

VENTILATOR INDUCED DIAPHRAGMATIC DYSFUNCTION

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Objectives

- Explain what is Ventilator Induced Diaphragmatic Dysfunction (VIDD)
- Clinical significance
- Evidence for VIDD
 - ▣ Animal and Human Studies
 - ▣ Muscular atrophy
 - ▣ Fiber remodeling
 - ▣ Oxidative stress
 - ▣ Structural injury
- Clinical relevance
- Potential therapeutic strategies
- Benefits of spontaneous breathing



What is VIDD

- Decreased diaphragm contractual force capacity and muscle endurance
- Diaphragmatic atrophy and histological changes
- Phrenic nerve impulse transmission remains normal up to 5 days
- Time dependent
- Human Studies
- Animal Studies
- Rat studies show that within 48 hours of diaphragmatic nonuse
 - ▣ 42% drop of pressure generated capacity of diaphragm



Clinical Significance of VIDD

- Muscular atrophy
- Decrease in muscle endurance
 - ▣ Decreased inspiratory muscle weakness (NIF)
 - ▣ Ventilatory fatigue during weaning process
- Cannot effectively take deep breaths to mobilize secretions



Clinical Significance of VIDD

- Weaning of patients from mechanical ventilation
 - ▣ 30% of patients on ventilator greater than 72 hours are difficult weans
 - ▣ 1% to 5 % may become ventilator dependent
 - ▣ Increased likelihood of VAP
 - ▣ Increased hospital cost
 - ▣ Increased ICU stay



Muscular atrophy

- Studies have demonstrated that prolonged CMV results in a rapid onset of diaphragmatic atrophy in several species (e.g., rats, rabbits, pigs, and humans!)
- 12 hrs to 18 hrs of CMV
 - ▣ Significant fiber atrophy in both slow and fast muscle fibers
- CMV-induced diaphragmatic atrophy is an extremely rapid and unique type of skeletal muscle wasting
- Diaphragmatic muscle atrophy greatly exceeds the time course of skeletal muscles wasting

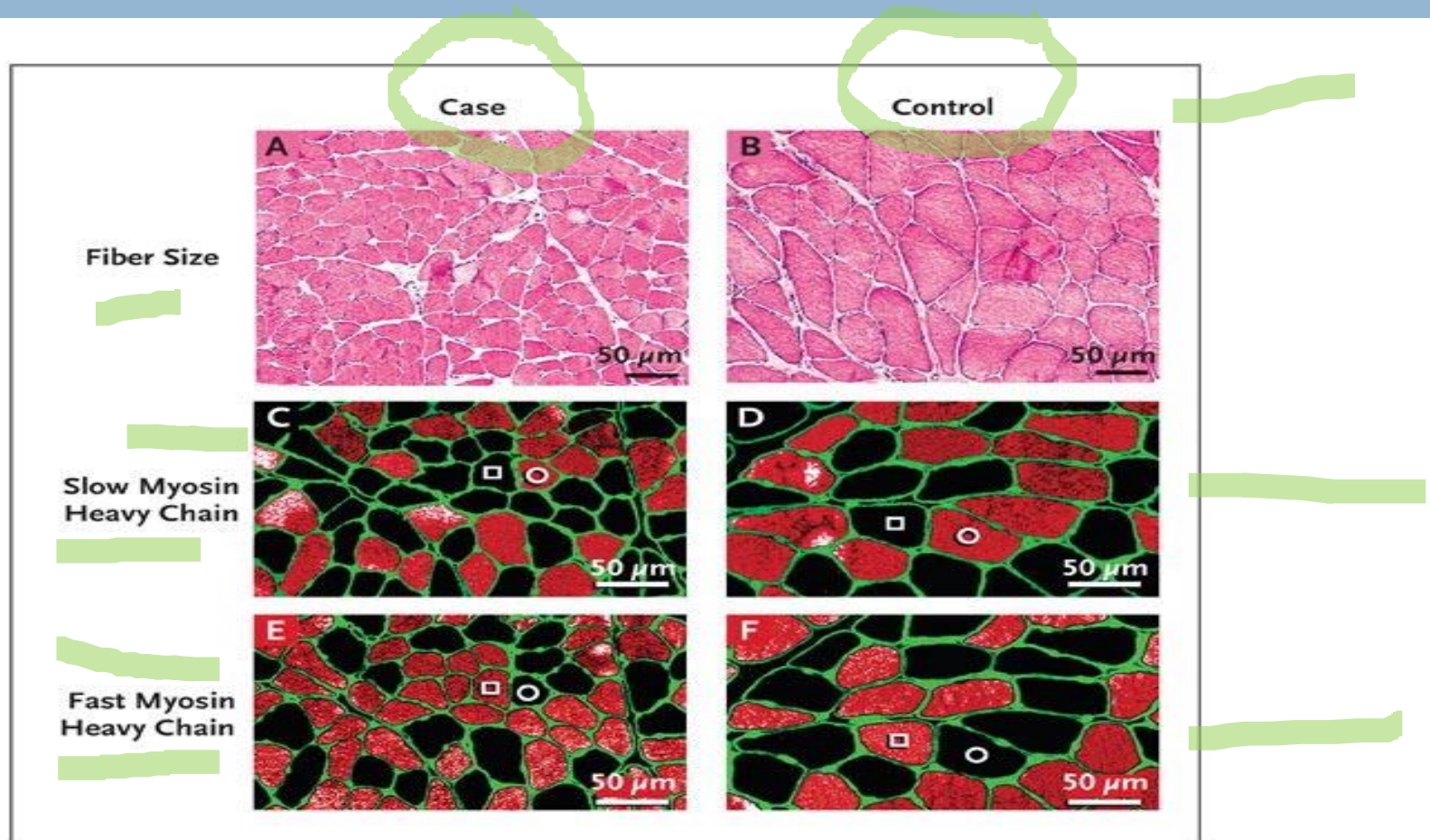


Muscular atrophy processes

- Muscle fiber atrophy is caused by two factors
 - ▣ Decreased protein synthesis
 - ▣ Increased protein breakdown (proteolysis)
- 5 hours of mechanical ventilation (animal studies)
 - ▣ 30% decrease of mixed muscle protein synthesis
 - ▣ 65% decrease of myosin heavy-chain-protein synthesis

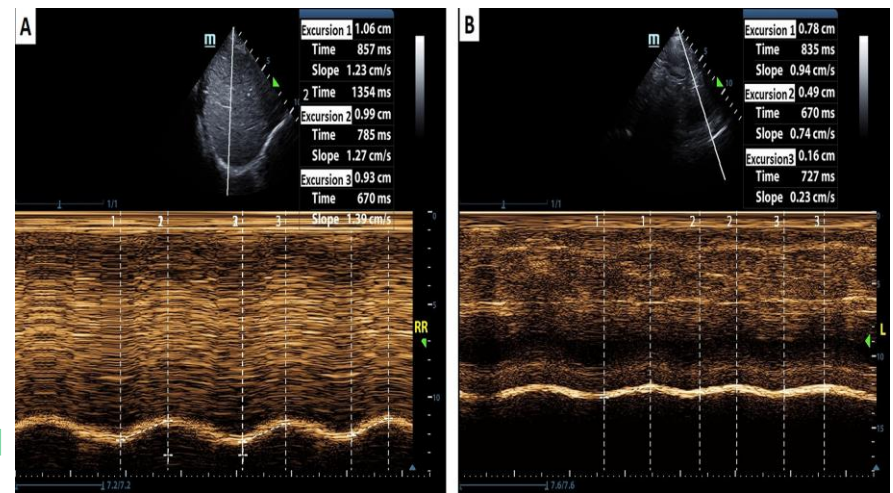


Representative Case and Control Diaphragm-Biopsy Specimens with Respect to Fiber Size (18 to 69 hours)



Muscular atrophy

- Neonates (human studies)
 - ▣ 12 days of MV
 - Histological data obtained immediately before death showed diffuse atrophy of the diaphragmatic fibers



Fiber Remodeling

- Diaphragm muscles
 - ▣ Slow twitch (type 1) used for endurance
 - ▣ Fast twitch (type 2) used for burst of muscular use
- During CMV modifications occur
 - ▣ ↓ 18 hours of type 1 and 2
 - ▣ ↓ force production
 - ▣ ↓ endurance
- Modification of fibers (increase in hybrid fibers)



Oxidative Stress from CMV

- Within 6 hours of MV
- Oxidative injury (protein oxidation and lipid peroxidation)
- When proteins are oxidized, they become more susceptible to proteolytic attack by the proteasome pathway of protein degradation
 - ▣ muscle atrophy
 - ▣ contractile dysfunction
 - ▣ protein degradation
 - ▣ reduction in muscle force production
- Antioxidant supplementation reduces oxidative stress and improves contractibility and endurance (Vitamin E and C)



Mechanism of Oxidative Stress

- Increase of protein oxidation and lipid peroxidation leading to muscle atrophy and contractile dysfunction
- Studies point to mitochondria as the main source of reactive oxygen species (ROS) regarding cellular respirations
- Trolox during CMV attenuated both contractile dysfunction and muscle proteolysis in the diaphragm



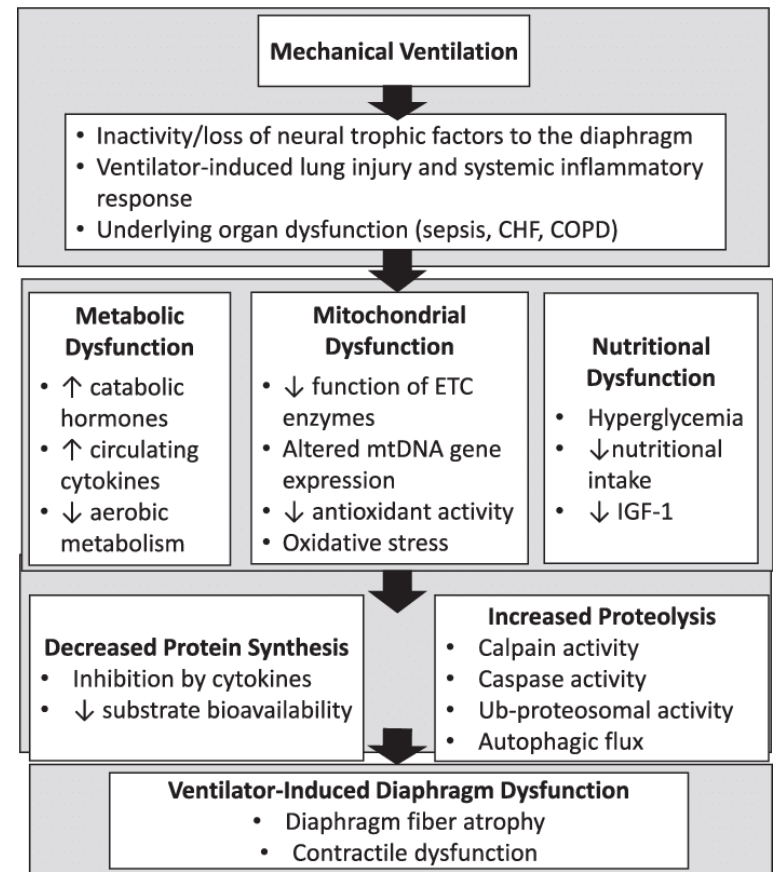
Structural Injury

- Loss of muscle fibers alone is doesn't account for the decrease in function
- Muscle fibers are disrupted within 48 hours of CMV
- Abnormalities include disrupted myofibrils, abnormal swelling of mitochondria, lipid droplets, and vacuoles
- Evidence says that a 70% decrease in muscle mass is required for loss of function
- 66% decrease in force generation due to myofibril disruption and damage (structural damage)



Therapeutic Strategies

Promote	Promote spontaneous breathing
Adjust	Adjust pressure support to allow patient comfort and adequate gas exchange
Target	Target the specific cellular pathways involved in muscle injury
Special	Special modes of mechanical ventilation



ETC: electron transport chain; mtDNA: mitochondrial DNA; IGF: insulin like growth factor; CHF: Chronic Heart Failure; COPD: Chronic Obstructive Pulmonary Disease



Therapeutic Strategies

- Pharmacological interventions
 - ▣ Vitamin E analogue Trolox prevents the loss of diaphragmatic contractility and attenuates atrophy
- Antioxidant supplement
 - ▣ Vitamins E and C was reported to reduce the duration of mechanical ventilation in comparison with nonsupplemented patients
- Proteolytic systems
 - ▣ Leupeptin (inhibitor of calpain/cathepsin)
 - ▣ Patients put on mechanical ventilation blocked atrophy, but also prevented intrinsic contractile impairment



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Ventilator-induced diaphragm dysfunction: translational mechanisms lead to therapeutic alternatives in the critically ill

[Oscar Peñuelas](#) , [Elena Keough](#), [Lucía López-Rodríguez](#), [Demetrio Carriedo](#), [Gesly Gonçalves](#), [Esther Barreiro](#) & [José Ángel Lorente](#)



Therapeutic Strategies with PS and NAVA (new study)

- *Effect of Neurally Adjusted Ventilatory Assist (NAVA) on prevention of ventilator-induced diaphragmatic dysfunction (VIDD) in ARDS rabbits*
- Randomized to Control Group, VC , NAVA, PS for 4 hours
- Superoxide dismutase and Glutathione were measured
- Light microscope and electron microscope viewing diaphragm fiber
 - ▣ PS group normal
 - ▣ NAVA group normal
 - ▣ VC group
 - Necrosis
 - Disrupted myofibrils
 - Swollen mitochondria
- Findings: NAVA groups has less oxidative stress, atrophy, and structural damage



Quiz# 1 What is this?

- Alveolar collapse that is not due to pneumothorax or hydrothorax
- Decrease in chest motion on the affected side
- Dullness to percussion
- Decreased to absent breath sounds
- Dyspnea, tachycardia, and cyanosis
- Radiologically findings
 - ▣ increase in density of the collapsed lung
 - ▣ reduced volume of the involved hemithorax
 - ▣ narrowed rib interspaces
 - ▣ elevated hemidiaphragm
 - ▣ mediastinal shift to the side of involvement



Dependant Atelectasis

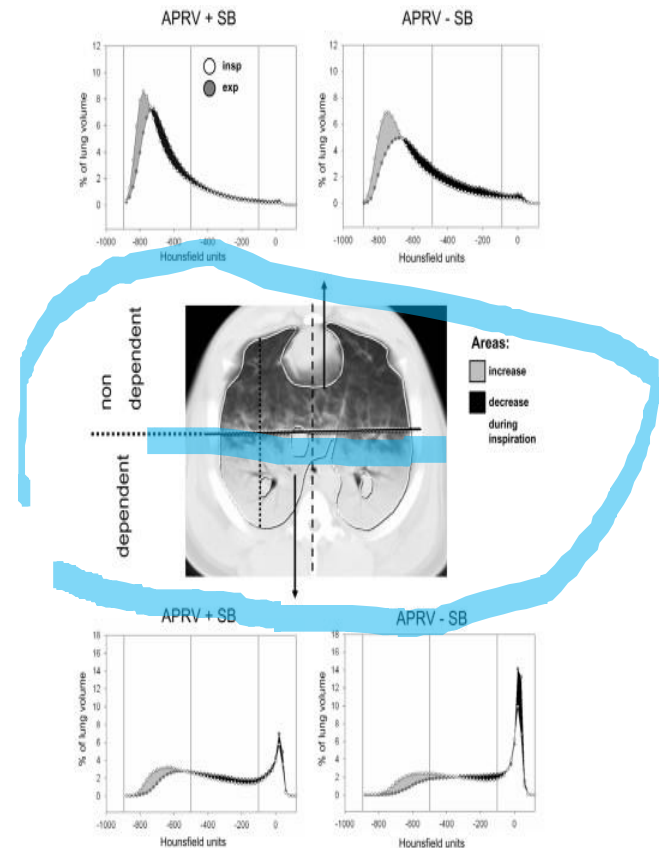
Dependent Atelectasis is more common in patients who are in a supine position on mechanical ventilation who don't spontaneous breath.

Weight of the lung is increased because of pulmonary edema; the dependent regions of the lung are compressed and collapse.

Increase pressure is required to reopen collapsed airways and alveoli.

It is believed that the increased weight of the lung (due to pulmonary edema, etc.) causes atelectasis and collapse in the dependent regions of the lung.

Dependent atelectasis usually appears as Ground-glass opacity, and often resolves when the patient changes from the supine to the prone position and/or spontaneous breaths.



Benefits of Spontaneous Breathing

- Spontaneous breathing improves shunt fraction and oxygenation
- Recruitment of collapsed lung regions by the contraction of the diaphragm
- Redistribution of blood flow to noncollapsed lung regions
- Improves hemodynamics by increasing venous return and cardiac output
- Prevents VIDD!



Benefits of Spontaneous Breathing

- Oxygenation
 - ▣ Studies show $\text{PaO}_2/\text{FIO}_2$ increased within 15 minutes after resuming spontaneous breathing in patients
- Engaging the diaphragm during spontaneous breathing attenuates atrophy and reactive oxidative stress
- Ventilation/Perfusion Distribution
 - ▣ Dead space ventilation was less with spontaneous breathing
- Reduction in atelectatic lung areas close to the diaphragm
- Reopening of dependent lung regions by diaphragmatic contractions increased PaO_2 substantially



ARDS and Spontaneous Breathing APRV Study

- Spontaneous breathing in any phase of the mechanical ventilator cycle is possible with airway pressure release ventilation (APRV)
- This study was designed to evaluate
 - ▣ “The effect of spontaneous breathing with APRV on gas exchange and cardiovascular function in patients at risk for ARDS”



ARDS and Spontaneous Breathing

- Alveolar collapse (atelectasis) is primarily in dependent lung regions resulting in severe hypoxemia
- Partial ventilatory support as compared with CMV
 - ▣ Improvement in ventilation-perfusion matching
- Diaphragmatic contraction augments distribution of ventilation to dependent and poorly aerated lung regions



ARDS and Spontaneous Breathing

- When spontaneous breathing was allowed
 - ▣ Gas exchange improved
 - ▣ $\text{Pa}_{\text{O}_2}/\text{FI}_{\text{O}_2}$ ratio increased
 - ▣ Lower shunt fraction
 - ▣ Distribution of ventilation to dependent lung areas
- APRV with spontaneous breathing
 - ▣ Lowest required doses of vasopressors and positive inotropes occurred with persisting spontaneous breathing during APRV



Spontaneous Breathing with APRV in ARDS Patients

- APRV was consistently associated
 - ▣ Shorter duration of ventilatory support
 - ▣ ICU stay
 - ▣ Improvement in cardiopulmonary function
- Results of this study show that partial ventilatory support with APRV
 - ▣ Reduction in sedation
 - ▣ Improved arterial oxygenation
 - ▣ Improved pulmonary compliance
 - ▣ Improved systemic blood flow
 - ▣ Decreased duration of ventilatory support and ICU stay
- Less Ventilator Induced Diaphragmatic Dysfunction



Summary

- Know what is VIDDD
- Engage the patient to breath with modes that improve patient interaction with the ventilator
- Understand the pathophysiology of VIDDD
- Encourage spontaneous breathing



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