Research

Acute respiratory distress syndrome: estimated incidence and mortality rate in a 5 million-person population base

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Received: 19 August 1997
Revisions requested: 13 November 1997
Revisions received: 20 January 1998
Accepted: 30 January 1998
Published: 12 March 1998

Crit Care 1998, **2**:29

(Print ISSN 1364-8535; Online ISSN 1466-609X)

Abstract

Background: Various estimates of the incidence and mortality rate of the acute (adult) respiratory distress syndrome (ARDS) have been published. The studies that led to those estimates were based on relatively small patient populations and employed variable diagnostic identifiers of ARDS. The purpose of this study was to estimate the incidence of ARDS and its mortality rate from a large database to which refined diagnostic criteria were applied. We conducted a retrospective review of all hospital discharges over a 4-year period, using screening criteria designed to select patients with ARDS. Discharges from all acute care hospitals in the state of Maryland were reviewed using a computer database from the Health Services Cost Review Commission (HSCRC). Patients ≥ 12 years of age were included. Screening criteria consisted of ICD-9 codes 518.5 and 518.82 cross-referenced with procedural codes for ventilatory support (96.70, 96.71 and 96.72). Data were normalized to the number of cases per 100,000 people.

Results: During the 4-year study period there were 2,501,147 hospitalizations. Applying the ICD-9 ARDS criteria yielded lower and upper limits of 159-205, 439-568, 531-694 and 529-720 cases of ARDS for 1992, 1993, 1994 and 1995, respectively. Normalizing for a population of 5 million yields yearly lower and upper limit rates of 3.2-4.2, 8.8-11.4, 10.6-13.8 and 10.5-14.2 cases of ARDS per 100,000 people. Mortality upper and lower limit rates based upon the same duration, admissions and population were 38-49%, 39-52%, 36-47%, and 36-49%, respectively.

Conclusions: The incidence of ARDS in Maryland is in the range of 10-14 cases per 100,000 people. The ARDS mortality rate is 36% to 52%, similar to that calculated in previous studies.

Keywords: acute respiratory distress syndrome, ARDS, incidence, mortality, respiratory failure

Introduction

The acute (adult) respiratory distress syndrome (ARDS) continues to cause substantial morbidity and mortality in the USA [1] and worldwide [2–4], but the incidence remains unclear. The National Heart and Lung Institute (NHLI) Task Force on Respiratory Distress Syndromes estimated the incidence of ARDS in the USA at 150,000 new cases per year [1]. The NHLI estimate translates to a population-based figure of 71 per 100,000. A recent prospective screening evaluation of hospitals in Utah [5] suggested that the incidence of ARDS is actually 'an order of magnitude less than' the NHLI estimate. The authors, Thomsen *et al*, estimated lower and upper limits for the incidence to be 4.8 and 8.3 cases of ARDS per 100,000 people. In 1988, Webster *et al*[2] calculated the incidence of ARDS in a limited British population to be 4.5 per 100,000 people, similar to Thomsen's estimate.

Villar and Slutsky [3] prospectively reviewed the incidence of ARDS in a controlled population of 703,710 during a 3-year period on the Canary Islands. Applying two sets of diagnostic criteria, the investigators found an incidence ranging from 1.5-3.5 cases per 100,000 people. Angus *et al* reported a much higher incidence of 50.7-64.3 per 100,000 people [4]. The Angus study, based on 109,874 hospital admissions from three states, Washington DC and the national Medicare database, used codes from the International Classification of Diseases, ninth edition (ICD-9), similar to those employed in the Thomsen study. However, Angus further refined the ICD-9 coding to include patients with > 96 h of ventilatory support. Preliminary data from another ongoing prospective study in a major university hospital revealed an incidence of ARDS of 25 per 100,000 [6].

The mortality rate associated with ARDS has also been difficult to quantify. The 1972 report from the NHLI quoted a range of mortality from 25% with optimal care to 70% in the absence of treatment. The American-European Consensus conference report [7] states that the 'published mortality rate of patients with ARDS varies from 10% to as high as 90%'. An effort to determine international hospital survival rates was undertaken by Vasilyev *et al* in 1995 [8]. A survey of both US and European respiratory ICUs determined that the survival rate was 33% (mortality 67%) over a 1-year period. Survival was higher in patients with acute respiratory failure secondary to pneumonia (63%) or postshock lung injury (67%), compared with respiratory failure resulting from sepsis (46%). According to Evans *et al*[6], the mortality rate is highest among patients with gastric aspiration, pneumonia and sepsis (60%).

In order to establish the incidence and mortality associated with ARDS in one of the 50 United States (Maryland), a retrospective review of Health Services Cost Review Commission data was undertaken.

Materials and methods

The Health Services Cost Review Commission (HSCRC) was established by the Maryland General Assembly in 1971 and given the authority to establish hospital rates. To achieve its rate-setting goals, the HSCRC collects data from all hospitals in the state. This includes demographic information, discharge diagnosis by the ICD-9 classification [9], utilization data such as length of hospital and ICU stay, and hospital charges. Since the HSCRC is a state agency, the information is available to the public.

Our methods and criteria were modifications of those used by Angus [4] and Thomsen [5]. The relevant ICD-9 codes are shown in Table 1. The HSCRC database was reviewed in a two-step process. The initial search was for all patients > 12 years old who were discharged between the beginning of 1992 and end of 1995 with ICD-9 codes 518.5 and 518.82 (Table 2), without additional constraint. The ICD-9 code 518.81 was not searched because its descriptors do not include ARDS. The second search incorporated the same ICD-9 codes with the additional mandate of ventilatory support (Table 2) (procedural codes 96.70, 96.71 and 96.72, established in 1991). The data were subsequently stratified into survivors and non-survivors.

Table 1

Respiratory disease codes from the International Classification of Diseases, 9th revision (ICD-9)

518.5	Pulmonary insufficiency following trauma and surgery
	Adult respiratory distress syndrome
	Pulmonary insufficiency following:
	shock
	surgery
	trauma
	Shock lung
	Excludes:
	Adult respiratory distress syndrome associated with other conditions (518.82)
	Pneumonia:
	aspiration (507.0)
	hypostatic (514)
	Respiratory failure in other conditions (518.81)
518.81	Respiratory failure
	Respiratory failure:
	NOS
	acute and/or chronic
	Excludes:
	Acute respiratory distress (518.82)
	Respiratory arrest (799.1)
	Respiratory failure, newborn (770.8)
518.82	Other pulmonary insufficiency, not elsewhere classified
	Acute respiratory distress
	Acute respiratory insufficiency
	Adult respiratory distress syndrome (NEC)
	Excludes:
	Adult respiratory distress syndrome following trauma and surgery (518.5)
	Pulmonary insufficiency following trauma and surgery (518.5)
	Respiratory distress:
	NOS (786.09)
	newborn (770.8)
	syndrome, newborn (769)
	Shock lung (518.5)
96.70	Continuous mechanical ventilation of unspecified duration
96.71	Continuous mechanical ventilation for < 96 h consecutively
96.72	Continuous mechanical ventilation for ≥96 h consecutively

NOS = not otherwise specified; NEC = not elsewhere classified.

The combination of ICD-9 disease and procedure codës representing the ICD-9 ARDS criteria mandates that the ARDS patient must meet all of the following criteria:

1. have a code directly indicating ARDS in the ICD-9 description;

2. be on concurrent ventilatory support, and

3. have required ≥ 4 days of ventilatory support unless the disease was fatal within that time (lower limit), or have

Table 2

Two-step search of the HSCRC database

Initial search		Additional constraints		Second search
518.5	Post-surgical or post-trauma ARDS; survivor or non-survivor	96.70	Ventilator duration NOS	518.5 + 96.71 518.5 + 96.72
518.82	ARDS unrelated to trauma or surgery;	96.71	Ventilator support < 4 days	518.82 + 96.71
	survivor or non-survivor	96.72	Ventilator support > 4 days	518.82 + 96.72

NOS = not otherwise specified.

Table 3

Numbers of patients with discharge diagnoses that include ARDS and ventilatory support descriptors

		1992	1993	1994	1995
1	Hospital discharges	629,881	621,209	625,020	625,037
2	ICD-9 518.5 only*	217	162	139	161
3	ICD-9 518.82 only*	97	71	69	58
4	518.5 + 96.71† ventilator < 4 days (expired/total)	10/35	27/116	32/158	42/179
5	518.5 + 96.72† ventilator > 4 days	72	245	315	296
6	518.82 + 96.71† ventilator < 4 days (expired/total)	9/30	28/68	19/74	24/78
7	518.82 + 96.72† ventilator > 4 days	68	139	165	167
8	518.5 + 96.70† ventilator duration NOS	0	1	2	3
9	518.82 + 96.70† ventilator NOS	0	0	5	1
	Total	519	802	927	942

NOS = not otherwise specified. *Patients coded for ARDS without further descriptors; †procedure codes 96.70, 96.71 and 96.72 were established in October 1991.

required ventilatory support of unspecified duration, survivors and non-survivors (upper limit).

ICD-9 procedure code 96.70 (ventilation support of unspecified duration) was reviewed to determine potential error introduced by failure to define ventilator duration.

Population data for the state of Maryland were extracted from the *Statistical Abstract of the United States*[10]. The ARDS incidence estimate was then normalized per 100,000 people in the population base.

Results

For the 4-year period covered by this study, 2,501,147 hospital discharges from the 52 acute care Maryland hospitals were screened. As revealed in Table 3, when ventilatory support is not a mandated criterion, a substantial number of patients are included, representing 15-42% of the total population of potential ARDS patients. During the years studied, the numbers of potential ARDS patients with ICD-9 codes 518.5 or 518.82 alone remained relatively stable, whereas the numbers of potential ARDS patients with additional codes indicating ventilatory support increased three to fourfold in each category. Further, the ICD-9 procedure code 96.70 (ventilatory support of

Table 4

Estimated ARDS incidence in Maryland, calculated from the application of ICD-9 ARDS criteria

	1992	1993	1994	1995
Population*	4914	4958	5006	5050‡
ARDS, all inclusive†	519	802	927	942
Cases/100,000	10.6	16.2	18.5	18.6
ICD-9 ARDS criteria Lower limit	159	439	513	529
ICD-9 ARDS criteria Upper limit	205	568	694	720
Cases/100,000				
Lower limit	3.2	8.8	10.6	10.5
Upper limit	4.2	11.4	13.8	14.2

*Expressed in thousands; †represents data from the initial search that did not mandate ventilatory support; ‡extrapolated from two previous years' growth rates (0.8% and 0.96%).

Table 5

Hospital-based mortality rate of patients with ICD-9 ARDS criteria

ICD-9 code	Ventilation (days)	1992	1993	1994	1995
518.5	< 4*	10/35	27/116	32/158	42/179
518.82	< 4*	9/30	28/68	19/74	24/78
518.5	> 4†	30/72	105/245	130/315	116/296
518.82	> 4†	29/68	67/139	69/165	79/167
Total expired (all categories)		78	227	250	216
Mortality					
Upper limit		49%	52%	47%	49%
Lower limit		38%	39%	36%	36%

Data is presented in fractional form as survivors over total patients within each category. *ICD-9 code 96.71; †ICD-9 code 96.72.

unspecified duration) contributes, at most, 0.7% to the patient population and is excluded from further consideration.

By applying the ICD-9 ARDS criteria described above, the 'lower limit' was generated by combining numerators of lines four and six with lines five and seven from Table 3. The 'upper limit' was generated by combining the denominators of lines four and six with lines five and seven. The resulting yearly estimates of ARDS patients in Maryland are shown in Table 4.

The in-hospital mortality rate by year and ICD-9 coding is shown in Table 5. Despite substantial increases in the number of patients with ARDS, the associated mortality rate has remained essentially unchanged.

Discussion

In attempting to define the 'magnitude of the problem', the NHLI task force conceded that ARDS was a relatively new syndrome (in 1971) and had not been included in the code of disease classification that was in existence at that time; they also conceded that relatively few physicians could make the diagnosis of ARDS reliably. Therefore, 'valid statistical data to document the magnitude of the health problem due to (A)RDS [are] virtually unobtainable' [1].

To estimate the frequency of ARDS, 'some members' of the NIH panel collected data 'on their own', representing 4650 hospital beds. During a 1-year period, 3200 patients with acute respiratory failure were seen, 'roughly one half classified as [having] (A)RDS'. In addition, six military hospitals were reviewed (duration undefined), representing 127,000 admissions and 1295 cases of 'acute respiratory failure', an incidence of approximately 1%. In neither case were the criteria to define ARDS stated explicitly nor was the overall population base defined. In addition, the NHLI task force results did not define the incidence of ARDS as a function of population.

The Thomsen study screened six of 40 Utah hospitals between 1 September 1989 and 31 August 1990. Relatively accepted criteria to diagnose ARDS [arterial/alveolar oxygen ratio < 0.2, bilateral infiltrates, pulmonary capillary wedge pressure (PCWP) < 15 and static compliance (Cs) < 50 ml/cmH_2O] were applied to patients from these six facilities. The actual mechanism or process of screening is undefined. The remaining 34 Utah hospitals were screened via the Utah Hospital Association registry, using discharge diagnoses identified by ICD-9 codes [5]. Codes 518.5, 518.81 and 518.82 (Table 1) were used as the sole indicators of ARDS. No further diagnostic classifiers were applied. Considerable effort was expended to ensure that the direct hospital 'screened' data were comparable to the Utah Hospital Association data. These two sources and types of data were then combined to develop a single database. Additionally, multiple estimates were applied to account for the transit of patients into and out of the state. Ultimately, Thomsen *et al* estimated an incidence of ARDS between 4.8 and 8.3 per 100,000 in a mostly rural state with a population of 1.7 million.

The commonly quoted study by Villar and Slutsky suggests an incidence of ARDS ranging from 1.5 to 3.5 cases per 100,000. This was a prospective 3-year study performed in the early to mid 1980s and based at a single referral hospital in the Canary Islands. All patients requiring mechanical ventilation, other than for anesthesia or immediate postoperative care, were believed to be hospitalized at this single referral center. The population base was estimated at 700,000. Although the study indicates a total of 23,920 admissions per year to all hospitals, the number of admissions to the study facility is not given; however, 1997 patients were admitted to the referral center's ICU. The incidence statistic is based on, at most, 74 patients with ARDS.

Webster, Cohen and Nunn [8] estimated the incidence of ARDS in the United Kingdom at 4.5 per 100,000. Their study was retrospective and based on data from 15 hospitals in a region with a population of 3.6 million. Data were collected from questionnaires sent to 'consultants' in charge of various ICUs. The response rate to the questionnaire was 88%. It is unclear whether information submitted by the consultants was based on objective hospital data or on recollection.

Angus *et al*[4] estimated the US national incidence of ARDS at 50.7-64.3 per 100,000. The Angus definition of ARDS and mechanism of acquiring data were essentially identical to those used in our study, with the addition of ICD-9 code 518.81 (ie respiratory failure not otherwise specified, acute, acute and chronic or chronic, and excluding acute respiratory distress). Specifically, the ICD-9 codes 518.5, 518.81 and 518.82 had to be further qualified with survival for > 96 h on mechanical ventilation or death within that period. The substantially higher incidence of ARDS in the study by Angus *et al* probably reflects the inclusion of ICD-9 code 518.81. Characteristics of recent studies are compared in Table 6.

During the study period, the population base for Maryland remained relatively stable at approximately 5 million, but the incidence of ARDS appeared to rise. Review of the data in Table x3 suggests that, during the study interval, fewer patients were discharged with diagnostic codes limited to 518.5 or 518.82 and that gradually more patients had added diagnostic procedure codes for ventilatory support. We suspect, therefore, that the incidence of ARDS may not be changing, but rather the use of the procedure codes may be improving. Over the 4-year interval studied, the population of patients meeting our ICD-9 ARDS criteria appears to have leveled off at approximately 500 to 700 patients per 5 million people.

The rationale for our selection of the specific ICD-9 descriptor pattern is as follows. Patients with ARDS, by definition, require ventilatory support; therefore, the combination of diagnostic criteria and ventilatory support is mandatory.

Fifty percent fewer patients fitted the ICD-9 ARDS criteria during the second search employing ICD-9 code 518.5 or 518.82 with the requirement of concurrent ventilatory support (compared with ICD-9 code 518.5 or 518.82 alone). Other authors [11] have suggested that applying only the ICD-9 codes of 518.5, 518.81, and 518.82 is adequately specific to describe ARDS. Our data indicate significant lack of specificity when coding only one descriptor.

Second, clinically, ARDS is a relatively long-term disease and highly unlikely to resolve within 4 days. Evans [6] observed a duration of ARDS of 3.8 to 12.2 days. Other investigators [12] noted median survival times of 13 days, suggesting significantly more than 4 days of ventilatory support. On the other hand, ARDS may be a rapidly fulminant disease [13]. Montgomery noted that, in a group of 32 patients with ARDS, 10 died within 72 h of onset.

To develop our lower limit, it was assumed that surviving patients with ICD-9 codes 518.5 and 518.82 who require fewer than 4 days of ventilatory support were mis-coded or mis-diagnosed and were, therefore, excluded from primary consideration. However, since the assumption of 'miscoding or mis-diagnosis' may be inappropriately exclusive, we developed the 'upper limit', which includes all patients coded for ARDS but requiring ventilation fewer than 4 days (survivors and non-survivors).

Table 6

Comparison of recent studies evaluating the incidence of ARDS

Study [reference]	Population	No of hospitals	Patient statistic*	Duration (years)
Current study	5,000,000	52	2,501,147	4
NIH [1]	?	4650 beds 6 hospitals	3200 127,000	1 (?)
Thomsen [5]	1,720,000	40 LDS hospital	19,050	1
Villar [3]	700,000	1	1997 ICU admissions	3
Webster [2]	3,600,000	15	5636 ICU admissions	1
Angus [4]	†	†	109,874 admissions	1-2
Evans [6]	741,000	15	1512 ICU admissions	1

*Any statistic that indicates number of patients in the study; †probably large, since the study is multi-regional. LDS = Latter Day Saints.

In the US, the ventilator procedure codes (96.70, 96.71 and 96.72) did not come into existence until October 1991. As shown in Table 4, there was an apparent 3.3 to 3.5-fold increase in the incidence of ARDS by the ICD-9 criteria. We believe this reflects increasing use of the ventilator procedure codes. In 1994 and 1995, the incidence stabilized, perhaps reflecting more uniform and complete ICD-9 diagnostic and procedural coding.

Our study's inclusion criteria were more restrictive than those of other studies that employed the ICD-9 coding system. Intuitively, more stringent criteria would be expected to yield fewer patients, all other variables being equal. However, our criteria yielded higher numbers of ARDS patients than the less restrictive criteria of Thomsen and Morris. The Utah study may have underestimated the frequency of ARDS because of a more limited population base or a shorter duration of study. Or perhaps the incidence of the disease is truly lower in a rural environment. On the other hand, perhaps patient diagnosis and therefore coding was less rigorous, leading to over-diagnosis in Maryland. Alternatively the disease might be more prevalent in a crowded urban environment.

The weakness of a computer-based data registry using the ICD-9 coding system is that no true physiological data are apparent. The first presumption is that knowledgeable clinicians will apply similar and reasonable criteria to diagnose ARDS. Second, it is assumed that record clerks will interpret medical records properly and code discharge diagnoses correctly. Third, there may be a coding bias designed to maximize reimbursement rather than correctly describe the disease entity. Fourth, our ICD-9 ARDS criteria may not be accepted in the medical community. Therefore, throughout this report, we have used the phrase 'ICD-9 ARDS criteria' instead of implying absolute certainty that the described patients truly have ARDS. We offer these criteria for consideration as a more specific computer-based set of descriptors. As such, these computer-based estimates of ARDS could serve for assessment of incidence, financial planning and impact studies. For instance, based on the estimated incidence of ARDS of 10.2 to 14.2 per 100,000 and a US population of 260 million (1994), the national incidence would be 27,300 to 36,920 new episodes of ARDS per year. Furthermore, such population-based ICD-9 statistics may be valuable for the development of tertiary referral centers for advanced treatment of ARDS. Such estimates, with lack of direct physiologic data, are not likely to be useful in evaluating specific therapeutic strategies, but may be useful to monitor trends.

Other assumptions of this study are that all Maryland residents are treated in hospitals within the state, and that all patients hospitalized in Maryland are state residents. Obviously, the hospitalized population is not that distinct, because Maryland borders other states and the District of Columbia, which offer a full range of medical care. However, since Maryland offers all primary, secondary and tertiary medical services, there is no necessity to leave the state for such care. The degree of error incurred by our assumptions is probably small, but unknown.

Finally, our mortality data are well within the middle range of those documented in other reports. With advanced technologies to support and treat established ARDS, the associated mortality may be declining. However, with other advanced technologies such as chemotherapeutic agents, bone marrow transplants and immunosuppressive agents, the opportunity for ARDS to develop seems greater. The direction of the mortality rate associated with ARDS will require long-term study.

Acknowledgements

This study would have been impossible without enormous assistance from Mr Richard Vincent of the St Paul Computer Center, which manages the computer database for the Maryland Health Cost Services Review Commission of the State of Maryland. We also acknowledge and thank Linda Kesselring, MS, ELS, for her extraordinary editorial assistance.

References

1. National Heart and Lung Institute, National Institutes of Health : **.** *Respiratory Distress Syndromes: Task Force Report on Problems, Research Approaches, Needs. Washington, DC: US Government Printing Office, DHEW Publication No (NIH) 73-432,* 1972:165-180.
2. Webster NR, Cohen AT, Nunn JF: **Adult respiratory distress syndrome - how many cases in the UK?** *Anaesthesia* 1988, **43:**923-926.
3. Villar J, Slutsky AS: **The incidence of the adult respiratory distress syndrome.** *Am Rev Respir Dis* 1989, **140:**814-816.
4. Angus DC, Linde-Zwirlbl WT, Clermont G, Newbold RC, Pinsky MR: **What's the incidence and mortality of ARDS in the US?** *Am J Respir Crit Care Med* 1996, **153:**A592.
5. Thomsen GE, Morris AH: **Incidence of the adult respiratory distress syndrome in the state of Utah.** *Am J Respir Crit Care Med* 1995, **152:**965-971.
6. Evans BH, Wachter JP, Wiener-Kronish , Luce JM: **Incidence of the adult respiratory distress syndrome in an urban population.** *Am Rev Respir Dis* 1988, **137:**A469.
7. Bernard GR, Artigas A, Brigham KL: **The American-European Consensus Conference of ARDS.** *Am J Respir Crit Care Med* 1994, **149:**818-824.
8. Vasilyev S, Schaap RN, Mortensen JD: **Hospital survival rates of patients with acute respiratory failure in modern respiratory intensive care units.** *Chest* 1995, **107:**1083-1088.
9. : **International Classification of Diseases, 9th revision.** *In Clinical Modification, 4th edn. Los Angeles, California: Practice Management Information Corporation (PMIC),* 1995.
10. : **.** *Statistical Abstract of the United States, 115th edn. The National Data Book. Washington, DC: US Department of Commerce, Economics and Statistics Administration, US Bureau of the Census,* 1995.
11. Thomsen G, Morris AH, Danino J, Ellsworth J, Wallace CJ: **Accuracy of ICD-9 coding in the diagnosis of ARDS.** *Am Rev Respir Dis* 1988, **145:**A81-.
12. Fowler AA, Hamman RF, Zerbe GO, Benson KN, Hyers TM: **Adult respiratory distress syndrome, prognosis after onset.** *Am Rev Respir Dis* 1985, **132:**472-478.
13. Montgomery AB, Stager MA, Carrico CJ, Hudson LD: **Causes of mortality in patients with the adult respiratory distress syndrome.** *Am Rev Respir Dis* 1985, **132:**485-489.