Kidney dysfunction and heart failure

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Introduction

The heart circulates a continuous supply of oxygenated blood through the body

Kidneys filter blood, extracting waste in form of urine and regulate water and salt levels to control blood pressure

Heart failure is a risk factor for kidney disease

Kidney disease is a risk factor for heart failure

Introduction

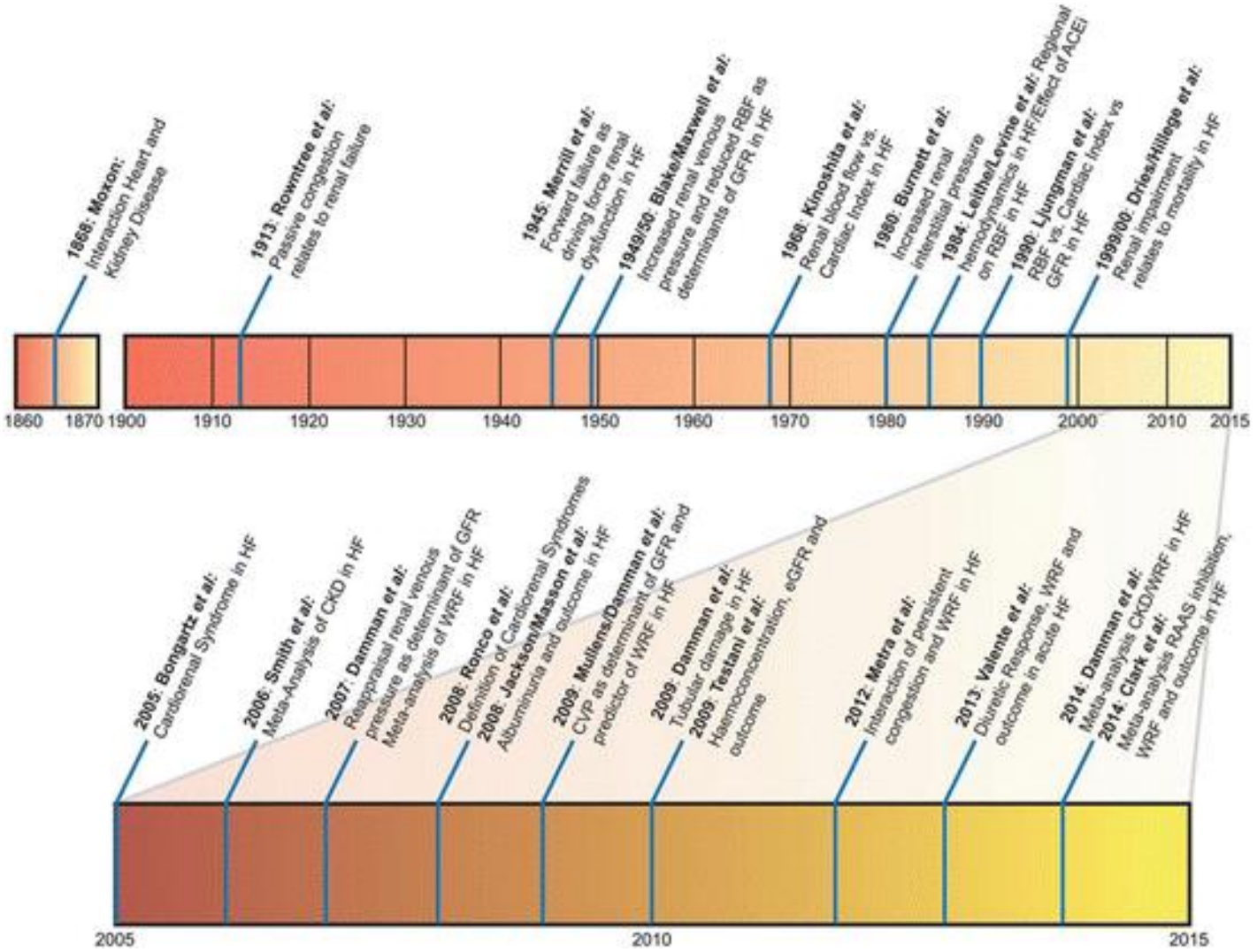
Control of blood pressure is key in management of both kidney failure and heart failure

Diuresis reduces blood pressure and removes excess fluid (kidneys excrete more water and salt), but may worsen kidney function

ACE inhibitors, beta blockers and aldosterone antagonists benefit heart failure, but may have a negative effect on renal function

Newer drugs: ARNIs and SGLT-2 inhibitors improve both heart failure and kidney disease

History of HF and KF interaction



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Ter Maaten JM, Voors AA. *Curr Approach Heart Fail* 2016. In Dorobantu M, Ruschitza F, Metra M (eds). Current approach to heart failure 2016. Springer.

Kidney disease

Chronic kidney disease (CKD) is a major public health problem, affecting 9-13% of general population

Incidence and prevalence of CKD has doubled in last decade

Cardiovascular disease (CVD) is the leading cause of death in patients with CKD

Chronic kidney disease

- **Definition-:** CKD is defined as abnormalities of kidney structure or function, **present for >3 months**, with implications for health.

❖ **Criteria for CKD (either of the following present for > 3 months)**

A.) Markers of kidney damage (one or more)

-Albuminuria (AER >30 mg/24 hours;ACR >30 mg/g [>3 mg/mmol])

-Urine sediment abnormalities

-Electrolyte and other abnormalities

-Abnormalities detected by histology

-Structural abnormalities detected by imaging

- H/o kidney transplantation

B.) Decreased GFR - GFR <60 ml/min/1.73 m2

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National Kidney Foundation. https://www.kidney.org/atoz/content/gfr (Accessed July 2022)

Kidney disease

CKD Classification and Staging

- **Green:** Low risk (LR)
- **Yellow:** Moderate risk (MR)
- **Orange:** High risk (HR)
- **Red:** Very high risk (VHR)

Kidney function stage GFR (ml/min/1.73m²) Description and range				Kidney damage stage Urine albumin/creatinine ratio Description and range		
				A1	A2	A3
				Normal to mild increase <30mg/g	Moderate increase 30-300 mg/g	Severe increase >300mg/g
	G1	Normal or high	≥90	LR	MR	HR
	G2	Mild decrease	60-89	LR	MR	HR
	G3a	Mild to moderate decrease	45-59	MR	HR	VHR
	G3b	Moderate to severe decrease	30-44	HR	VHR	VHR
	G4	Severe decrease	15-29	VHR	VHR	VHR
	G5	Kidney failure	<15	VHR	VHR	VHR

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National Kidney Foundation. https://www.kidney.org/atoz/content/gfr (Accessed July 2022)

Heart failure

Heart failure (HF) is a serious public health challenge and a leading cause of mortality, with a prevalence of 2-5% in general population, rising sharply in elderly

50% of patients with HF die within 4 years of diagnosis; 40% of patient admitted to hospital with HF are dead or readmitted within 1 year

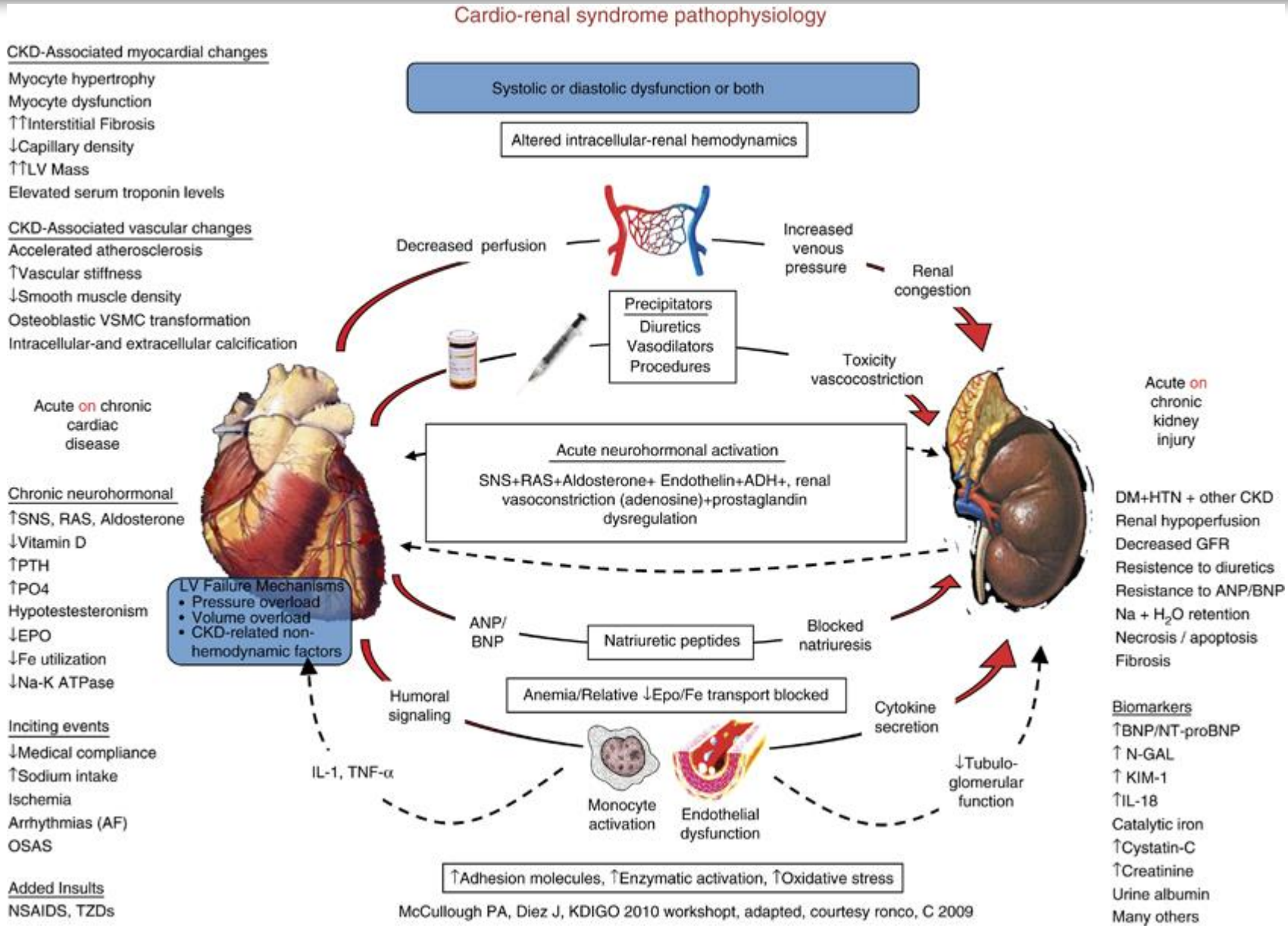
CKD and HF have many shared risk factors

McMurray JJ, Stewart S. Epidemiology, aetiology, and prognosis of heart failure. *Heart* 2000;83:596-602.

Table 5 Proposed mechanism in cardiorenal interaction.

Common factors for heart and kidney
Traditional cardiovascular risk factors
Smoking
Obesity
Hypertension
Diabetes
Dyspilidemia
Other risk factors
Malnutrition
Genetic risk factors
Humorally mediated factors
Elevated sympathetic nervous system
Elevated renin-angiotensin system
Other common factors
Inflammation
Endothelial dysfunction
Immune mediated damage
Oxidative stress
Coagulation imbalance
Treatment related factors
Undertreatment
Toxic agents
Organ-specific factors
Hemodynamics mediated factors
Decreased cardiac output (heart)
Renal hypoperfusion (heart)
Elevated venous pressure (heart)
Sodium and water retention (kidney)
Hypertension (kidney)
Other specific factors
Brain natriuretic peptide (heart)
Anemia (kidney)
Uremic solute retention (kidney)
Calcium and phosphate abnormality (kidney)
Electrolyte, acid-base imbalances (kidney)

Cardiorenal syndrome



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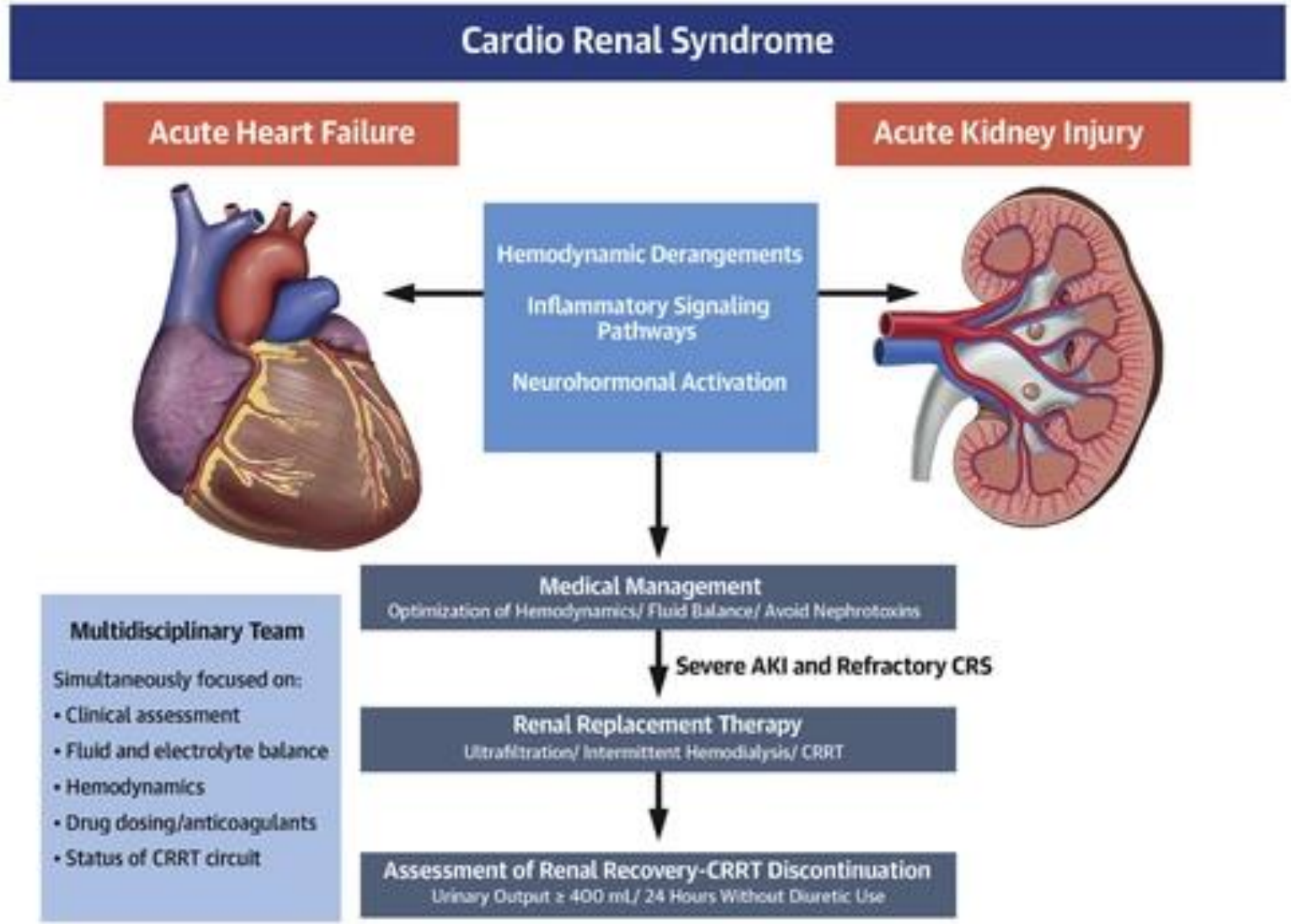
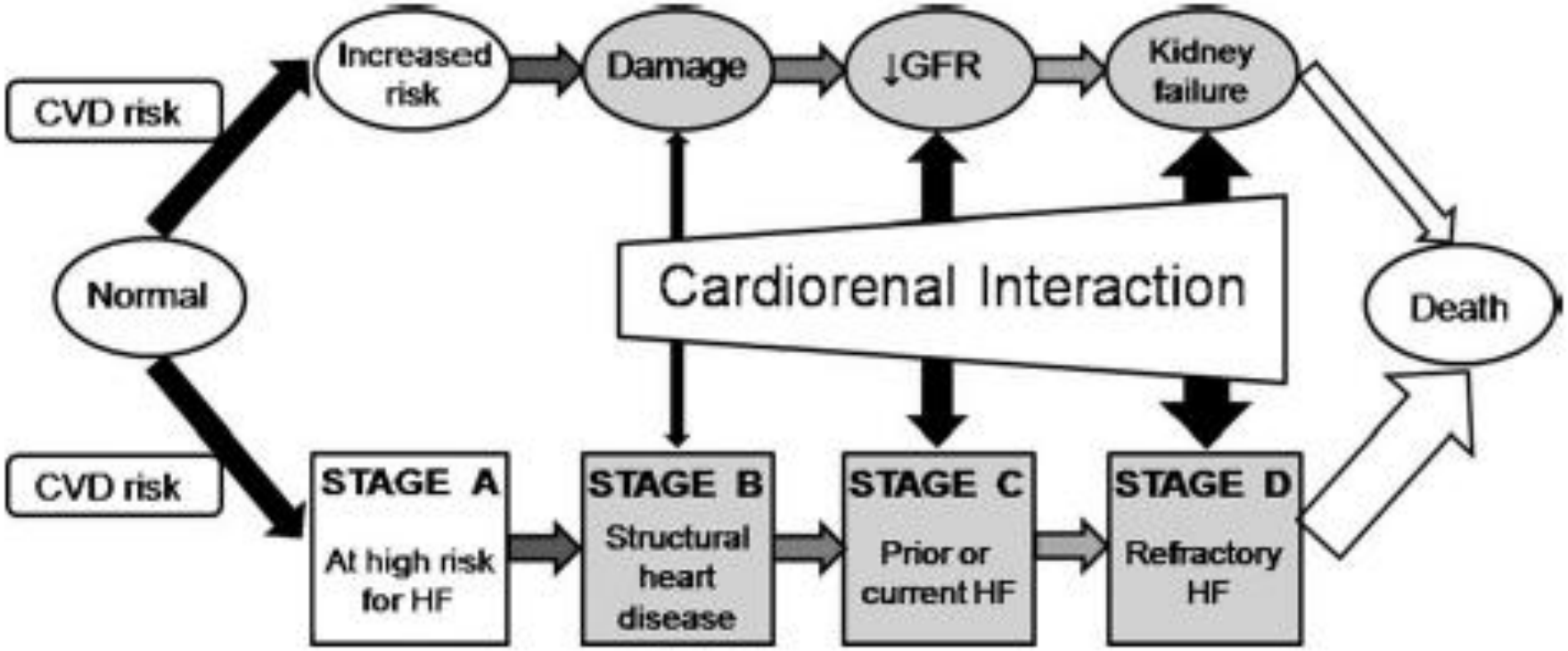


Jentzer, J.C. et al. J Am Coll Cardiol. 2020;76(9):1084-101.

Cardiorenal syndrome

Type of CRS	Description
Type 1 (acute CRS)	Rapid worsening of cardiac function leads to acute kidney injury
Type 2 (chronic CRS)	Chronic abnormalities in cardiac function lead to progressive chronic kidney disease
Type 3 (acute renocardiac syndrome)	Acute, primary worsening of kidney function leads to acute cardiac dysfunction
Type 4 (chronic renocardiac syndrome)	Primary chronic kidney disease contributes to decreased cardiac function, left ventricular hypertrophy, diastolic dysfunction and increase risk of cardiovascular events
Type 5 (secondary CRS)	Acute or chronic systemic disorders (e.g. diabetes mellitus) cause combined cardiac and renal dysfunction

Cardiorenal interaction



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Cardiorenal interaction

Table 4 Prevalence and hazard of chronic kidney disease in patients with chronic heart failure.

Ref. no.	Study	Year	No. of pts	NYHA	Age, years	Male, %	EF, %	BP or HTN	DM, %	RASI, %	eGFR < 60,%	Follow-up	Outcome	Adjusted hazard comparing with pts without CKD for the outcome
17	SOLVD-T	2000	2,161	I–IV	60.7	81.5	24.7	40.4%	24.9	50.3	35.7	–	All-cause mortality	1.41 for eGFR <60[a]
18	PRIME-II	2000	1,906	III–IV	64.7	80.4	26.2	121.6/ 75.1 mmHg	20.7	91.6	49 (eGFR ≤ 58)	277 days (median)	All-cause mortality	1.91 for eGFR 44–58 2.85 for eGFR <44
19	DIG	2002	585	II/III: 85%	65	73.9	35	128.3/ 75.3 mmHg	40.3	88	50 (eGFR ≤ 63.8)	2.6 years (median)	All-cause mortality	1.6 for eGFR 47–64[a] 2.1 for eGFR 18–48[a]
20	McClellan	2002	665	–	75.7	40	38.4	66%	44	54	38[b]	–	All-cause mortality	1.24 at 1-year mortality[b]
21	UK-HEART	2002	553	II/III: 98%	62.7	76	42	–	0	82	–	–	All-cause mortality	1.09 in each 10 μmol/l increase of creatinine
22	CHARM	2006	2,680	II–IV	65.3	66.6	38.5	128.2/ 73.6 mmHg	37.2	45.5	36	34.4 months	CV death + HF hospitalization	1.54 for eGFR 45–59.9 1.86 for eGFR <45
23	ANCHOR	2006	59,772	–	71.8	54.2	NA	61%	32.4	24	39.2	2.07 years (median)	All-cause mortality + HF hospitalization	1.39 for eGFR 30–44 2.28 for eGFR 15–29
24	CHART	2008	920	II–IV	68.3	65.1	49.3[c]	39.2%[c]	19.3[c]	69.1[c]	42.7	3.45 years	All-cause mortality + HF hospitalization	1.31 for eGFR 30–59 1.56 for eGFR <30
25	JCARE-CARD	2009	2,013	1.8 (mean)	71.5	58.7	44.8	54.5%	30.7	ACEI: 36.7 ARB: 46.1	70.3	2.4 years	All-cause mortality	1.26 for eGFR 30–59 2.48 for eGFR <30

EF, ejection fraction; BP, mean blood pressure; HTN, hypertension; DM, diabetes mellitus; RASI, renin–angiotensin-system inhibitor; eGFR, estimated glomerular filtration rate (ml/min/1.73 m^2); pts, patients; CKD, chronic kidney disease; HF, heart failure; CV, cardiovascular; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

[a] ml/min.

[b] CKD was defined by serum creatinine of ≥1.4 mg/dl for women and ≥1.5 mg/dl for men.

[c] Data were retrieved from the previous study that included 1154 patients.

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Ahmed A, Campbell RC. Epidemiology of chronic kidney disease in heart failure. *Heart Fail Clin* 2008;4(4):387-399.

Meta-analyses of renal impairment in HF

Author	Year	Population	Total *n*	Main results
Smith[12]	2006	Acute and chronic HF	CKD: 80 098 WRF: 12 634	• CKD present in 63% of patients • Baseline CKD associated with mortality: HR 1.56 (1.53–1.60) • WRF associated with mortality: HR 1.47 (1.26–1.72)
Tonelli[66]	2006	CV disease, including chronic HF	Total: 1 371 990 HF: 78 272	• CKD present in 33% of patients • Baseline CK associated with mortality: HR 1.78 (1.57–2.01)
Damman[13]	2007	Acute and chronic HF	HF: 18 634	• WRF occurred in 25% of patients • WRF associated with mortality: OR 1.62 (1.45–1.82) • WRF associated with HF hospitalizations: OR 1.30 (1.04–1.62)
Clark[24]	2014	Chronic HF patients included in RAAS-inhibitor trials	HF: 20 573	• WRF occurred in 13 and 9.6% with RAAS inhibitors and placebo, respectively. • WRF associated with mortality RR: 1.36 (1.25–1.48), in both treatment groups • RAAS inhibition reduced mortality even despite WRF: RR 0.72 (0.62–0.84)
Damman[8]	2014	Acute and chronic HF	CKD: 1 076 104 WRF: 49 890	• CKD present in 32% of patients • Baseline CKD associated with mortality: OR 2.34 (2.20–2.50) • WRF associated with mortality: OR 1.81 (1.55–2.12) • Evidence of publication bias for studies on WRF

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Damman K, et al. Renal impairment, worsening renal function, and outcome in patients with heart failure: an updated meta-analysis. *European Heart Journal* 2014;35(7):455–469.

Case Presentation

Mr LM, 45 year old man, married father of 3, was a teacher

NYHA functional class I-II baseline, obese

9 month history of progressive decline in effort tolerance, shortness of breath, fatigue, difficulty walking uphill or up stairs. Swelling of the legs, 3 pillow orthopnoea and episodes of paroxysmal nocturnal dyspnoea. Occasional reports of wheeze

Seen at day hospital and diagnosed with asthma: no improvement on MDI and short courses of prednisone

Case Presentation

Now, sleeps sitting in chair. Difficulty with all ADLs including self care. Has been off work for past three months

On examination: overweight, 3+ pitting oedema, warm peripheries, HR 98 bpm, RR 20 bpm, BP 90/62 mmHg, pallor, JVP 7 cm with prominent CV waves.
Chest: Bibasal crackles, dullness in right base
CVS: Apex displaced to midaxillary line, 6th ICS. No heave. Normal S1 and S2, S3 gallop. 3/6 PSM, clinically has MR and TR.

Assessment: Heart failure
?Dilated cardiomyopathy/?Hypertensive heart disease/?Rheumatic heart disease/IHD unlikely

Case Presentation

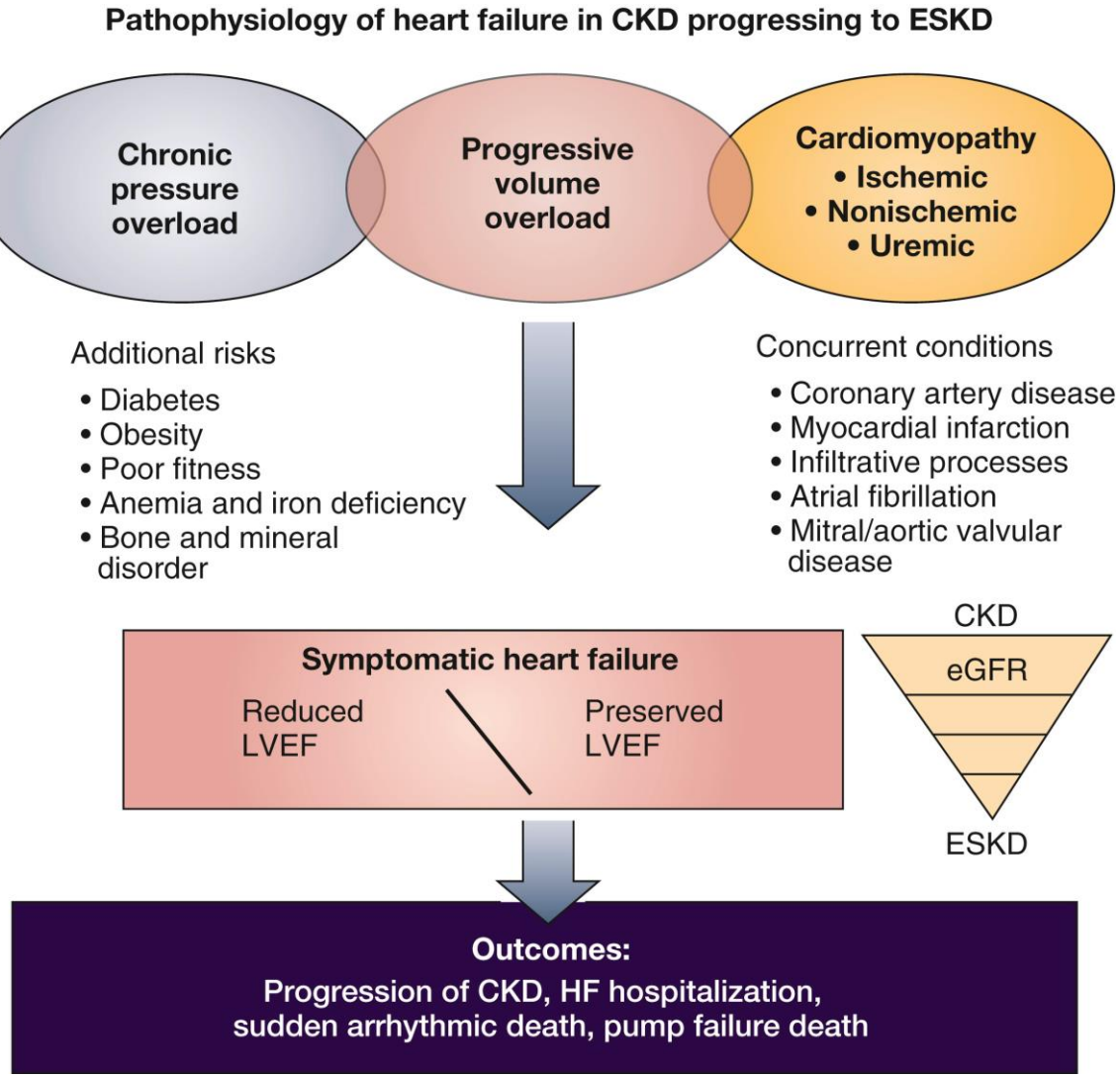
Echo:
LVEDD 66 mm, EF 28%, thin LV walls, global hypokinesia of all LV segments, moderate MR and moderate TR, RV pressure 38 mmHg

Bloods:
Hb 8.1 g/dL; MCV 86 fL; WCC 7.1 10^9/L; Plt 189 10^9/L
Na 129 mmol/L; K 5.8 mmol/L; U 16 mmol/L; Cr 214 µmol/L
GFR 35 mL/min/1.73m^2

Case Presentation

What is your approach to management?

Renal function, HF and mortality risk



House AA, et al. Heart failure in chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) controversies conference. *Kidney Int* 2019;95(6):1304-1317.

Managing HF in patient with renal dysfunction

1. Dietary salt restriction and diuretics:

To control fluid overload and symptoms

Effect on morbidity and mortality unknown

Loop diuretics should be first line

Managing HF in patient with renal dysfunction

2. Managing anaemia in CKD and ESRD:

Anaemia associated with LV hypertrophy and LV dilation

Anaemia should be treated according to guidelines used in CKD population (including IV iron replacement)

Managing HF in patient with renal dysfunction

3. Hyperphoshataemia, secondary hyperparathyroidism and vitamin D deficiency:

Associated with LV hypertrophy and LV dysfunction

Achieving adequate phosphate, calcium, vitamin D and PTH levels is a good goal in CKD

Symptom benefits

Benefits in preventing or improving HF not proven

Managing HF in patient with renal dysfunction

4. Beta-blockers:

In CKD and non-CKD patients with HF with reduced systolic function, beta-blockers shown to reduce mortality and hospitalisation rates

Treatment should be started slow and up-titrated and monitored

The role of beta-blockers

Managing HF in patient with renal dysfunction

5. Angiotensin converting enzyme inhibitors (ACE inhibitors) and angiotensin receptor blockers (ARBs):

ACE inhibitors and ARBs have a favourable effect on survival in patients with CKD and HF

Indicated in all patients with mild to moderate CKD (stages 1 to 3)

Retard progression to renal replacement therapy

In patients with advanced CKD, the benefits of ACE inhibitors/ARBs have not been proven

Need to monitor blood pressure, potassium levels and development of acute kidney injury

Managing HF in patient with renal dysfunction

6. Mineralocorticoid receptor (aldosterone) antagonists

Relatively contraindicated in stages 1 to 3

May rarely be considered for management of HF in patients with renal dysfunction

Only use at low doses

Carefully monitor serum potassium

Absolute contraindication in stages 4 and 5

Managing HF in patient with renal dysfunction

7. Digoxin

Relatively contraindicated in HF with kidney dysfunction

May be considered in poorly controlled HF with high-ventricular rate atrial fibrillation in presence of optimal dose of RAAS inhibitors and beta-blockers

Use at low doses in kidney disease

Monitor serum levels regularly

Managing HF in patient with renal dysfunction

8. Angiotensin receptor neprolysin inhibitors (ARNIs)

ARNIs improve outcomes in patients with CKD and in patients with HF

ARNIs enhance activity of natriuretic peptide system producing natriuresis, diuresis and inhibition of the RAAS system; ARNIs inhibit the sympathetic nervous system

Improve blood pressure control in patients with CKD; but associated with higher risk of hypotension compared to ACE inhibitors

ARNI use associated with reduction in loop diuretic requirement

Retard progression to renal replacement therapy

Need to closely monitor electrolytes

Managing HF in patient with renal dysfunction

9. Sodium-glucose cotransporter-2 (SGLT-2) inhibitors

SGLT-2 inhibitors are effective at slowing progression of CKD

SGLT-2 inhibitors reduce development of heart failure and are associated with symptom improvement and in QOL in patients with HF; reduce loop diuretic requirement

SGLT-2 inhibitors lower risk of kidney failure, death and heart failure in people with kidney disease and type 2 diabetes

SGLT-2 inhibitors prevent development of heart in non-diabetic patients and are also effective in treatment of heart failure in patients without diabetes

May be used together with an ACE inhibitor or an ARNI

May increase risk of urinary tract infections

Managing HF in patient with renal dysfunction

10. Cardiac resynchronisation therapy:

Limited evidence

No recommendations can be made about CRT for HF in CKD

Managing HF in patient with renal dysfunction

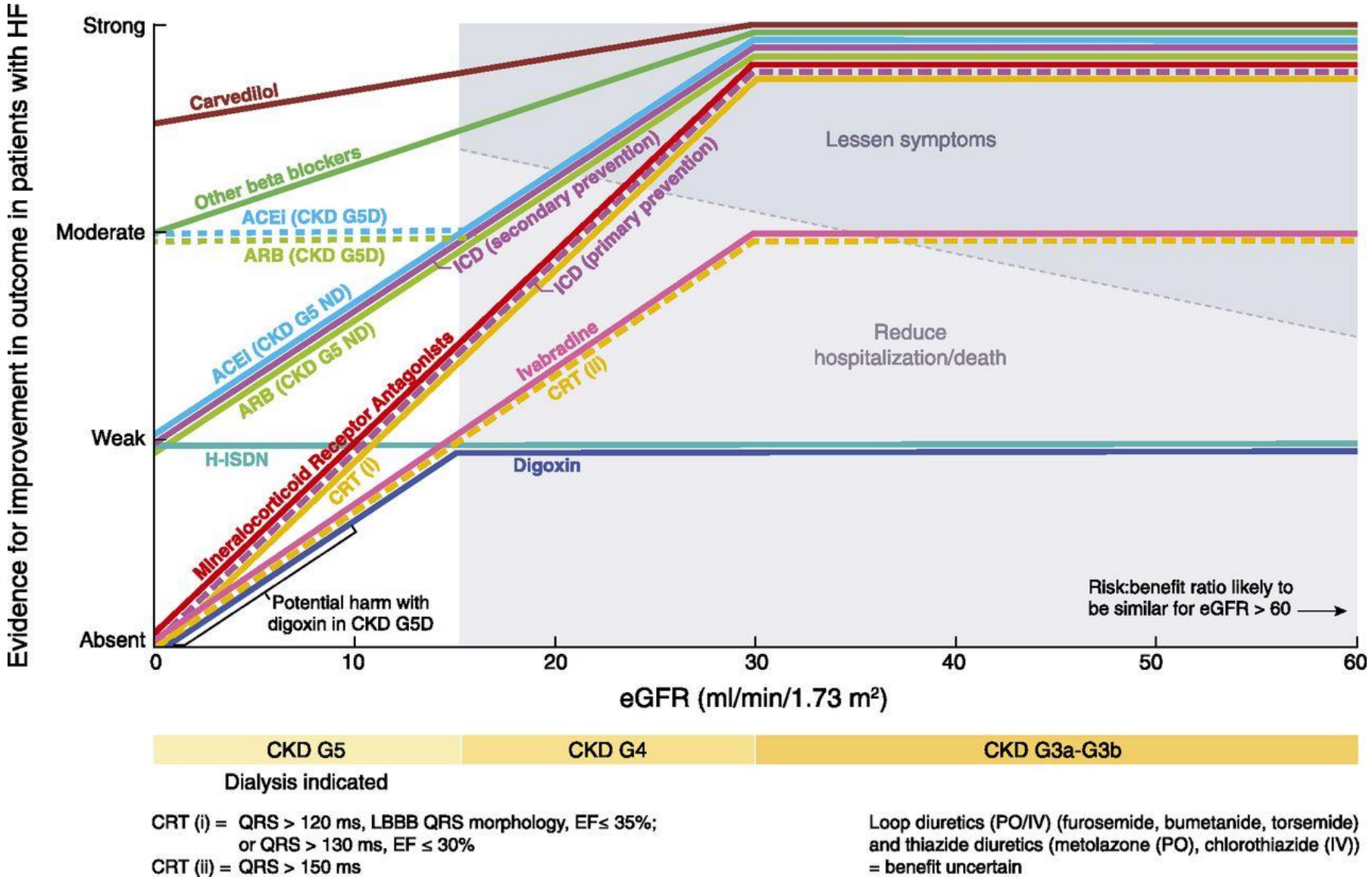
11. Renal replacement therapy:

Role of modality of dialysis is unclear, but likely irrelevant

Adequate ultrafiltration is crucial for controlling volume overload

Large volume ultrafiltration associated with myocardial stunning

High-flow arteriovenous fistulae should be avoided: contribute to volume overload, high cardiac output, eccentric LVH and worsening HF



Evidence of benefit from ARNI and SGLT-2 inhibitors is also high

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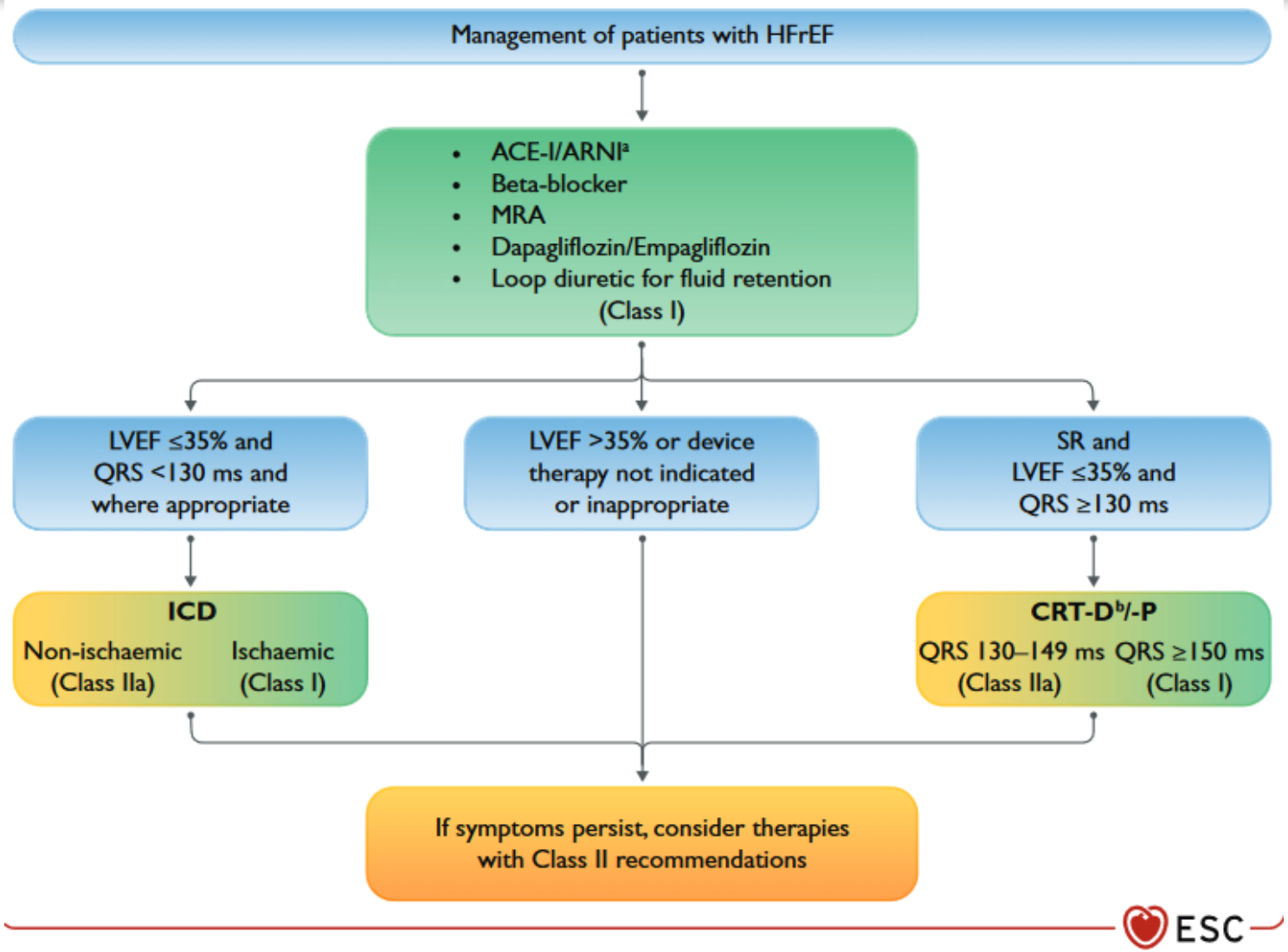
Banerjee D, et al. Management of heart failure patient with CKD. *CJASN* 2021;16(7):1131-1139.

Management



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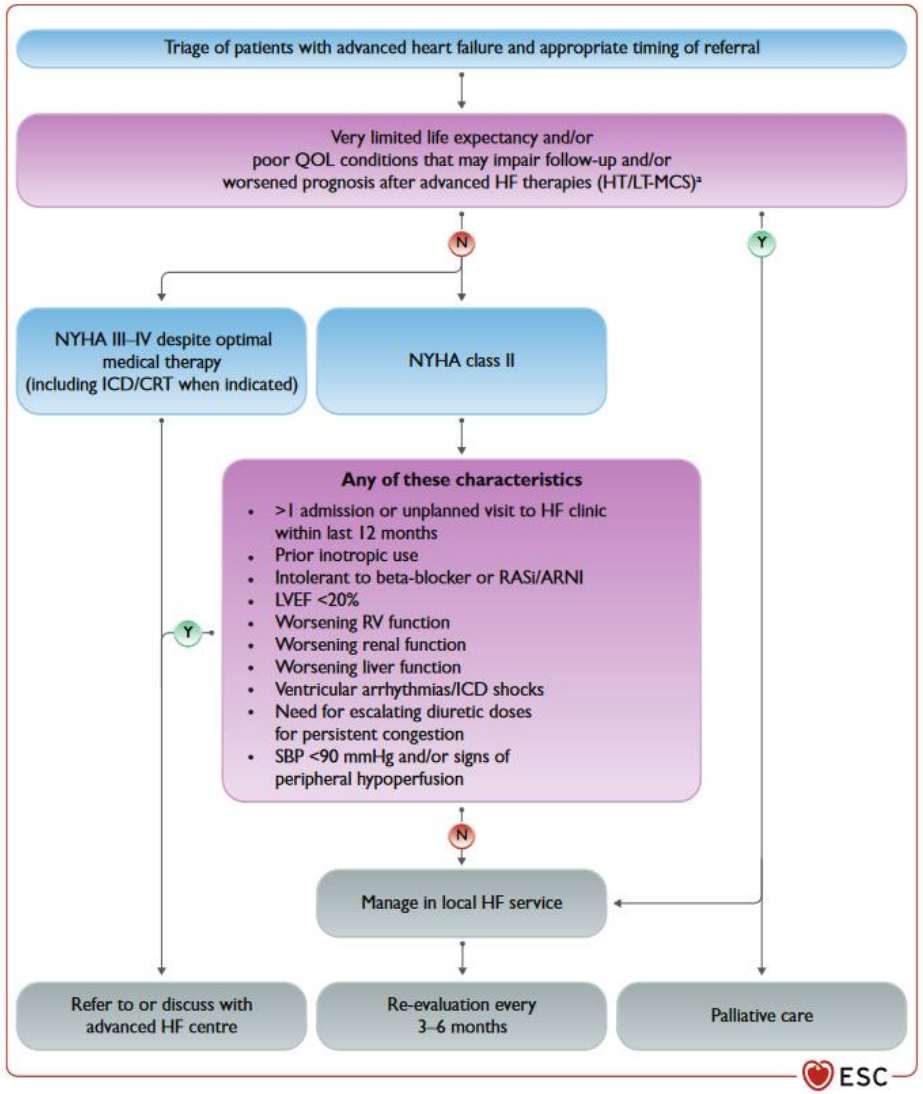
McDonagh TA, et al. , 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2021;42(36):3599-3726.

Management



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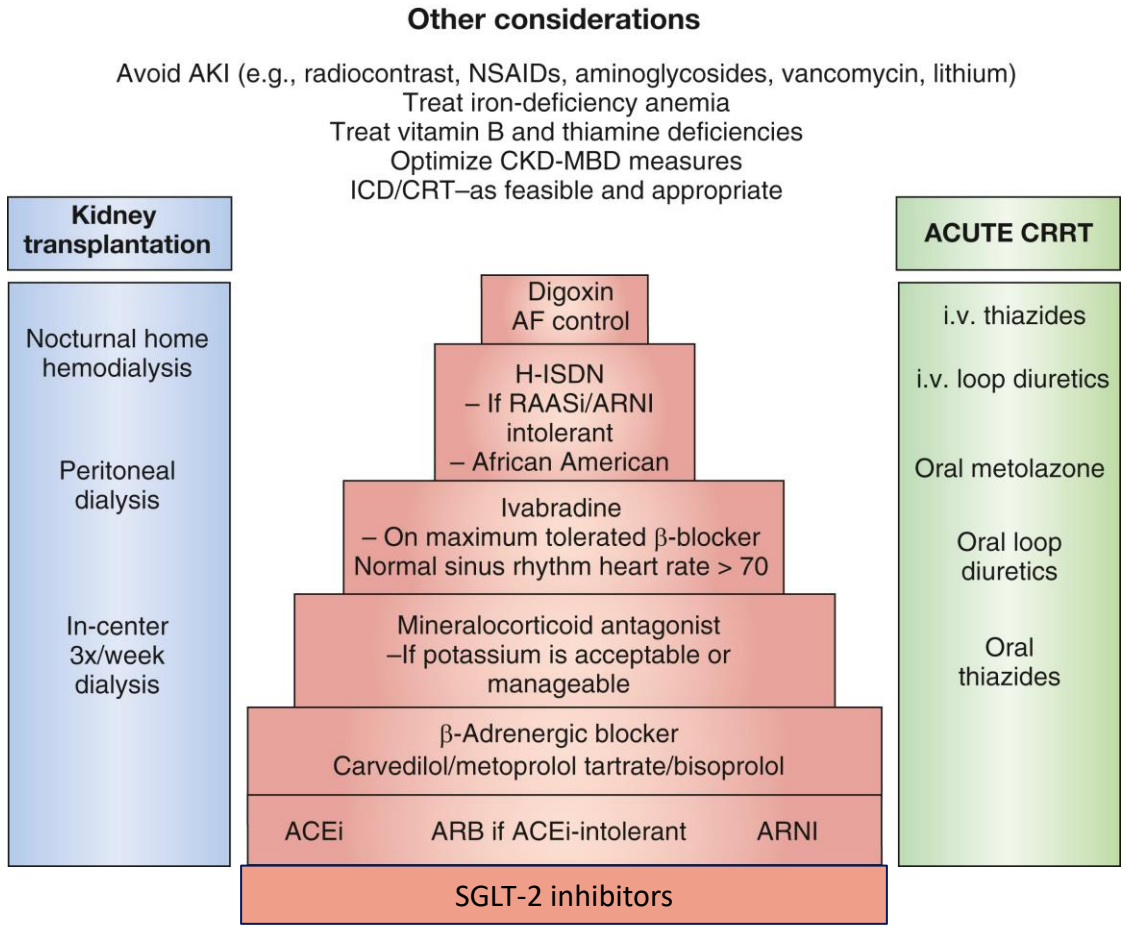
Principles of management



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Conclusions

CKD and HF are common; often coexist and share aetiology and risk factors

Individuals with CKD have greater risk of CV death

More than 40% of HF patients have CKD and presence of kidney dysfunction worsens HF; renal dysfunction occurs commonly in all forms of HF

Updated definition of cardiorenal syndrome

Pharmacotherapy may be difficult to manage and requires close monitoring

Beta-blockers, ACE inhibitors/ARBs, ARNIs and SGLT-2 inhibitors are associated with improved outcomes in patients with HF and CKD

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Thank you for your attention!

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HF ACADEMY COURSE OVERVIEW

This **free CPD accredited educational program** was developed by cardiologists who are members of the Heart Failure Society of South Africa and is aimed at those who are interested in improving services for people with heart failure, including **not only doctors, but also nurses and pharmacists**. The course comprises 5 modules that provide a basic review of heart failure care and each module is individually **CPD accredited for 5 CPD points** with the HPCSA. Following the completion of all 5 modules, a **Certificate of Competency** in basic heart failure management will be awarded by HeFSSA.

COURSE LEARNING OBJECTIVES

- ✓ Raise the awareness of heart failure among health care professionals
- ✓ Improve the prevention, diagnosis, treatment and long – term management of heart failure
- ✓ Ensure equity of care for all patients with heart failure
- ✓ Support and empower patients with heart failure and their families or other caregivers to engage proactively in long – term care

COURSE DIRECTORS

Prof Nash Ranjith
City Hospital
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Dr Martin Mpe
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Prof Nqoba Tsabedze
University of the Witwatersrand

Dr Tony Lachman
Victoria Hospital

Prof Mpiko Ntsekhe
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