Acute Hypoxemic Respiratory Failure: Acute Lung Injury and Acute Respiratory Distress Syndrome. A Review.

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ABSTRACT

Severe arterial hypoxemia that is resistant to supplemental oxygen is a common reason for admission to ICU. This form of respiratory failure termed acute hypoxemic respiratory failure (AHRF) has two notable forms: Acute Lung Injury (ALI) and the more severe Acute Respiratory Distress Syndrome (ARDS), with diagnostic criteria based on refractory hypoxemia and a classical radiological appearance. It is common, and is likely to exist outside the intensive care setting and therefore is a condition relevant to all clinicians. Genetically predisposed individuals exposed to environmental triggers which can be intra or extra pulmonary in nature manifest an inflammatory response that causes damage to alveolar epithelial cells and vasculature, impairing gas exchange and can lead to multiple organ failure. Management centers around supportive care and treatment of the cause. However evidence supports use of low tidal volume ventilator settings and conservative intravenous fluid strategies. Long term outcomes are related to neuromuscular, cognitive and psychological issues rather than pulmonary, and rehabilitation during recovery needs to focus on this.

INTRODUCTION

Acute Hypoxemic Respiratory Failure (AHRF) is a continuum of clinical and radiographic changes affecting the lungs, characterized by acute onset severe hypoxemia, not related to left atrial hypertension, occurring at any age. At one end lies acute lung injury (ALI) and at the severe end of this spectrum lies Acute Respiratory Distress Syndrome (ARDS). It was first described by Ashbaugh in 1967. This landmark paper described a group of 12 patients with acute onset dyspnea, severe hypoxemia, diffuse infiltrates on chest radiography, decreased lung compliance and required positive end expiratory pressure (PEEP) for ventilation.[1]

This initial description gave only vague criteria for diagnosis, focused on the most severe end of the continuum and was not specific enough to exclude other conditions. A more precise definition was described by Murray et al. in 1988 using a 4 point lung injury scoring system including the level of PEEP used in ventilation, ratio of arterial oxygen tension to fraction of inspired oxygen (PaO_2 /FiO_2), static lung compliance and chest radiography changes[2]. Despite being more specific and assessing severity it was too large and complex for practical purposes in the ICU setting.

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DEFINITION

It was not until 1994 that The American –European Consensus Conference on ARDS set the criteria used today to define both ALI and ARDS in research and clinical medicine. It recommended ALI be defined as "a syndrome of inflammation and increased permeability that is associated with a constellation of clinical, radiological and physiological abnormalities that cannot be explained by, but may coexist with, left atrial or pulmonary capillary hypertension"[3]. They distinguished between ALI and ARDS based upon the degree of hypoxemia present, as determined by the ratio of partial pressure of arterial oxygen to fractional inspired oxygen concentration (PaO_2 /FiO_2), with ALI patients demonstrating a milder level of hypoxaemia. Additionally ARDS changed from Adult Respiratory Distress Syndrome to Acute Respiratory Distress Syndrome to account for its occurrence at all ages.

Table1. Diagnostic Criteria for ALI and ARDS

DIAGNOSIS AND PROBLEMS RELATED TO THIS

There are no gold standard radiological, laboratory or

Table1. Diagnostic Criteria for ALI and ARDS		
	Criteria for ALI	**Criteria for ARDS**
Onset	Acute	Acute
Hypoxemia	Pao_2/Fio_2 < 300	Pao_2/Fio_2 < 200
Chest Radiological Appearance	Bilateral Pulmonary Infiltrations which may or may not be symmetrical	Bilateral Pulmonary Infiltrations which may or may not be symmetrical
Pulmonary Capillary Wedge Pressure (in mmHg)	<18 or no clinical evidence of left atrial hypertension	<18 or no clinical evidence of left atrial hypertension

pathological tests to diagnosis ALI and ARDS and patients are diagnosed based on the criteria agreed in 1994. In practice ALI and ARDS are clinically under-diagnosed, with reported rates ranging between 20 to 48% of actual cases.[4]This is due to poor reliability of the criteria related to;

- Non-specific radiological findings which are subject to inter-observer variability.
- Oxygenation criteria is independent of inspired oxygen concentration or ventilator settings including tidal volumes and PEEP.
- Excluding cardiac causes of pulmonary edema including left ventricular failure, mitral regurgitation and cardiogenic shock, in the ICU setting is difficult even when pulmonary artery catheters are used.
- The definition includes a heterogeneous population who behave very differently in response to treatment, duration of mechanical ventilation and severity of pulmonary dysfunction.

EPIDEMIOLOGY

Incidence

Inconsistent definitions of ALI and ARDS in large databases of hospital admissions, variations in the application of AECC definition in different studies and variations in different at risk population have hampered obtaining accurate estimates of incidence. However incidence of ALI is reported as 17-34 per 100,000 person years[5] with mean age of approximately 60 yrs, mortality of 35-40% and ratio of ALI to ARDS around 70% however these figures are less consistent internationally. A recent prospective population-based cohort study in a single US county demonstrated a higher incidence around 78.9 per 100,000 person years and inferred from this that 190,600 cases could occur in the USA alone each year.[6] This variation is likely due to problems with reliability of diagnosis as illustrated above.

Risk Factors

Acute Lung Injury is a multi-factorial process which occurs due to environmental triggers occurring in genetically predisposed individuals, as ALI-inducing events are common, yet only a fraction of those exposed develop the syndrome.

Direct Lung Injury	**Indirect Lung Injury**
Common	
Pneumonia	
Aspiration of gastric contents	**Common**
Less Common	Sepsis
Pulmonary contusion	Severe trauma with shock and multiple transfusions
Fat / Amniotic fluid embolism	**Less Common**
High Altitude	Burns
Near Drowning	Disseminated intravascular-coagulation
Inhalation Injury	Cardiopulmonary bypass
Reperfusion Injury	Drug overdose-(heroin, barbiturates)
	Acute pancreatitis
	Transfusion of blood products

Environmental triggers for developing ALI can be divided into those causing direct and those causing indirect lung injury, with sepsis, either intrapulmonary or extra pulmonary being the commonest cause.

Table 2 Direct and Indirect triggers for ALI

At present there is research into the role of genetic factors and how they contribute to susceptibility and prognosis[7]. Secondary factors including chronic alcohol abuse, chronic lung disease and low serum pH may increase risk of developing ALI. There may be factors which are protective against its development, such as diabetes in septic shock patients[8] but further research is required.

PATHOLOGY AND PATHOPHYSIOLOGY

In cases of ALI and ARDS, it is useful to distinguish between the early phase of lung injury and subsequent events[9]. By light microscopy, the early appearance is of interstial and alveolar edema, capillary congestion, and intra-alveolar hemorrhage with minimal evidence of cellular injury. By electron microscopy, changes of endothelial swelling, widening of intercellular

junctions, increased number of pinocytotic vesicles, and disruption and denudation of basement membrane are prominent. Inflammatory cell infiltration of lung interstium is generally subtle. During this early *exudative* phase of diffuse alveolar damage (DAD), pulmonary edema and its clinical effects are most pronounced. Over the ensuing days, hyaline membrane formation in the alveolar spaces becomes prominent. Inflammatory cells become more numerous within interstium. There is extensive necrosis of type I alveolar cells.

The late phase of ARDS is dominated by disordered healing. This can occur as early as 7 to 10 days after initial injury and may result in extensive pulmonary fibrosis. This has been termed the *proliferative* or *fibroproliferative* phase. Type II alveolar cells proliferate along alveolar septae and alveolar walls; fibroblasts and myofibroblasts become more numerous. Evidence of lung flooding is less prominent.

It is thought ALI patients follow a similar pathophysiological process independent of the etiology. This occurs in two phases; acute and resolution, with a possible third fibrotic phase occurring in a proportion of patients.

Acute Phase

This is characterised by alveolar flooding with protein rich fluid secondary to a loss of integrity of the normal alveolar capillary base, with a heterogeneous pattern of alveolar involvement.

Both types of alveolar epithelial cells are damaged in ALI, likely via neutrophil mediation, with macrophages secreting pro-inflammatory cytokines, oxidants, proteases, leucotrienes and platelet activating factor.

Damage to type I alveolar epithelial cells causes disruption to alveolar-capillary barrier integrity and allows lung interstitial fluid, proteins, neutrophils, red blood cells and fibroblasts to leak into the alveoli.

Damage to type II cells decreases surfactant production and that produced is of low quality, likely to be inactivated by fluid now in alveoli, which leads to atelectasis. Additionally there is impaired replacement of type I alveolar epithelial cells and an inability to transport ions and therefore remove fluid from the alveoli.

Coagulation abnormalities occur including abnormal fibrinolysis and formation of platelet and fibrin rich thrombi which result in microvascular occlusion, causing intrapulmonary shunting leading to hypoxaemia.

Ventilation-perfusion mismatch, secondary to alveolar collapse and flooding, decreases the number of individual alveoli ventilated, which in turn increases alveolar dead space, leading to hypercapnia and respiratory acidosis. Additionally pulmonary compliance decreases and patients start to hyperventilate in an attempt to compensate the above changes.

The release of inflammatory mediators from damaged lung tissue triggers systemic inflammation and systemic inflammatory response syndrome (SIRS) which may progress to multiple organ failure, a leading cause of death in ARDS patients.

Resolution Phase

This phase is dependent on repair of alveolar epithelium and clearance of pulmonary edema and removal of proteins from alveolar space.

The type II alveolar epithelial cells proliferate across the alveolar basement membrane and then differentiate into type I cells. Fluid is removed by initial movement of sodium ions out of the alveoli via active transport in type II alveolar epithelial cells, with water then following, down a concentration gradient through channels in the type I alveolar epithelial cells.

Soluble proteins are removed by diffusion and non soluble proteins by endocytosis and transcytosis of type I alveolar epithelial cells and phagocytosis by macrophages.

Fibrotic Phase

Some patients do not undergo the resolution phase but progress to fibrosing alveolitis, with fibrosis being present at autopsy in 55% non-survivors of ARDS.[10] This occurs by the alveolar spaces filling with inflammatory cells, blood vessels and abnormal and excessive deposition of extracellular matrix proteins especially collagen fibres.[11] Interstitial and alveolar fibrosis develops, with an associated decrease in pulmonary compliance and only partial resolution of pulmonary edema with continued hypoxemia.

APPROACH TO DIAGNOSIS OF ALI and ARDS

CLINICAL PRESENTATION

Acute Phase

Bedside appearance of patients with ALI and ARDS resulting from different etiologies is remarkably similar. Marked tachypnea and dyspnea are invariably present. Physical examination may reveal diffuse crackles in pulmonary edema or focal signs of consolidation in case of lobar pneumonia. Distressed patients with AHRF have initial room air blood gas results with Pao2 in range of 30 to 55 mm of Hg and Spo2 < 85% and they typically do not achieve Spo2 of > 90% with oxygen by nasal mask suggesting a large shunt. If oxygen by mask or cannula raises Spo2 > 95% other causes of respiratory distress should be considered.

Resolution Phase

This phase usually occurs after around 7 days after onset of ALI, where a resolution of hypoxaemia and improvement in lung compliance is seen.

Fibrotic Phase

There is persistent impairment of gas exchange and decreased compliance. In severe cases it can progress to pulmonary hypertension through damage to pulmonary capillaries and even severe right heart failure, with the signs and symptoms of this developing over time

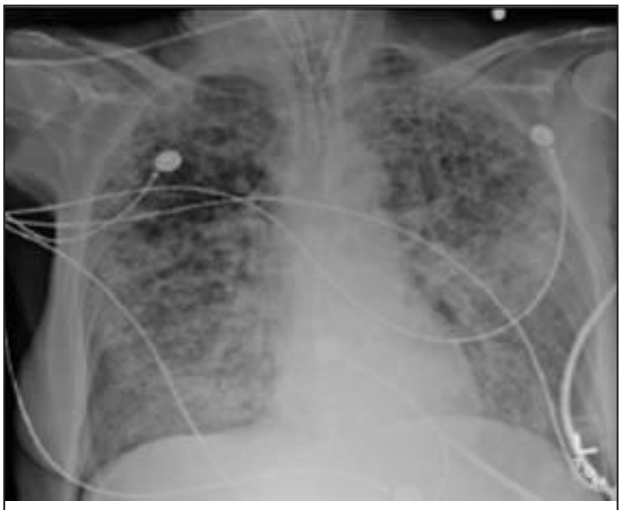
.CLINICAL SETTING

ALI and ARDS commonly arise in a typical clinical context. Sepsis, pneumonia, trauma, multiple transfusions, and acid aspiration account for majority of cases. Less common causes include pancreatitis, near drowning, fat embolism, viral pneumonias, and drug toxicities.[12] Cause for cardiogenic pulmonary edema may be evident in form of abnormal heart sounds or murmur, abnormal electrocardiogram, or enzymes indicative of cardiac ischemia. Overzealous fluid administration in setting of renal failure & LV dysfunction also can lead to it

INVESTIGATIONS

CHEST RADIOGRAPH

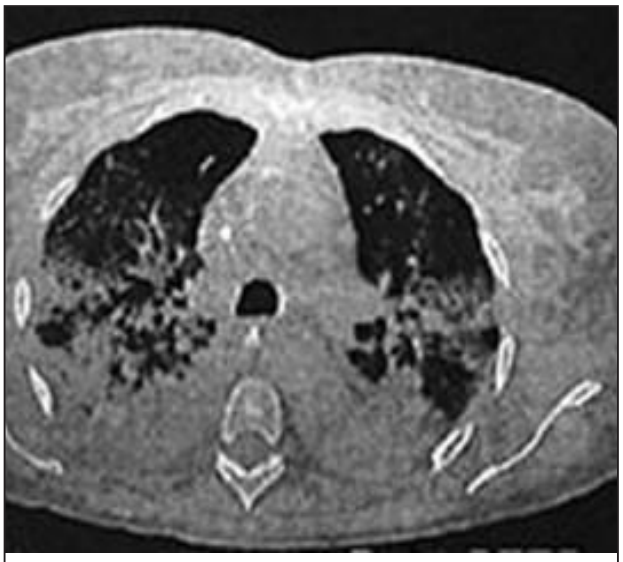
CXR is widely used tool to assess AHRF but is not very accurate in differentiating hydrostatic edema from increased permeability edema. Features that suggest hydrostatic edema include increased heart size, increased width of vascular pedicle, vascular redistribution towards upper lobes, and a centrifugal pattern of spread with a perihilar bat's wing distribution of edema. Absence of these findings and patchy peripheral infiltrates suggest ALI / ARDS. Pleural effusions may be present.



Chest radiograph in ARDS

Computed tomography of ALI /ARDS

Computed tomography of the chest can show the heterogeneous nature of ALI, with dependent areas of the lung showing patchy consolidation with air bronchograms, atelectasis and fibrosis. Pneumothorax not visualized on CXR may also be evident



Computed tomography of ALI/ARDS

ECHOCARDIOGRAPHY

Echocardiography is a noninvasive tool that helps to differentiate cardiogenic pulmonary edema from

noncardiogenic one. LV dilatation, regional or global wall motion abnormalities and significant mitral regurgitation on Doppler imaging support cardiogenic edema. Normal systolic and diastolic cardiac functions suggest increased permeability edema.

RIGHT HEART CATHETERIZATION

Right heart catheterization is often performed in patients of pulmonary edema, although the benefits continue to be debated. It has also been suggested that the technology itself contributes to a poor patient outcome, hence its routine use can not be recommended.[13] However it can be used to address specific questions regarding ventricular functions, adequacy of volume resuscitation, the degree of intrapulmonary shunt and the adequacy of cardiac output and oxygen saturation of mixed venous / central venous blood.

MANAGEMENT

The aims of management are to provide good supportive care, maintain oxygenation and to diagnose and treat the underlying cause and other comorbidities as making the diagnosis of ALI is not equivalent to diagnosing the patient's underlying problem. If the precipitating cause of ALI is unclear, one should consider performing early fiberoptic bronchoscopy to obtain bronchial washings for microbiologic and cytologic analysis.

General Care

Good supportive care, as for all ICU patients, should include nutritional support with an aim for early enteral feeding, good glycaemic control and deep venous thrombosis and stress ulceration prophylaxis. It is important to identify and treat any underlying infections with antibiotics targeted at culture sensitivities and if unavailable, towards common organisms specific to infection site.

It is not uncommon for ALI patients to die from uncontrolled infection rather than primary respiratory failure.Ventilator associated pneumonia is common in patients with ALI and can be difficult to diagnoses, as ALI radiological findings can mask new consolidation and raised white cell count and pyrexia may already be present.

VENTILATOR MANAGEMENT

Principles of ventilation in ALI are to maintain adequate gas exchange until cell damage resolves whilst avoiding ventilator associated injury from;

- Barotrauma and volutrauma – alveolar overdistension associated with ventilation at high tidal volumes and pressure.
- Biotrauma – repeated opening and closing of collapsed alveoli causing shearing stress which can initiate a proinflammatory process.

Lungs in patients with ALI are heterogeneous and therefore can react variably to changes in ventilator settings. Therefore settings which provide adequate oxygenation, may damage more "healthy" areas of lung.[14]

Goals and Priorities of Lung protective Approach

The lung protective approach to ventilator management has the same oxygenation goal of arterial saturation > 88% to 90%. However it gives higher priority to protection from ventilator induced lung injury (VILI) than to normalization of Pco_2 and pH.[15] This is achieved by decreasing the tidal volume from 10 to 15ml / kg body weight to tidal volumes of 4 to 6 ml / kg predicted body weight and limiting plateau pressure to < 30 cm H_2O following the NIH ARDS Network study demonstrating mortality and other benefits in lower tidal volume group. Oxygenation goal should be achieved by using incremental FIO_2-PEEP combinations as in the ARDS Network study.

NIH-NHLBI ARDS Network Low Tidal Volume Ventilation Strategy[16]

Part I. Ventilator set up and adjustment

1) Calculate predicted body weight (PBW).
2) Use assist/control mode and set initial tidal volume to 8 ml / kg PBW.
3) Reduce TV by 1 ml / kg intervals every 2 hrs until TV = 6ml / kg.
4) Set initial RR to approximate baseline minute ventilation (but not > 35).
5) Adjust TV and RR to achieve plateau pressure and pH goals.
6) Set inspiratory flow rate above patients demand usually > 80L/min, adjust flow rate to achieve goal of I:E ratio of 1:1-1.3.

Part II. Oxygenation goal: Pao_2 = 55-80 mm of Hg or Spo_2 = 88-95%

1. Use these incremental Fio_2-PEEP combination

Fio_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12
Fio_2	0.7	0.8	0.9	0.9	0.9	1.0	1.0	1.0
PEEP	14	14	14	16	18	20	22	24

Part III. Plateau pressure (Pplat) goal: 30 cm H_2O.

1. Check Pplat, Spo_2, RR, TV, and ABG every 4 hrs and after each change in PEEP or TV.
2. If Pplat > 30cm, decrease TV by 1ml / kg steps. (minimum TV 4ml / kg)
3. If Pplat<25cm and TV<6ml/kg, increase TV by 1ml/kg until Pplat >25cm or TV=6ml/kg.
4. If Pplat <30cm and breath stacking occurs, increase TV by 1ml/kg increments to a maximum of 8ml/kg as long as Pplat remains<30cm

Part IV. pH Goal: 7.30-7.45

Acidosis management: pH <7.30

1. If pH < 7.30, increase RR until pH >7.30 or RR=35
2. If pH <7.3 and RR = 35if RR =35 and $Paco_2$ < 25 mm, may give $NaHCO_3$.
3. If pH < 7.15 and $NaHCO_3$ given, TV may be increased in 1ml/kg steps until pH > 7.15. (Pplat limit may be exceeded)

Alkalosis management: pH > 7.45: Decrease RR if possible.

ADJUNCTS TO CORE VENTILATORY MANAGEMENT

PERMISSIVE HYPERCAPNIA

Traditionally patients have been ventilated to maintain normal Pco_2 using larger tidal volumes. In patients with severe lung injury this can amplify preexisting lung injury by inducing VILI. Increasing evidence points to the efficacy and safety of allowing Pco_2 to rise modestly while using low tidal volumes and plateau pressures. Some contraindications to this strategy include, increased intra cranial pressure, acute cerebrovascular accident, Severe pulmonary hypertension, Myocardial ischemia, Right ventricular failure, uncorrected metabolic acidosis, pregnancy.[17]

PRONE POSITIONING

There is sufficient evidence to suggest that prone positioning in ALI and ARDS patients improves oxygenation however it does not translate in to survival benefit.[18] It may be used as a salvage therapy for severe hypoxemia. Pco_2 response following prone positioning may have prognostic value.

RECRUITMENT MANEUVERS

Recruitment maneuvers evolved from "sighs". They were part of open lung strategy, the justification for their use is they "recruit" or open totally or partially collapsed alveoli which would be than kept open by high level of PEEP.[19] Evidence is lacking that recruitment maneuvers alone improve clinically significant outcomes such as mortality or ventilator free days.

PRESSURE- CONTROL VENTILATION AND INVERSE RATIO VENTILATION

Pressure-control ventilation is favored by some as it limits maximal peak airway pressure. It also limits static end-inspiratory pressure. ARDS Net study limited end inspiratory pressure to 30 cm. Inverse ratio ventilation (IRV) entails use of prolonged inspiratory time (I:E ratio >1) with either a volume cycled or pressure cycled mode. A subset of patients with hypoxia refractory to conventional modes responded to IRV.[20] An important caution when using this mode is that both auto PEEP and higher mean alveolar pressure typical of this mode tend to reduce cardiac output. Auto PEEP also needs to be monitored regularly.

HIGH-FREQUENCY OSCILLATORY VENTILATION

If excessive excursion during tidal volume breathing is associated with lung injury, it seems reasonable to assume that ventilation with very small tidal volumes at high frequencies would be associated with least possible VILI and potentially with improved outcome, however its role in clinical practice remains unclear.[21] HFOV holds promise in the ventilator management of ALI and ARDS.

EXTRACORPOREAL MEMBRANE OXYGENATION AND EXTRACORPOREAL CO_2 REMOVAL.

The use of extracorporeal gas exchange such as extracorporeal membrane oxygenation (ECMO) and extracorporeal CO_2 removal ($ECCO_2R$) to adequately oxygenate and ventilate the patient while allowing the lungs to rest was viewed as an attractive strategy for management of ALI and ARDS. However this has not

been supported by clinical outcome studies.[22] Some centers continue to offer ECMO as salvage therapy for severe ARDS

SALVAGE INTERVENTIONS

TRACHEAL GAS INSUFFLATION (TGI).

It involves introducing fresh gas near carina through modified endotracheal tube. The added flow washes CO_2 rich gas out of the trachea (and via turbulence out of small airways as well), reducing anatomic dead space thus helps reducing $PaCo_2$.[23] Potential risks include tracheal erosions, Oxygen toxicity, hemodynamic compromise, larger tidal volume potentially increasing risk of VILI.

PARTIAL LIQUID VENTILATION.

Partial liquid ventilation using perfluorocarbons instilled in to trachea of patients with ARDS has been found to be both safe and efficacious in improving gas exchange in both adults [24] and children. However as they are radiodense lungs appear white making it impossible to use chest radiography to detect new shadows or to follow progress of healing.

ROLE OFNON INVASIVE VENTILATION

The role of non invasive ventilation in ALI/ARDS is less clear. It may reduce the need for intubation and improve outcome in some selected patients of ALI and ARDS who are immunosupressed for some reason and have high chances of nosocomial infections , do not have severe oxygenation defect, hemodynamic instability, altered mental status and can be closely observed and readily intubated in case NIV failure.

FLUID MANAGEMENT

RESTRICTIVE ("DRY") FLUID MANAGEMENT

The optimal fluid management in patients with ALI and ARDS remains uncertain. The rationale for restricting fluids in ALI and ARDS suggests that if edemagenesis could be diminished early after lung injury, the duration of potentially dangerous ventilator, PEEP, and oxygen therapy could be reduced and outcome conceivably improved.

The ARDSnet FACTT study looked at two fluid regimens comparing liberal fluid management (a net gain of approximately 1 litre per day) with a conservative fluid management (zero net gain over first seven days).[25] Although there was no significant difference in the primary outcome of 60 day mortality, the conservative management group had improved lung function, shortened duration of mechanical ventilation and intensive care and had no increased incidence of shock or use of renal replacement. This is supported by a recent retrospective review, which concluded negative cumulative fluid balance at day 4 of acute lung injury is associated with significantly lower mortality, independent of other measures of severity of illness.[25]

PHARMACOTHERAPY

To date no pharmacological agent has been demonstrated to reduce mortality among patients with ALI. However ALI encompasses a wide range of patients with varying etiology and comorbidities. It may be that on subdividing ALI patients, some therapies may be suitable for specific circumstances but at present there is little literature to support this.

CORTICOSTEROIDS

Despite the potential for steroids to benefit ALI patients due to anti-inflammatory properties, clinical trials demonstrate no improved mortality when given early or late in disease progression and given concerns regarding their role in development of neuromuscular disorders associated with critical illness, a recent large randomised controlled trial argued against steroid use in ALI[26]

INHALED NITRIC OXIDE

Despite providing selective vasodilatation of pulmonary arterioles and capillaries that subserve ventilated alveoli and improving ventilation perfusion mismatch, trials have only showed short lived improvement in oxygenation and no change in mortality with nitric oxide use. At present it plays no role in standard ALI treatment and should be reserved for rescue therapy in patients difficult to oxygenate.[27]

EXOGENOUS SURFACTANT

Dramatic response to surfactant therapy in respiratory distress syndrome of prematurity and presence of surfactant abnormalities in ALI and ARDS prompted their use in these conditions. However since the 1980's numerous randomized controlled trials have demonstrated no benefit from synthetic, natural or recombinant surfactant use in adults with ALI.[28]

INTRAVENOUS SALBUTAMOL

Beta 2 agonists were shown to be experimentally

beneficial in ALI due to increasing fluid clearance from alveolar space, anti-inflammatory properties and bronchodilation.[29] The BALTI trial published in 2006, investigated the effects of intravenous salbutamol in patients with ARDS. It showed decreased lung water at day 7, lowered Murray lung injury scores and lower end expiratory plateau pressures but an increase in incidence of supraventricular tachycardias and therefore further investigation is needed before it can be recommended as treatment for ALI.[30]

MORTALITY

Mortality rates of patients with ALI and ARDS are similar, with both being around 35-40%.[3] Controversy exists regarding whether mortality rates in ALI are decreasing,[31] or have stayed static.[32] Nonetheless death in patients with ALI is rarely from unsupportable hypoxaemic respiratory failure but from complications of the underlying predisposing conditions or multiple organ failure.

OUTCOMES

Long term problems are related to neuromuscular, neurocognitive and psychological dysfunction rather than pulmonary dysfunction. There is poor understanding of the mechanisms which cause these sequele and therefore prevention of these outcomes and planning rehabilitation can be difficult.

Long Term Outcomes in ARDS survivors

Neuromuscular dysfunction

critical illness polyneuropathy

critical illness myopathy.

entrapment neuropathy.

Neurocognitive dysfunction involving

memory

executive function

attention

concentration

Psychological dysfunction

Post traumatic stress disorder

Depression

Anxiety

Others

Pulmonary dysfunction

Tracheostomy site complications

Striae

Frozen joints

CONCLUSION

Acute hypoxemic respiratory failure (ALI and ARDS) is common and encountered in non ICU setting as well. Despite standardized identification criteria and advances in management, morbidity and mortality is significant. Low tidal volume ventilation strategy and conservative fluid therapy have improved survival. Ongoing research is still needed to hone the diagnostic criteria, define genetic risk factors and develop new treatment strategies to improve outcome. The new challenge for clinicians is how to address the long term outcomes of survivors and their relatives which will be an increasingly important problem in the future.

REFERENCES

1) Ashbaugh DG, Bigelow DB, Petty TL et al. Acute Respiratory Distress in Adults. Lancet. 1967; 2: 319-323

2) Murray JF, Matthay MA, Luce JM et al. An expanded definition of the adult respiratory distress syndrome. Am Rev Respir Dis. 1988; 138: 720-723

3) Bernard GR, Artigas A, Brigham KL et al. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes and clinical trial coordination. Am. J. Respir. Crit. Care Med. 1994 Mar; 149 (3 Pt 1): 818-824

4) Rubenfeld GD, Herridge MS. Epidemiology and Outcomes of Acute Lung Injury. Chest. 2007; 131 (2): 554-562

5) McCallum NS, Evans TW. Epidemiology of Acute Lung Injury. Current Opinion in Critical Care. 2005: 11; 43-49

6) Rubenfeld GD, Caldwell E, Peabody E et al. Incidence and outcomes of acute lung injury. N Engl J Med 2005; 353: 1685-1693

7) Kamp R, Sun X, Garcia JG. Making genomics functional: deciphering the genetics of acute lung injury. Proc Am Thorac Soci. 2008; 5: 348-53

8) Moss M, Guidot DM, Stienberg KP et al. Diabetic patients have a decreased incidence of acute respiratory distress syndrome. Critical Care

Medicine 2000; 28:2187-2192

9) Ware LB, Matthay MA : The acute respiratory distress syndrome. N Eng J Med 342:1334,2000

10) Meduri GU. Late adult respiratory distress syndrome. New Horiz 1993; 1:563-577

11) Rocco PRM, Santos CD, Pelosi P. Lung parenchyma remodelling in acute respiratory distress syndrome. Minerva Anestesiologica. 2009; 75: 730-740

12) Steinberg K P, Hudson L D: Acute lung injury and acute respiratory distress syndrome. The clinical syndrome. Clin Chest Med 21:401.2000

13) Connors AF, Speroff T, Dawson NV, et al: The effectivenessof Right heart catheterization in the initial care of critically ill patients. JAMA 276:916,1996.

14) Gattinoni L, Pesenti A. The concept of "baby lung" Intensive Care Med 2005; 31: 776-784

15) Brower RG: Mechanical ventilation in acute lung injury and ARDS. Crit Care Clin 18:1, 2002.

16) ARDSnet investigators, ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and acute respiratory distress syndrome. N Eng J Med 342:1301,2000

17) Tuxen DV: Permissive hypercapnic ventilation. Am J Respir Crit Care Med 150:870, 1994.

18) Gattinoni L, Tognoni G, Pesenti A, et al: Effect of prone positioning on survival of patients with acute respiratory failure. N Eng J Med:345:568, 2001.

19) Marini JJ, Gattinoni L: Ventilatory management of acute respiratioy distress syndrome: a consensus of two. Crit Care Med 32:250,2004.

20) Tharratt RS, Allen RP, Albertson TE: Pressure control inverse ratio ventilation in severe adult respiratory failure. Chest 94:755,1988.

21) Derdak S: High frequency oscillatory ventilation for acute respiratory distress syndrome in adult patients. Crit care Med 31:S317,2003

22) Morris AH, Wallace CJ, Menlove RL, et al: Randomized clinical trial of pressure controlled inverse ratio ventilation and extracorporeal CO_2 removal for adult respiratory distress syndrome. Am J Respir Crit Care Med 149:295, 1994.

23) Carter C, Adams AB, Stone M, et al: Tracheal gas insufflations during late exhalation efficiently reduces $PaCO_2$ in experimental acute lung injury. Intensive Care Med 28:504, 2002.

24) Hirschl RB, Croce M, Gore D: Prospective randomized controlled pilot study of partial liquid ventilation in adult acute respiratory distress syndrome. Am J Respir Crit Care Med 165:781,2002.

25) The Acute Respiratory Distress Syndrome Network. Comparison of Two Fluid Management Strategies in Acute Lung Injury. New Engl J Med. 2006; 354: 2564-2575

26) The Acute Respiratory Distress Syndrome Network. Efficacy and safety of corticosteroids for persistent acute respiratory distress syndrome. N Engl J Med 2006; 354: 1671-1684

27) Calfee CS, Matthay MA. Nonventilatory treatments for acute lung injury and ARDS. Chest 2007; 131(3): 913-920

28) Spragg RG, Lewis JF, Wurst W, et al: Treatment of acute respiratory distress syndrome with recombinant surfactant protein C surfactant. Am J Respir Crit Care Med 167:1562, 2003.

29) Groshaus HE, Manocha S, Walley KR et al. Science review: Mechanisms of beta-receptor stimulation-induced improvement of acute lung injury and pulmonary oedema. Critical Care 2004; 8 (4): 234-242

30) Perkins GD, McAuley DF, Thickett DR et al. The ß-Agonist Lung Injury Trial (BALTI): A Randomized Placebo-controlled Clinical Trial Am J Respir Crit Care Med. 2006; 173:281-287

31) Perkins GD, McAuley DF, Thickett DR et al. The ß-Agonist Lung Injury Trial (BALTI): A Randomized Placebo-controlled Clinical Trial Am J Respir Crit Care Med. 2006; 173:281-287

32) Phua J, Badia JR, Adhikari NK et al. Has mortality from acute respiratory distress syndrome decreased over time?: a systematic review. Am J Respir Crit Care Med. 2009 Feb; 179(3): 220-227