Community of Practice

OF HEARTS & KIDNEYS
Understanding the Cardiorenal Relationship

Disclosures

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Ad Boards/Speakers Bureau/Consulting: Astra-Zeneca, Bayer, Janssen, Otsuka, Pfizer

Scientific Committee/speaker: Liv Bio Pharma, CHEP+

Grants/Research: CIHR, KMH

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Scientific Committee/speaker: AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Cytokinetics, Eli Lilly, GSK, Janssen, Medtronic, Merck, Novartis, Novo-Nordisk, Otsuka, Pfizer, Roche, Salubrisbio, Servier and Vifor Pharma

Grants/Research: AstraZeneca, Bayer, Boehringer Ingelheim, Merck, Novartis and Pfizer

Other: Canadian Medical and Surgical KT Group, CCS, CHFS, Charite, EOCI, Liv, Medscape, Ology, PACE-CME, Radcliffe, Reach MD, Translational Medicine Academy

Learning Objectives

1. Explore the interdependent relationship between the heart and kidneys
2. Identify patients with an elevated cardiorenal risk within your practice
3. Appraise treatment options for patients with elevated cardiorenal risk

Short Term Falls in eGFR due to Higher Dose of Diuretic or Adjustment of RAASi were NOT Associated with Worse Outcomes

- Therefore:
  - Treat the patient to make the heart better, even if on the short term, renal function falls
  - **A healthier heart makes healthier kidneys**

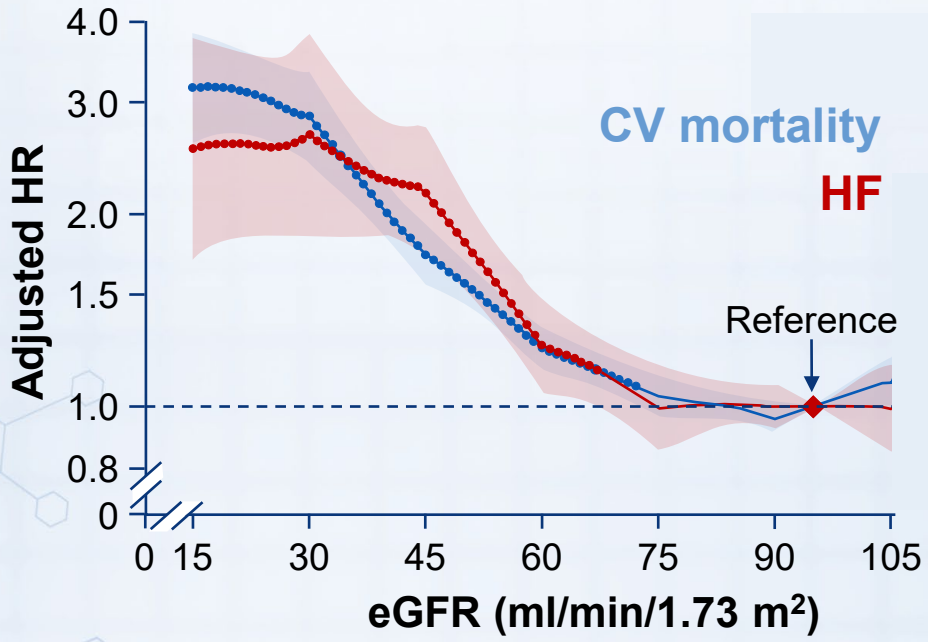
Tobe SW, Canadian J Cardiology vol 34: 2018, 1261-1263
Adapted from: Mascarenhas J, CJC 34, 2018: 1325-1332

Patients with T2D and CKD Have a High Risk of Hospitalisation for HF and CV Death

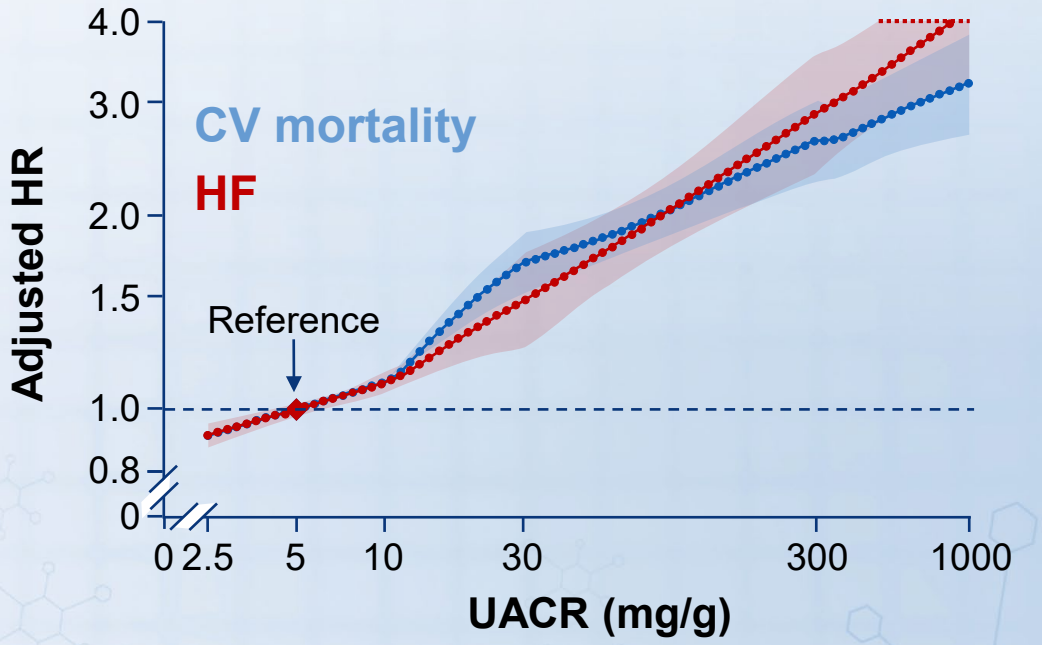
CV risk increases as eGFR falls below ~75 ml/min/1.73 m^2

DM Increases risk

eGFR (ml/min/1.73 m^2)*#,2



UACR (mg/g)*,2



*Adjusted for age, sex, race or ethnic origin, smoking, SBP, antihypertensive drugs, diabetes, total and high-density lipoprotein cholesterol concentrations, and albuminuria (UACR or dipstick) or eGFR, as appropriate;
#Figure adapted from Matsushita K, *et al.* 2015
CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HF, heart failure; SBP, systolic blood pressure; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio

1. Matsushita K, *et al. Lancet Diabetes Endocrinol* 2015;3:514–525; 2. Fox CS, *et al. Lancet* 2012;380:1662–1673

KDIGO HEAT MAP

GFR categories (ml/min/1.73 m²) Description and range				Albuminuria categories Description and range		
				A1	A2	A3
CKD is classified based on: • Cause (C) • GFR (G) • Albuminuria (A)				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
	G1	Normal or high	≥90	Screen 1	Treat 1	Treat 3
	G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat 3
	G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat 3
	G3b	Moderately to severely decreased	30–44	Treat 2	Treat 3	Treat 3
	G4	Severely decreased	15–29	Treat* 3	Treat* 3	Treat 4+
	G5	Kidney failure	<15	Treat 4+	Treat 4+	Treat 4+

Low risk (if no other markers of kidney disease, no CKD)
Moderately increased risk
High risk
Very high risk

Increasing risk

Increasing risk

Prognosis worsens with decreasing eGFR or increasing albuminuria

- All-cause mortality
- CV mortality
- ESKD
- AKI
- Progressive CKD

Green is representative of low risk, yellow of moderately increased risk, orange of high risk, and red of very high risk
AKI, acute kidney injury; CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; GFR, glomerular filtration rate; UACR, urine albumin-to-creatinine ratio
Kidney Disease: Improving Global Outcomes. *Kidney Int Suppl* 2020;98:1–S115.

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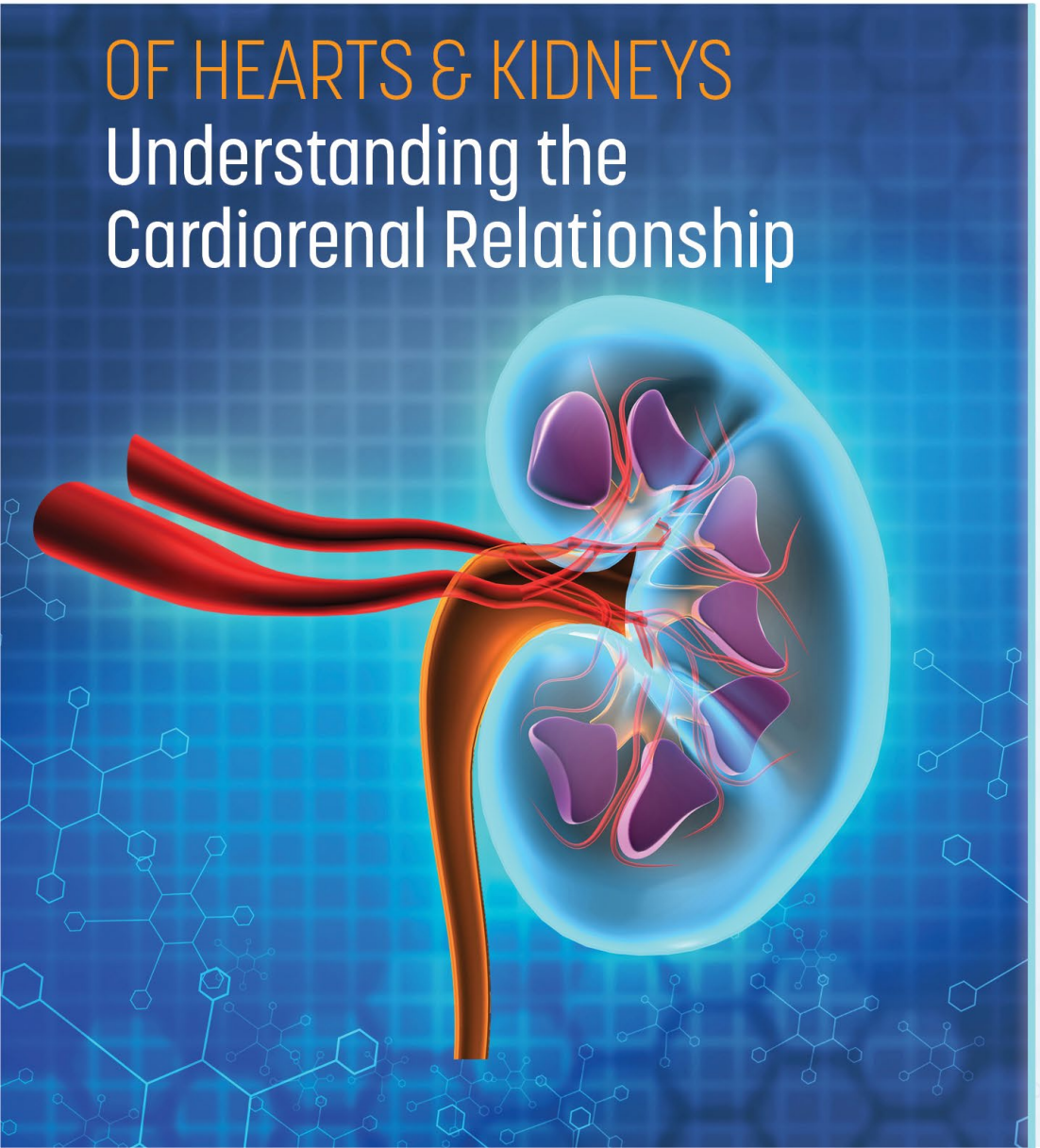
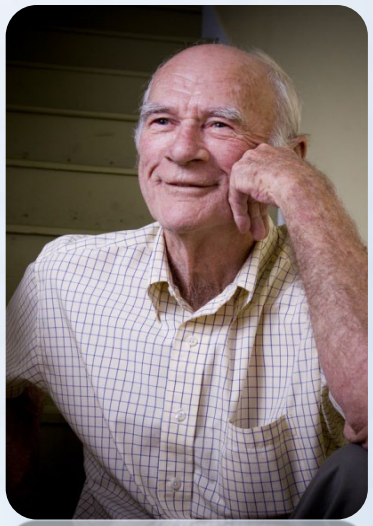


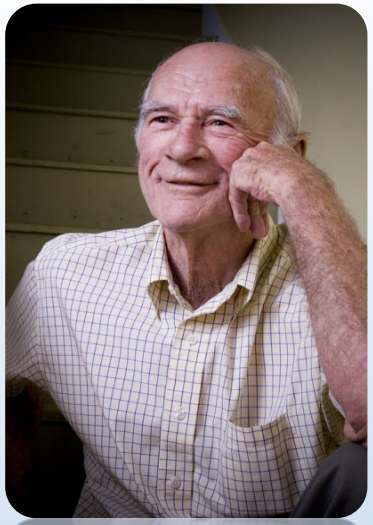
Case #1: Heart and Hypertension HFpEF



Cliff

A 76-year-old man presents to your office with worsening shortness of breath

Case #1: Heart and Hypertension HFpEF



Cliff
A 76-year-old man presents to your office with worsening shortness of breath

Present lifestyle

- Non-smoker, averages 2 beers/day
- Married; 2 children out of town

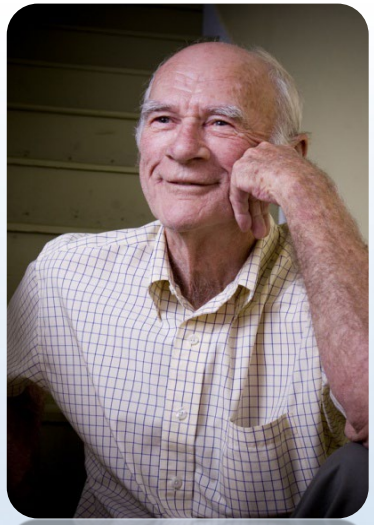
- Last 3 months
  - He noted dyspnea with exertion while climbing the stairs at home
- Last month
  - He woke up from sleep with dyspnea and had to sit on the edge of his bed
  - He noticed that he is winded after his usual walks with the dog
  - No chest pain, no cough, no edema, no palpitations

Past history

- Hypertension
- Diagnosed and treated for 10 years
- Acute myocardial infarction
- 6 years ago (thrombolysed) preserved LV function immediately after discharge
- Recent Echo LVEF 50- 55%, no valvular abnormalities
- Osteoarthritis

Current Medications

- Hydrochlorothiazide 25 mg OD
- Amlodipine 5 mg OD
- Ramipril 5 mg OD
- ECASA 81 mg OD
- Rosuvastatin 10 mg OD

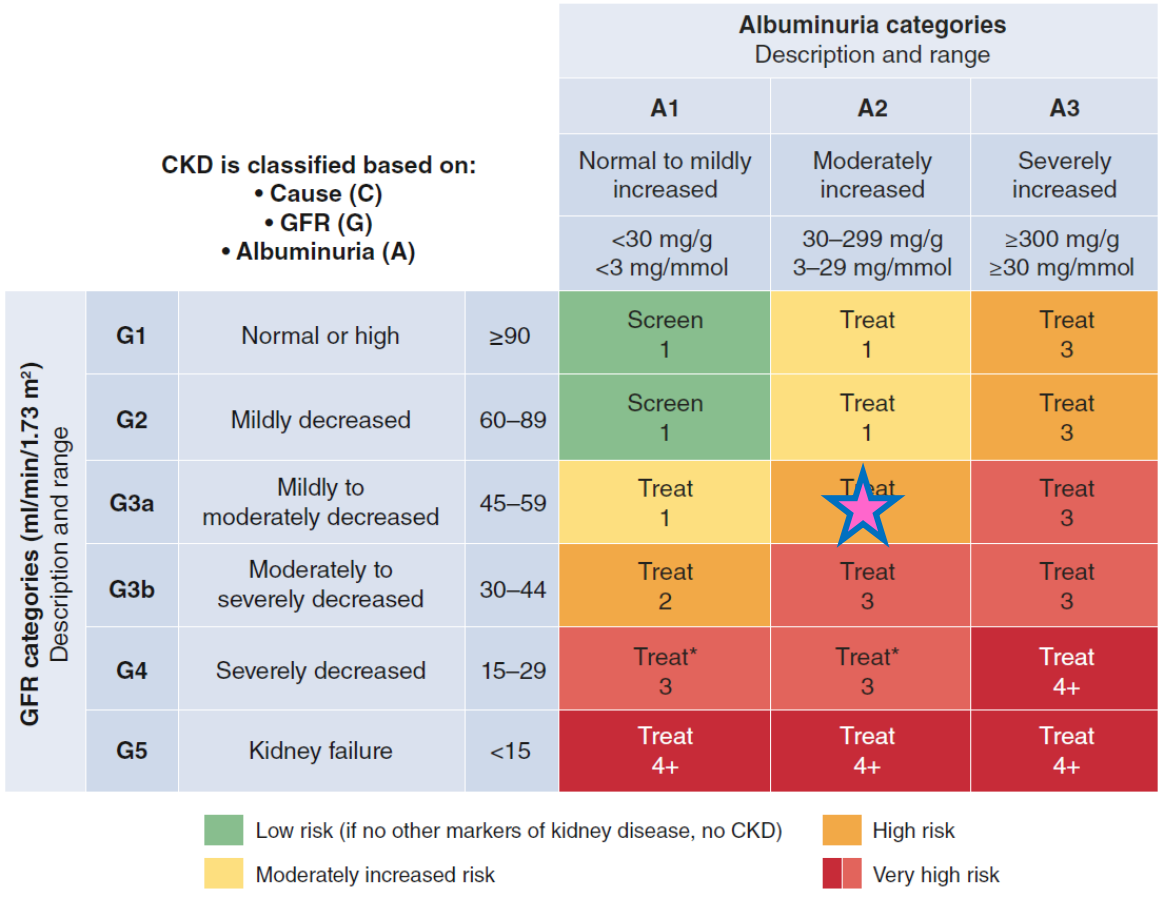


Physical Examination

- Height: 172 cm
- Weight: 85 kg
- Waist 102 cm
- BMI: 28.7 kg/m2
- BP (left arm, seated):
  - 144/84 mmHg using an automated device
- Pulse: 96 regular
- Not dyspneic at rest
- No edema
- Lungs clear on chest exam

Cliff's Lab Results

Test	Results	Normal Values
Glucose	6.5 mmol/L	4.0-8.0 mmol/L
Urea	6.8 mmol/L	3.0-7.0 mmol/L
Creatinine	105 µmol/L eGFR 50 ml/min	44-106 µmol/L
K	4.3 mmol/L	3.5-5.0 mmol/L
Hb	112 g/L	115-165 g/L
ACR	11 mg/mmol	< 3
NT-PRO-BNP	350 pg/ml	



Question: How Can We Improve Cliff's Heart & Kidney Outcomes?

76-year-old man presents to your office with worsening shortness of breath.

Diagnosis: HFpEF, albuminuric CKD

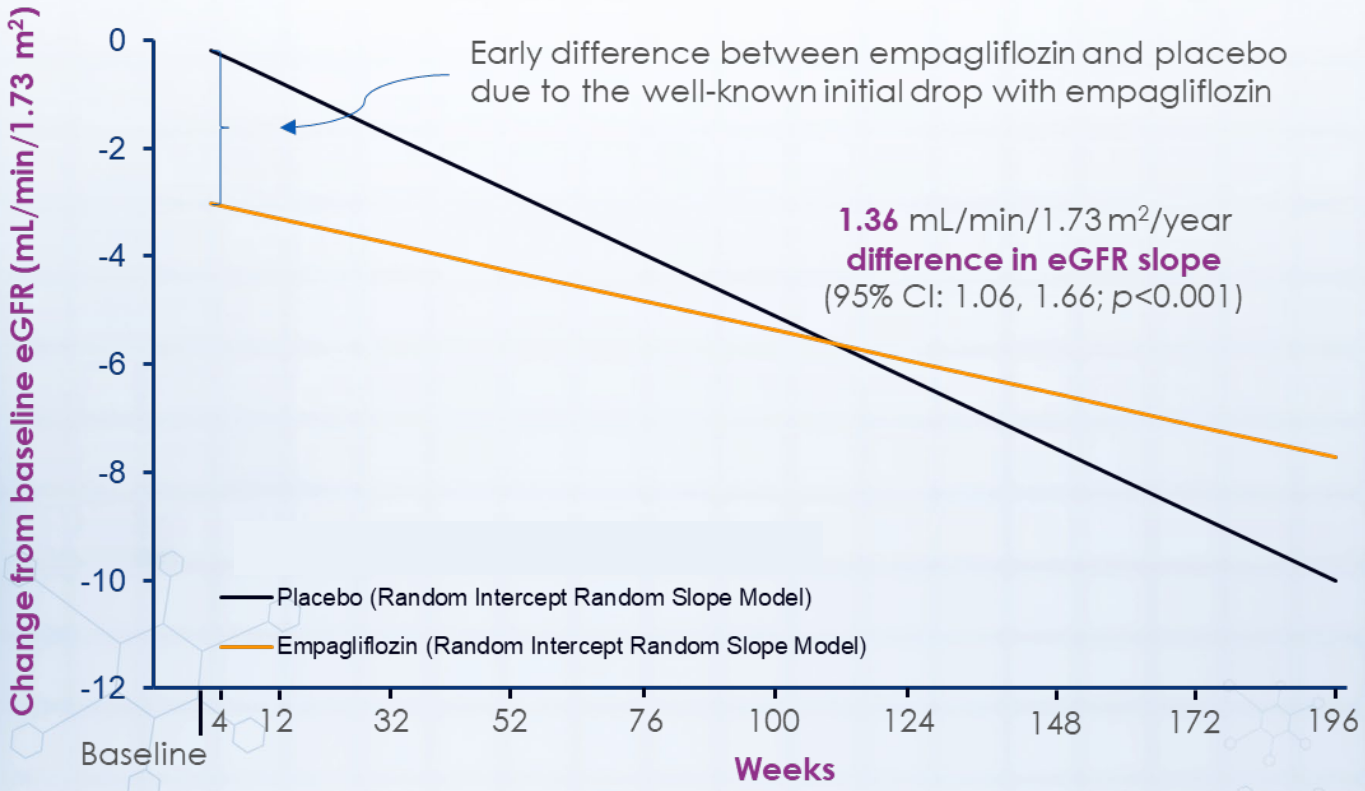
Current Meds

- Hydrochlorothiazide 25 mg OD
- Amlodipine 5 mg OD
- Ramipril 5 mg OD
- ECASA 81 mg OD
- Rosuvastatin 10 mg OD

Recommended therapy?

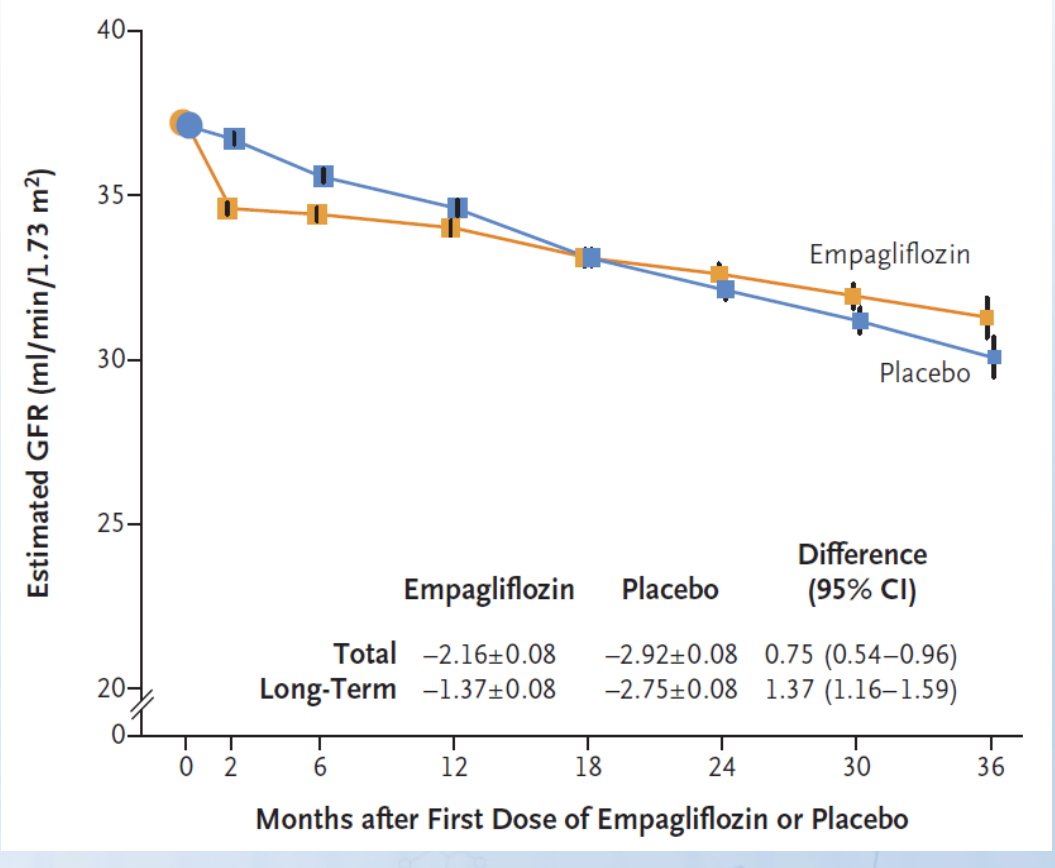
Using your tubes, vote at your tables for which therapy you would next!

EMPEROR PRESERVED: Empagliflozin Significantly Reduced the Decline in eGFR Slope



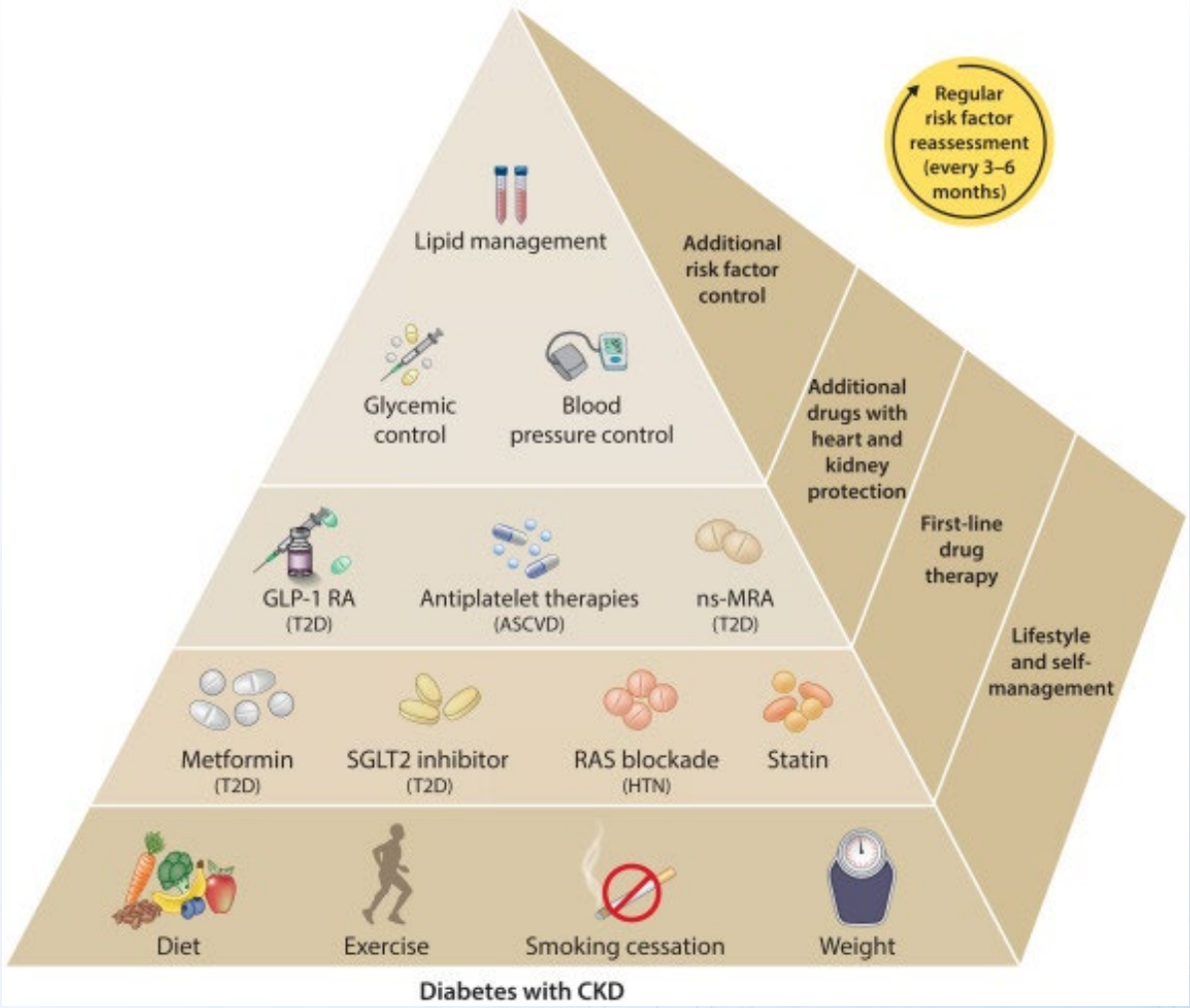
eGFR slope = rate of decline (and is a measure for long-term renal function). eGFR slope is analyzed based on on-treatment data using a random coefficient model including age, baseline eGFR and baseline LVEF as linear covariates and sex, region, baseline diabetes status, and baseline by time and treatment by time interactions as fixed effects; the model allows for randomly varying slope and intercept between patients.
CI, Confidence Interval; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; SE, standard error.
Developed from data reported in Anker S et al. N Engl J Med. 2021. DOI:10.1056/NEJMoa2107038

EMPA-Kidney: Acute and Long-term eGFR Trajectories



Herrington WG, NEJM 2022 Nov 4 doi: 10.1056/NEJMoa2204233

KDIGO 2022 - Guideline Recommendations



Rossing, Peter, M. Luiza Caramori, Juliana C.N. Chan, Hiddo J.L. Heerspink, Clint Hurst, Kamlesh Khunti, Adrian Liew, et al. "KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease." *Kidney International* 102, no. 5 (November 2022): S1–127. https://doi.org/10.1016/j.kint.2022.06.008.

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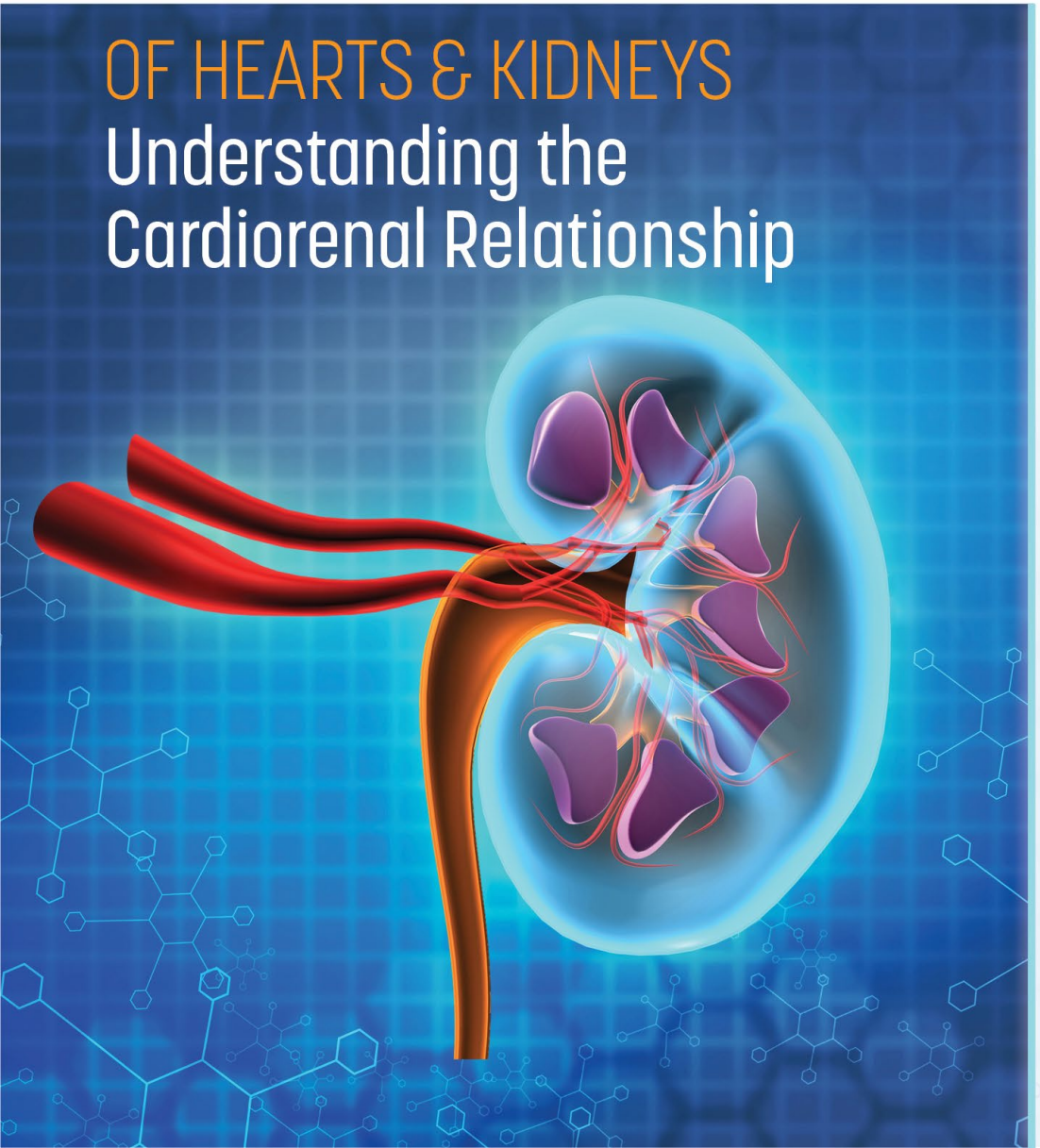


Case #2: CKD and Diabetes – Advanced Nephropathy

Asha

72-year-old woman

Case:
Management of Cardiorenal Risk in Patient with CKD

- Asha is a 72-year-old mother living with her son
- She has CKD, hypertension, and diabetes and they are worried about prevention of kidney disease and cardiovascular disease

PMHx:

- CKD (stage G4, A3)
- Hypertension (x 10 years)
- Type 2 Diabetes (x 20 years)

Social:

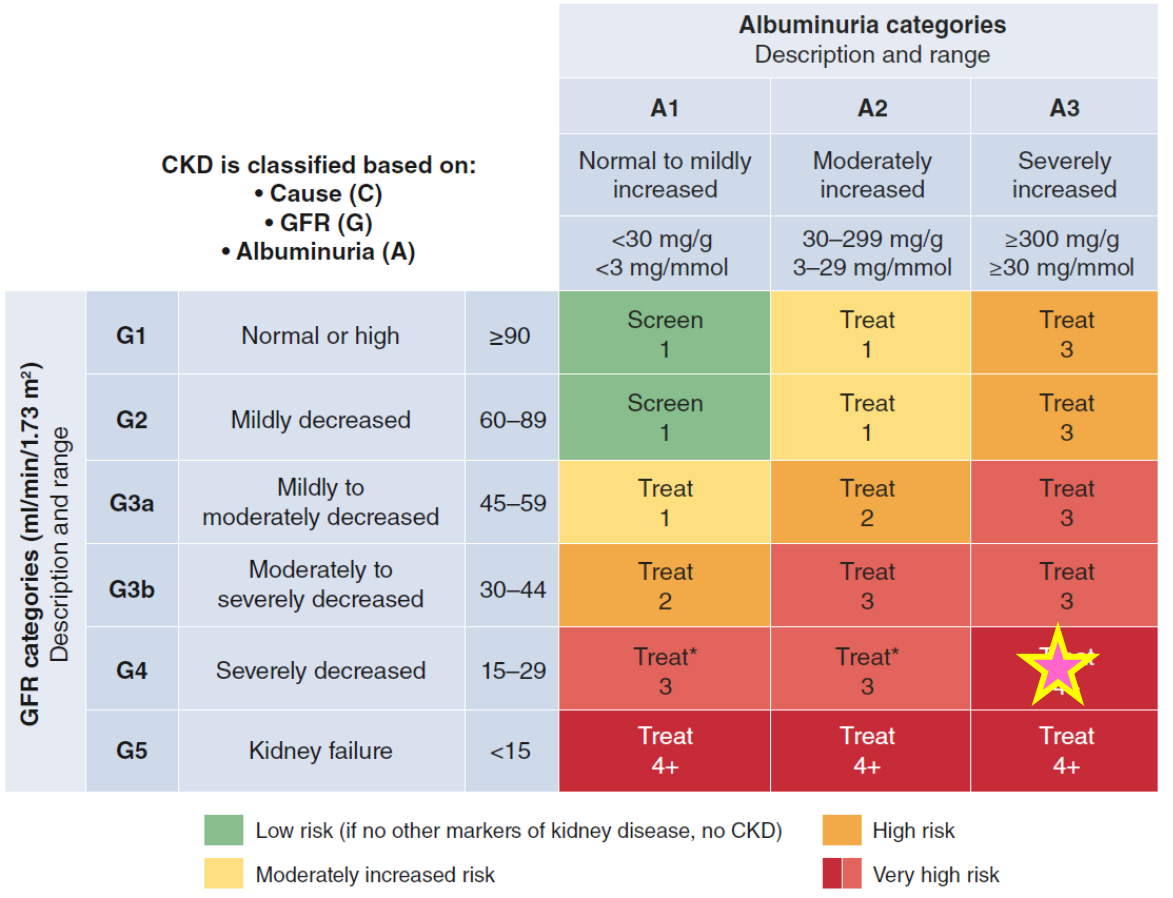
- Retired
- Non-smoker

Medications:

- Ramipril 10 mg
- Amlodipine 5 mg
- Indapamide 1.25 mg
- Semaglutide 1 mg sc/week
- Rosuvastatin 5 mg

Asha's Lab Results

Test	Asha	Normal Values
HbA1c	7.5%	4.5-5.7%
Creatinine	165 umol/L	44-106 µmol/L
eGFR	**28**	**>60**
K	5.1 mmol/L	3.5-5 mmol/L
ACR	**105 mg/mmol**	**< 3 mg/mmol**



Question:
How Can We Improve Asha's Heart & Kidney Outcomes?

Medications:

- Ramipril 10 mg
- Amlodipine 5 mg
- Indapamide 1.25 mg
- Semaglutide 1 mg sc/week
- Rosuvastatin 5 mg
- **BP 125/62 mm Hg**
- **HR 72 bpm**
- **Pedal edema 2+**

Recommended therapy?

Using your tubes, vote at your tables for which therapy you would next!

Case Completion:
Management of Cardiorenal Risk in Patient with CKD

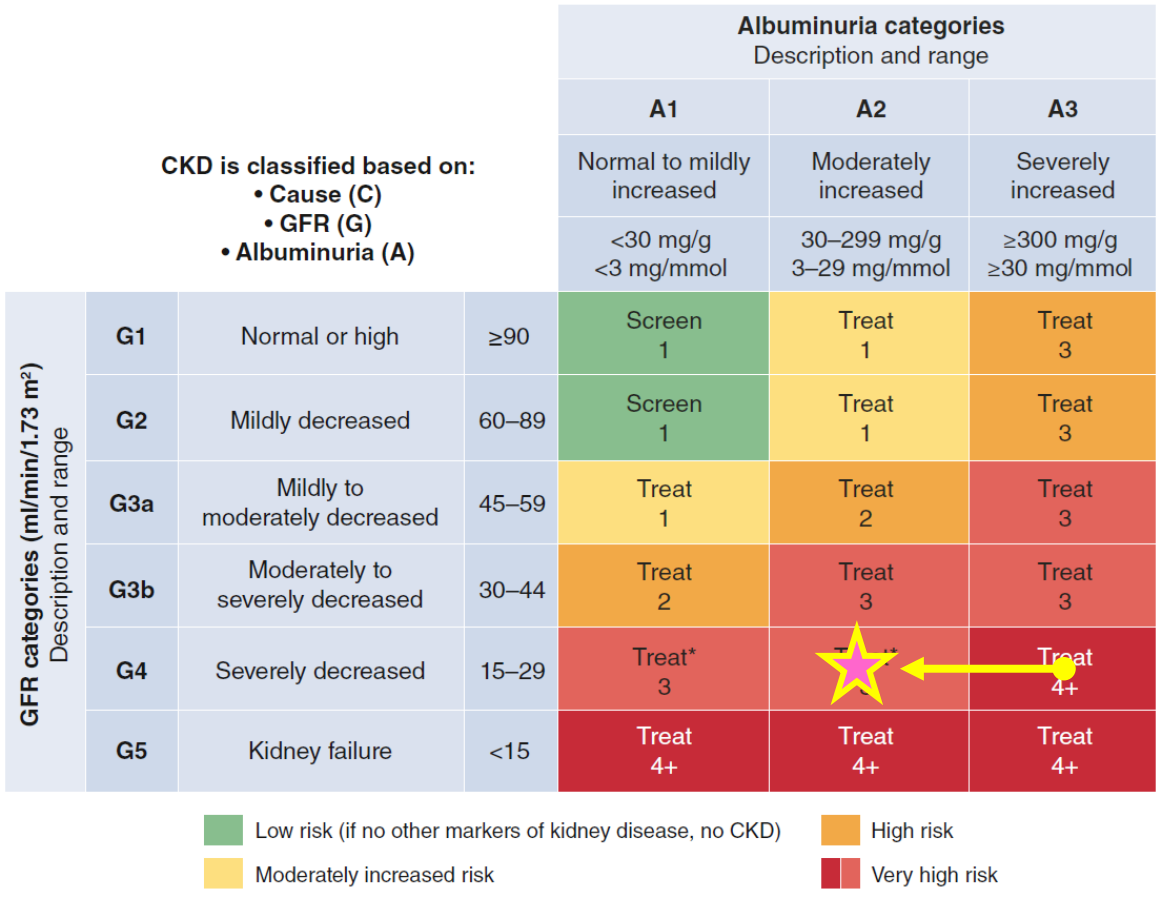
Asha is a 72-year-old female **BP 128/56**
Meds:

- Ramipril 10 mg
- Amlodipine 7.5 mg
- Indapamide 2.5 mg
- Semaglutide 1 mg sc/week
- **Empagliflozin 10 mg**
- Rosuvastatin 5 mg

- Asha is physically active with 30 minutes of brisk walking at least 5 days of the week
- She has lowered sodium in their diet to <2 g per day
- **Asha is appreciative that her edema resolved after the addition of empagliflozin**
- Asha is at significantly higher risk of renal and CVD and will benefit from additional therapy with finerenone when available if her K is controlled

Asha's Lab Results - Follow Up

Test	Asha Before	Asha After	Normal Values
HbA1c	**7.5**	**7.5**	4.5-5.7 %
Creatinine	**165**	**185**	44-106 umol/L
eGFR	**28**	**24**	**>60**
K	**5.1**	**4.8**	3.5-5 mmol/L
ACR	**105**	**48**	**< 3 mg/mmol**



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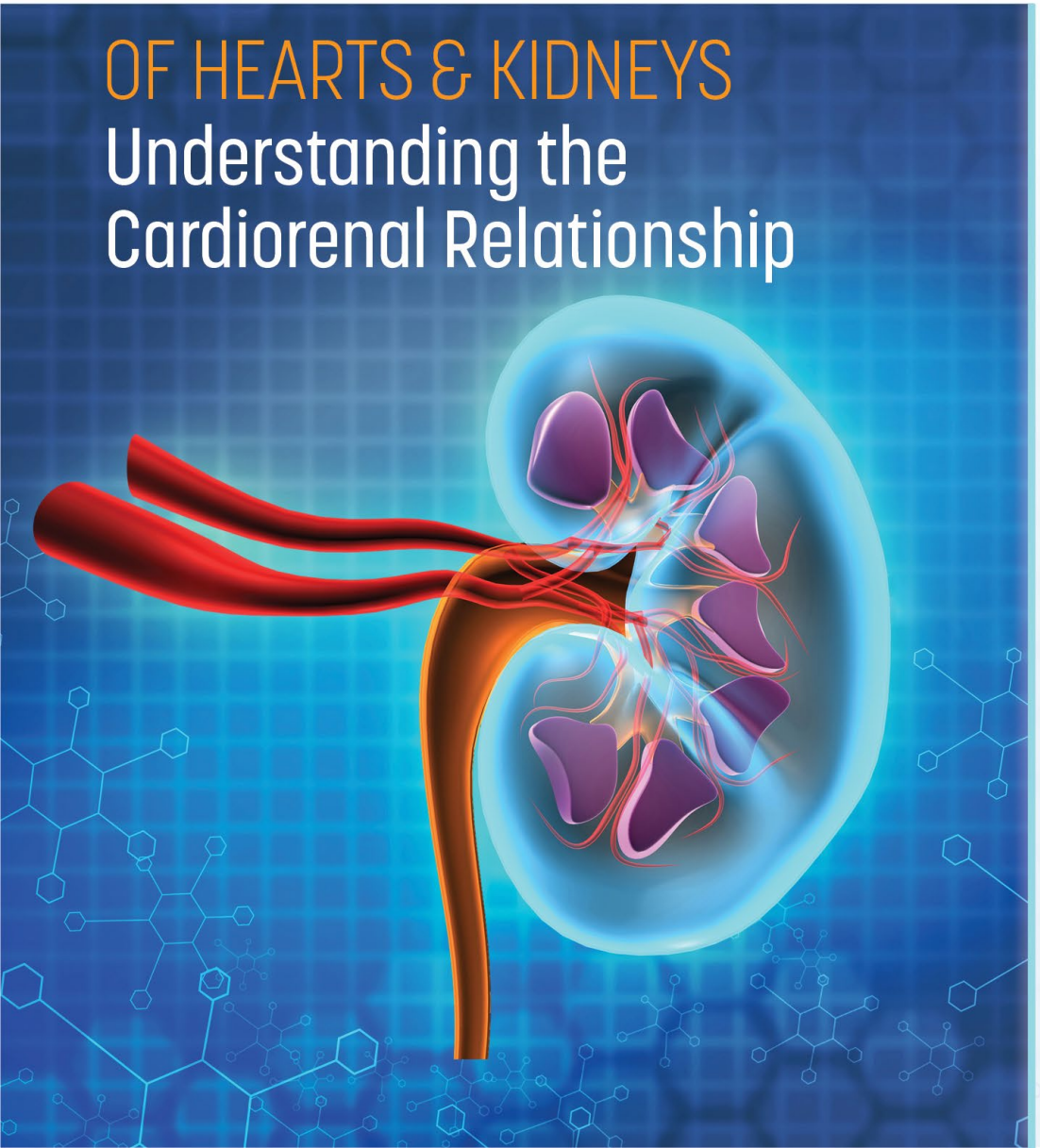


Case #3: HFrEF and Diabetes

Mr. Wynded
67-year-old man

Failing Triple Therapy: What's the Next Step?

- Mr. Wynded, 67-year-old man
- **Past medical history:**
  - Hypertension, type 2 diabetes, dyslipidemia,
  - Ex-smoker
  - VF arrest and anterior STEMI (May 2017): PCI to LAD and LCx with 2 drug-eluting stents, complicated by cardiogenic shock
  - ICD implanted July 2017 for LVEF 20% and transient episodes of complete heart block
- Presents to clinic with a 2-week history of increasing peripheral edema, orthopnea, PND, and dyspnea with minimal exertion

Clinic Visit: Decompensated HF

Medications:

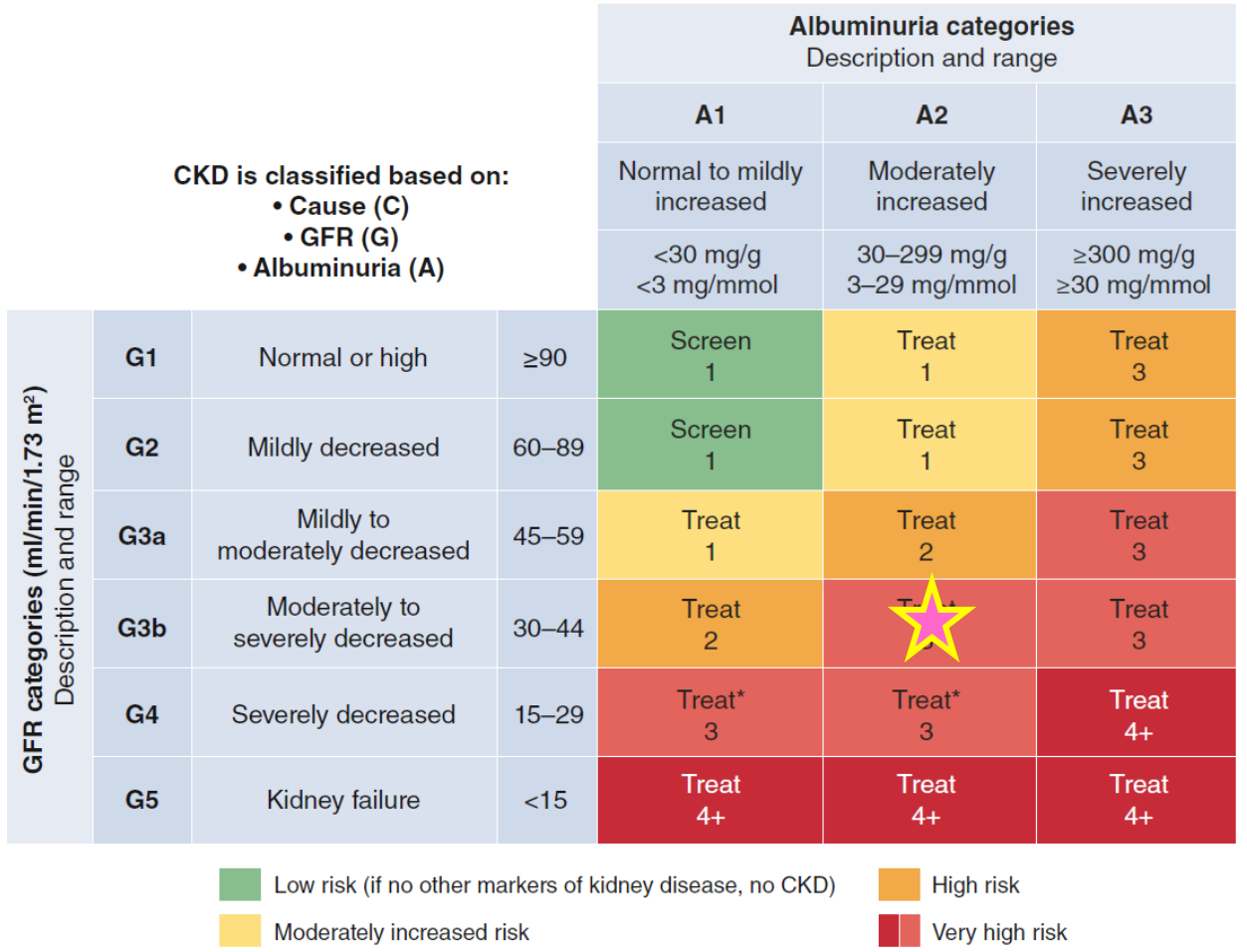
- Bisoprolol 10 mg OD
- Sacubitril valsartan 49/51 mg BID
- Spironolactone 50 mg OD
- Furosemide 80 mg BID
- ASA 81 mg OD
- Metformin 500 mg BID
- Atorvastatin 80 mg qhs

On examination:

- 94/77 mmHg, 68 bpm
- Decreased air entry right lower lobe of lung, JVP elevated at earlobe, 2+ pitting edema to lower calves bilaterally
- ECG: normal sinus rhythm at 62 beats/min with old anterior MI
- Echo: LVEF 30%
- Mild MR

Mr. Wynded's Lab Results

Test	Results	Normal Values
Fasting Glucose	6.2	4.0–8.0 mmol/L
HbA1c	6.2%	4.5–5.7%
Creatinine	178	44–106 µmol/L
eGFR	33	>60
Na	140	135–145 mmol/L
K	3.6	3.5–5 mmol/L
ACR	5.5	< 3.0 mg/mmol



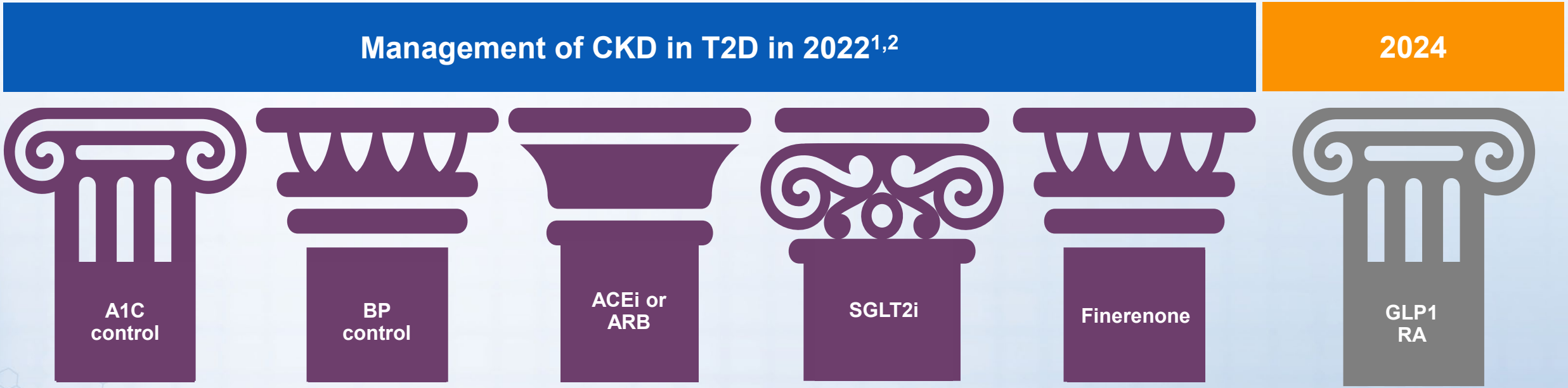
Question:
How Can We Improve Mr. Wynded's Heart & Kidney Outcomes?

a. Increase his sacubitril valsartan
b. Add ivabradine
c. Add a SGLT2 inhibitor
d. All of the above are appropriate

Recommended therapy?

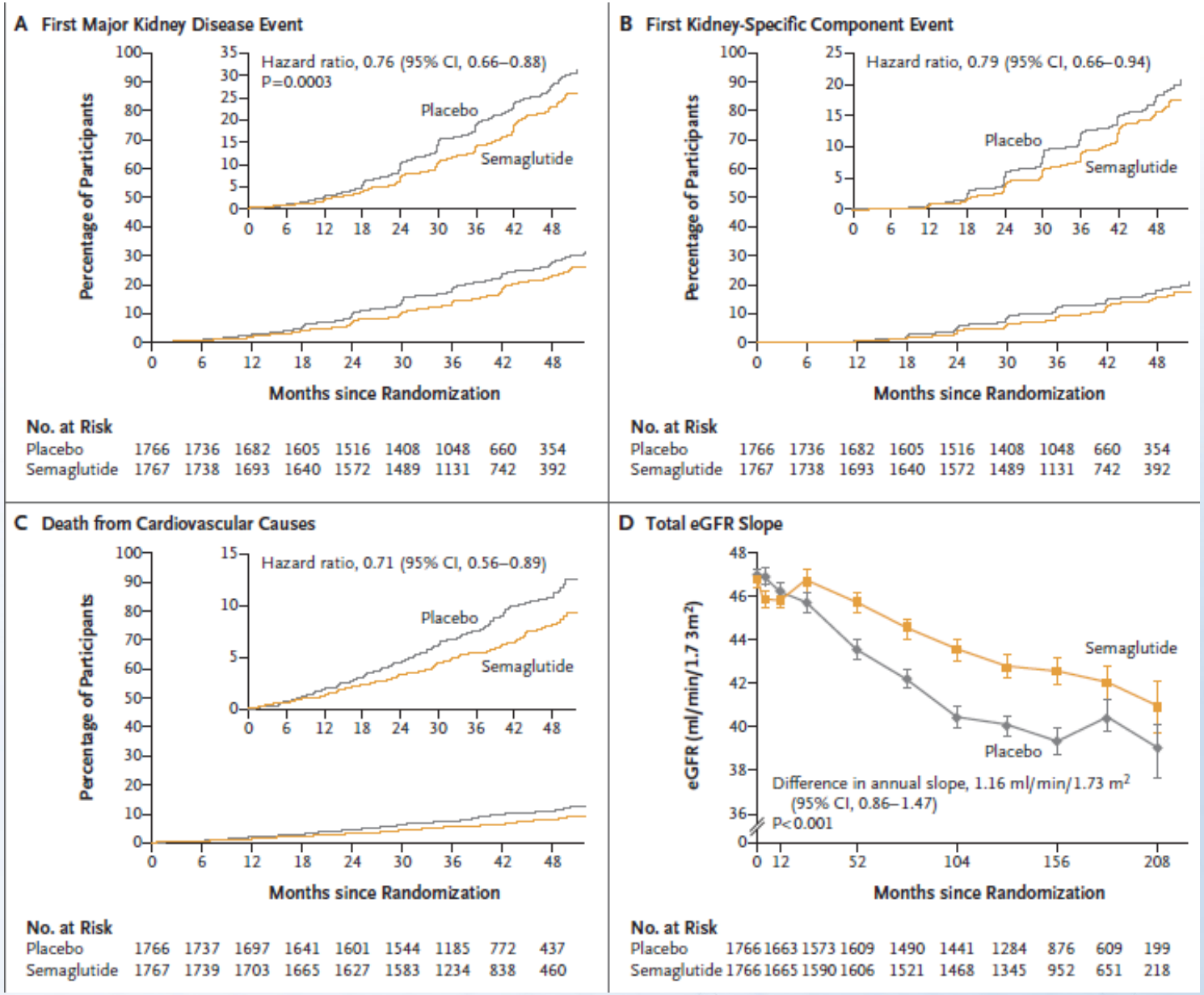
Using your tubes, vote at your tables for which therapy you would next!

KDIGO 2022 - Guideline Recommendations



A1C, glycated hemoglobin; ACEi, angiotensin-converting enzyme inhibitor; ACR, albumin-creatinine ratio; ADA, American Diabetes Association; ARB, angiotensin II receptor blocker; BP, blood pressure; CKD, chronic kidney disease; CV, cardiovascular, eGFR, estimated glomerular filtration rate; nsMRA, non-steroidal mineralocorticoid receptor antagonist; RAS, renin-angiotensis system; SGLT2i, sodium-glucose cotransporter 2 inhibitor; T2D, type 2 diabetes.

1. Diabetes Canada Clinical Practice Guidelines Expert Committee. Can J Diabetes 2018;42 :S201–209.
2. Diabetes Canada Clinical Practice Guidelines Expert Committee. Can J Diabetes. 2020 Oct;44(7):575-591.
3. American Diabetes Association Professional Practice Committee. Diabetes Care. 2022 Jan 1;45(Suppl 1):S175-S184. doi: 10.2337/dc22-S011.
4. de Boer IH, Khunti K, Sadusky T, et al. Diabetes Care. 2022 Oct 3:dci220027.



Vlado Perkovic, NEJM - Today

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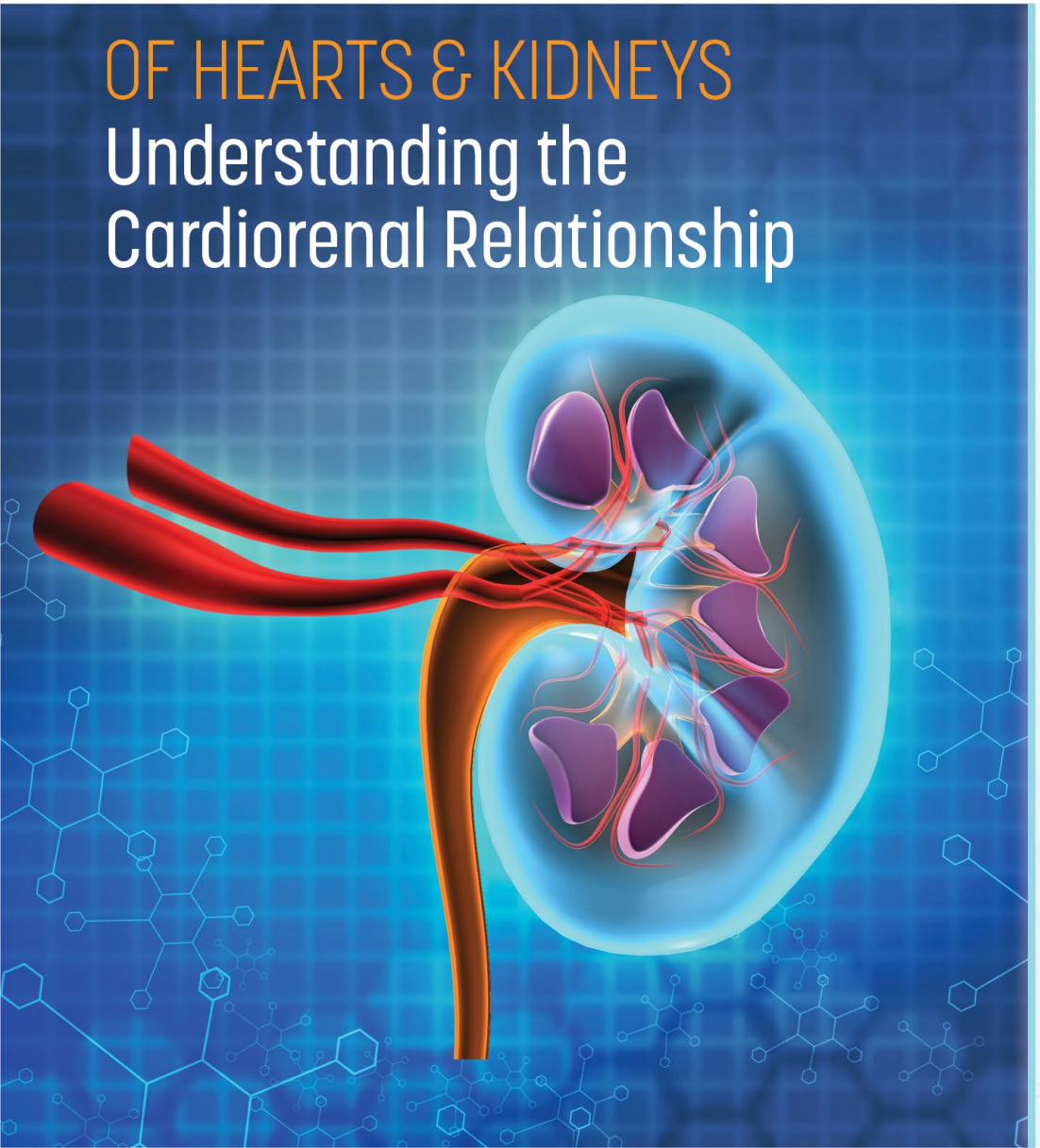

Evaluation

Please take a moment to complete the session evaluation by scanning the QR code below. (also found on your table)

Next Up! ***Please proceed back downstairs to the Ballroom for lunch and the symposium Weighing in on HFpEF: A Review of the Clinical Evidence and Emerging Therapies for HFpEF***