

Long-term Outcome and Disease Control in Near-fatal Asthma

W C Tan,**FAMS, FRACP, FCCP*, K P Lim,**, T P Ng,****FAMS, MPPHM, FACOM*, T C Chao,*****FAMS, FRCPath, FRCPA*,
Y Y Ong,†*FAMS, M Med (Int Med), MRACP*, Y C Chee,‡*FAMS, FRCP (Lond), FRACP*

Abstract

Patients who have survived an episode of intubation and mechanical ventilation for acute respiratory failure due to a severe and unresponsive asthmatic attack are considered to have experienced a near-fatal asthma (NFA) attack. Such patients are at a higher risk of similar severe attacks and hence of death in the future.

The aims of the study were to: (i) evaluate the outcome; (ii) identify any persistent deficiencies in asthma management, and (iii) assess self-management knowledge in survivors of NFA. Ninety-three consecutive patients who had been treated for NFA in the Intensive Care Unit of an urban teaching hospital in Singapore from 1992 to 1997 were studied. All hospital records were reviewed retrospectively. Survivors were then invited to attend a questionnaire interview and to have lung function tests performed. Of the original cohort (OC) of 93 patients with NFA (mean age 55.2 years), 18 (19% OC) patients (mean age 64 years) had died while in hospital and 75 (81% OC) patients survived the initial episode of NFA and were discharged home (DH). The long-term outcome of this DH group was: 13 patients had died (17% DH) and 62 (83% DH) survived. Of these survivors, 35 were interviewed while 27 declined or were not contactable. This interview yielded the following information:

- (i) Hospitalisation in the past year: 66 % had no hospital admission; of the 31.4 % who had 2 or more admissions, most had a further NFA attack.*
- (ii) Health care: The majority of patients (71.4%) were monitored by a single doctor.*
- (iii) Patient knowledge of disease management was deemed good to fair for trigger avoidance (77%), for appropriate drug usage (97%).*
- (iv) Satisfactory inhaler skill (80%).*

NFA is associated with a high intrahospital and long-term mortality. Although most survivors of NFA appeared to have satisfactory care and a fair understanding of medication usage, a significant minority continue to pose much morbidity and risk for death.

Ann Acad Med Singapore 1999; 28:384-8

Key words: *Asthma, Ethnic, Mortality, Race, Trends*

Introduction

Rising trends in mortality in asthma have been reported from many countries, including Asian countries such as Hong Kong.¹⁻³ Asthma deaths have been associated with a number of avoidable factors such as deficiencies in personal and professional management that can potentially be remedied if identified.⁴⁻¹¹ Furthermore, a history of near-fatal asthma (NFA) has been shown to be a risk factor for subsequent death from asthma. Available data on patients who have suffered a near-fatal asthmatic attack showed an increased long-term mortal-

ity rate.¹²⁻¹⁴ A six-year follow-up study of 145 such patients found a post hospitalisation mortality of 10.2% at one year, 14.4% at three years, and 22.6% at six years.¹² Most of the deaths were due to recurrent severe asthmatic attacks. Most of these patients were not receiving close follow-up with structured review of objective tests of pulmonary function.

NFA resemble fatal cases in many aspects including asthma severity, frequency of symptoms, frequency of hospital care, compliance with medications, types of medication used, quality of personal asthma care and

* Professor

** Medical Student (Elective Period), Department of Medicine, National University of Singapore

*** Associate Professor

Department of Community, Occupational and Family Medicine, National University of Singapore

**** Special Forensic Advisor

Department of Forensic Medicine, Ministry of Health

† Head

Department of Respiratory and Critical Care Medicine, Singapore General Hospital

‡ Head

Department of General Medicine, Tan Tock Seng Hospital

Address for Reprints: Dr WC Tan, Department of Medicine, National University of Singapore, Faculty of Medicine, Lower Kent Ridge Road, Singapore 119260.

psychiatric profile.¹⁵⁻¹⁸ They could provide a surrogate group for study into the problems associated with the risk of asthma deaths. Resultant data could yield information for life-saving intervention.

The aims of this study were: to evaluate prospectively the long-term outcome, identify any deficiencies in asthma management and assess knowledge in survivors of NFA.

Materials and Methods

This study was conducted from September 1997 to December 1997. Patients who had been treated for a severe attack of asthma requiring close surveillance and management in the medical intensive care unit of the National University Hospital were studied. All patients had a well-established history of asthma. All patients fulfilled the American Thoracic criteria for the diagnosis of asthma. Asthma was considered only if there was a convincing history of asthma supported by recurrent episodes of wheezing and dyspnoea requiring medical intervention and prompt response to bronchodilators, and /or evidence of significant reversibility of airway obstruction ascertained by spirometric measurements before or after the episode of NFA. Patients were considered to have suffered NFA if they arrived at the hospital in respiratory arrest or had overt respiratory failure despite vigorous conventional treatment. Respiratory failure was defined as the need for mechanical ventilation or $\text{PaCO}_2 > 50$ mmHg and / or altered conscious state.^{14,18}

The study design consisted of three parts:

1. A retrospective review of all the case records of consecutive patients admitted into the medical intensive care unit of the National University Hospital during a five-year period from January 1992 to September 1997.
2. The details and confirmation of all deaths of the patients studied were obtained through the National Registry of births and deaths.
3. A prospective interview using a structured respiratory questionnaire based on those used in the New Zealand mortality studies^{10,19,20} was administered prospectively by one investigator (LKP) to survivors of NFA who consented to be interviewed. The aims of this interview were to assess disease severity based on that recommended by the global initiative for asthma (GINA);* and to obtain information after the episode of NFA, on health care provision and utilisation,²² patient education; patient adherence to asthma medication regimens¹⁰ and patient attitude towards their disease. Responses were reviewed by one clinician and one epidemiologist from the study team and collective judgement was made.

Data Analysis

The following data were obtained: fatal asthma or

intrahospital mortality for the initial severe asthmatic attack and NFA or long-term mortality occurring after hospital discharge for the initial severe asthmatic attack.

Data obtained from the response to the questionnaire interview included asthma severity as scored according to the GINA guidelines;²¹ health care quality (number of changes of primary care providers for asthma); number of hospitalisations; patient knowledge about asthma; and inhaler technique were assessed by expressing the patient's score for the correct answers as a percentage of the best achievable score. In the 35 patients who were interviewed, the clinical severity scoring according to the GINA guidelines²¹ was determined at the interview and compared with that assessed from the MICU case notes.

The survival curve (Fig. 1) was displayed using the actuarial life table method of SPSS version 9.0.

Results

Ninety-three patients, mean age 55.2 years, were identified as having suffered NFA treated in the MICU from 1992 to 1997. The smoking status of the patients consisted of 49% never-smokers; 37% ex-smokers and 14% current smokers of less than 5 pack years. Patients with significant smoking history (>5 pack years) and likely chronic obstructive lung disease were not included in the study. Ten patients had a diagnosis of concomitant ischaemic heart disease. A total of 31 patients, mean age 68.4 years, had died during the study period September to December 1997. Sixty-two survivors, mean age 50 years, were identified at the time of the study. Of the survivors, 35 patients, mean age 49.5 years, agreed to be interviewed. Of the remaining 27 patients who were not interviewed, mean age 50.8 years, 10 refused the invitation and 17 were not contactable due to change in address or emigration.

Mortality

There were 31 deaths registered during the study

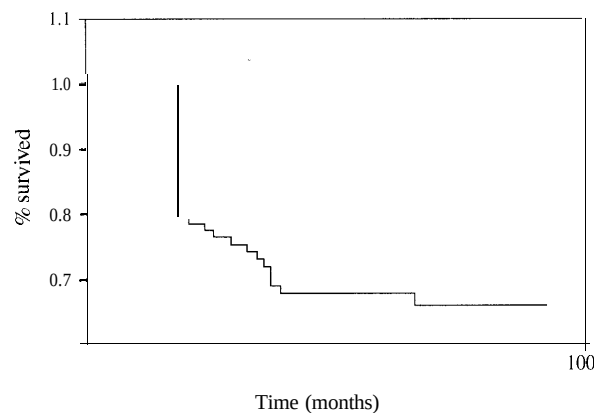


Fig. 1. Survival (%) of patients discharged from the MICU.

period, giving an overall mortality of 33%. The short-term intrahospital mortality rate was 19.4% (18/93). Seventy-five patients were discharged from hospital after the index NFA episode. Information from the National Registry indicated that a further 13 out of these 75 initial survivors who were discharged for the index NFA episode had subsequently died giving an additional long-term mortality rate of 17.3% for the initial survivors. Nine of these deaths occurred in another hospital while 4 occurred at home. The long-term survival is represented in Figure 1.

The immediate causes of death in the 18 asthmatics during the initial ICU admission are shown in Table I. Anoxic brain damage and cardiopulmonary arrest on arrival at the emergency room were the main causes of death. In patients who had not had a cardiopulmonary arrest at the time of presentation at the hospital, the causes of death were from associated diseases or complications such as pneumonia, cardiac failure, cerebral haemorrhage and peritonitis.

Table II shows the details (certified causes of death, venue of death and time from the initial ICU admission) for the long-term mortality of 13 patients who survived the initial ICU admission for NFA and were discharged from hospital but who subsequently died during the period of the study.

Disease Severity of Survivors

In the 35 survivors who were interviewed, disease severity (GINA score) prior to admission to hospital for NFA, as assessed from the MICU case notes was compared with the GINA score obtained during the interview and are shown in Fig. 2. There was a shift of the GINA score towards the less severe category at the time of the interview compared to that before the index NFA episode.

Health Care Provision and Utilisation

A summary of the results of the questionnaire interview is shown in Table III.

TABLE I: CAUSES OF DEATH IN 18 ASTHMATICS DURING INITIAL INTENSIVE CARE UNIT ADMISSION

Main cause of death	No.	Sex
Anoxic brain damage	4	4F/-
Cardiopulmonary arrest on arrival	8	7F/1M
Complications		
. Cardiac failure	1	1F/-
. Pneumonia	2	1F/1M
. Cerebral bleed	2	-/2M
. Peritonitis	1	1F/-
Total	18	14F/4M

The significant minority of patients (34.4%) had 1 or more hospitalisations during the year prior to the interview. In patients who had 2 or more hospital admissions, at least one of these (75%) was for another episode of NFA. Analysis of the response to the question on the health care provision showed that the majority of patients (71.4%) received regular supervision of asthma control from one doctor. Private general practitioners and hospital specialists formed the two main categories of doctors consulted (45.7% and 40.0% respectively). Traditional medicine (including herbal) was also utilised by 17.1% of the patients interviewed.

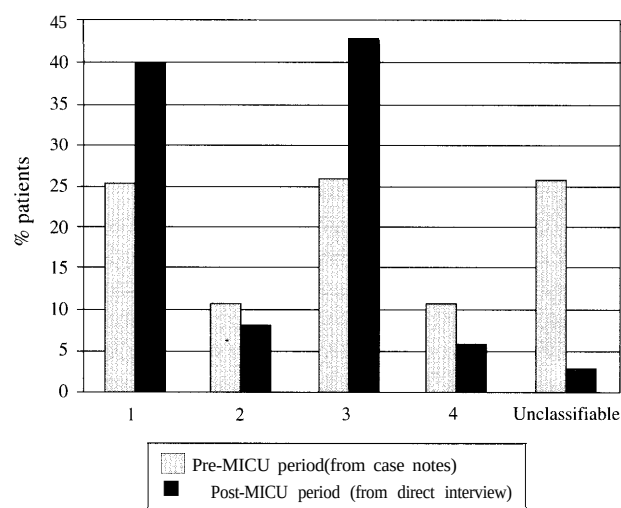
Patient Education and Knowledge

Over half the patients (51.4%) were judged to be

TABLE II: CERTIFIED CAUSES OF DEATH AFTER SURVIVING INITIAL MEDICAL INTENSIVE CARE UNIT (MICU) ADMISSION

Certified death	No.	Venue	Time from initial MICU
Asthma	3	Hospital	13 to 56 months
	1	Home	
COPD	3	Hospital	1 to 16 months
	1	Home	
Pneumonia	1	Hospital	19 months
Cancer	2	Home	8 to 22 months
	1	Hospital	

COPD: chronic obstructive pulmonary disease



- 1 -Intermittent asthma
- 2-Mild persistent asthma
- 3-Moderate persistent asthma
- 4-Severe persistent asthma

Unclassifiable-Information inadequate for assignment of category

Fig. 2. Comparison of asthma severity score (GINA) during initial MICU and at time of interview.

TABLE III: MORBIDITY AND HEALTH CARE PROVISION IN 3.5 INTERVIEWED SURVIVORS OF NEAR-FATAL ASTHMA

	Percentage
Hospitalisation (past year)	
0	65.7
2 – 3*	17.1
4 or more*	14.3
Health care supervision	
1 doctor	71.4
2 – 3 doctors	22.9
>3 doctors	5.7
Patient knowledge of management	
Fair to good	65.7
Inhaler technique	
Fair to good	80.0
Patient attitude	
“Self efficacy” (confidence)	91.4

*This includes 1 or more MICU admission in 75% of cases.

adequately informed of the basic underlying mechanism of the illness as well as ways of controlling it. 74.3% of those interviewed admitted to receiving formal instructions on inhaler technique. Although 80% of those interviewed and tested used the MDI satisfactorily, only 19.4% knew of the different actions of the two main groups of inhalers: bronchodilators and inhaled steroids.

Patient Attitude

Self confidence in asthma self management and confidence in their doctors were expressed by 32 out of 35 (91.4%) patients.

Discussion

NFA is associated with a high intrahospital and an excess long-term mortality. The high intrahospital mortality is similar to that in an earlier report.²³ The current study shows a post hospitalisation mortality of 19% over a median period of 19 months, range 1 to 56 months. These data confirm findings reported in other developed countries where published data had shown an increased long-term mortality rate.¹²⁻¹⁴ A six-year follow-up study of 145 such patients found a post hospitalisation mortality of 10.2% at one year, 14.4% at three years, and 22.6% at six years? Most of the deaths were due to recurrent severe asthmatic attacks. The current study thus supports previous observations that the most powerful predictive feature in the history that a severe asthmatic attack may be life threatening in any history of prior intubation and mechanical ventilation for asthma.⁷

The reasons for the high long-term mortality rate were not obvious. Our data showed that the certified causes of death were due to asthma as well as to other causes, such

as chronic obstructive pulmonary disease and lung cancer. A recent population study showed that there is an excess death due to chronic obstructive lung disease in asthmatic subjects compared with non-asthmatic persons.²⁴ It is therefore conceivable that part of the excess mortality the current study could be due to chronic bronchitis and emphysema, as there might be some misclassification between asthma and chronic bronchitis in the elderly. Nonetheless, the long-term mortality data also showed that deaths directly attributable to another severe attack of asthma occurred in this cohort of survivors of an initial NFA episode.

Various reasons have been proposed to explain the increased risk of death and near death from asthma, including asthma severity, frequency of symptoms, frequency of hospital care, compliance with medications, types of medication used, quality of personal asthma care and psychiatric profile.¹⁵⁻¹⁷ Several authors noted that most of these patients were not receiving close follow-up with structured review of objective tests of pulmonary function. Conversely, other authors observed that regular follow-up care was associated with improved long-term survival.^{13,14} The importance of the approach of secondary prevention was emphasised in a study of 12 survivors of a near-fatal asthmatic attack, which found that of the 7 who returned for regular follow-up visits, all survived. Of the 5 who did not, 2 died from asthma within 18 months.¹³

In this study, asthma severity (GINA score) in the survivors lessened after discharge for NFA. This is likely to be the effect of careful follow-up and treatment modification. Similar effects have been shown by Ruffin et al¹⁴ who documented a progressive improvement in bronchial hyper-responsiveness with closely supervised care of NFA patients. The GINA score supported the clinical impression from other studies^{15,18} namely, that fatal and NFA could occur in asthmatics of all grades of severity.

The findings in our study were discrepant in some ways. Most survivors in our study appeared to have satisfactory health care and a overall fair but patchy understanding of medication usage. Furthermore, the change in the pattern of the GINA score suggested a lessening in asthma severity in survivors of NFA. Despite these, adverse long-term characteristics such as frequent hospitalisation, repeated MICU admissions for NFA episodes and high death rates persisted in a sizeable minority of NFA survivors.

There are several potential reasons for these findings:

- The current usage of GINA score may not be sufficiently objective to be used as a marker of severity,
- Baseline asthma severity is not the only risk factor for a life-threatening asthma attack,
- Another possible explanation for the above findings may lie in self-denial. Survivors of NFA paradoxi-

cally show denial of their illness and anxiety also appears to be higher in the family members than in the patients themselves.²⁵ Denial is a natural mechanism for dealing with a situation that is perceived to be beyond one's control. That denial may be present in the patients interviewed with consequent poor application of knowledge, was inferred from the discrepancy between the high level of self confidence in self management and the frequency of recurrent hospitalisations.

We identified two problems in the interpretation of the results of the study. In this study the descriptive data were derived from a small number of subjects interviewed, and may not be representative of all those who survived. Nonetheless, the findings are similar to those reported in several large studies of NFA in Europe, Australia and North America.¹²⁻¹⁸ Longer term evaluation of a larger group of well characterised near-fatal asthmatics from several hospitals is needed to validate the current data. The second problem lies in the predominantly descriptive case-series design of the study. The data in this study are of importance as it confirms a high long-term mortality rate in asthmatics who have survived a NFA episode and provides insight into the medical management of NFA cases for planning and evaluative purposes. However, the interpretation should be cautious due to the lack of a matched control group and the inclusion of smokers, with the potential risk of studying mortality rates of a chronic obstructive disease as well as asthma. More comparative research is needed, using a case-control or cohort study design. Despite these caveats, the risk of death from another episode of severe asthma in patients who had a previous episode of NFA is unequivocally shown in this study.

Acknowledgements

We thank the patients who participated in the study; the National Registration Department of Singapore for their help in ascertaining the details of death ; and to Ms Nancy Woon for preparation of the manuscript.

REFERENCES

1. Weiss K B, Wagener D K. Changing patterns of asthma mortality: identifying target populations at high risk. *JAMA* 1990; 264:1683-7.
2. Sears M R. Worldwide trend in asthma mortality. *Bull Int Union Tuberc Lung Dis* 1991; 66:79-83.
3. So S Y, Ng M M, Ip M S, Lam W K. Rising asthma mortality in young males in Hong Kong, 1976-85. *Respir Med* 1990; 84:457-61.
4. Robertson C F, Rubinfeld A R, Bowes G. Death from asthma in Victoria; a twelve month survey. *Med J Aust* 1990; 152:511-7.
5. Sears M R, Rea H H, Beaglehole R, Gillies A J, Holst P E, O'Donnell T V, et al. Asthma mortality in New Zealand: a two-year national study. *NZ Med J* 1985; 98:271-5.
6. British Thoracic Association. Deaths from asthma in two regions of England. *BMJ* 1982; 285:1251-5.
7. Rea H H, Scragg R, Jackson R, Beaglehole R, Fenwick J, Sutherland D C. A case control study of deaths from asthma. *Thorax* 1987; 41:833-9.
8. Clark N M, Starr-Schneidkraut N J. Management of asthma by patients and families. *Am J Respir Crit Care Med* 1994; 149:S54-66.
9. Pearce N, Grainger J, Atkinson M, Crane J, Burgess C, Culling C, et al. Case-control study of prescribed fenoterol and death from asthma in New Zealand, 1977-81. *Thorax* 1990; 45:170-5.
10. Rand C S, Wise R A. Measuring adherence to asthma medication regimens. *Am J Respir Crit Care Med* 1994; 149:S69-76.
11. Turner M O, Noertjojo K, Vedal S, Bai T, Crump S, Fitzgerald J M. Risk factors for near-fatal asthma. A case-control study in hospitalised patients with asthma. *Am J Respir Crit Care Med* 1998; 157:1804-9.
12. Marquette C H, Saulnier F, Leroy O, Wallaert B, Chopin C, Demarcq J M, et al. Long-term prognosis of near-fatal asthma. A 6-year follow-up study of 145 asthmatics patients who underwent mechanical ventilation for a near-fatal attack of asthma. *Am Rev Respir Dis* 1992; 146:76.
13. Molino N A, Nannini L J, Rebuck A S, Slutsky A S. The fatality-prone asthmatic patient. Follow-up study after near fatal attacks. *Chest* 1992; 101:621.
14. Ruffin R E, Latimer K M, Schembri D A. Longitudinal study of near-fatal asthma. *Chest* 1991; 99:77-83.
15. Richard G N, Kolbe J, Fenwick J, Rea H H. Demographic characteristics of patients with severe life threatening asthma: comparison with asthma deaths. *Thorax* 1993; 48:1105-9.
16. Beasley R, Pearce N, Crane J. Use of near fatal asthma for investigating asthma deaths [editorial comments]. *Thorax* 1993; 48:1093-4.
17. Campbell D A, McLennan G, Coates J R, Frith P A, Gluyas P A, Latimer K M, et al. A comparison of asthma deaths and near fatal asthma attacks in South Australia. *Eur Respir J* 1994; 7:490-7.
18. Campbell D A, Luke C G, McLennan G, Coates J, Frith P A, Gluyas P A, et al. Near-fatal asthma in South Australia: descriptive features and medication use. *Aust NZ J Med* 1996; 26:356-62.
19. Richards J M Jr, Hemstreet M T. Measures of life quality, role performance, and functional status in asthma research. *Am J Respir Crit Care Med* 1994; 149:S31-9.
20. Kolbe J, Vamus M, James F, Elkind G, Garrett J. Assessment of practical knowledge of self-management of acute asthma [see comments]. *Chest* 1996; 109:86-90.
21. Global Initiative for Asthma (GINA)-Global Strategy for Asthma Management and Prevention. United States: National Institutes of Health (National Heart, Lung & Blood Institute), January 1995. NHLBI/WHO Workshop Report, March 1993, Publication No. 95-3659.
22. Vollmer W, Osbourne M, Buist A S. Uses and limitations of mortality and health care utilisation statistics in asthma research. *Am J Respir Crit Care Med* 1994; 149:S79-87.
23. Lee K H, Tan W C, Lim T K. Severe asthma. *Singapore Med J* 1997; 38:238-43.
24. Huovinen E, Jaakko K, Vesterinen E, Koskenvuo M. Mortality of adults with asthma: a prospective cohort study. *Thorax* 1997; 52:49-54.
25. Yallowlees P M, Ruffin R E. Psychological defences and coping styles in patients following a life-threatening attack of asthma. *Chest* 1989; 95:1298.