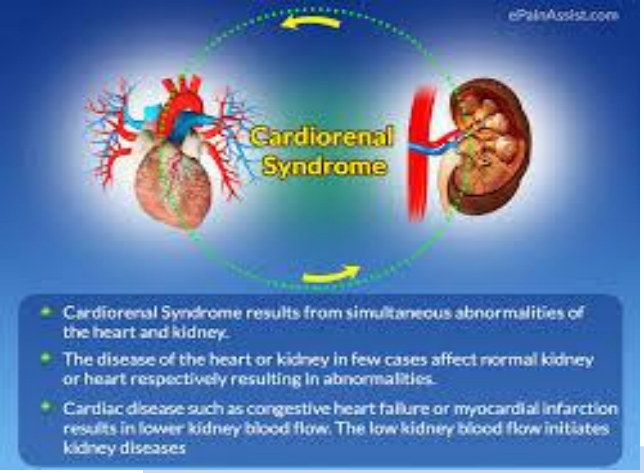
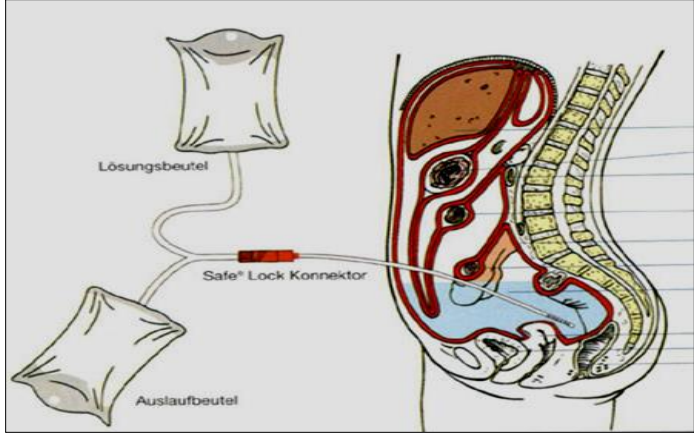




Peritoneal dialysis in cardo-renal syndrome

Dr. F. Ahmadi

Professor Of nephrology

TUMS

Introduction

- Heart failure (HF) is a medical condition with high mortality rate affecting quality of life adversely with accompanying symptoms and frequent hospitalization
- According to the classification by ejection fraction (EF) in current cardiology guidelines, an EF of ≥50% is defined as HF with preserved EF, an EF<40%as HF with reduced EF and EF 40-49% is classified as grey zone

Introduction

- The prevalence is 1-2% in adult population in developed countries, however, this rate is above 10% in individuals older than 70 years of age
- Glomerular filtration rate (GFR) is <60cc/min in 30-60% patient with HF
- Renal dysfunction has a greater impact on mortality than impaired cardiac function [EF and New York Heart Association (NYHA) class] in advanced HF patient

Introduction

- A small group of CHF patients, estimated to be between 50 000 and 200 000 individuals in the United States, are resistant to conventional therapy
- Most, if not all, patients with treatment-resistant CHF have underlying cardio-renal syndrome
- Chronic renal dysfunction is a common finding in RCHF patients, either as a primary cause as seen in type 4 CRS or as a secondary consequence as seen in type 2 CRS

Introduction

- Despite advancements in diagnosis and treatment, the HF population is expected to expand to more than 8 million by 2030 due to the increase in the proportion of aging population as well as the improving number of patients surviving ischemic events

Cardiorenal syndrome classification

CRS Type I (Acute Cardio-Renal Syndrome)

Abrupt worsening of cardiac function (e.g. decompensated congestive heart failure or acute cardiogenic shock) leading to acute kidney injury

Key Concept: prevent decompensation of stable heart failure

CRS Type II (Chronic Cardio-Renal Syndrome)

Chronic abnormalities in cardiac function (e.g. chronic congestive heart failure) causing progressive and permanent chronic kidney disease

Key Concept: ***optimal medical and device treatment of HF with blood pressure and volume control***

CRS Type III (Acute Reno-Cardiac Syndrome)

Abrupt worsening of renal function (e.g. Contrast or bypass surgery induced AKI) causing acute cardiac disorder (e.g. heart failure, arrhythmia, ischemia)

Key Concept: prevent AKI and reduce the risk of acute Reno-Cardiac Syndrome

CRS Type IV (Chronic Reno-Cardiac Syndrome)

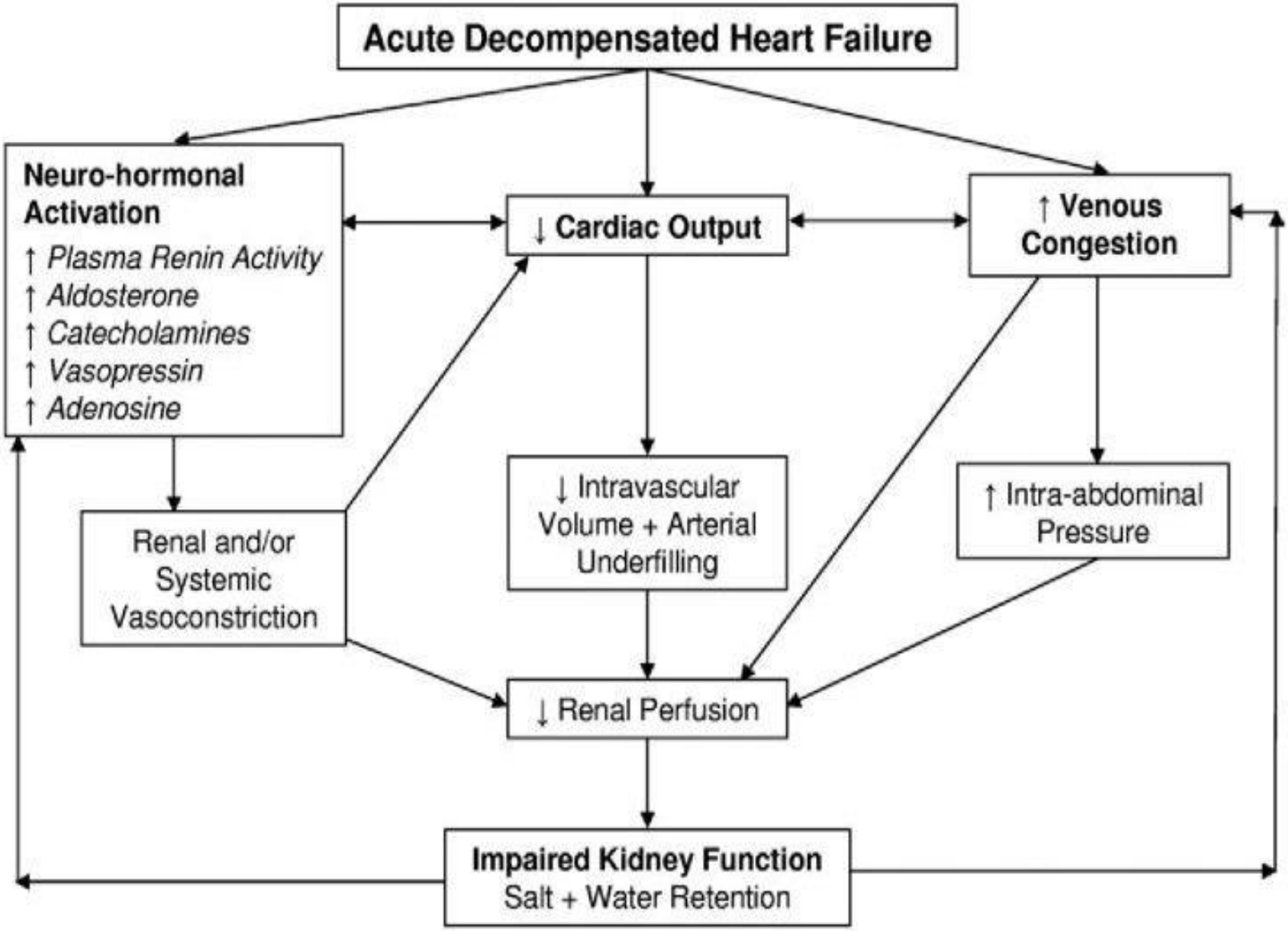
Chronic kidney disease contributing to decreased cardiac function, cardiac hypertrophy and/or increased risk of adverse cardiovascular events

Key Concept: attenuate the progression of CKD and reduce the risk of Chronic Reno-Cardiac Syndrome

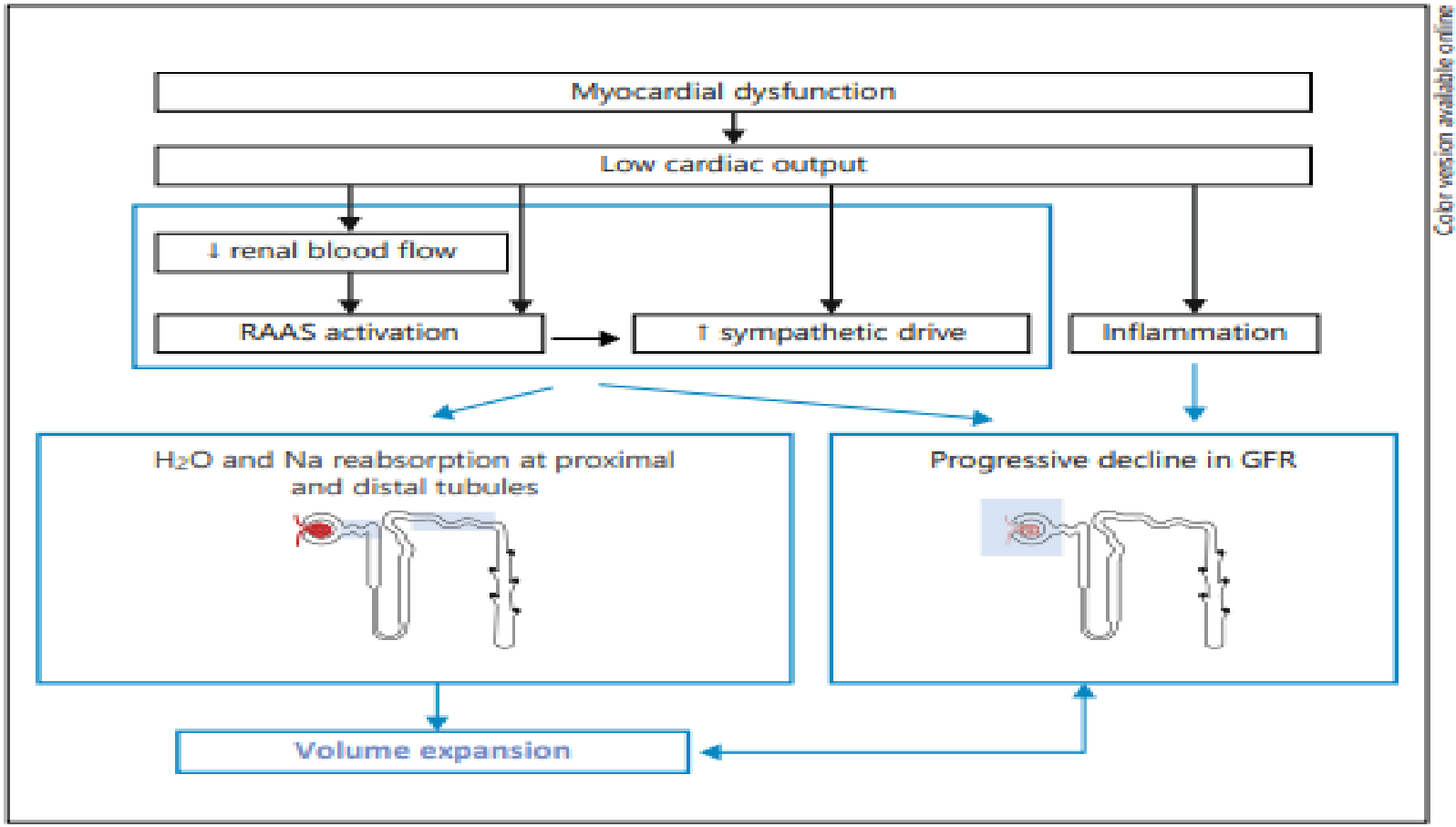
CRS Type V (Secondary Cardio-Renal Syndrome)

Systemic condition (e.g. diabetes mellitus, sepsis) causing both cardiac and renal dysfunction

Key Concept: treat the underlying systemic illness to minimize end-organ injury



Pathophysiological pathways of kidney injury in the setting of myocardial dysfunction



Blood Purif 2015;40:45–52

Potential biologic targets for the prevention of CRS

Target	Rationale
Neurohormonal activation	Excess neurohormonal activity leads to progression of LV and renal dysfunction
RAAS	
Sympathetic nervous system	
Endothelin	
Arginine vasopressin	
Chronic sodium and volume balance	Volume depletion is a risk for AKI
	Chronic volume overload contributes to the development of HF
Inflammation	Linked to plaque rupture and ACS
Tumour necrosis factor alpha	Associated with cardiac and renal fibrosis
	Concurrent malnutrition, inflammation and atherosclerosis syndrome in dialysis patients strongly predicts mortality
Nitric oxide metabolism	Endogenous paracrine defence against endothelial injury
Asymmetric dimethylarginine	
Oxidative injury	Secondary event in acute cardiac and organ injury that leads to greater zones of cell death
Adenosine receptors	Adenosine receptors modulate coronary and renal blood flow
Chronic cardiac ischaemia in haemodialysis patients	Possibly contributes to progressive LV diastolic and systolic dysfunction
Tissue hypoxia	Associated with progression of kidney disease, LV hypertrophy, HF and death
Anaemia	
CKD-BMD	Hyperphosphataemia related to cardiovascular calcification and mortality
	Vitamin D deficiency and hyperparathyroidism associated with LV hypertrophy, cardiovascular events and mortality
Uraemia (elevated plasma urea, phosphorus, etc.)	Associated with multiple pathological alterations including increased thrombosis and decreased platelet aggregation, damage to heart and cardiovascular tree and increased susceptibility to infection
Hyperlipidaemia	Association to atherosclerosis (CAD, nephrosclerosis)

Nephrol Dial Transplant (2010) 25: 1777–1784

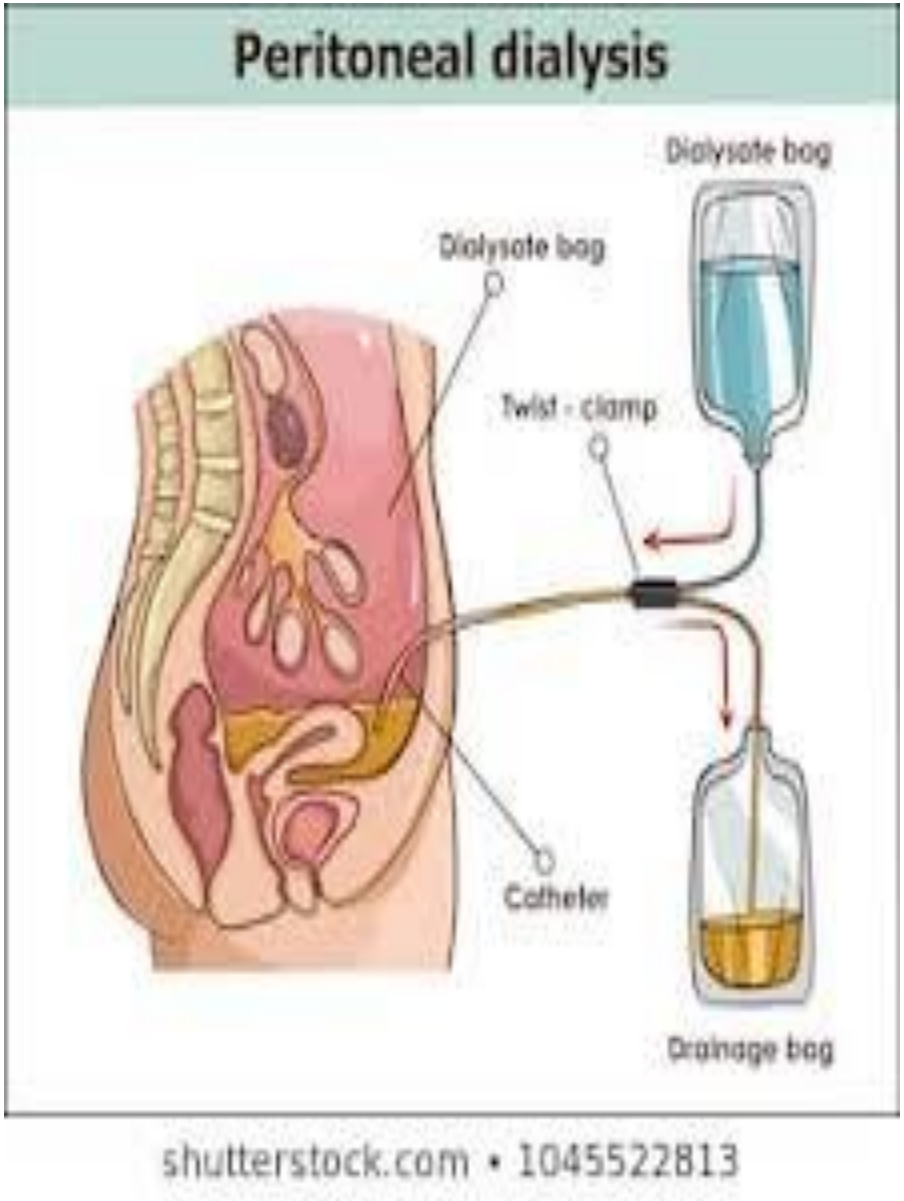
Pharmacological agents used in the management of CRS

- ACE inhibitors and ARBS
- Beta-blockers
- Aldosterone antagonists
- Diuretics
- Digoxin
- Hydralazine and nitrates
- Inotropic agents
- Vasopressin antagonist
- Endothelin antagonists

CaReSyAn

Cardio**Re**nal **Sy**ndrome **An**alysis:
Joining forces to reduce cardiovascular burden in chronic kidney disease

- Peritoneal dialysis (PD) ,a home-based therapy for uremia characterized by slow and gradual fluid removal, was first tried by Mailloux et al. to successfully treat nonuremic RCHF in 1964



Mechanism of Therapeutic Action of PD:

- PD continuously draws ultrafiltrate; its physiologic effect therefore has a lesser risk of abrupt hypotension that would exaggerate organ hypoxia and kidney damage
- UF in PD is driven by the osmotic power of the PD solution (glucose or glucose polymer) indwelling within the peritoneal cavity which is drained through the extended network of microvessels in the visceral and parietal peritoneum

Peritoneal Dialysis International January 2013 – Vol. 33, No. 1

Mechanism of Therapeutic Action of PD:

- The metabolic effects of PD therapy—such as glucose load from the solution, and correction of acidosis—favor the correction of nutrition and anemia
- the removal of proinflammatory factors (for example, tumor necrosis factor α and cardiac depressant factor) into the PD fluid might improve cardiac function
- PD preserves residual kidney function by slowing fluid removal, leading to less stimulation of the renin– angiotensin system or the sympathetic nervous system, or both

Peritoneal Dialysis International, January 2013 – Vol. 33, No. 1

JOURNAL OF THE INTERNATIONAL SOCIETY FOR PERITONEAL DIALYSIS
Peritoneal Dialysis INTERNATIONAL

Review

Defining the role of peritoneal dialysis in management of congestive heart failure

Amir Kazory & Joanne M. Bargman

Pages 533-543 | Received 01 May 2019, Accepted 25 Jun 2019, Accepted author version posted online: 26 Jun 2019, Published online: 02 Jul 2019

- Congestion is the primary reason for hospitalization of patients with acute heart failure and is a key driver of adverse outcomes
- Renal dysfunction and diuretic resistance are common findings in advanced heart failure.
- Peritoneal dialysis, a home-based therapeutic modality, has the ability for efficient removal of salt and water to treat congestion while sparing the kidneys.

Review

Defining the role of peritoneal dialysis in management of congestive heart failure

Amir Kazory & Joanne M. Bargman

Pages 533-543 | Received 01 May 2019, Accepted 25 Jun 2019, Accepted author version posted online: 26 Jun 2019, Published online: 02 Jul 2019

- Several clinical trials have confirmed the feasibility of peritoneal dialysis for management of refractory heart failure
- Reduction in hospital readmission, improvement of functional status, and quality of life are among beneficial impacts of peritoneal dialysis in this setting.
- Peritoneal dialysis is a highly flexible modality and can easily be adjusted to the patients' characteristics and clinical needs that might vary over time.

Review

Defining the role of peritoneal dialysis in management of congestive heart failure

Amir Kazory & Joanne M. Bargman

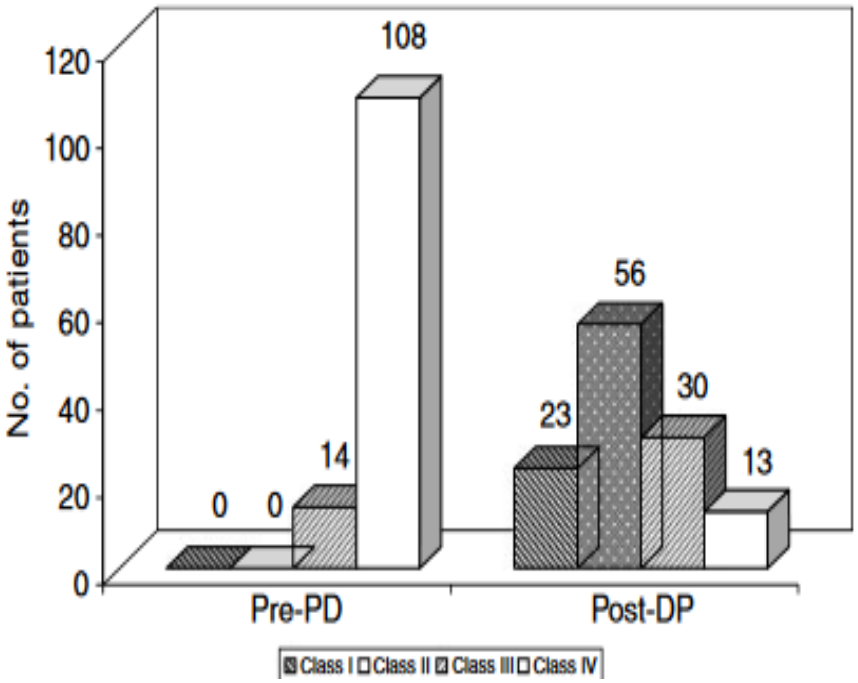
Pages 533-543 | Received 01 May 2019, Accepted 25 Jun 2019, Accepted author version posted online: 26 Jun 2019, Published online: 02 Jul 2019

- Peritoneal dialysis can provide patients with the opportunity to fully benefit from the established therapies of heart failure that would otherwise be challenging to use (e.g. risk of hyperkalemia with renin-angiotensin-aldosterone inhibition).
- Future studies are needed to explore whether peritoneal dialysis can have a role in the reduction of heart failure-associated health-care expenditure and patient survival.
- Designing interdisciplinary collaborative programs with the involvement of cardiologists and nephrologists would be crucial for the implementation and success of this initiative

Place of peritoneal dialysis in the management of treatment-resistant congestive heart failure

R Mehrotra[1,2], P Kathuria[3]

- The effect of PD on the functional status of 122patients with Class III (n¼14) and Class IV (n¼108) patient

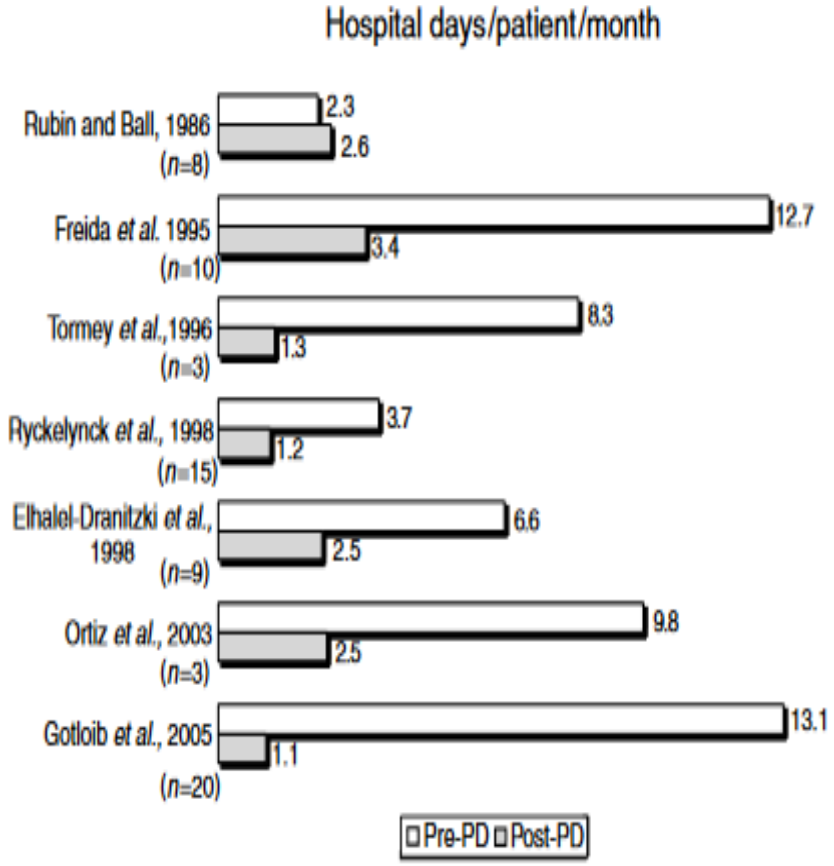


Kidney International(2006)70, S67–S7

Place of peritoneal dialysis in the management of treatment-resistant congestive heart failure

R Mehrotra[1,2], P Kathuria[3]

- The effect of ambulatory PD on hospitalizations of patients with severe refractory CHF



Kidney International(2006)70, S67–S71

Can Peritoneal Dialysis Decrease Mortality Rate?

- In a study, five-year mortality after diagnosis was found to be 52.6% for HF patients, 24.4% in patients under sixty years old, and 54.4% in patients above 80 years old
- In a prospective study by Núñez et al in 2012, it was reported that the mortality rate was lower in PD group than in conventional treatment group (HF = 0.40; 95% CI, 0.21-0.75; p=0.005) Rev Esp Cardiol (Engl Ed) 2012;65:986-9

Potential roles of ambulatory peritoneal ultrafiltration in patients with refractory congestive heart failure

- Restore diuretic responsiveness
- Bridge therapy (e.g., valve repair/replacement or cardiac transplantation)Palliative therapy
- Improve symptoms and exercise tolerance
- Preserve residual renal function (compared to extracorporeal ultrafiltration)
- Reduce hospitalizations
- Improve quality of life

Kidney International(2006)70, S67–S7

The advantages of peritoneal ultrafiltration in heart failure treatment

- Slow and controlled in PD
- Effective in protecting residual renal functions
- Prevents rebound neurohumoral activation
- Higher amount of removed sodium besides diuretic treatment
- Eliminates cytokines that may have negative effects on the heart
- Conventional treatment is more efficient in terms of cost
- Reduces hospitalization
- Regression in heart failure

Med Bull Haseki 2017;55:165-74

In which conditions should peritoneal ultrafiltration be recommended for patients with heart failure?

- Despite standard medical treatment, hospitalization due to acute decomposed HF over 2-3 times per year
- Despite standard medical treatment, NYHA classes 3-4 HF
- Advanced hypotension and/or hemodynamic instability and/or no need inotrope
- Side effects observed with standard medical treatment (hyperkalemia, hypotension etc.)
- Mental and physical capacity that can be done PD carefully

Med Bull Haseki 2017;55:165-74

BioMed Research International
IMPACT FACTOR 2.20

Effectiveness and Safety of Peritoneal Dialysis Treatment in Patients with Refractory Congestive Heart Failure due to Chronic Cardiorenal Syndrome

Qiuyuan Shao, Yangyang Xia, [...], and Chunming Jiang

- The benefit of PD on the improvement of survival and LVEF was limited
- The impairment of exercise tolerance indicated by NYHA classification was markedly improved
- The technique survival was remarkably high with low rate of PD-associated complications
- The hospital readmission was evidently decreased
- Our data suggest that PD is a safe and feasible alternative treatment for RCHF with type 2 CRS

Int. J. Mol. Sci. **2019**, *20*(11), 2610; https://doi.org/10.3390/ijms20112610 Open Access

Article

Effect of Peritoneal Dialysis on Serum Fibrosis Biomarkers in Patients with Refractory Congestive Heart Failure

by Margarita Kunin * ✉, Vered Carmon, Pazit Beckerman and Dganit Dinour

- Failing hearts display increased expression of MMP-2 and its endogenous inhibitor tissue inhibitor of metalloproteinases I (TIMP-1) at transcript- and protein- levels
- MMP-2 and TIMP-1 have been demonstrated to contribute to ventricular remodeling and myocardial apoptosis in experimental HF mode
- A decrease in the serum fibrosis markers following PD treatment was demonstrated.

The studies of peritoneal ultrafiltration in heart failure

Study	Type of study, years	Number of the patients	Mean of age (years)	Follow up period (month)	Compared situations	Effect of PD; on hospitalization*, on GFR	Effect of PD; on NHYA, on EF, on PAP
Courivaud et al. (58)	Retrospective two center 2014	126	72±11	16±16	Before and after PD at the same patient group	Decrease in hospitalization N/A on GFR	N/A on NHYA increase in EF N/A on PAP
Bertoli et al. (56)	Retrospective multicenter 2014	48	74±9	At least 6 months	Before and after PD at the same patient group	Decrease in hospitalization non effective on GFR	Decrease on NYHA increase in EF decrease on PAP
Kunin et al. (63)	Prospective 2013	37	66 (median)	42	Before and after PD at the same patient group	Decrease in hospitalization decrease in GFR	Decrease on NYHA non effective on EF N/A on PAP
Núñez et al.** (65)	Prospective 2012	62	74	16 (median)	PD and control group	Decrease in hospitalization	N/A on NHYA non effective on EF N/A on PAP
Koch et al. (69)	Prospective single center 2012	118	73±11	13.3±14	Before and after PD at the same patient group	N/A on hospitalization decrease in GFR	Decrease on NYHA non effective on EF non effective on PAP
Sánchez et al. (68)	Prospective single center 2010	17	64±9	15±9	Before and after PD at the same patient group	Decrease in hospitalization non effective on GFR	Decrease on NYHA non effective on EF decrease on PAP
Nakayama et al. (42)	Prospective single center 2010	12	81±6	26.5 (median)	Before and after PD at the same patient group	N/A on hospitalization non effective on GFR	Decrease on NYHA non effective on EF N/A on PAP
Gotloib et al. (47)	Prospective single center 2005	20	65±7	19.8±7.3	Before and after PD at the same patient group	Decrease in hospitalization N/A on GFR	Decrease in NYHA N/A on EF N/A on PAP

*Admission to acute decomposed heart failure
**Mortality was reduced with peritoneal dialysis
PD: Peritoneal dialysis, GFR: Glomerular filtration rate, NHYA: The New York Heart Association, EF: Ejection fraction, PAP: Pulmonary artery pressure, N/A: Not available

Med Bull Haseki 2017;55:165-74

Determinants of ultrafiltration with peritoneal dialysis

- Patient-related factors ：Peritoneal transport rate
- Dialysis prescription: Volume of dialysate Osmotic/oncotic agent Dextrose or icodextrin Tonicity of dextrose-based dialysate (1.5, 2.5, or 4.25%)
- Duration of dwell ：Shorter dwells with dextrose Long dwells with icodextrin

Kidney International(2006)70, S67–S7

Sodium and PD

- Impairment in sodium excretion starts in early subclinical stages of HF
- Sodium is the major determinant of extracellular volume, and its key role in retention of fluid and development of congestion has widely been recognized.
- loop diuretics tend to generate hypotonic urine that contains about (50-100) mmol/L of sodium, the concentration of sodium in PD ultrafiltrate has been reported to be as high as 130-150 mmol/L

Cytokines and PD

- Atrial natriuretic peptide, tumor necrosis factor-α, interleukin-1, and interleukin-6 are known to increase apoptosis of cardiac myocyte and to have negative inotropic effect
- These mediators whose molecular weight ranges between 500 and 30000 Dalton can penetrate from the peritoneal membrane, by this way PD allows clearance of these agents while contributing to the support for the heart directly

Icodextrin

- Serious consideration should be given to icodextrin use in this clinical context where the primary goal is extraction of sodium-rich fluid.
- Icodextrin optimizes SR by elimination of the initial sodium-sieving phase because it does not activate aquaporins
- Accordingly, it has been shown that one single nocturnal icodextrin exchange can successfully manage volume overload in patients with refractory HF

Icodextrin

- In a recent study on more than 5,000 newly diagnosed end-stage renal disease patients undergoing PD, icodextrin users had an overall 26% lower incidence of HF compared to nonusers (13.7 vs. 18.6 per 1,000 person-years, ratio 0.67, $p < 0.01$)

Pharmacoepidemiol Drug Saf. 2018 Apr;27(4):447–52

NEFROLOGIA 2018;38(1):87–91

Sociedad Española de Nefrología

nefrología
Revista de la Sociedad Española de Nefrología
www.revistanefrologia.com

Case report

Hyponatremia in refractory congestive heart failure patients treated with icodextrin-based peritoneal dialysis: A case series

Margarita Kunin, Liat Ganon, Eli J. Holtzman, Dganit Dinour*

- Hyponatremia in refractory CHF patients is multifactorial. In rare cases, icodextrin may contribute to clinically relevant hyponatremia if the hyponatremia is compounded by other factors. Severe hyponatremia in icodextrin users was associated with poorer survival and is most likely a marker of advanced heart disease

PD Modalities

- Continuous ambulatory PD (CAPD) is generally believed to result in higher SR than automated PD (APD) by virtue of typically having less frequent and longer cycles (and hence less sodium sieving)
- However, some authors have suggested that both modalities could result in similar sodium elimination with optimal PD prescription
- Recent meta-analysis including 683 patients from 7 studies concluded that CAPD is associated with significantly higher SR compared with APD (141 vs. 86 mmol/day, respectively, $p = 0.015$) J Nephrol. 2018 Jul 5

Categories of prescriptions used for ambulatory peritoneal ultrafiltration

- Intermittent peritoneal dialysis – manual or automated a. Health-care provider dependent b. Self-care
- Continuous ambulatory peritoneal dialysis
- Automated peritoneal dialysis
- Single night time exchange with icodextrin

Blood Purification

In-Depth Review

Blood Purif 2015;40:45–52
DOI: 10.1159/000430084

Published online: June 24, 2015

Peritoneal Dialysis for Chronic Congestive Heart Failure

Karlien François[a, b] Claudio Ronco[c] Joanne M. Bargman[a]

Table 1. Examples of PD prescription in heart failure

	Day	Night
Scenario 1: adequate residual kidney function but need for fluid removal		
CAPD	dry	1 × 7.5% or 4.25%
	1 × 7.5% or 4.25%	dry
	2 × 2.5%	1 × 2.5%
APD	dry	2–3 × 2.5%
Scenario 2: inadequate residual kidney function thus need for solute and fluid removal		
CAPD	2–3 × 2.5%	1 × 2.5%
	2–3 × 2.5%	1 × 7.5% or 4.25%
APD	7.5% or 4.25%	3 × 2.5%

Potential Future Approaches

- Low-Sodium Peritoneal Dialysate(e.g., 115–126 mmol/L)
- Bimodal Peritoneal Dialysate : There have been suggestions for use of combined solutions with icodextrin and glucose (i.e., “bimodal solution”) in a study by Freida et al. the authors reported an impressive increase in the estimated ultrafiltration volume and SR of 150 and 147%, respectively, for their bimodal solution (sodium 121 mmol/L) compared to icodextrin alone

Cardiorenal Med 2019;9:117-124

Potential Future Approaches

- Twice-Daily Icodextrin
- Adapted APD The first phase includes cycles with short dwell time (e.g., 45 min) and small fill volumes (e.g., 1,500 mL) to primarily promote ultrafiltration, and the second phase consists of cycles with long dwell time (e.g., 150 min) and large dwell volumes (e.g., 3,000 mL) to facilitate solute (e.g., sodium) removal

Cardiorenal Med 2019;9:117-124

Proposed approaches for enhancement of sodium extraction in peritoneal dialysis for heart failure

- Icodextrin use rather than glucose-based solutions
- Continuous ambulatory peritoneal dialysis rather than automated peritoneal dialysis
- Addition of mid-day exchange
- Increase in dialysate volume
- Optimization of dwell time (sodium sieving vs. back diffusion)
- Increase in ultrafiltrate volume (e.g., use of higher concentrations of glucose)
- Supine position
- Consideration of tidal volume
- Low-sodium dialysate
- Bimodal dialysate
- Consideration of twice-daily icodextrin
- Adapted automated peritoneal dialysis

Cardiorenal Med 2019;9:117-124

CardioRenal Medicine