# RENAL INSUFFICIENCY MANAGEMENT IN HEART FAILURE

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# Introduction

- Renal dysfunction is one of the most important comorbidities in heart failure
- It is a predictor of poor outcome
- Become more common in the near future due to the improved survival of heart failure patients

# Potential Challenges for CRS Managment

- Heterogeneous and complex pathophysiology
- Contradictory therapeutic choices
- Symptomatic therapies for fluid removal with no benefit on improving survival
- No single success-guaranteed treatment
- Diagnostic challenges

# CRS Managment

Excluding Potentially reversible causes, including hypotension, dehydration, drug effects and renovascular disease

- More intensive diuretic treatment
- ACEIs and ARBs
- Ultrafiltration and RRT
- Consider increase bleeding risk with aspirin , clopidogrel and anticoagulants
- Dose adjustments and careful monitoring of drug plasma level
- Anaemia treatment

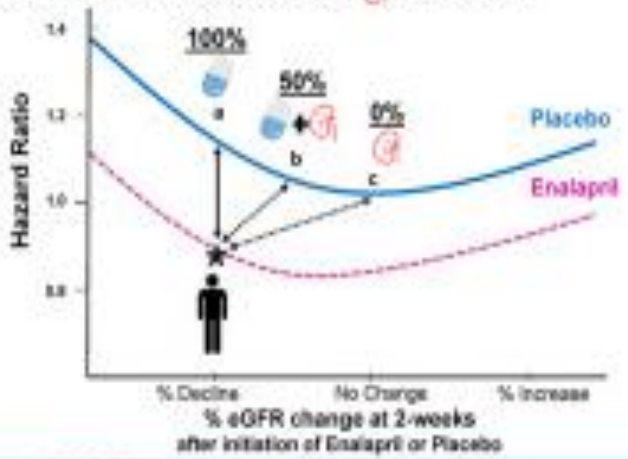
# ACE inhibitor

- In minority  of patiens: increase in GFR
  but  most patient:  moderate reduction in GFR
- chronic eGFR decline not significantly different compared to not taking (SOLVD trials )
- No absolute serum creatinine level that is a contraindication to the use of ACEIs/ARBs

## Acute declines in estimated glomerular filtration rate on enalapril and mortality and cardiovascular outcomes in patients with heart failure with reduced ejection fraction

**Different Reference Groups**

*Depending on Assumptions of Degree of Medication-driven ( ) eGFR decline versus non-Medication-driven ( ) eGFR decline*




**Studies Of Left Ventricular Dysfunction Trial**

*6,245 patients with HFrEF randomized to enalapril vs placebo*

Examples of different thresholds of %eGFR decline on enalapril that are significantly associated with improved outcomes:

| Placebo Reference Group | All-cause Mortality HR (95% CI) | Heart Failure Hospitalization HR (95% CI) |
|---|---|---|
| Point a "Magnified" | 40% decline 0.77 (0.62, 0.96) | 40% decline 0.55 (0.43, 0.70) |
| Point b "Intermediate" | 15% decline 0.86 (0.77, 0.97) | 40% decline 0.67 (0.51, 0.88) |
| Point c "Conservative" | 10% decline 0.87 (0.77, 0.99) | 35% decline 0.79 (0.61, 0.99) |

**CONCLUSION:**

In patients with HFrEF, competing reasons beyond moderate acute eGFR decline with ACE inhibitors ought to be considered before their use is withdrawn

ISN kidney INTERNATIONAL

McCallum, (2019)

# *SOLVD trials*

# ACE inhibitor adjustment in CRS

- Stop if:
  Cr increase > 100% above the baseline
  Serum Cr rise >3.5 mg/dl
  Estimated GFR, 20ml/min/1.73m2

- Half the dose when:
  Cr increase 50 to 100% above the baseline
  Serum Cr rise 3 to 3.5 mg/dl
  Estimated GFR 20 to 25 ml/min/1.73m2

# DIURETICS

**TABLE I** - European Society of Cardiology 2016 guidelines on diuretic use and ultrafiltration in heart failure

| | Class | Level |
|---|---|---|
| Diuretics are recommended to improve symptoms and exercise capacity in patients with signs and/or symptoms of congestion | I | B |
| Diuretics should be considered to reduce the risk of HF hospitalization in patients with signs and/or symptoms of congestion | IIa | B |
| Diuretics are recommended in congested patients with HFpEF or HFmrEF to alleviate symptoms and signs | I | B |
| A thiazide diuretic (or if the patient is being treated with a thiazide diuretic, switching to a loop diuretic) is recommended | I | C |
| Intravenous loop diuretics are recommended for all patients with AHF admitted with sign/symptoms of fluid overload to improve symptoms. It is recommended to regularly monitor symptoms, urine output, renal function and electrolytes during use of i.v. diuretics | I | C |
| In patients with new-onset AHF or those with chronic, decompensated HF not receiving oral diuretics, the initial recommended dose should be 20-40 mg i.v. furosemide (or equivalent); for those on chronic diuretic therapy, initial i.v. dose should be at least equivalent to oral dose | I | B |
| It is recommended to give diuretics either as intermittent boluses or as a continuous infusion, and the dose and duration should be adjusted according to the patient's symptoms and clinical status | I | B |
| Combination of loop diuretic with either thiazide-type diuretic or spironolactone may be considered in patients with resistant edema or insufficient symptomatic response | IIb | C |
| Ultrafiltration may be considered for patients with refractory congestion, who have failed to respond to diuretic-based strategies | IIb | B |
| Renal replacement therapy should be considered in patients with refractory volume overload and acute kidney injury | IIa | C |

AHF = acute heart failure; HF = heart failure; HFpEF = heart failure with preserved ejection fraction; HFmEF = heart failure with mid-range ejection fraction.

# continuous infusion vs intermittent boluses of Loop Diuretic

Continuous infusion benefits :

- – Lower risk of *rebound* sodium retention
- _ Greater efficacy and efficiency
- – Smaller fluctuations of intravascular volume status with reduced neurohumoral activation and lower incidence of WRF
- – Lower ototoxicity

## Continuous versus bolus intermittent loop diuretic infusion in acutely decompensated heart failure: a prospective randomized trial

Alberto Palazzuoli, Marco Pellegrini, Gaetano Ruocco, Giuseppe Martini, Beatrice Franci, Maria Stella Campagna, Marilyn Gilleman, Ranuccio Nuti, Peter A McCullough & Claudio Ronco

## Diuretic efficacy of high dose furosemide in severe heart failure: Bolus injection versus continuous infusion

MD Tom P.J. Dormans [a], MD, PhD Joseph J.M. van Meyel [*], MD, PhD Paul G.G. Gerlag [†], Yuen Tan [a], PhD Frans G.M. Russel [a], MD, PhD Paul Smits [a]

## A meta-analysis of continuous vs intermittent infusion of loop diuretics in hospitalized patients

Fahad Alqahtani MD [a], Ioannis Koulouridis MD, MS [a, b], Paweena Susantitaphong MD [a, b, c], Khagendra Dahal MD [a], Bertrand L. Jaber MD, MS [a, b]

## Continuous infusion of loop diuretics are safer and more effective than intermittent administration for people with congestive heart failure

## Continuous infusion vs. intermittent bolus injection of furosemide in acute decompensated heart failure: systematic review and meta-analysis of randomised controlled trials

K. T. Ng[1] and J. L. L. Yap[2]

# DIURETIC RESISTANCE

- failure to achieve the therapeutically desired reduction in edema even when a maximal dose of diuretic
- Prevalence among HF patients : 20-30%a
- Practical definition:
  weight change of 0 to 2.7 kg per 40 mg of furosemide (or equivalent)
  a urinary diuretic response <1400 ml per 40 mg of furosemide (or equivalent)
  a fractional excretion of sodium at baseline <0.2%
  a urinary sodium concentration and urinary furosemide concentration ratio (both obtained from spot urine samples) <2 mmol/mg and/or lower chloride levels at baseline (97 to 103 mEq/l

- fractional sodium excretion lower than 0.2% or the failure to excrete at least 90 mmol of sodium within 72 hours under treatment with furosemide 160 mg i.v. b.i.d.

# Causes of diuretic resistance

- *Incorrect diagnosis*
- *Nonadherence to recommended sodium and/or fluid restriction*
- *Poor diuretic delivery to the nephron lumen*
- *Reduced diuretic secretion*
- *Insufficient kidney response to drug*

TABLE II - Causes of diuretic resistance and pseudoresistance

| Compliance and dietetic factors | Acute and chronic comorbidities | Cardiac factors | Pharmacological causes |
|---|---|---|---|
| Unrestricted water intake | Pneumonia | Arrhythmias | NSAIDs |
| Unrestricted sodium intake | Pulmonary embolism | Hypertension | Negative inotropes |
| No monitoring of body weight | COPD | Ischemia | Inadequate diuretic therapy |
| | Thyroid disease | Valvular | |
| | Anemia | Endocarditis | |
| | Surgical stress | | |
| | AKI | | |
| | CKD | | |

AKI = acute kidney injury; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; NSAIDs = nonsteroidal antiinflammatory drugs.

# Diuretic Resistance Approach

- Intravenous diuretics
- Increase diuretic dose (Doses of ≥500 mg/day of oral furosemide were safe)
- Use alternative loop diuretic
- Continuous infusion
- Combination of intravenous loop diuretics with diuretics from different classes
- Hypertonic saline
- Dopamine
- Ultrafiltration

***Nesiritide should not be used in loop diuretic resistance***

## Aquapheresis Therapy

- Therapy to **safely achieve euvolemia** (dry weight)
- Uses a simplified form of ultrafiltration

| | |
|---|---|
| - Quick and easy device setup: | less than 10 mins |
| - Low blood flow: | 20-40 mL/min |
| - Low blood volume: | **33 mL** |
| - Precise fluid removal rates: | 10-500 mL/hour |

- **Inpatient** or **outpatient** settings
  - ICU, CCU, MICU, telemetry, stepdown, observation, ED, outpatient clinics
- **Peripheral** or **central** venous access
  - Flexible access sites and catheters
- Diverse physician prescription
- **No clinically significant impact on electrolyte balance, blood pressure or heart rate**

*Think of it as a "mechanical diuretic"...*

# advantages of ultrafiltration

- Less neurohormonal activation
- 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
- Sustainability of the beneficial effects
- Improvement in diuretic resistance, natriuresis, and urine output
- Decreased rate of heart failure related rehospitalization
- Decreased hospital length of stay

# Disadvantages of Ultrafiltration

- Lack of protective effect on renal function
- Lack of effect on markers of mortality
- Possible need for placement of midline or central venous catheter
- Need for additional training for staff and physicians
- Need for anticoagulation
- Complications related to extracorporeal circuit
- Lack of widely accepted guidelines for its use
- Lack of data on the long-term outcomes
- High cost

## Ultrafiltration Versus Usual Care for Hospitalized Patients With Heart Failure: The Relief for Acutely Fluid-Overloaded Patients With Decompensated Congestive Heart Failure (RAPID-CHF) Trial

Heart Failure

**Conclusions:**

The early application of UF for patients with CHF was feasible, well-tolerated, and resulted in significant weight loss and fluid removal. A larger trial is underway to determine the relative efficacy of UF versus standard care in acute decompensated heart failure.

## Ultrafiltration Versus Intravenous Diuretics for Patients Hospitalized for Acute Decompensated Heart Failure

Heart Failure

### Conclusions

In summary, the UNLOAD trial conclusively shows that early ultrafiltration safely produces greater weight and fluid loss than intravenous loop diuretics in hypervolemic HF patients. Ultrafiltration significantly decreased rehospitalizations for HF and unscheduled medical visits. The cost-effectiveness of ultrafiltration is not established; however, this treatment may have favorable economic implications for patients and payers owing to reduced resource utilization after the index hospitalzation. Mechanisms linking different methods of fluid removal to clinical benefit deserve further study.

## Effects of ULTRAfiltration vs. DIureticS on clinical, biohumoral and haemodynamic variables in patients with deCOmpensated heart failure: the ULTRADISCO study

### Conclusions

In patients with advanced HF, ultrafiltration facilitates a greater clinical improvement compared with diuretic infusion by ameliorating haemodynamics (assessed using a minimally invasive methodology) without a marked increase in aldosterone or NT-proBNP levels.

ELSEVIER

Journal of Cardiac Failure

Volume 20, Issue 1, January 2014, Pages 9-17

Clinical Trial

## Continuous Ultrafiltration for Congestive Heart Failure: The CUORE Trial

### Conclusions

In HF patients with severe fluid overload, first-line treatment with ultrafiltration is associated with a prolonged clinical stabilization and a greater freedom from rehospitalization for congestive HF.

# Ultrafiltration in Decompensated Heart Failure with Cardiorenal Syndrome

Bradley A. Bart, M.D., Steven R. Goldsmith, M.D., Kerry L. Lee, Ph.D., Michael M. Givertz, M.D., Christopher M. O'Connor, M.D., David A. Bull, M.D., Margaret M. Redfield, M.D., Anita Deswal, M.D., M.P.H., Jean L. Rouleau, M.D., Martin M. LeWinter, M.D., Elizabeth O. Ofili, M.D., M.P.H., Lynne W. Stevenson, M.D., et al., for the Heart Failure Clinical Research Network

**CONCLUSIONS**

In a randomized trial involving patients hospitalized for acute decompensated heart failure, worsened renal function, and persistent congestion, the use of a stepped pharmacologic-therapy algorithm was superior to a strategy of ultrafiltration for the preservation of renal function at 96 hours, with a similar amount of weight loss with the two approaches. Ultrafiltration was associated with a higher rate of adverse events. (Funded by the National Heart, Lung, and Blood Institute;

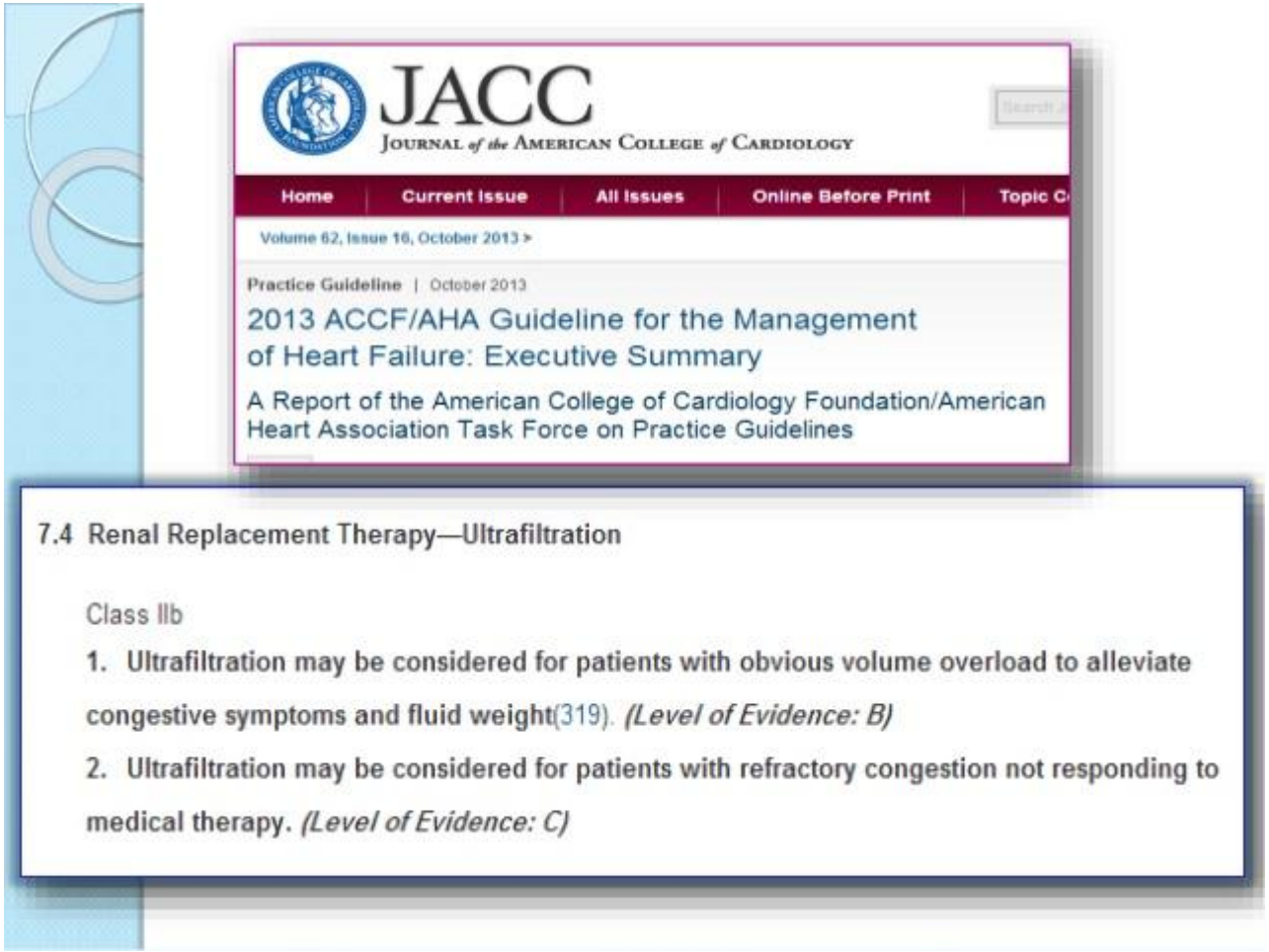
## Efficacy and Safety of Ultrafiltration in Decompensated Heart Failure Patients With Renal Insufficiency

A Meta-Analysis

Zhong Cheng, Lan Wang, Ye Gu, Shao Hu

Seven RCTs with 569 participants were eligible for analysis.

UF is an effective and safe therapeutic strategy and produces greater weight loss and fluid removal without affecting renal function, mortality, or rehospitalization in patients with decompensated heart failure complicated by renal insufficiency.



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Volume 62, Issue 16, October 2013 >

Practice Guideline | October 2013

2013 ACCF/AHA Guideline for the Management of Heart Failure: Executive Summary

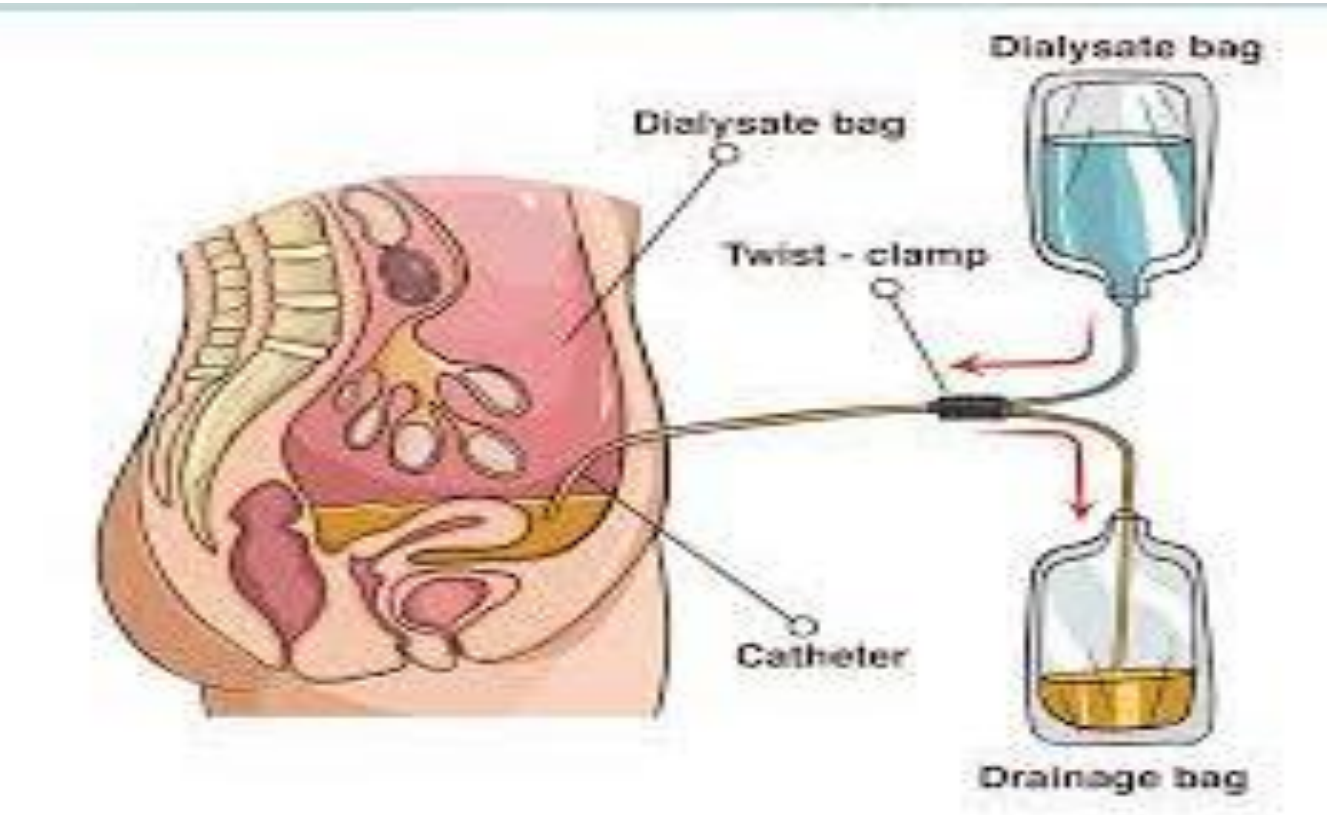
A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

7.4 Renal Replacement Therapy—Ultrafiltration

Class IIb

1. Ultrafiltration may be considered for patients with obvious volume overload to alleviate congestive symptoms and fluid weight(319). *(Level of Evidence: B)*
2. Ultrafiltration may be considered for patients with refractory congestion not responding to medical therapy. *(Level of Evidence: C)*

# The use of peritoneal dialysis in heart failure



# Rationale for Ultrafiltration by PD in CHF

- **Gentle ultrafiltration**
- **Minimal impact of peritoneal ultrafiltration on haemodynamic**
- **Compared to HD, slower decline in residual kidney function**
- **It is performed at home(psychosocial aspect of this treatment modality)**
- **It is technically simple with fewer facility requirements**
- **It has a reasonable cost**
- **Reinstituted of drugs which had to be stopped**

# Miscellaneous benefits for PD in CHF

- **Treatment of ascitis : no more paracentesis**
- **Decompress liver and intestinal edema:less abdominal discomfort**
- **Use of intraperitoneal medications**

# HOME MASSAGES

- **Treat the whole patient and treat for long term**
- **individualize the treatment based on the etiology**
- **Early diagnosis is important for better survival**
- **Cardiorenal syndrome requires an interprofessional team approach**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