Use of Ultrafiltration for Volume Management in COVID-19 Patients

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About the Aquadex SmartFlow™ System

The Aquadex SmartFlow system delivers clinically proven therapy using a simple, flexible and smart method of removing excess fluid from patients suffering from hypervolemia (fluid overload). The Aquadex SmartFlow system is indicated for temporary (up to 8 hours) or extended (longer than 8 hours in patients who require hospitalization) use in adult and pediatric patients weighing 20 kg or more whose fluid overload is unresponsive to medical management, including diuretics. All treatments must be administered by a health care provider, within an outpatient or inpatient clinical setting, under physician prescription, both having received training in extracorporeal therapies.

Panelists & Disclosures

Dr. Amir Kazory, MD, FASN, University of Florida

- Baxter - Cardiology Advisory Board
- CHF Solutions, Inc. - Medical Advisory Board
- Relypsa, Inc. – Consultant
- W. L. Gore & Associates, Inc. - Consultant

Dr. Maria DeVita, MD, FACP, FASN, Lenox Hill Hospital

- Consultant Vascular Therapies – serving as medial monitor for a Phase 3 trial on AVF for hemodialysis

Dr. Mehdi Oloomi, MD, Mount Sinai Medical Center

- CHF Solutions, Inc. - Medical Advisory Board

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Learning Objectives

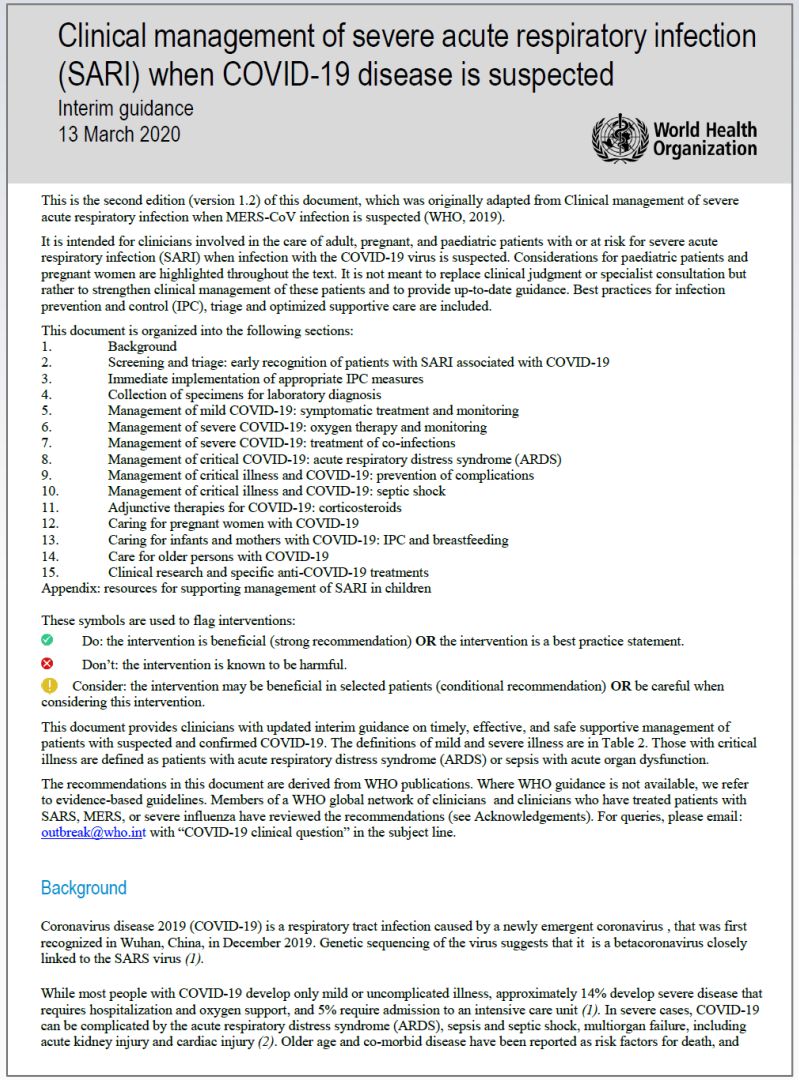
- Discuss the WHO protocol and the importance of identifying volume overload in COVID-19 infected patients
- Understand the risks associated with volume overload, the importance of maintaining fluid balance, and the benefits of using ultrafiltration in patients with volume overload
- Discuss training and personnel required to quickly implement access to ultrafiltration
- Hear real-world critical care patient case studies

WHO Guidance on Treatment of COVID-19

Dr. Mehdi Oloomi, MD

Mount Sinai Medical Center

Clinical Management of Severe Acute Respiratory Infection (SARI) when COVID-19 Disease Is Suspected (*Interim Guidance, 13 March 2020, WHO*)



Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected

Interim guidance
13 March 2020

World Health Organization

This is the second edition (version 1.2) of this document, which was originally adapted from Clinical management of severe acute respiratory infection when MERS-CoV infection is suspected (WHO, 2019).

It is intended for clinicians involved in the care of adult, pregnant, and paediatric patients with or at risk for severe acute respiratory infection (SARI) when infection with the COVID-19 virus is suspected. Considerations for paediatric patients and pregnant women are highlighted throughout the text. It is not meant to replace clinical judgment or specialist consultation but rather to strengthen clinical management of these patients and to provide up-to-date guidance. Best practices for infection prevention and control (IPC), triage and optimized supportive care are included.

This document is organized into the following sections:

1. Background
2. Screening and triage: early recognition of patients with SARI associated with COVID-19
3. Immediate implementation of appropriate IPC measures
4. Collection of specimens for laboratory diagnosis
5. Management of mild COVID-19: symptomatic treatment and monitoring
6. Management of severe COVID-19: oxygen therapy and monitoring
7. Management of severe COVID-19: treatment of co-infections
8. Management of critical COVID-19: acute respiratory distress syndrome (ARDS)
9. Management of critical illness and COVID-19: prevention of complications
10. Management of critical illness and COVID-19: septic shock
11. Adjunctive therapies for COVID-19: corticosteroids
12. Caring for pregnant women with COVID-19
13. Caring for infants and mothers with COVID-19: IPC and breastfeeding
14. Care for older persons with COVID-19
15. Clinical research and specific anti-COVID-19 treatments

Appendix: resources for supporting management of SARI in children

These symbols are used to flag interventions:

Do: the intervention is beneficial (strong recommendation) **OR** the intervention is a best practice statement.

Don't: the intervention is known to be harmful.

Consider: the intervention may be beneficial in selected patients (conditional recommendation) **OR** be careful when considering this intervention.

This document provides clinicians with updated interim guidance on timely, effective, and safe supportive management of patients with suspected and confirmed COVID-19. The definitions of mild and severe illness are in Table 2. Those with critical illness are defined as patients with acute respiratory distress syndrome (ARDS) or sepsis with acute organ dysfunction.

The recommendations in this document are derived from WHO publications. Where WHO guidance is not available, we refer to evidence-based guidelines. Members of a WHO global network of clinicians and clinicians who have treated patients with SARS, MERS, or severe influenza have reviewed the recommendations (see Acknowledgements). For queries, please email: outbreak@who.int with "COVID-19 clinical question" in the subject line.

Background

Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by a newly emergent coronavirus , that was first recognized in Wuhan, China, in December 2019. Genetic sequencing of the virus suggests that it is a betacoronavirus closely linked to the SARS virus *(1)*.

While most people with COVID-19 develop only mild or uncomplicated illness, approximately 14% develop severe disease that requires hospitalization and oxygen support, and 5% require admission to an intensive care unit *(1)*. In severe cases, COVID-19 can be complicated by the acute respiratory distress syndrome (ARDS), sepsis and septic shock, multiorgan failure, including acute kidney injury and cardiac injury *(2)*. Older age and co-morbid disease have been reported as risk factors for death, and

"… In severe cases, COVID-19 can be complicated by the acute respiratory distress syndrome (ARDS), sepsis and septic shock, multiorgan failure, including acute kidney injury and cardiac injury." (p.1)

"**Fluid resuscitation may lead to volume overload**, including respiratory failure, particularly with ARDS. If there is no response to fluid loading or signs of volume overload appear (e.g. jugular venous distension, crackles on lung auscultation, pulmonary oedema on imaging, or hepatomegaly in children), then reduce or discontinue fluid administration. This step is particularly important in patients with hypoxemic respiratory failure." (p. 9)

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Clinical Course of COVID-19

ARDS: Acute Respiratory Distress Syndrome
MOF: Multiple Organ Failure

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Risk Factor for Severe COVID-19*

- Age
- Cardiovascular Disease
- Diabetes Mellitus
- Chronic Respiratory Disease

* CDC-COVID-19 (March/7/2020)

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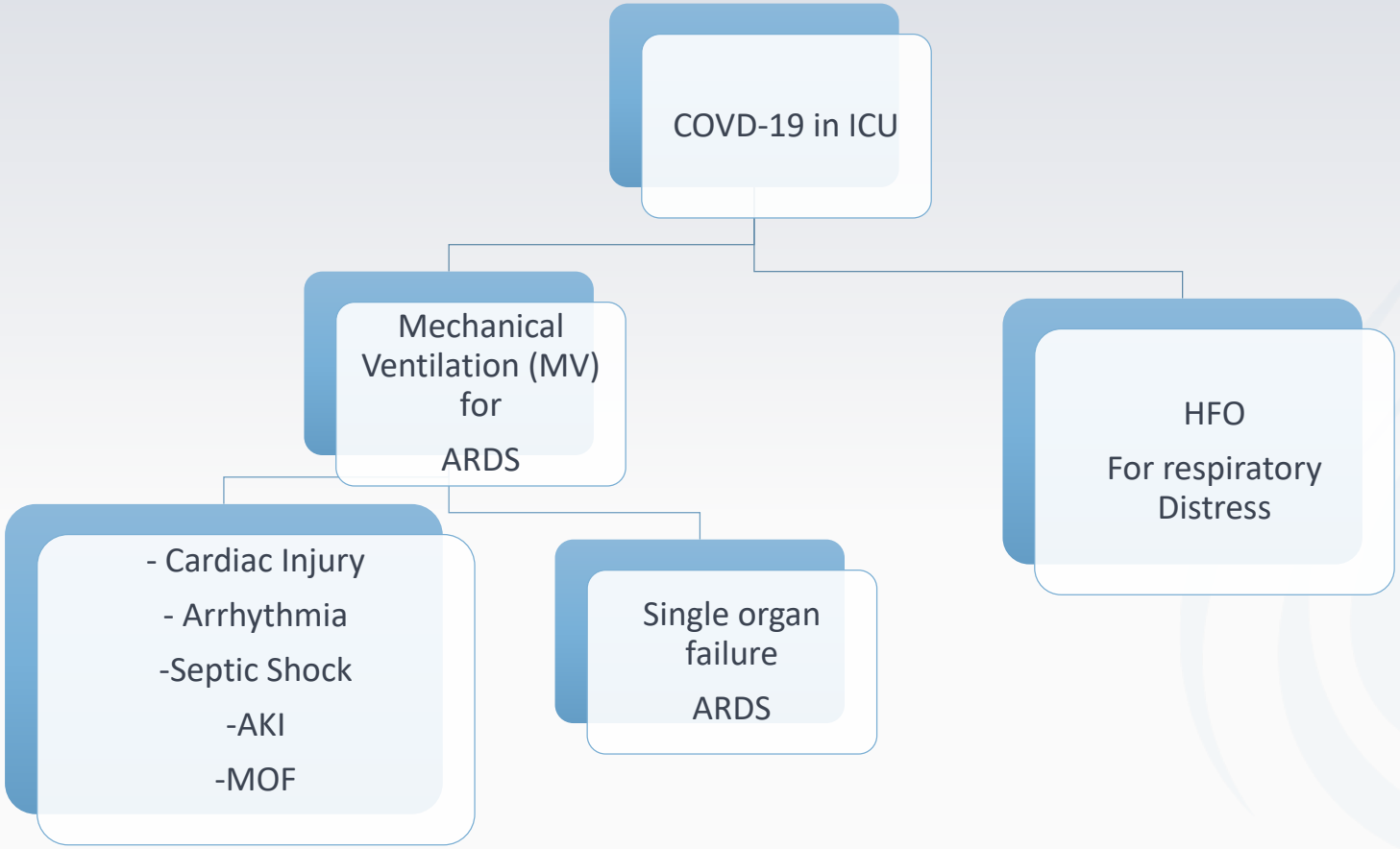
Hospital Course of COVID-19



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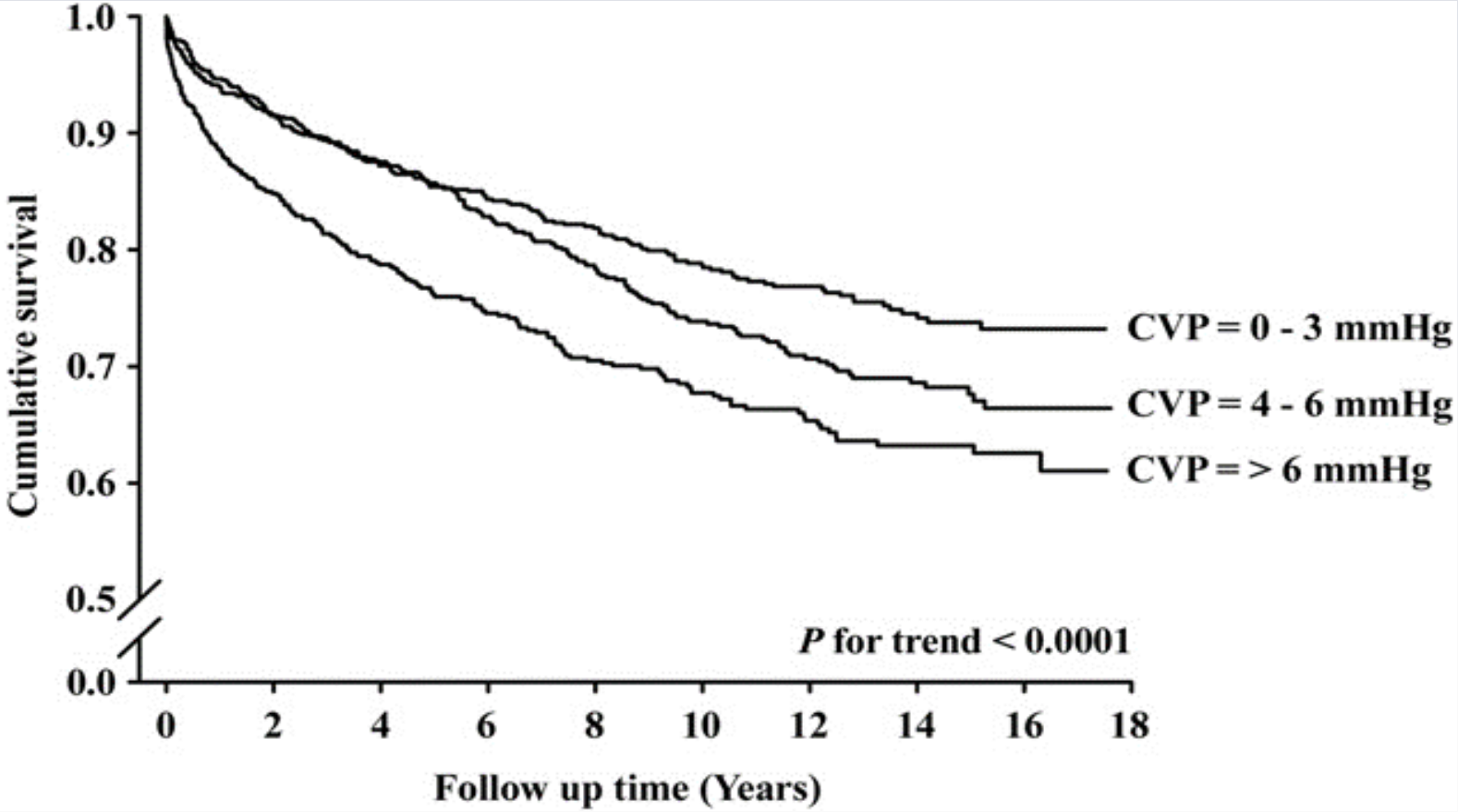
Venous Congestion in Patients with Cardiovascular Disease



Increased central venous pressure is associated with impaired renal function and all-cause mortality in a broad spectrum of patients with cardiovascular disease

Source: Damman K et al. J Am Coll Cardiol 2009 Feb 17;53(7): 582-588.

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Volume Overload

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Ultrafiltration & Aquadex SmartFlow

Panel

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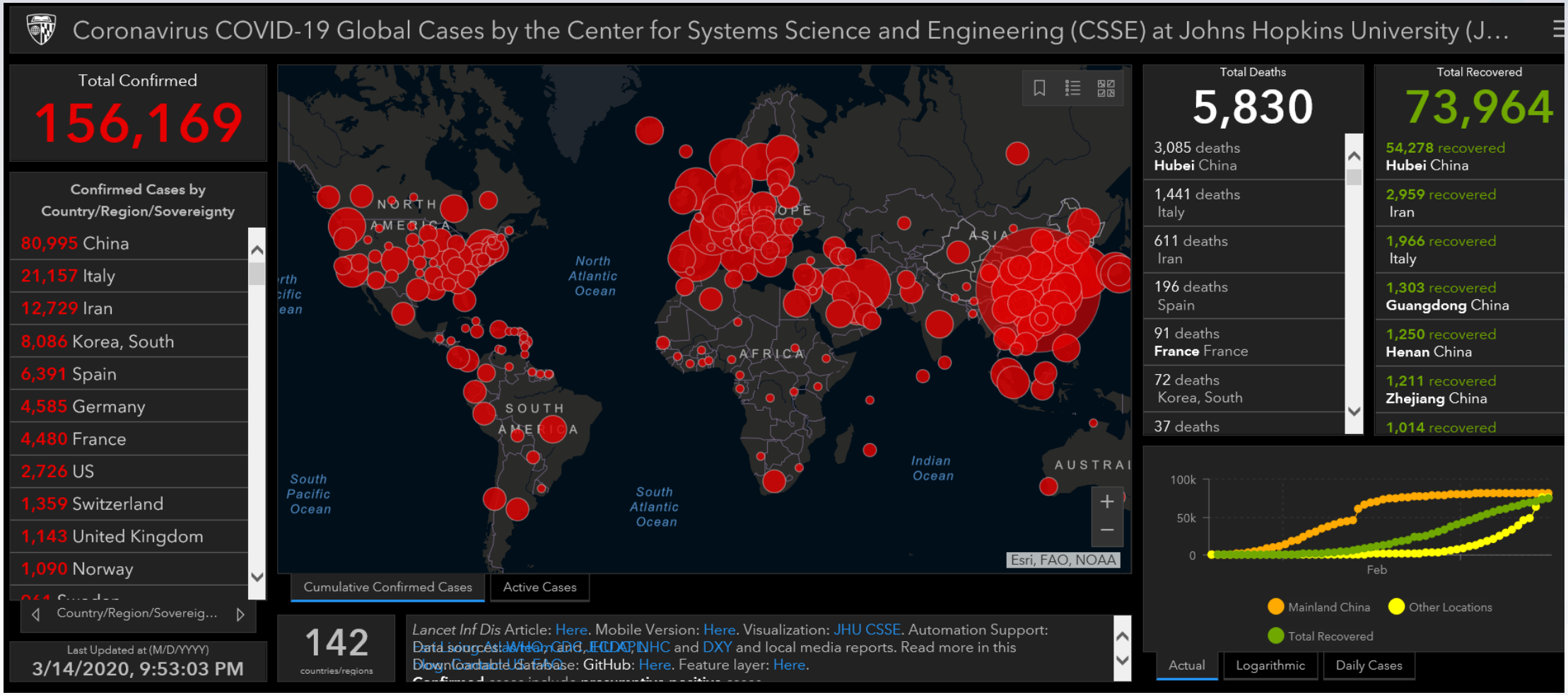
COVID-19 Pandemic



https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6 Access: March 14 at 10:00 PM

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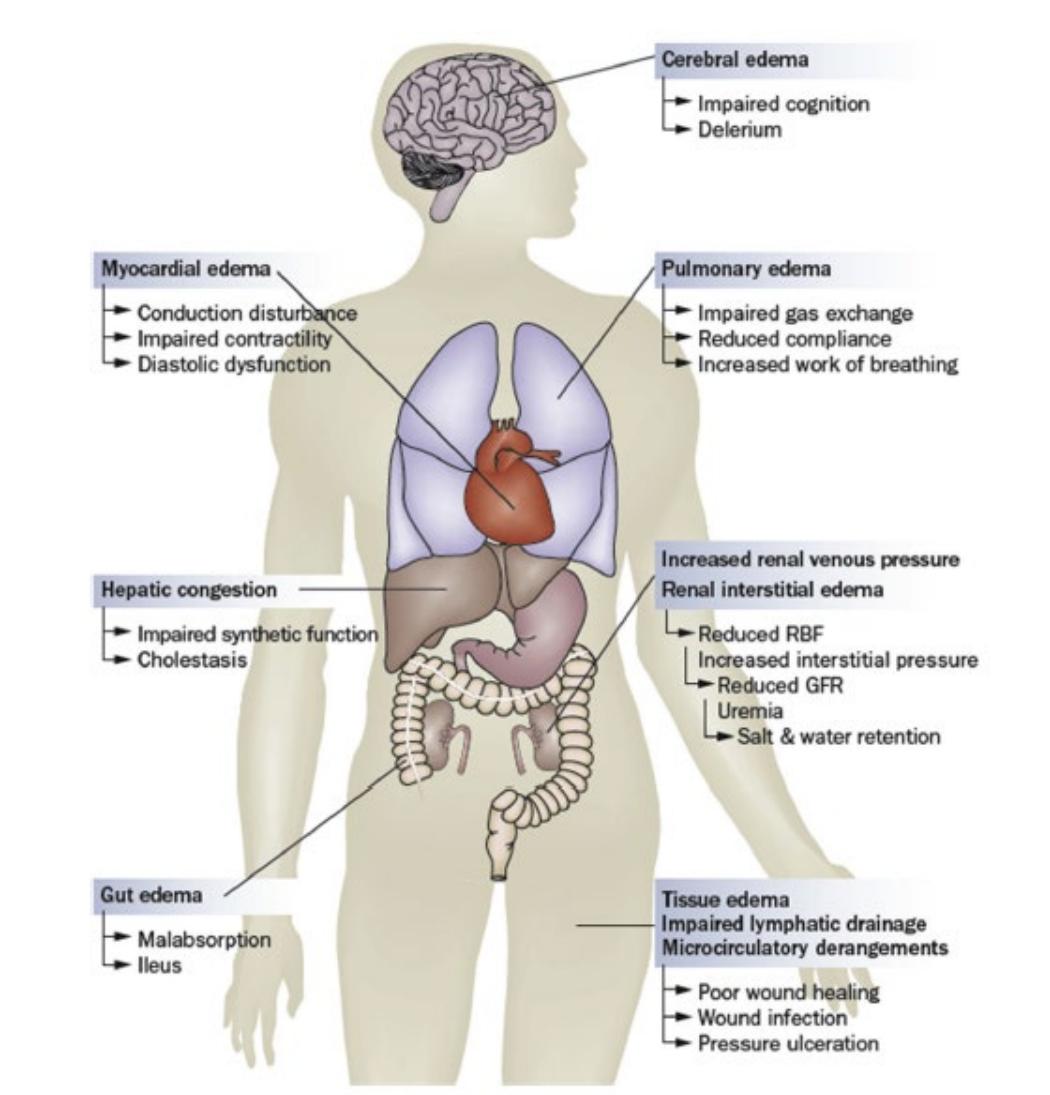
Volume Overload – Detrimental Effects



- Cerebral Edema
- Pulmonary Edema
- Increased Renal Venous Pressure
- Renal Interstitial Edema
- Tissue Edema
- Impaired Lymphatic Drainage
- Microcirculatory Derangements
- Gut Edema
- Hepatic Congestion
- Myocardial Edema

Prowle JR et al. Nat Rev Nephrol 2010;6:110

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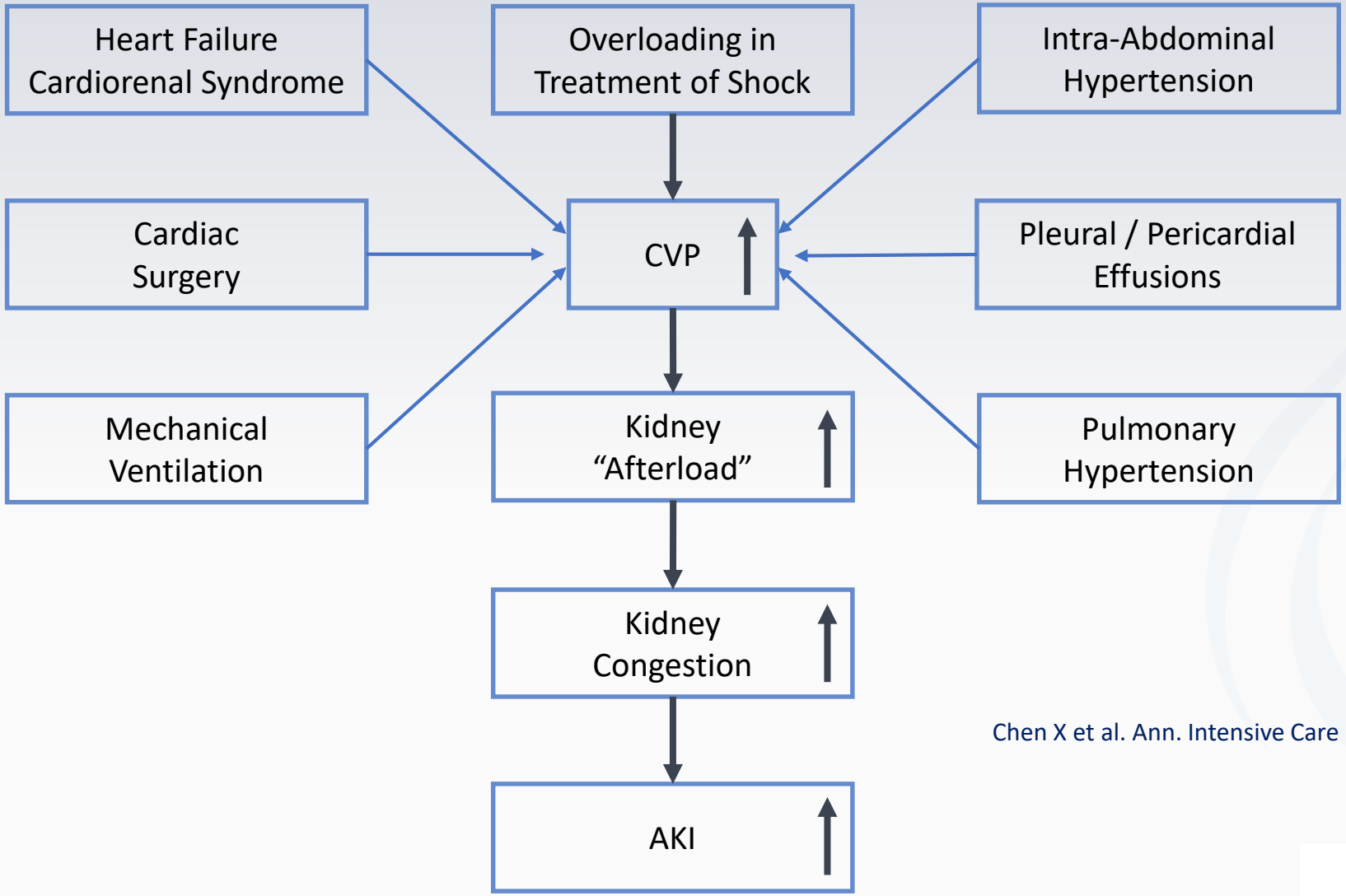
Volume Overload and the Kidney



Chen X et al. Ann. Intensive Care 2018;8:91

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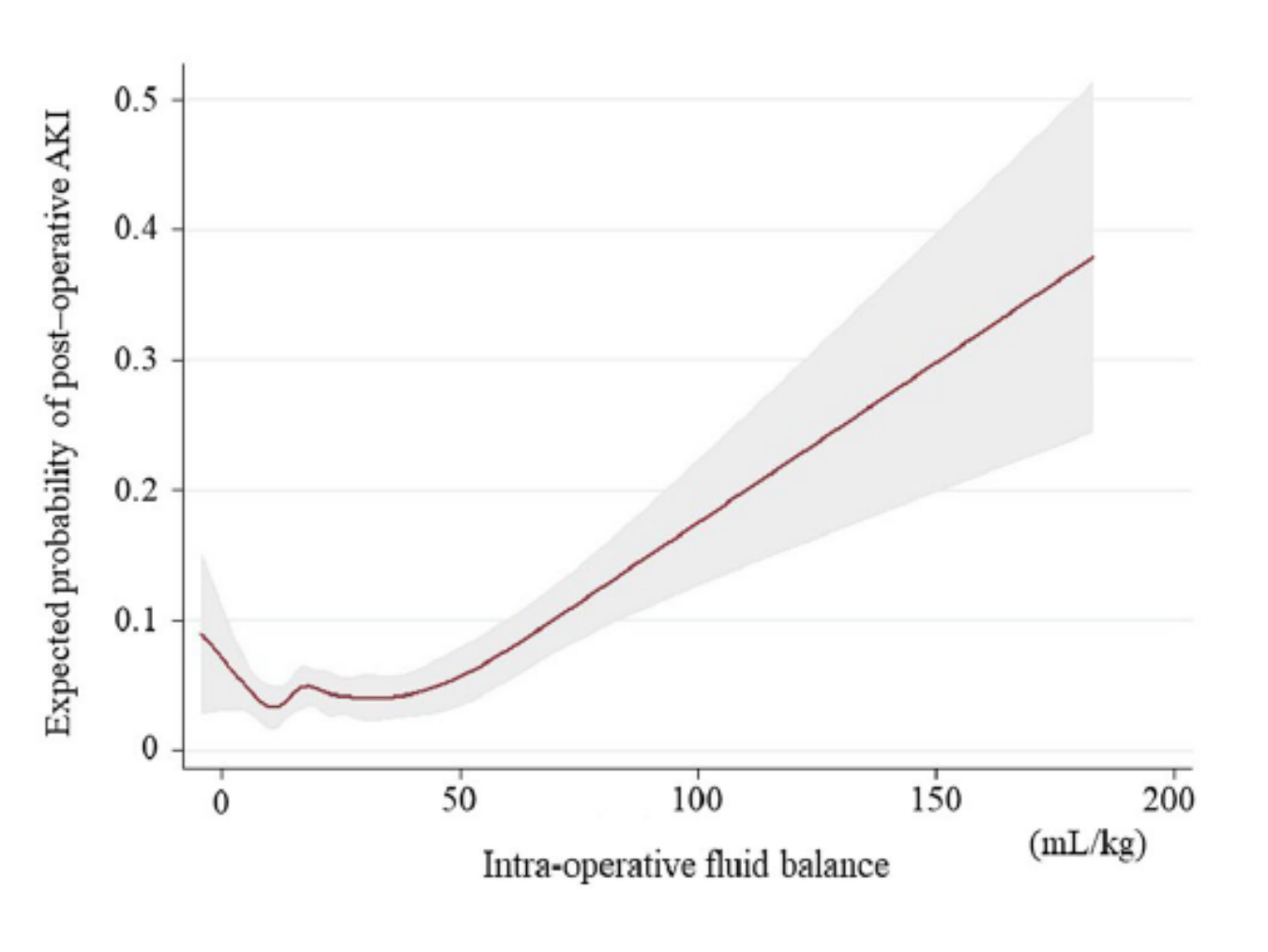
Volume Overload and the Kidney – Intraoperative Fluid Balance



NARA-AKI cohort study
n=5168

Murashima M et al. J Neph 2019 doi.org/10.1007/s40620-019-00688-x

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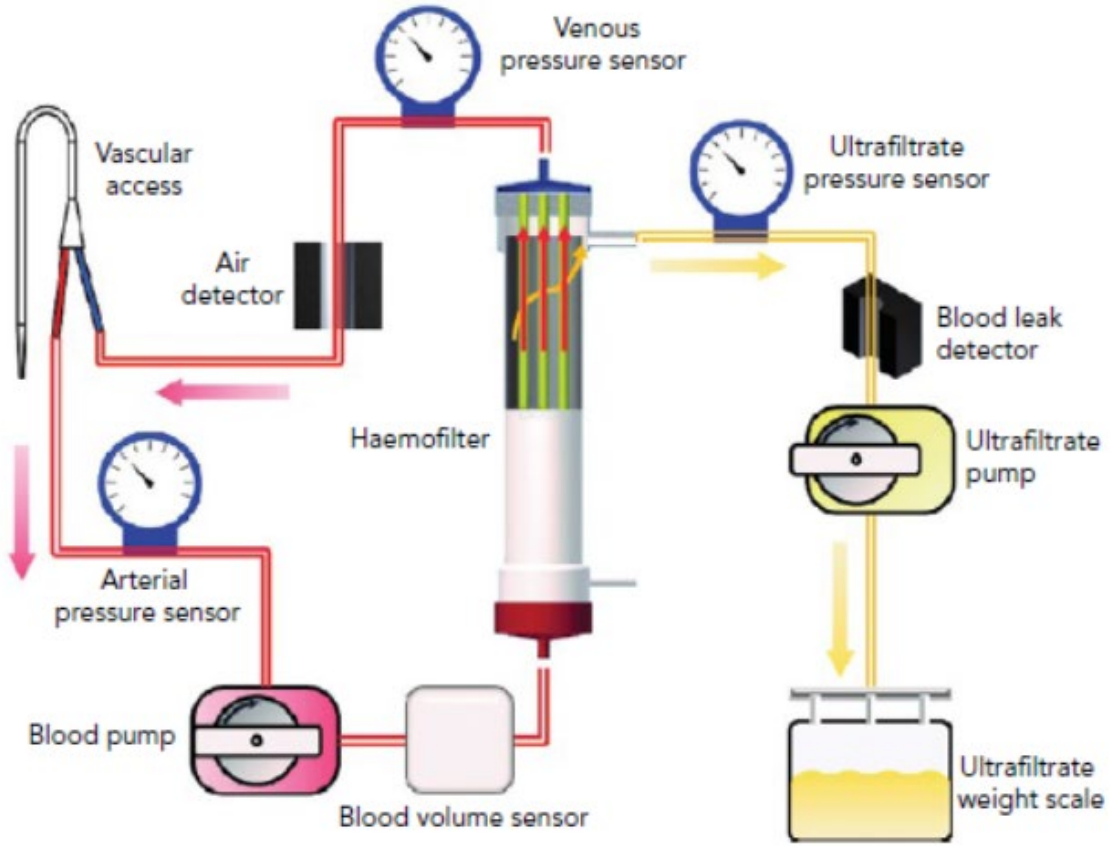
Ultrafiltration Therapy

Figure 1A: Ultrafiltration Circuit



Costanzo MR. Card Fail Rev 2019;5:9–18

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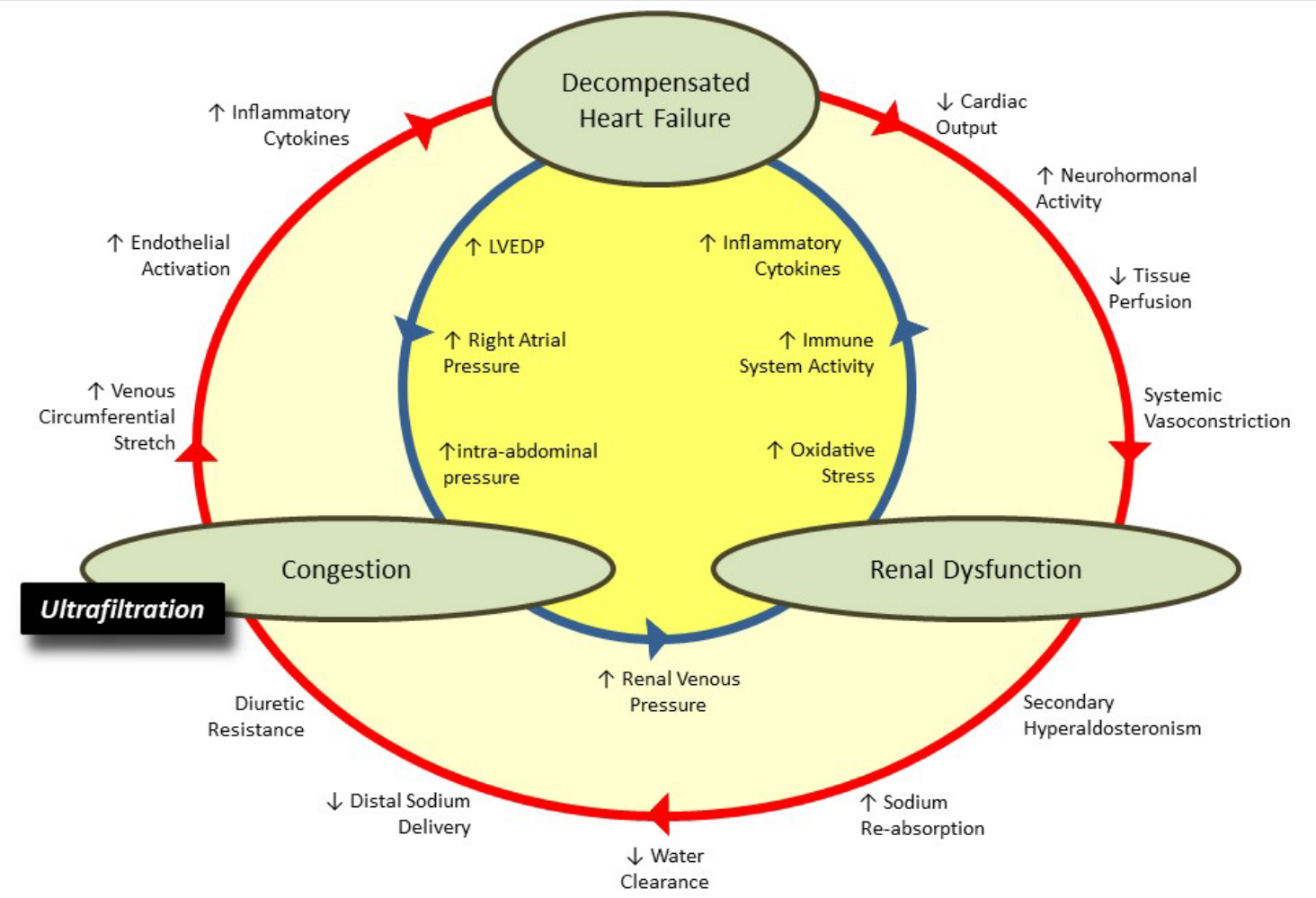
Congestion – Bi-directional Relationship with Heart and Kidney



Bidirectional pathways linking congestion, heart failure, and renal dysfunction.

Decompensation of heart failure can lead to deterioration in renal function via exacerbated neurohormonal activity (i.e., low forward flow) or through fluid overload and renal venous congestion (i.e., high backward pressure).

Ultrafiltration could counter these maladaptive interactions mainly through correction of congestion.

Kazory A. Clin J Am Soc Nephrol 2016;11:1463-71

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Decongestion – Potential Shortcomings of Diuretics

Direct activation of renin-angiotensin-aldosterone system
Deterioration in renal function
Electrolyte abnormalities (e.g. hypokalemia and hypomagnesemia)
Suboptimal natriuresis (production of hypotonic urine)
Development of diuretic resistance
Unpredictability of the therapeutic response
Lack of clarity on the practical aspects of use (e.g. optimal dosing strategy)
Non-renal adverse effects (e.g. ototoxicity and hypersensitivity)

Kazory A. Clin J Am Soc Nephrol 2013;8:1816-28

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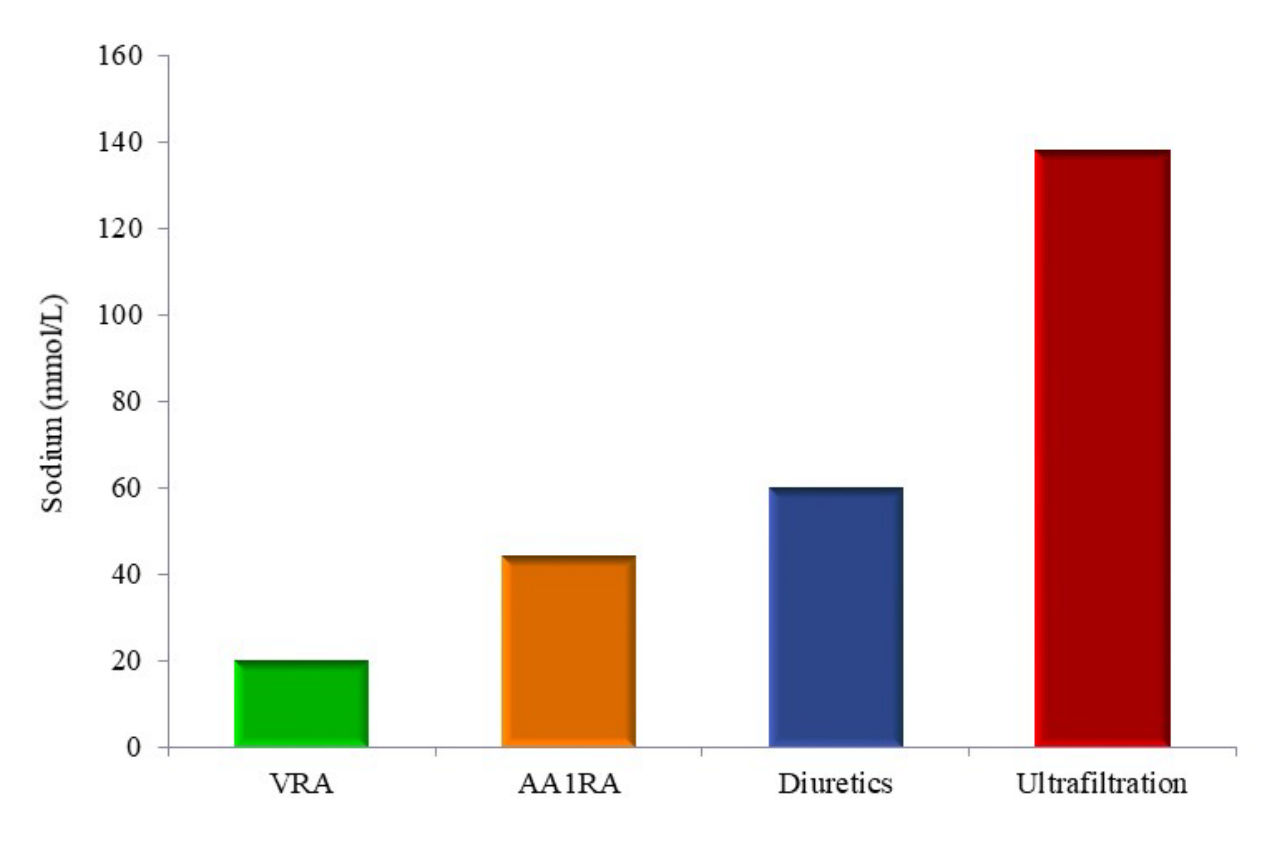
Decongestion – Proposed Advantages of Ultrafiltration

Reduction in renal venous congestion and improvement in renal hemodynamics
Rapid and adjustable removal of fluid and improvement in symptoms of congestion
Higher mass clearance of sodium
Decreased risk of electrolyte abnormalities (e.g. hypokalemia)
Lack of neurohormonal activation (SNS, RAAS, and AVP)
Sustainability of the beneficial effects (e.g. impact on neurohormonal axis)
Improvement in diuretic resistance, natriuresis, and urine output
Decreased rate of heart failure-related re-hospitalizations
Decreased hospital length of stay
Availability of dedicated ultrafiltration devices that are portable, user-friendly, with minimal extracorporeal volume (35 ml), and the ability of functioning with low blood flow rates (10-40 ml/min)

Kazory A. Clin J Am Soc Nephrol 2013;8:1816-28

Ultrafiltration – Advantageous Sodium Removal



Because ultrafiltrate extracted through convective forces is isotonic, it removes a significantly higher amount of sodium compared with hypotonic urine produced by diuretics and other available pharmacologic agents. Given that UF also extracts fluid more efficiently and rapidly compared with diuretics[1,2] and that it is reported to enhance natriuresis[3,4] this effect can be further potentiated possibly leading to longer-lasting results".

VRA: Vasopressin Receptor Antagonists
AA1RA: Adenosine-A1 receptor antagonists.

1.Bart BA, et al,: RAPID-CHF trial. J Am Coll Cardiol **46**: 2043–2046, 2005
2.Costanzo MR, et. al. UNLOAD. J Am Coll Cardiol 49: 675–683, 2007
3.Guazzi MD, et. al., Apparent paradox of neurohumoral axis inhibition after body fluid volume depletion in patients with chronic congestive heart failure and water retention. Br Heart J **72**: 534–539, 1994
4.Marenzi G, Lauri G, Grazi M, Assanelli E, Campodonico J, Agostoni P: Circulatory response to fluid overload removal by extracorporeal ultrafiltration in refractory congestive heart failure. J Am Coll Cardiol 38: 963–968, 2001

Kazory A. Clin J Am Soc Nephrol 2013;8:1816-28

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Aquadex SmartFlow – Simplified Ultrafiltration

Safe and predictable method to achieve euvolemia

- Removes isotonic plasma water with no changes to a patient's electrolytes
- Low extracorporeal volume (35 mL)
- Low blood flow rate (10-40 mL/min)
- Precise control of rate and amount of fluid removed (up to 500 mL/hr)
- Hematocrit (Hct) & SvO_2 monitoring

Ease of Use

- Performed at patient bedside
- May be prescribed by any physician trained in extracorporeal therapy, allowing for timely initiation of therapy
- Highly automated setup and operation
- Central venous access or peripheral access with Aquadex catheter (dELC)
- Often used with up to 4:1 Patient/Nurse ratio
- Portability enables patient to ambulate and rapid device deployment capability

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Thank You

Q&A