A multidisciplinary clinical dialogue: Optimizing long-term goals: practical approaches to novel potassium binder use in cardiorenal care

Aaron Wong, MBCHB, MD, FRCP, CAS (Heart Failure)

Consultant Cardiologist and General Physician

Princess of Wales Hospital, Wales, United Kingdom

Honorary Clinical Lecturer, University of Cardiff

James Burton, MD

Honorary Consultant Nephrologist

Professor of Renal Medicine and Associate Dean for Clinical Research at the University of Leicester

Leicester, United Kingdom

Speaker disclosures

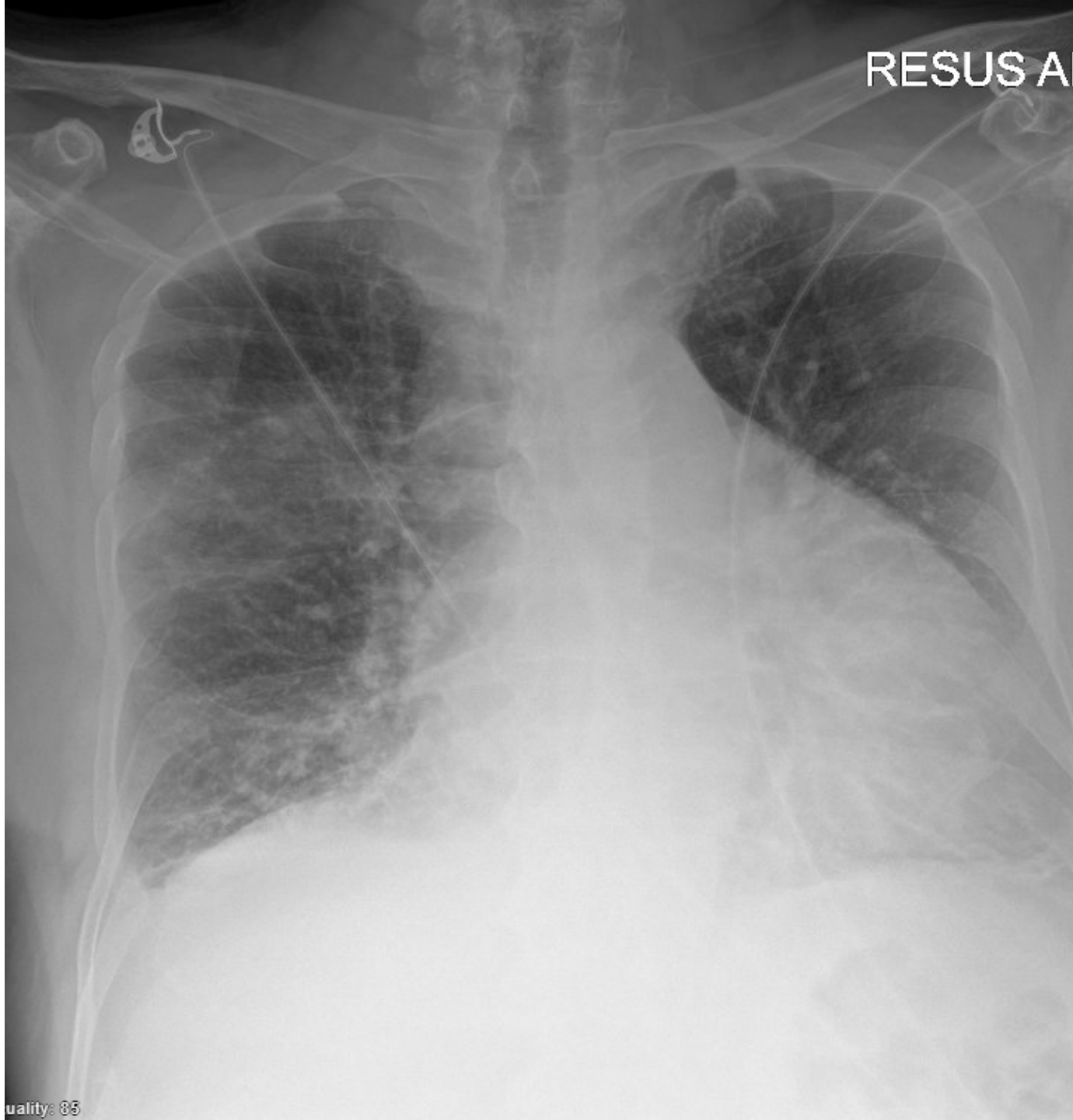
Dr Aaron Wong

- Received funding for education and attends courses from Servier, Novartis, Menarini, Pharmacosmos, NAPP, Amarin
- Principal Investigator for TRANSITION-HF, IRONMAN, ReliefHF , DAPA-MI, VICTOR-HF, Realize K trials
- Received speaker's fees and consultation fees from Novartis, AstraZeneca , Pharmacosmos, Menarini, Boehringer Ingelheim, Lilly, Bayer and Roche

Dr James Burton

Case Study

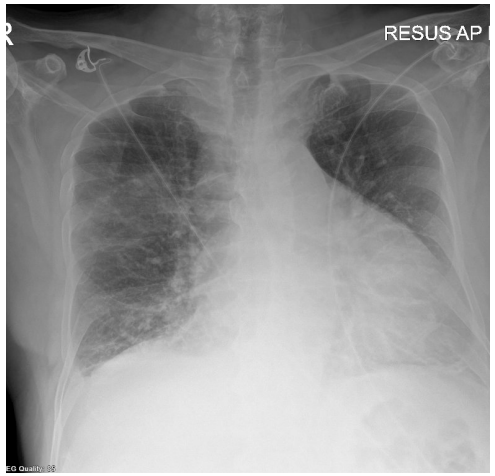
- 77-year-old male
- T2DM, Hypertension, CKD, AF
- April 2022 Admission
  - Dyspnea, Abdominal distension
  - AF, cardioverted in A&E
  - LVEF 30-35%
  - K 5.5 mmol/L, Cre 147 umol/L. Na 135 mmol/L, eGFR 40 mL/min per 1.73 m^2
  - NTproBNP 4280 ng/L
  - Normal TFT, CRP 22 mg/L



Pre-admission Medications

- Metformin
- Linagliptin 5mg od
- Simvastatin 20mg od
- Bisoprolol 2.5mg bd
- Digoxin 125mcg od
- Apixaban 5mg bd
- Ramipril 5mg od

Next step of Management



- T2DM, Hypertension, CKD. AF
  - LEVF 30-35%
  - K 5.5 mmol/L,
  - Cre 147 umol/L
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  - NTproBNP 4280 ng/L

Management of congestion with loop diuretics
Consider novel potassium binder
Initiate Dapagliflozin
Start Sacubitril/ Valsartan
Dipstix urine/ Send urinary ACR/ renal tract ultrasound

Persistence of congestion during the hospitalization is the most important prognostic factor and WRF has a clinical significance only when occurring in patients with persistent fluid overload.

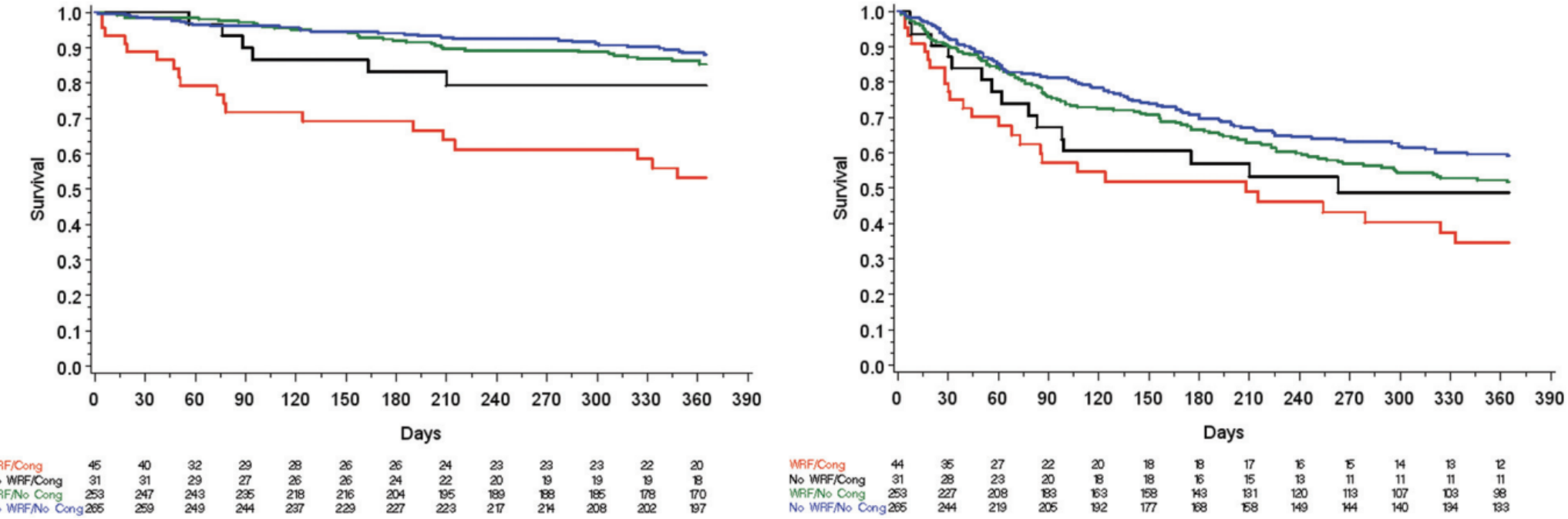


Figure. Outcome for 1-year death or urgent heart transplantation (Tx) (**left**) and for the combined end point of 1-year death, urgent heart transplantation, or heart failure (HF) readmission (**right**) for the patients subdivided on the basis of the development of worsening renal function (WRF) and on the presence of signs of congestion (Cong) at discharge. The number of patients at risk is shown at the bottom.

Metra et al. Congestion and Worsening Renal Function in AHF. Circ Heart Fail. 2012;5:54-62.)

Discharge medications

- Metformin
- Linagliptin 5mg od
- Simvastatin 20mg od
- Bisoprolol 2.5mg bd
- Digoxin 125mcg od
- Apixaban 5mg bd
- Eplerenone 25mg alternate day
- Dapagliflozin 10mg od
- Sacubitril/Valsartan 50mg bd
- Furosemide 40mg bd

New Medications

- Discharge on the 28 April 2022
- For outpatient heart failure specialist nurse follow up
- GP to check U&E in 2 weeks.

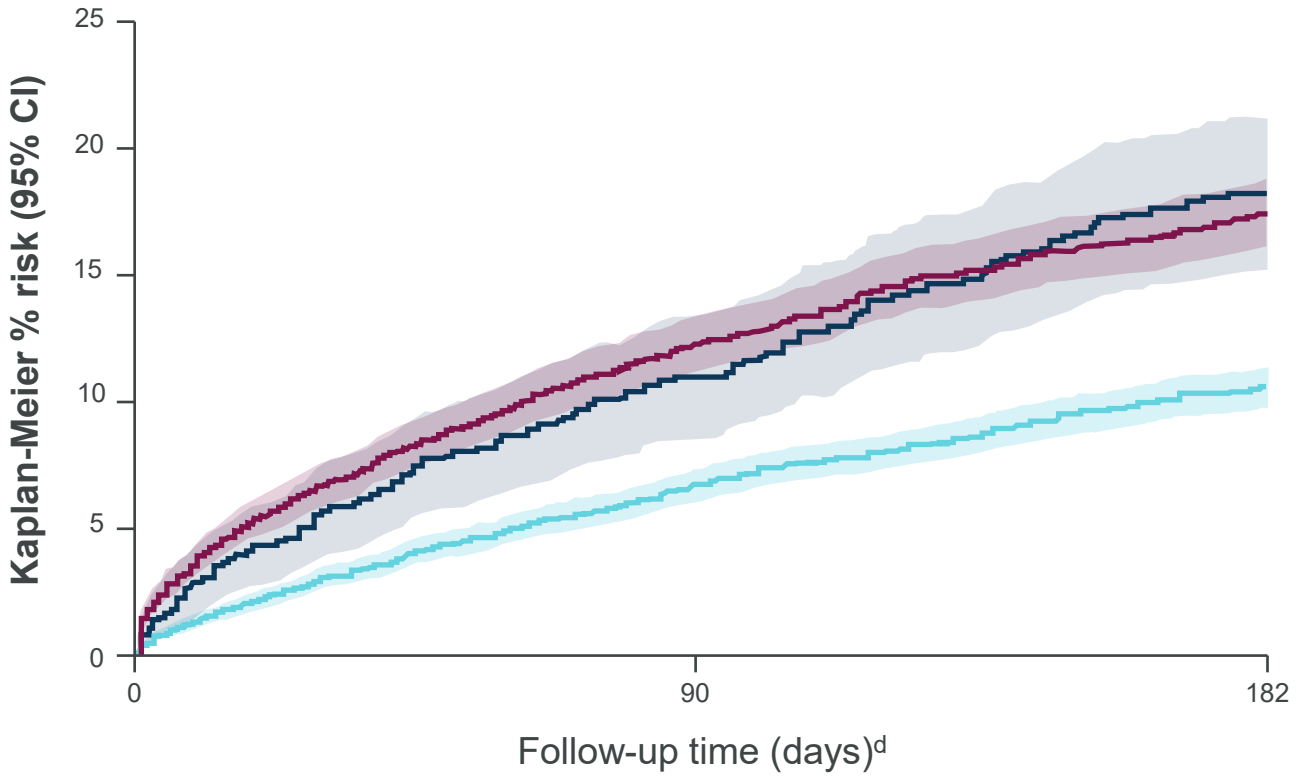
Attended A&E on the 8 May 2022

- Lowish BP, Diuretics withheld
- Discharge

Electrolyte Profile (Authorised [A])			
Sodium	136	mmol/L	133-146
Potassium	5.0	mmol/L	3.5-5.3
Urea	**29.2**	**mmol/L**	**H 2.5-7.8**
Creatinine	**203**	**umol/L**	**H 58-110**
Estimated GFR	28	ml/min/1.73m2	

RAASi dose reduction is just as harmful as RAASi discontinuation[1]

Risk of the composite outcome of progression to end stage kidney disease[a] and HF-related hospitalisations[b] was 51% with RAASi dose reduction and 55% with RAASi discontinuation compared to the risk with RAASi maintenance[c]



Change in RAASi following a hyperkalaemia event:

- Discontinued
- Down-titrated at least one of the RAASi types by at least 25%
- Maintained the same dose for all RAASi types or up-titrated their dose in any RAASi type

Risk in patients with HF

Note: An observational study that utilised the US EHR data in 15,488 adult patients with CKD Stage 3-4 and/or HF with an index hyperkalaemia event between July 2019 and September 2021. Hyperkalaemia defined using ICD-10-E87.5 or ICD-9-276.7 code. RAASi includes ACEi, ARB, ARNI, and MRA.

[a]Initiation of haemodialysis or a diagnosis of end stage kidney disease or CKD stage 5 in any position recorded in hospital, emergency, or outpatient setting; [b]Hospitalisations with HF and emergency visits for HF; [c]*P*<0.001 for each comparison. Adjusted for age, sex, history of hyperkalaemia, diabetes, HF, CKD including stage, and baseline use of ACEi, ARB, ARNi, and MRA, respectively. [d]Patients still at risk at follow-up day: discontinued, day 0, n = 3,223; day 90, n = 2,805; day 120, n = 2,044; down-titrated, day 0, n = 650; day 90, n = 557; day 120, n = 391; maintained, day 0, n = 5,922; day 90, n = 5,280; day 120, n = 3,800.

Kanda E, et al. *BMC Nephrol*. 2023;24(1):18.

Among patients with advanced and progressive chronic kidney disease, the discontinuation of RAS inhibitors was not associated with a significant difference in eGFR at 3 years

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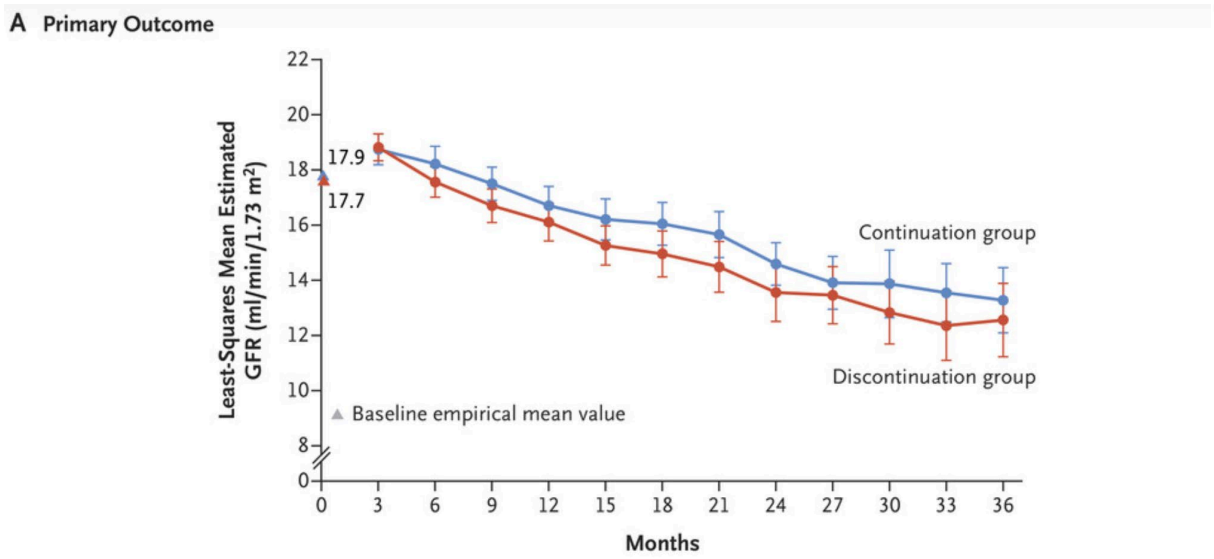
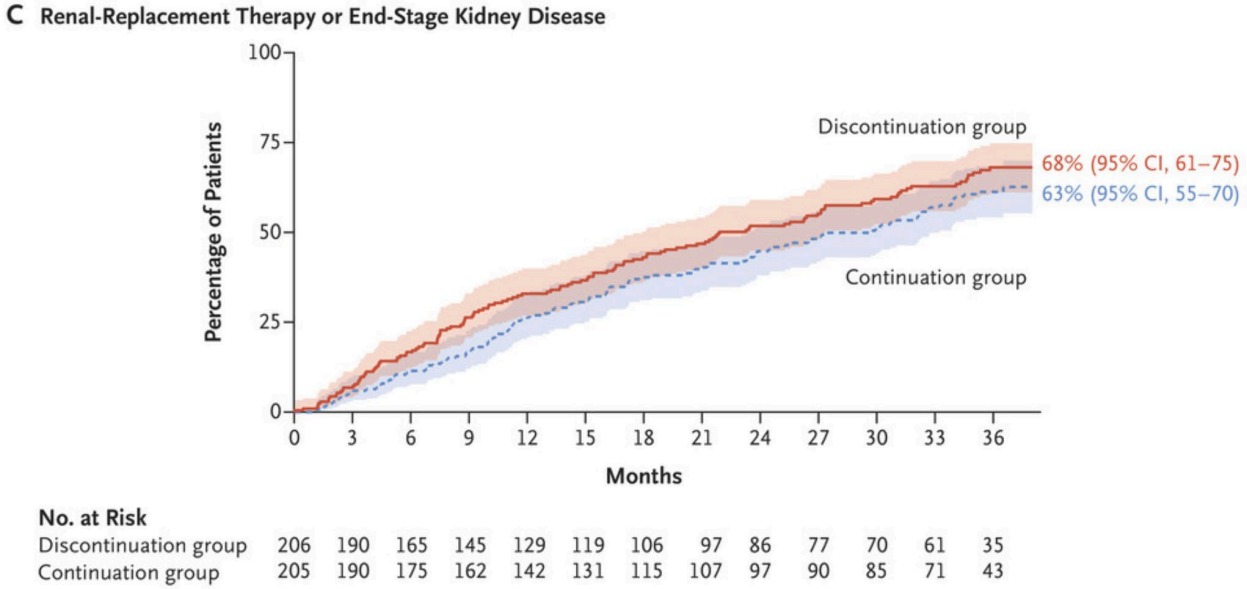
Renin–Angiotensin System Inhibition in Advanced Chronic Kidney Disease

Sunil Bhandari, Ph.D., Samir Mehta, M.Sc., Arif Khwaja, Ph.D., John G.F. Cleland, M.D., Natalie Ives, M.Sc., Elizabeth Brettell, B.Sc., Marie Chadburn, Ph.D., and Paul Cockwell, Ph.D., for the STOP ACEi Trial Investigators*





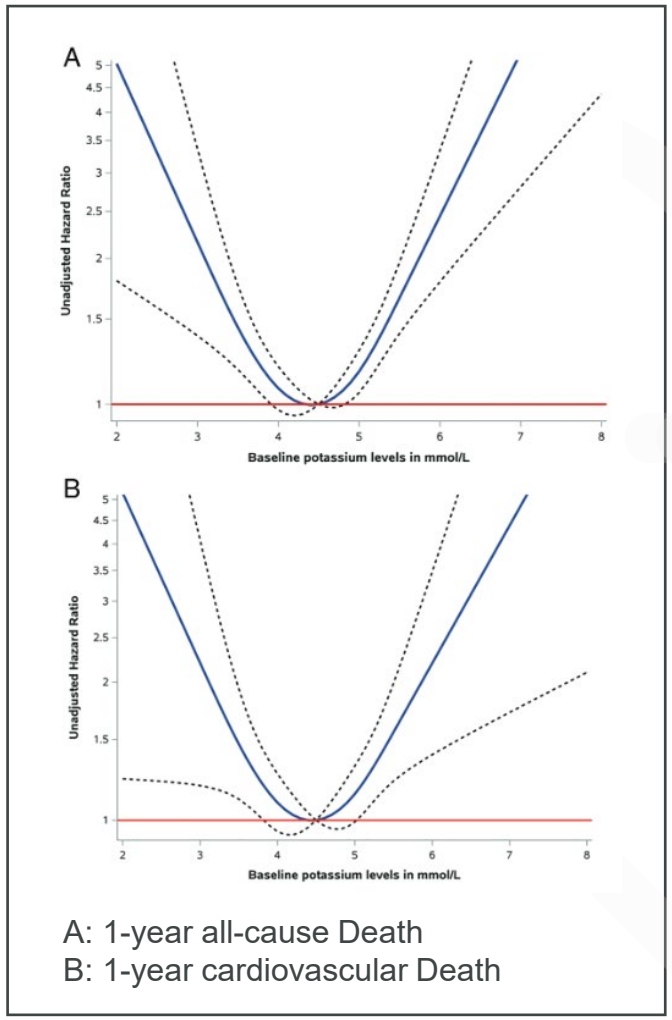
Seen in HF clinic 24 May 2022

- NTproBNP 5700
- BP 112/74
- HR 88 AF
- Fatigue, NYHA 2

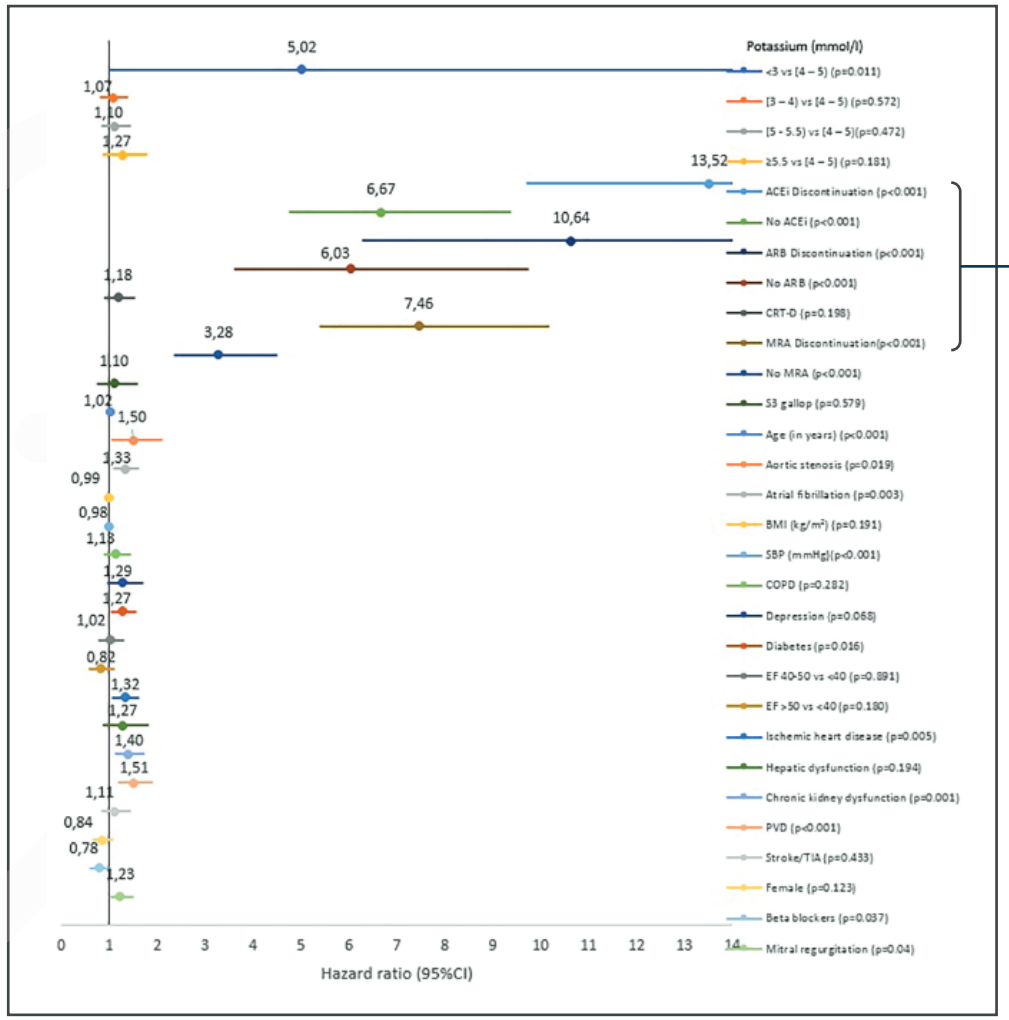
- HF Meds:
  - Bisoprolol 2.5mg bd
  - Eplerenone 25mg alternate day
  - Sacubitril/Valsartan 50mg bd
  - Dapagliflozin 10mg od
  - Furosemide 40mg PRN
  - No change of HF meds optimisation
  - Review in a few weeks' time

Electrolyte Profile (Authorised [A])				
Sodium	140	mmol/L		133-146
Potassium	5.3	mmol/L		3.5-5.3
Urea	**13.3**	**mmol/L**	**H**	**2.5-7.8**
Creatinine	**112**	**umol/L**	**H**	**58-110**
Estimated GFR	55	ml/min/1.73m2		

ESC-HFA-EORP Heart Failure Long-Term Registry[1]



A: 1-year all-cause Death
B: 1-year cardiovascular Death



Unravelling the interplay between hyperkalaemia, renin–angiotensin–aldosterone inhibitor use and clinical outcomes.

When adjusting for RAASi discontinuation, HK was no longer associated with mortality, suggesting that HK may be a risk marker for RAASi discontinuation rather than a risk factor for worse outcomes.

RAASi discontinuations
Strongest Predictor of all-cause and cardiovascular death, independent of serum potassium at baseline

1. P. Rossignol *et al. Eur J Heart Fail*, 2020;22(8):1378-1389.

ESC European Society of Cardiology

European Journal of Heart Failure (2022) **24**, 1467–1477
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POSITION PAPER

An international Delphi consensus regarding best practice recommendations for hyperkalaemia across the cardiorenal spectrum

James O. Burton[1]*, Andrew J.S. Coats[2], Csaba P. Kovesdy[3], Biff F. Palmer[4], Ileana L. Piña[5], Giuseppe Rosano[6], Manish M. Sood[7], and Shelley Zieroth[8]

Recommendations

Based on the results obtained, the authors offer the following recommendations:

1. Hyperkalaemia should be recognized as a predictable, treatable, and manageable side effect of optimal heart failure/chronic kidney disease therapy in people with a history or at high-risk of hyperkalaemia.
2. RAASi use should not be de-escalated or discontinued due to hyperkalaemia unless alternative measures of hyperkalaemia management have been optimized.
3. Novel K^+ binders should be the preferred agent to manage hyperkalaemia, and should be used to enable and maintain optimized RAASi therapy.
4. For high-risk individuals that are currently not hyperkalaemic, a thorough history is critical to inform preventative measures.
5. Closer cross-specialty collaboration would help optimize outcomes for individuals with cardiorenal disease. Clinical teams should be encouraged and supported to identify suitable methods to achieve this within their care setting.
6. Consistent treatment approach should be the goal of new and updated guidelines that support people with cardiorenal disease, and cross-specialty support should be sought for these to ensure aligned clinical practice.