Quick Review: ARDS

T Fujii, B Phillips

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Abstract

This article reviews briefly the main points of Adult Respiratory Distress Syndrome (ARDS). Lung Injury can be divided into Acute Lung Injury (ALI) and ARDS.

ALI: A CONDITION INVOLVING IMPAIRED OXYGENATION

Defined as:

- A ratio of the partial pressure of arterial oxygenation (PaO2) to the fraction of inspired oxygen (FiO2) that is < 300 regardless of whether or how much positive end-expiratory pressure is used to provide respiratory support
- Bilateral pulmonary infiltrates on chest radiograph
- Pulmonary Artery Occlusion Pressure of < 18 mmHg or no clinical evidence of elevated left atrial pressure

ALI is an acute change in lung function, typically in gas exchange via a lack of prevention in abnormal water or solute accumulation within the alveolar spaces.

This functional injury, which can be identified histologically as diffuse alveolar damage, is the result of structural changes in the alveolocapillary unit. Injury to the membrane disrupts the endothelial barrier, leading to subsequent development of noncardiogenic pulmonary edema through increased vascular permeability. As the air spaces fill with fluid, the gas exchange and mechanical properties of the lung deteriorate

When the injury is “severe”, we have recognizable clinical features of ARDS.

Definition of ARDS includes the three same components as ALI, except:

The ratio of PaO2/FiO2 must be < 200, regardless of the level of PEEP but these are operational definitions!

REMEMBER THE FUNCTIONAL & PATHOLOGICAL DERANGEMENTS THAT RESULT IN THIS CONDITION

PREDISPOSING FACTORS – ARDS

Direct Injury

- Inhalation Injury (i.e. Burns)
- Aspiration (i.e. chemical pneumonitis)

Indirect Injury

- Bacterial Sepsis (i.e. endotoxemia)
- Pancreatitis

With some of these “predisposing conditions”, the risk of A.R.D.S. is substantial

Gastric Aspiration & Sepsis: Overall Mortality of 30 - 40 %

OVERALL MORTALITY ARDS

Typically reported to be greater than 50%

Most deaths result from underlying illness, sepsis, or multiorgan dysfunction

Recent studies (within the last decade), have demonstrated a decrease in mortality from 60 to 40 % Steinberg et al. 1993, Schuyta et al. 1992

DIAGNOSTIC STUDIES: THE CXR

The CXR may be “normal” for a period of time (hours - days) following the precipitating event [e.g. sepsis]

Full progression to diffuse, bilateral alveolar infiltrates ordinarily takes place within 4 - 24 hours after the first abnormal radiographic signs appear

The shadows within the lung parenchyma may be very similar to those identified in CHF

As alveolar filling continues, more of the lung parenchyma is involved - leading at times to a near-total “white-out” of both fields

CXR's are strongly influenced by the effects of therapy

- IV Fluids can increase alveolar content
- Diuretic agents may decrease total content
- PEEP increases lung inflation thereby reducing regional lung density

Remember... your treatment may produce the appearance of radiographic improvement despite continued severe abnormalities in gas exchange !

DIAGNOSTIC STUDIES: COMPUTED TOMOGRAPHY

Despite what appears to be a UNIVERSAL involvement of all lung fields on standard CXR, C.T. will often reveal patchy areas of infiltrate interspersed with normal-appearing lung !

Degree of lung involvement on C.T. correlates with the efficiency of gas exchange and underlying lung compliance (Gattioni et al. 1988)

C.T. can also reveal Barotrauma or localized infection

- i.e. loculated empyema or abscess

With appropriate precautions & continuous monitoring, clinically-indicated tomography can and should be undertaken in all but the most unstable A.R.D.S. patients

GAS EXCHANGE: THE ABG'S (VITAL!)

Initial studies: Respiratory Alkalosis w/ Hypoxemia

- the hypoxemia is relatively resistant to supplemental oxygen

As fluid accumulation progresses, the hypoxemia worsens

- leads, eventually, to the point of ventilatory support

The efficiency of gas exchange [PaO2/FiO2] at the onset of A.R.D.S., has correlated to patient outcome Bone et al. 1989

Dead-space ventilation is markedly increased in patients with ARDS. This translates into a high rate of minute ventilation. [RR x Vt] to maintain effective carbon dioxide elimination. If the problem in this disease, is integrity of the alveolocapillary membrane - then how do we measure it's barrier function ?

“MEASURING” MEMBRANE PERMEABILITY:

Analyze the Protein Content within the Alveolus or you can measure the flux of radiolabeled proteins

When this is done, the pulmonary edema that we see in ARDS appears to be noncardiogenic in etiology! Drake & Lane 1988

The amount of extravascular water within the lungs can also be measured

- Thermal Indocyanine Green Technique
- Rarely done in the clinical setting

How much fluid do we normally have in our lungs ?

Upper-limit of Normal: 500 cc's The “average” ARDS patient: 1500 cc's

Can be as much as 6 - 8 times normal (4 liters of fluid)... Mitchell et al. 1992

BRONCHOALVEOLAR LAVAGE:

Usually employed to document nosocomial infection

- can be safely performed in A.R.D.S. patients
- has never been prospectively validated
- can identify opportunistic lung infections presenting as ARDS

2 findings in ARDS: [non-specific]

- Increased # PMN's (nearly 80 % of the total cell population)
- Eosinophilia(these patients may respond to corticosteroids) Allen et al. 1989

What is the role of invasive hemodynamic monitoring ?

first of all, what does it mean ?

where did it come from ?

Preload: EDV (the load that stretches a muscle prior to contraction)

Afterload: SVR (the load that must be moved during muscle contraction)

Contractility: the velocity of muscle shortening at a constant preload and afterload

Compliance: the length that a muscle is stretched by a given preload

Heart Rate: Several Effects on overall Cardiac Function there is not a diagnostic hemodynamic profile for ARDS

Characteristic Features of A.R.D.S.

- Pulmonary Edema
- High Cardiac Output
- Low PA Occlusion Pressure

There are conditions that mimic the "A.R.D.S. Features":

- Partially-treated Volume Overload
- "Flash Pulmonary Edema" both of these cause a transient elevation in the filling pressures as well as alveolar congestion

Hemodynamics can also be elevated with:

- Increased Intrathoracic Pressure (artifactual)
- Fluid Administration for Hypotension (therapeutic)

Cardiac Function can also be depressed:

- Acidosis
- Hypoxia
- Sepsis-related Depressant Phenomenon

Which creates a confusing hemodynamic combination in the setting of developing-lung injury Parrillo et al. 1990. Despite all of these caveats, invasive cardiac monitoring can play a direct role in management of A.R.D.S. i.e. during the early phase to "rule out" Cardiogenic Edema & during subsequent management - to optimize fluid balance while efficiently maximizing cardiac performance.

Is it possible to measure the Lung Injury, itself ? No !

Murray et al.(1989) devised a semiquantitative score in an attempt to "measure" the degree of lung injury

- But, it has never been correlated to outcome
- APACHE & MP Models have been used but, again, their usefulness has never been validated !

TREATMENT OF ARDS:

NONPHARMACOLOGIC THERAPY.....PHARMACOLOGIC THERAPY

Currently, specific measures to correct the abnormality in vascular permeability or to limit the degree of inflammatory reaction present in ARDS, do not exist.

Clinical management involves primarily supportive measures aimed at maintaining cellular and physiologic function, while the acute lung injury resolves.

What cellular functions are you trying to maintain ?

- Alveolar Gas Exchange
- Organ Perfusion
- Aerobic Metabolism

There are very few therapeutic regimens which have been thoroughly evaluated; thus, many treatments are CONTROVERSIAL !

NONPHARMOCOLOGICAL APPROACHES

MECHANICAL VENTILATION: PRESSURE VS. VOLUME

Goals in providing support

- Preserve Arterial Oxygen Saturation
- Prevent complications from elevated airway pressuresi.e. Peak Airway Pressures > 40 cmH2O
- Minimize "oxygen toxicity" [FiO2 < 0.6] Dreyfuss et al. 1992 Marino 1998

Tidal Volume

- large volumes & high airway pressures have been

implicated as causes of gross lung injury & direct injury to the alveolar-endothelial membrane Dreyfuss et al. 1988

- 12 - 15 ml/kg : “old surgical dogma”
- 6 - 10 ml/kg [6 - 8 ml/kg]: “new surgical dogma”

Studies in support of 6ml/kg

Leatherman et al. 1991
Kisski et al. 1992
Lee et al. 1990

Improved hemodynamic performance with fewer pulmonary complications in patients with ARDS or respiratory failure. Remember, lung impedance, a function of airway resistance & tissue compliance, changes frequently in ARDS - requiring close monitoring of the tidal volume in maintaining the preselected level while avoiding elevated pressures

PEEP:

Theory: increases lung volume by limiting the degree of alveolar closure

Problem: there are no prospective studies of how or when PEEP should be used in A.R.D.S.

Prophylactic-PEEP: will NOT prevent ARDS in patients at risk Pepe et al. 1984

Routine Low-Level PEEP [5 cmH2O]

- May limit atelectasis
- May improve arterial oxygenation
- Has never been proven harmful Kollef & Schuster 1995

Apply PEEP in small increments (3 - 5 cmH2O)
Use it to achieve acceptable arterial saturations, > 90 %
Use it to lower the FiO2 Level
Follow the Airway Pressures !

Evaluate the clinical effect by monitoring BP, urine output, hemodynamic parameters, gas exchange, & most importantly - oxygen delivery.

Permissive Hypercapnea

- Theory: controlled hypoventilation with subsequent hypercapnea avoid detrimental increases in peak airway pressure
- Gradual increases of PaCO2 are well tolerated (up to 100 mmHg) - and marked acidosis (pH < 7.25) can be corrected with sodium bicarbonate

Inverse Ratio Ventilation

- Theory: by prolonging inspiration time, mean airway pressure is increased (allowing a subsequent increase in oxygen diffusion) while maintaining acceptable peak airway pressures
- Problem: there are no prospective, randomized trials !

I:E Ventilation, Articles in Support

- Gurevitch et al. 1986
- Tharrat et al. 1988
- Lain et al. 1989
- Marcy & Marini 1991
- East et al. 1992

NEJM 1995 REVIEW ARTICLE: ARDS & I:E

Inverse ratio ventilation should still be considered experimental since it has not been prospectively evaluated... therefore, until further studies have been performed, we recommend that ‘reversal' be considered only when acceptable arterial oxygenation cannot be achieved with a PEEP <15 cm H20 or when the use of PEEP is associated with excessive peak airway pressures.

However, “Reverse Ventilation” usually requires heavy sedation & paralysis

- neuromuscular blockade during the management of respiratory failure is occasionally associated with prolonged weakness & muscular paralysis Hansen & Cowen 1994

** the Benefit of paralytics & sedatives must be weighed against potential effects

PATIENT REPOSITIONING:

West Zone's of the Lung

Lung infiltrates are not uniformly distributed in A.R.D.S.

- Changes in position can improve oxygenation by altering the distribution of perfusion to ventilated areas (Piehl & Brown 1976)
- The Prone PositionComplicatedLogistic Nightmare - but the theory is sound !

PRONE = "DIMENSIONAL VENTILATION"

Arteriovenous shunting is a well-documented event in the critical care setting. Ventilation-perfusion differences can be, in part, attributed to alterations in the functional integrity of dependent lung zones. Over time, through gravitational influences, oxygenation declines without necessarily a progression of the histological injury.

Ray et al. Immobility, hypoxemia, and pulmonary arteriovenous shunting

Arch Surg, 1974.

3 groups of anesthetized dogs with induced-respiratory failure

- Group I: Control, left immobile
- Group II: Test 1, side-to-side every hour
- Group III: Test 2, side-to-side every half-hour

Group I: PaO2 values fell sharply - with a clinically significant shunt

Group II: PaO2 values moderate improvement, still with a significant shunt

Group III: PaO2 values returned to normalRay et al. 1974

In unilateral lung disease, the lateral decubitus position has been employed to improve blood distribution to the unaffected lung. (Remolina 1981)

In bilateral disease (e.g. ARDS), atelectasis and edema are mainly distributed in the posterobasal areas

- the prone position has demonstrated a "shifting" of the involved areas with improvement of PaO2 Langer et al. 1988

The Literature

- Piehl & Brown. Use of extreme position changes in acute respiratory failure. Crit Care Med 1976;413-4.
- Douglas et al. Improved oxygenation in patients with acute respiratory failure: the prone position. Am Rev Respir Dis 1977;115:559-66.
- Langer et al. The prone position in ARDS patients: a clinical study. Chest 1988;94:103-7.

The basic mechanisms underlying pathophysiologic cellular injury in A.R.D.S. are not known, but some evidence suggests that Tissue Perfusion is a key factor !

Russel et al, 1990 - reported that patients who died of A.R.D.S. had significantly lower values for oxygen delivery & consumption than the survivors

Although controversial - it is important to understand the role of oxygen delivery & consumption...

OXYGEN TRANSPORT:

- What are the "transport variables" ?
- What is their role in ARDS ?
- Is there any benefit to "supranormal" levels ?

The Transport Variables:

Oxygen Content, [CaO2] Oxygen Delivery, [DO2] Oxygen Uptake, [VO2] Extraction Ratio, [ER]

Specific recommendations:

in the treatment of A.R.D.S. based on hemodynamics & oxygen transport, can not be made.

However, it is important to ensure that a "sufficient" oxygen delivery is maintained - as judged by the adequacy of tissue perfusion.

FLUID MANAGEMENT IN ARDS:

In A.R.D.S., the primary problem is vascular permeability - however, increased hydrostatic forces can still worsen alveolar content

Pulmonary Function & Outcome are BETTER in patients who lose weight or whose PA-Occlusion Pressure falls as a result of fluid restriction or diuresis Simmons et al. 1987, Humphrey et al. 1990

- Must Avoid Hypovolemia (Impaired Renal

Clearance)

- Central Monitoring is critically important

GOAL OF THERAPY

to achieve the lowest possible PA-Occlusion Pressure consistent with an “adequate” cardiac output - (especially during the first few days after onset) while correcting any compromise in end-organ function (the benefit of this for more than 3 -4 days is unclear)

Diuretics & Fluid Restrictions can help to reduce total lung water

[which would work with Hydrostatic Pulmonary Edema]

ARDS is an INFLAMMATORY CONDITION & these methods are not as effective

Pharmacologic Treatment:

“you name it, and it's been tried...”

Exogenous Surfactant
Corticosteroids
Antioxidants
Vasodilators
Antiendotoxin
Ketoconazole
Nitric Oxide
Eicosanoid Inhibitors
Vasoconstrictors
Pentoxifylline

“Yet, what actually works ?”

CORTICOSTEROIDS:

Corticosteroids alter the host's inflammatory response

A.R.D.S is an “inflammatory process”

Prospective, multicenter, placebo-controlled studies have demonstrated that patients with ARDS do NOT benefit from high doses of corticosteroids administered early in the disease process Bernard et al. 1987, Luce et al. 1988 Bone et al. 1987

However, there are anecdotal reports suggesting that steroids may be useful during the

Fibroproliferative Phase of A.R.D.S.

Also, eosinophilia (either in the blood or lungs), may be an indication to administer corticosteroids

Tx: 2 - 4 mg Prednisone/kg/day, started 7 - 14 days after onset, in patients with severe disease; tapering is based on clinical response

NITRIC OXIDE:

Can act as a selective pulmonary vasodilator [5 - 80 ppm]

Despite, academic interest - all current studies of Nitric Oxide have been stopped [November 1997]

- Clinical Significance vs. Statistical Significance
- Cost / Benefit Ratio

ANTIBIOTICS:

Main Risk: Development of Resistant Organisms, which may cause “late-infection” and subsequent mortality. Patients with A.R.D.S., may have fever, leukocytosis, & pulmonary infiltrates yet no histologic evidence of pneumonia

- now, what do you do ?

If Sepsis is thought to be the cause, a trial of empiric antibiotic coverage is reasonable EARLY in the disease process. In the later phases of A.R.D.S., antibiotics should be reserved for clear indications of infection

- Appropriate Cultures
- Bronchoalveolar Lavage

There appears to be no scientific role for routine administration of prophylactic antibiotics in A.R.D.S. Kollef et al. 1995

MANAGEMENT: OF ARDS: THE RECOVERY PHASE

Most patients who die of ARDS, do so within the first two weeks of their illness

For those who survive, “recovery” takes weeks to months

General Supportive Care Issues:

- Ventilatory Support (i.e. Barotrauma / Tracheostomy)
- Nutritional Support (i.e. PEG vs. Jejunostomy)
- Nosocomial Infections (Pneumonia / UTI's...)

- "Stress-related" GI Bleeding

References

Author Information

Tisha K. Fujii, DO
Dept. of Trauma & Critical Care , Boston University School of Medicine, Boston Medical Center

Bradley J. Phillips, MD
Dept. of Trauma & Critical Care , Boston University School of Medicine, Boston Medical Center