

Intensive care admission

Patients on admission to ICU were moderately ill, with a median APACHE II score of 12 (IQR, 8–15) with an arterial partial pressure of carbon dioxide ($Paco_2$) level of 41 mmHg (*n* = 103; range, 22–118 mmHg) and a median oxygen saturation measured by pulse oximetry (Spo_2) level of 92% (range, 40–100%).

Non-invasive ventilation

Of the 270 admissions to the ICU, 79 patients (29%) received NIV, with rescue invasive ventilation required in 11 patients (14%). Three patients needed ongoing NIV following invasive ventilation. On commencing NIV, the median $Paco_2$ level was 44 mmHg (*n* = 97; IQR, 37–49 mmHg; range, 21–119 mmHg). The median total time spent receiving NIV was 8 hours (IQR, 4–17 h; range, 0.2–62 h), representing a median of 62% (IQR, 21–100%; range, 2–100%) of the hours spent in the ICU. B-PS was used as the sole NIV mode in 64 patients (81%) and continuous positive airway pressure in 11 patients (14%).

B-PS used a median inspiratory positive airway pressure of 12 cmH_2O (IQR, 10–14 cmH_2O; range, 7–40 cmH_2O) and a positive end-expiratory pressure (PEEP) of 5 cmH_2O (IQR, 5–7 cmH_2O; range, 1–15 cmH_2O). In those patients only receiving continuous positive airway pressure, the median airway pressure was 5 cmH_2O (IQR, 5–6 cmH_2O; range, 3–15 cmH_2O).

Invasive ventilation

Of the 68 patients (25%) who received invasive ventilation, 63 (93%) received volume cycled synchronised intermittent mechanical ventilation (SIMV-VC), which was the initial mode used in the ICU in 80% of patients. The ventilation mode initiated in the emergency department was not recorded in our survey. A pressure-based strategy was used in 29 patients (43%), pressure-controlled

Table 2. Summary of drug use during admission to the intensive care unit (ICU)

	n = 270 (%)	Proportion of ICU admission time of medication use Median (IQR) [range]
Systemic corticosteroids		1 (1–1) [0.08–1]
Total	232 (86%)	
Enteral	131 (49%)	
Parenteral	192 (71%)	
Dexamethasone	3 (1%)	
Hydrocortisone	181 (67%)	
Methylprednisolone	14 (5%)	
Prednisolone	131 (49%)	
Dose (prednisone equivalent) (mg)		75 (5–100) [10–625]
> 150 mg/day	4 (1%)	
Short-acting ß-agonist		1 (1–1) [0.06–1]
Total	263 (97%)	
MDI	28 (10%)	
Nebuliser	245 (91%)	
Intravenous infusion	69 (26%)	
Inhaled anticholinergic		1 (0.5–1) [0.08–1]
Total	238 (88%)	
MDI	27 (10%)	
Nebuliser	228 (84%)	
ICS		0.73 (0.5–1) [0.08–1]
Total	56 (21%)	
MDI	33 (12%)	
Nebuliser	24 (9%)	
Magnesium	91 (34%)	0.5 (0.33–0.66) [0.08–1]
Antibiotics	126 (47%)	1 (0.5–1) [0.08–1]
Antivirals	22 (8%)	
Non-selective catecholamines		
Total	38 (14%)	0.5 (0.33–0.73) [0.08–1]
Nebuliser	15 (6%)	0.41 (0.25–0.6) [0.14–1]
Intravenous infusion	23 (9%)	0.42 (0.29–0.75) [0.25–1]
Emergency parenteral adrenaline	3 (1%)	
Methylxanthines		0.68 (0.4–1) [0.125–1]
Total	38 (14%)	
Enteral	9 (3%)	
Intravenous infusion	33 (12%)	
Long-acting ß-agonist	32 (12%)	1 (0.5–1) [0.2–1]
Ketamine infusion	12 (4%)	0.4 (0.17–0.60) [0.125–1]
Inhalational anaesthetic	2 (1%)	0.14 (0.09–0.18) [0.09–0.18]

ICS = inhaled corticosteroids. IQR = interquartile range. MDI = metered-dose inhaler.

synchronised intermittent mechanical ventilation (SIMV-PC) in nine patients (13%), bilevel in 15 patients (22%), pressure cycled assist control (AC-PC) in two patients (3%), with one patient (1%) each receiving either airway pressure release ventilation, adaptive support ventilation or pressure regulated volume control. Only one ventilation mode was used in 47 patients (64%). Some patients received multiple modes during the admission, with two modes used in 18 patients (24%) and three modes in three patients (4%), exclusive of spontaneous weaning modes. Invasive ventilation continued for a median of 2.6 days (IQR, 1.0–5.2 days; range, 0.17–19.5 days). The median minimum respiratory rate used was ten breaths per minute (IQR, 8–12; range, 4–18), with a median tidal volume of 0.61 L (IQR, 0.55–0.70 L; range, 0.32–1.85 L). There were 21 patients with tidal volumes greater than 0.8 L while receiving a mandatory rate of mechanical ventilation. Twelve of these patients (57%) were ventilated with a pressure targeted strategy, while the remainder were all receiving SIMV-VC. Measurements of auto-PEEP were available in the clinical record in only 23 patients (31%). The median highest auto-PEEP recorded was 10 cmH_2O (IQR, 7–13 cmH_2O; range, 13–24 cmH_2O).

Table 3. Clinical outcomes

	***n* = 265 (%)**
Days in ICU, median (IQR) [range]	2 (2–4) [1–24]
Complications in ICU	
All electrolyte disturbances	91 (33%)
Hypokalaemia	75 (28%)
Hypophosphataemia	13 (5%)
Hyperkalaemia	2 (1%)
Hypomagnesaemia	3 (1%)
Hyponatraemia	3 (1%)
Hypocalcaemia	4 (1%)
Hyperglycaemia needing treatment	63 (24%)
Lactic acidosis	21 (8%)
Pneumonia	14 (5%)
Myopathy	10 (4%)
Atelectasis	8 (3%)
Pneumomediastinum	3 (1%)
Pneumothorax	2 (1%)
Diaphragm paralysis	1 (< 1%)
Cardiac arrhythmia needing treatment	8 (3%)
Myocardial infarction	8 (3%)
Hypoxic brain injury	3 (1%)
Discharge management plan documented when deemed applicable	105/200 (53%)
Asthma education when deemed applicable	122/202 (60%)
Hospital outcome	
Died in hospital	3 (1%)
Home and independent	246 (93%)
Home and not independent	9 (3%)
Transfer to another hospital	7 (3%)
Not documented	5 (2%)

ICU = intensive care unit. IQR = interquartile range.

During invasive ventilation, the median highest value of $Paco_2$ was 53 mmHg (IQR, 44–67 mmHg; range, 21–130 mmHg). The median percentage of the total invasive ventilation time in which the patient remained hypercapnic ($Paco_2$ > 45 mmHg) was 50% (IQR, 21–71%; range, 0–100%), with eight patients remaining hypercapnic after cessation of invasive ventilation. These patients only had mild hypercapnia, with a median $Paco_2$ at the time of weaning of 49 mmHg (IQR, 48.5–52 mmHg; range, 46–58 mmHg). The median maximum inspiratory:expiratory (I:E) ratio was 1:4.3 (IQR, 1:3.6–1:7; range, 1:1.7–1:19), in which the most prolonged I:E ratios were associated with low mandatory respiratory rates. The minimal setting of PEEP was a median of 5 cmH_2O (IQR, 0–9 cmH_2O; range, 0–20 cmH_2O), with the highest recorded median peak inspiratory pressure being 38 cmH_2O (IQR, 27–48 cmH_2O; range, 15–85 cmH_2O). Plateau pressures were inconsistently recorded to be available for analysis. Arterial partial pressure of oxygen (Pao_2) was recorded for patients receiving any form of ventilation. The highest median Pao_2 was 317 mmHg (IQR, 220–427 mmHg; range, 55–650 mmHg).

Pharmacological management

The pharmacological details of management were available for 265 episodes of ICU care (Table 2). All patients received some form of adrenergic agonist via SABA (263; 99%), $ß_2$-agonist intravenous infusion (69; 26%), inhaled adrenaline (15; 6%) or an adrenaline intravenous infusion (23; 9%). There were 20 patients (8%) who received both intravenous infusions of catecholamines and nebulised SABA, 12 patients (5%) received both inhaled SABA and non-selective catecholamines, while one patient received inhaled and intravenous catecholamines in addition to short term nebulised SABA on the same day. Anticholinergics were used in 238 patients (90%). Systemic corticosteroids were used in 232 patients (88%), the formulations, predominantly hydrocortisone and prednisolone (median prednisiolone equivalent dose, 75 mg/day). Three patients received dexamethasone. Inhaled corticosteroids were given to 56 patients (21%). Antibiotics were used in 126

patients (48%) and antivirals in 22 (8%). Inhaled or nebulised and systemic corticosteroids were received concurrently in 43 patients (16%) for whom systemic corticosteroid dose remained greater than 15 mg in prednisolone equivalents.

Clinical outcomes

Clinical outcomes are summarised in Table 3. Although most patients (*n* = 246; 93% of the 265 patients with information available) were able to be discharged home and were independent, three patients (1%) died in hospital (two while admitted to the ICU), nine (3%) were able to be discharged home but were not independent, and seven (3%) needed to be transferred to another hospital. The median length of ICU stay was 2 days (IQR, 2–4 days; range, 1–24 days). Common electrolyte disturbances were hypokalaemia (75; 28%), hyperglycaemia needing treatment (63; 23%) and hypophosphataemia (13; 5%). Additional common complications included lactic acidosis (21; 8%), myopathy (10; 4%) and nosocomial pneumonia (14; 5%), with hypoxic brain injury occurring in three patients (1%).

In univariate modelling, the development of myopathy was associated with APACHE II score, antibiotic use, time with hypercapnia, cumulative dose of prednisolone while in the ICU, ventilation hours and hyperglycaemia needing treatment, with ventilation hours and hyperglycaemia being independent predictors (Table 4). All patients with myopathy had been invasively ventilated.

When patients remained in their original hospital and with a documented discharge to ward based care (*n* = 254), 135 (53%) were cared for most commonly by general medical physicians (102; 40%). In patients for whom a discharge management plan was considered applicable, 105 (*n* = 200; 53%) received a documented asthma management plan and 122 (*n* = 202; 60%) had documentation of asthma education before discharge. We could not find any predictors for documentation of an asthma management plan at discharge (online Appendix, Table S4). However, the only predictor of documentation of asthma education occurring during the admission was when care was under specialist thoracic medicine after ICU discharge (Table 5).

We were unable to find specific predictors of NIV failure. Patients needing both NIV and invasive ventilation were not predicted by APACHE II score ($P = 0.10$), currently smoking ($P = 0.74$), asthma control in the month before presentation ($P = 0.81$), weight ($P = 0.94$), age ($P = 0.88$), the number of comorbidities ($P = 0.2$), the number of previous admissions ($P = 0.41$), worst Spo_2 level before ICU admission ($P = 0.88$), worst $Paco_2$ level before ICU admission ($P = 0.78$), history of obstructive sleep apnoea ($P = 0.74$), mood disorder ($P = 0.58$) or antibiotic use ($P = 0.71$). No patients with a history of diabetes mellitus needed to receive invasive ventilation after NIV.

Table 4. Associations of myopathy present at intensive care unit (ICU) discharge*

Univariate models	Odds ratio (95% CI)	*P*
Lactic acidosis	1.49 (0.2–12.5)	0.72
APACHE II	1.11 (1.03–1.20)	0.01
Number of comorbidities	0.77 (0.41–1.42)	0.36
Gender	2.23 (0.63–7.89)	0.22
Non-invasive ventilation	0.34 (0.04–2.73)	0.25
Antibiotic use	5.20 (1.08–25.0)	0.02
Hypercapnia (hours)	1.07 (1.04–1.11)	< 0.001
Prednisone cumulative dose in ICU (mg)	1.001 (1.0003–1.002)	0.06
Ventilation hours	1.02 (1.01–1.02)	< 0.001
Hyperglycaemia needing treatment	35.15 (4.35–283.60)	< 0.001
Electrolyte disturbance	0.49 (0.10–2.35)	0.34
Hypokalaemia	0.30 (0.04–2.42)	0.19
Hypomagnesaemia	7.11 (0.72–70.20)	0.16
Hypophosphataemia	2.30 (0.27–19.63)	0.49
Multiple regression model		
Ventilation hours	1.02 (1.01–1.02)	< 0.001
Hyperglycaemia needing treatment	31.56 (2.10–474.11)	0.01

APACHE = Acute Physiology and Chronic Health Evaluation. * Calibration of model: Hosmer–Lemeshow, goodness of fit ($\chi^2 = 0.54$; $P = 0.91$). Discrimination of model: area under receiver operating characteristic (ROC) curve (0.97).

Discussion

Our study found a low overall mortality of LTA, consistent with previous findings.[3,4] Previous studies have noted that most mortality occurs before hospital admission,[15] with in-hospital mortality largely attributed to inadequate observation, limited recognition of respiratory failure or deficient treatment.[16] Most patients did not meet current guidelines for recommended maintenance or acute exacerbation therapy;[17,18] smoking was common, and many struggled with asthma symptoms for some time before hospital presentation.[15]

Treatment options in LTA are mainly extrapolated from severe

Table 5. Associations of documentation of asthma education*

Univariate models	Odds ratio (95% CI)	*P*
Age	0.99 (0.98–1.01)	0.17
APACHE II	1.00 (0.95–1.04)	0.87
Number of comorbidities	0.81 (0.63–1.03)	0.09
Myopathy	5.45 (0.67–44.42)	0.11
Number of previous admissions	0.97 (0.84–1.12)	0.66
Non-invasive ventilation	1.10 (0.55–2.16)	0.80
Invasive ventilation	0.83 (0.44–1.57)	0.58
Smoking (compared with current smoking)		0.17
Non-smoker	0.58 (0.27–1.24)	
Previous smoker	0.53 (0.25–1.14)	
Asthma control (compared with well controlled)		0.34
Somewhat controlled	1.87 (0.74–4.69)	
Poorly controlled	1.16 (0.53–2.55)	
Corticosteroid accumulated dose in ICU (prednisone equivalent) (mg)	0.99 (0.99–0.99)	0.01
Ventilation hours	0.99 (0.99–1.02)	0.48
Non-invasive ventilation	1.09 (0.55–2.16)	0.80
Invasive ventilation	0.84 (0.44–1.57)	0.58
ICU discharge care (compared with general medical care)		0.001
Shared specialist/general care	1.49 (0.48–4.65)	
Specialist thoracic care	3.18 (1.72–5.86)	
Multiple regression		0.0002
Corticosteroid accumulated dose in ICU (prednisone equivalent) (mg)	0.99 (0.99–0.99)	0.05
ICU discharge care (compared with general medical care)		0.001
Shared specialist/general care	1.59 (0.49–5.14)	
Specialist thoracic care	3.0 (1.61–5.54)	

APACHE = Acute Physiology and Chronic Health Evaluation. ICU = intensive care unit. * Calibration of model: Hosmer–Lemeshow, goodness of fit (χ^2 = 9.88; *P* = 0.27). Discrimination of model: area under receiver operating characteristic (ROC) curve (0.67).

presentations.[19] There was variability in the use of intravenous $ß_2$-agonists and catecholamines. With no documented advantage of parenteral administration of bronchodilators, prescription may relate to a clinical assessment of the efficacy of nebulisation therapy with drug delivery better assured parenterally.[20] Nebulised therapy was more common than metered-dose aerosol despite lack of documented efficacy. Drug delivery varies with nebuliser type, ventilator mode and gas flow parameters, with the optimal method of aerosolised drug delivery in ventilated patients remaining unclear.[21] There does not seem to be a difference in aerosolised drug delivery efficacy with NIV compared with spontaneous breathing,[22] although studies in patients with significant airflow obstruction are lacking. Not all patients received inhaled anticholinergic agents although their safety and beneficial adjunct to $ß_2$-agonists have been demonstrated.[23-25] Some 18% of patients were receiving antibiotics before hospital presentation, which increased to 48% during their ICU admission despite not generally being needed in LTA.[19] Data were not collected for microbiological confirmation of infection. In a life-threatening situation in which pulmonary infiltrates are present on x-rays, it would be a difficult decision to withhold antibiotics while awaiting culture confirmation. Clearly, appropriate early de-escalation as part of ward-based care is important.

Not all patients received systemic corticosteroids while in the ICU, perhaps reflecting the speed of recovery and administration before ICU admission. The median dose of systemic corticosteroids in equivalents of prednisolone was 75 mg and is consistent with guidelines for adults.[17] Prescription of larger doses (eight patients), largely pulse methylprednisolone,[26-28] was in the absence of evidence-based support. The individual response to systemic corticosteroids is variable and is related to the degree of obstruction.[29] Although for mild to moderate asthma, inhaled corticosteroids may be used as an alternative to systemic administration,[30] the addition of inhaled corticosteroids to systemic corticosteroids does not improve clinical outcomes and the effects in ventilated patients are unknown.[31] Parenteral and enteral corticosteroids would appear equivalent, except in patients thought to have systemic absorption issues.[32-34]

The use of adjunctive agents was variable in our cohort, with a limited evidence base.[35] No patient received inhaled helium-oxygen admixtures, with limited evidence to support its use and limited availability.[19] Parenteral administration of magnesium was consistent with guidelines. Lack of use as a continuous infusion to target a particular serum

level would be in keeping with maintenance of a normal serum concentration.[17] Guideline recommendations for aminophylline remain confusing, with continued support in children,[18] but not in adults,[17] hampered by a lack of pharmacokinetic and pharmacodynamic data in the critically ill.[36]

Ketamine was rarely used in our cohort. It has limited clinical efficacy as a bronchodilator salvage therapy. The propensity for increased airway secretions may also be undesirable. It has usually been reserved for patients receiving mechanical ventilation due to its anaesthetic properties.[37] However, nebulised ketamine has been reported and awaits further efficacy evaluation.[38] Inhalational anaesthetics were also rarely used. The literature supporting their use is based on the pharmacological potential for adrenergic receptor stimulation, direct bronchodilation, histamine antagonism and interference with hypercapnic bronchoconstriction[39] and physiological before-and-after studies.[40] Hypotension is common, with inotropic support required and with prolonged administration and associations with neuropathy, renal impairment and hepatotoxicity.[40]

NIV is commonly used in LTA, with low complication and similar deterioration rates (4.5–12 %), as found in our study.[41] Benefits remain inconclusive,[42] with higher mortality rates in those patients deteriorating on NIV, as is the case for most other respiratory conditions.[43] The need for invasive ventilation in patients receiving NIV is largely predicted by the severity of respiratory failure,[42-44] concomitant diagnosis of pneumonia, the number of prior asthma admissions and comorbid diabetes mellitus.[45] We could not confirm these associations using antibiotic therapy and worst Spo_2 as a surrogate for a pneumonia diagnosis.

In our study, although both pressure and volume strategies were employed, preference was for volume cycled ventilation. There is no recommended consensus on the mode of invasive ventilation that should be used, and perhaps consistent institutional preference is most important.[44] Most strategies aim for controlled hypercapnia, avoiding air trapping and heterogenous ventilation.[44] There were no significant gains in lung emptying beyond an expiratory time of 4 seconds and no PEEP,[46] although there may be some improvement in dynamic airway closure by small amounts of PEEP between 1 and 3 cmH_2O.[47] Measures of auto-PEEP, persisting expiratory flow when the next breath is delivered or dynamic trapped volume may be used when making ventilation changes to ensure lung emptying, but are not commonly recorded in the chart. Our study suggests that there were patients with mixed disease needing higher PEEP than would be recommended for severe asthma. Some tidal volumes were large, suggesting that improved monitoring of this parameter is required, especially when using a pressure mode. I:E ratios were generally managed to facilitate prolonged expiration. The use of high-flow oxygen therapy (HFO_2) was not able to be determined accurately in our study. Some publications have suggested that HFO_2 in severe asthma may prolong length of stay due to a delay in instituting positive pressure ventilation,[48] but further specific study is needed for benefit over conventional oxygen therapy.[49]

Myopathy potentially delays ventilator weaning and prolongs hospital length of stay. We found that myopathy was associated with the duration of mechanical ventilation and hyperglycaemia. Hyperglycaemia, oxidative stress and depletion of troponin T has been shown to weaken diaphragm strength[50] and, more generally, is recognised as a risk for post-critical illness weakness.[51]

National and international guidelines support referral of patients with LTA to specialists with expertise in ambulatory management and asthma education — a structured approach and management of comorbidities that may not be readily available outside larger centres.[52] Our cohort had poor documentation of an asthma management plan or having received asthma education, also observed by others.[53] A designated patient education role held by clinical staff may improve readmission rates by ensuring education occurs.[54] This is an important issue as the one-year post-discharge mortality in LTA is 10%, with women, smokers and patients over the age of 40 years disproportionately represented.[55] The mortality rate remains high for 10 years after discharge, particularly in those patients requiring mechanical ventilation.[56] A "recollection" of the case history while in post-ICU ward care would be a variable addition to improve the detail of clinical notes and could be part of asthma education before discharge.

This study represents a contemporary summary of intensive care asthma management within two of Australia's states and territories. It is important because the detail of clinical care in LTA is under-reported.[57] Variation in practice is recognised in ambulatory care but has not been characterised previously for LTA.[58] The study is limited by its retrospective nature and surety of data, such as interval symptoms, auto-PEEP documentation, asthma education and discharge planning. Modelling for predictors of mortality was not performed due to its rarity. Although the time frame for the study was prolonged due to significant staff movement, the data are reflective of current practice.

Conclusion

There is a significant variability in the management of critically severe asthma within ICUs, particularly related to the use of second-line therapies. Many modes of mechanical ventilation are used with an overall successful outcome, suggesting that familiarity with ventilatory approaches may be more important than any particular technique.

Avoiding hyperglycaemia may be important to prevent the development of myopathy. We need to ensure that patients with LTA have a well documented history, particularly in relation to preventable risks, and receive recommended ambulatory care and education.

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Competing interests

None declared.

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