

Clinical Pearls for management of End Stage Heart Disease

PCAND Meeting – December 12th, 2024

Dr. Lynn Straatman and Dr. Conor Barker

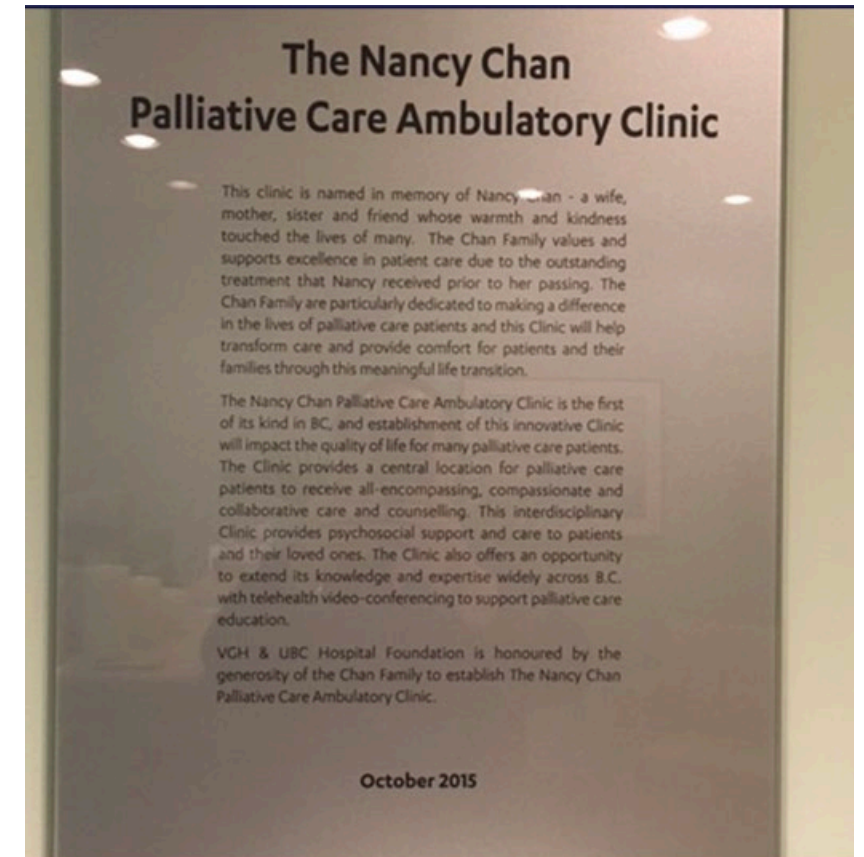
Vancouver Community Palliative Care Program, Nancy Chan Ambulatory Palliative Care Clinic

Case: Ms. CHF

- 83F with a history of HFpEF and severe mitral regurgitation
- Cardiac History:
 - Heart Failure Preserved Ejection Fraction (EF 77% Nov 2022)
 - Severe mitral regurgitation with mitral valve replacement in 2012, not candidate for repeat replacement (mitral mean gradient 10mmHg Nov 2022)
 - Bioprosthetic aortic valve replacement in 2002, repeat in 2012
 - Ischemic cardiomyopathy with CABG x1 in 2012
- Additional PMHx:
 - Cerebral vascular disease, MOCA 23/30, HTN, DLD, CKD, Hypothyroidism, Anxiety, Osteoporosis, Hearing Impairment, GERD

Referral to Palliative Care

- Cardiology clinic follow up Nov 2022
 - not a candidate for transcatheter or surgical intervention, referred for second opinion
 - Thought to be on maximal medical therapy
- Referred to ambulatory palliative care clinic Dec 2022 for symptom management (dyspnea and anxiety)



Initial palliative care clinic visit (Dec 2022)

- Lives with her husband in Vancouver, retired school teacher, supportive daughter who lives close by
- Multiple hospital admission the past 6 months for CHF
- Dyspnea on exertion and presyncope. Insomnia and anxiety. No dyspnea at rest, no chest pain, no palpitations.
- BP 94/68, HR 74 (reg), pansystolic murmur, JVP not elevated, no edema.
- Recent K+ 5.3, Cr 62 and eGFR 80
- GOC reviewed and agreeable to more of a symptom focused approach

Medication

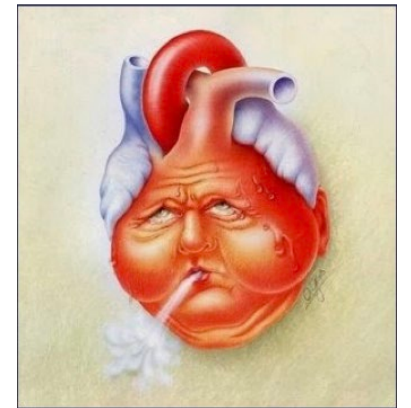
- Bisoprolol 2.5mg daily
- Furosemide 40mg in morning and 20mg in evening
- Potassium supplement 40mg daily
- Clopidogrel 75mg PO daily
- Levothyroxine 75 mcg qHS
- Aledronate 70mg PO weekly
- Pantoprazole 40mg daily
- Buspirone 5mg BID

Conclusion of this visit:

- Clopidogrel, Bisoprolol and potassium stopped.
- Hydromorphone 0.25mg PO qHS added (unable to do PRN)
- Consideration for Nitroglycerin 0.2mg/h patch
- Had been on prior but were inadvertently discontinued during last hospital stay and restarted in clinic
 - Mirtazapine 15mg PO qHS
 - Quetiapine 25mg PO qHS
- No CPR form signed

Ongoing In Clinic Follow up Issues (Jan – April 2023)

- Ongoing falls at home, found to be euvolemic so Furosemide decreased to 20mg daily.
- Admitted to hospital 2 weeks later for CHF and K⁺ 2.5, received IV Furosemide and K⁺ replacement. Discharged on Furosemide 40mg daily and 20mg PRN and potassium supplement, and increased Hydromorphone 0.5mg PO qHS.
- Ongoing fluid overload in clinic, switched to Bumetanide 1mg PO daily and added Hydromorphone 0.25mg PO q2h PRN.



- Fluctuating fluid status and new palpitations, Bumetanide dose adjusted between 1-2mg daily (Diuretic Action Plan with Bumetanide 1mg PO if weight increase >1kg) and Digoxin 0.0625mg added.
- Hydromorphone increased to 0.25mg PO TID and 0.5mg PO qHS with improvement in dyspnea
- Ongoing intermittent palpitations but HR noted to be irregular and 56-66bpm, so no further increase in Digoxin.

Transitions in Care (April 2023 – Oct 2023)

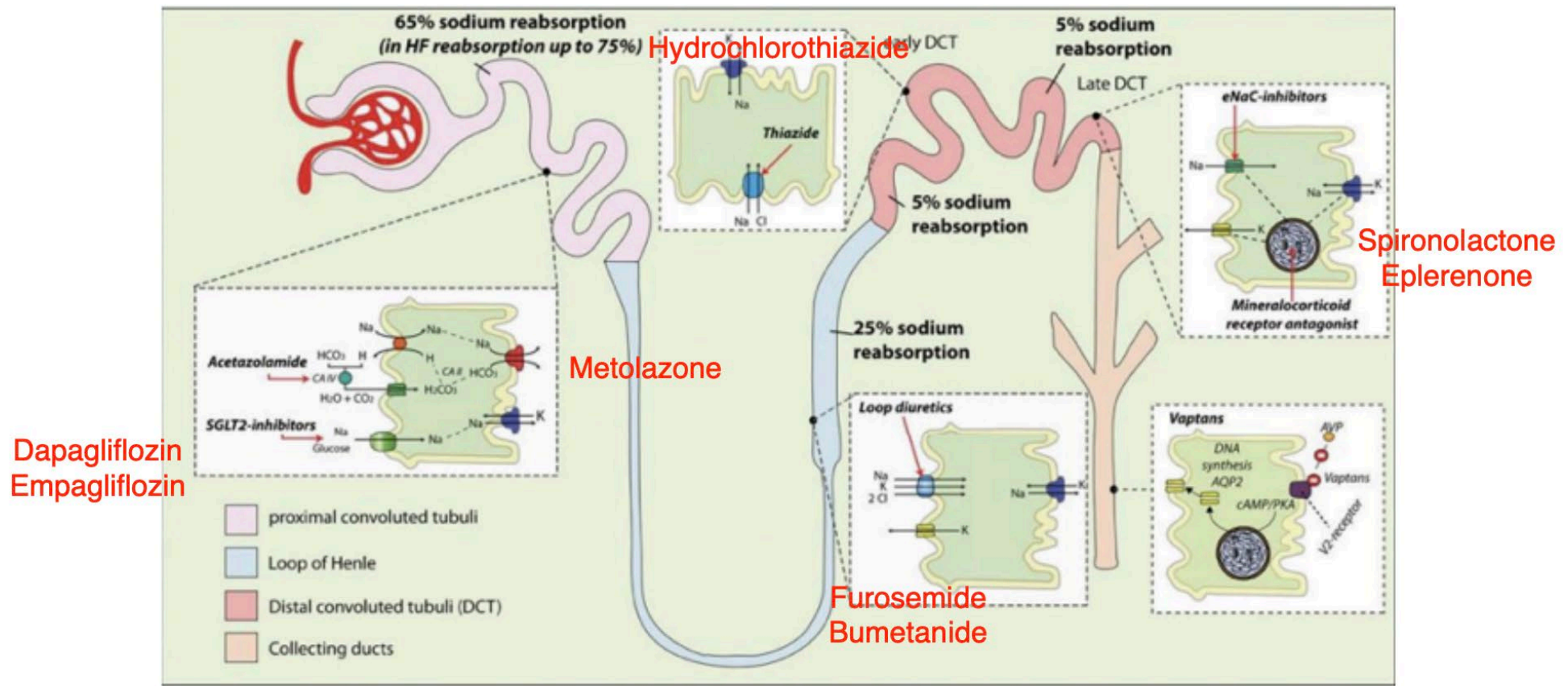
- April 2023 (Symptom Management – Reassessment for Surgery):
 - Cardiac Surgeon second opinion: discussed redo AVR and MVR, mortality risk ~10% and morbidity risk 50-60% with likelihood of requiring LTC if any complications.
 - She was not happy with QOL despite ongoing symptom management and decided to pursue surgery, booked for June 2023.
- May 2023 (ER Visit for increasing symptom burden):
 - Assessed in ED for dyspnea/palpitations, BNP >9000, treated with extra Bumetanide 0.5-1mg daily x1 week but BNP continues to increase (26,000).

Transitions in Care (April 2023 – Oct 2023)

- June 2023 (Back to Symptom Management only and EOL):
 - Despite BNP improving to 2600 and weight slowly improving with extra Bumetanide she was not felt to be a candidate for surgery anymore and procedure was cancelled.
- July-Sept 2023
 - Ongoing dyspnea/slow functional decline – continued on Bumetanide 1mg daily and 0.5mg PRN and Digoxin 0.0625mg daily, Hydromorphone reduced to 0.5mg BID.
- Oct 2023 (Transition from home to hospice)
 - Increased follow up at home by community palliative nurses as her function declined.
 - Admitted to hospice and died three days later.

Pharmacological Treatment of Volume Overload

- Diuretic therapy
- Vasodilators
 - ACE/ARB/ARNI
 - Nitroglycerin
 - PDE5 inhibitors



Loop Diuretics

Furosemide (Lasix), Bumetanide (Bumex)

- Highly protein-bound organic anions secreted across the proximal convoluted tubule where they act on sodium-potassium chloride channel in thick ascending loop of Henle to inhibit Na^+ reabsorption to promote delivery of Na^+ to distal tubule
- Steep dose-response curve and threshold dose below which they do not produce natriuresis
- “High ceiling” diuretics: progressive increase in their dose promotes more natriuresis but after certain maximal dose the effect plateaus

Loop diuretic resistance in HF

- Heavily protein-bound (> 90%) and requires sufficient plasma levels as renal perfusion is often reduced in HF, resulting in decreased secretion of loop diuretics.
- Also impacted by decreased plasma protein content in cachexia / malnutrition.
- Bioavailability is highly variable for oral furosemide and determined by gastrointestinal tract absorption, which is impaired by reduced cardiac output and bowel edema.
- Chronic use of loop diuretics induces compensatory distal tubular sodium reabsorption through tubular cell hypertrophy, leading to reduced natriuresis and need for progressive dose increase over disease course.

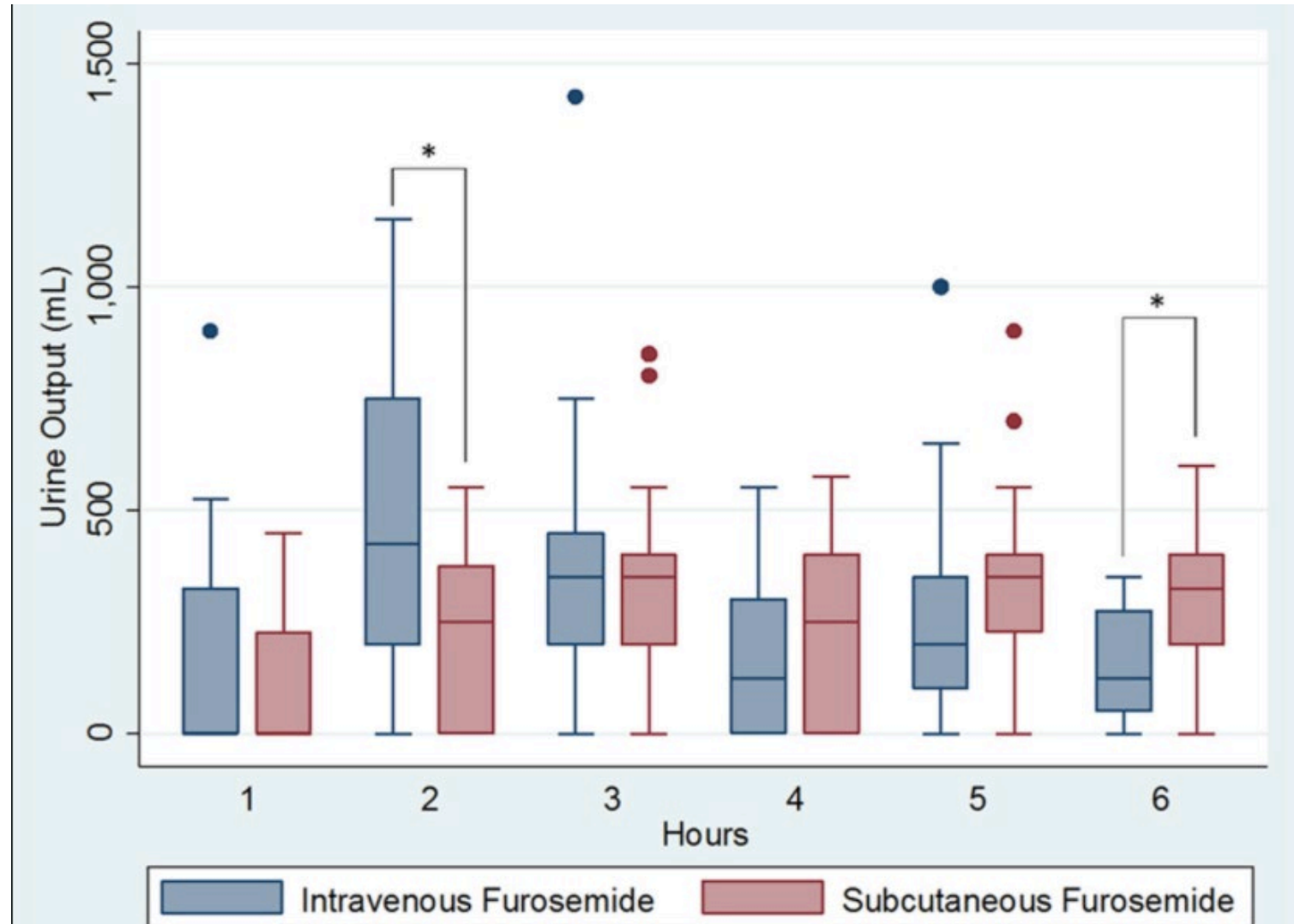
Furosemide vs. Bumetanide

Characteristics	Furosemide (Lasix)	Bumetanide (Bumex)
Half-life (hours)	1.5-2	1-1.5
Bioavailability	10-100	80-100
Initial oral dosing (mg)	20 - 40	0.5 – 1
Relative potency	40	1
IV to oral dosing	1:2	1:1 (IV not available in Canada)
Maximum dosing in 24 hours (mg)	600	10
Duration of effect (hours)	~ 6	4-6

Efficacy of Intravenous Furosemide Versus a Novel, pH-Neutral Furosemide Formulation Administered Subcutaneously in Outpatients With Worsening Heart Failure

JACC: Heart Failure

Volume 6, Issue 1, January 2018, Pages 65-70



Sodium-Glucose Linked Transporter-2 Inhibitors (SGLT2)

Empagliflozin (Jardiance), dapagliflozin (Farxiga), canagliflozin (Invokana).

- Inhibit proximal sodium absorption.
- Modest natriuretic effect of SGLT2 in addition to loop diuretics from glucosuric effect.
- Disease modifying therapeutic agent in symptomatic patients with chronic HFrEF.
- Decreases magnesium excretion and increased uric acid excretion and not known to worsen renal potassium excretion like loop diuretics.

Diuretic Class		Dose Range (daily)	Bioavailability	Onset of Action
Loop (Act on the loop of Henle)	Furosemide (Lasix)	20 - 360 mg	10 - 100%	PO - 30 -90 minutes IV - 30 -60 minutes SC - 30 - 90 minutes
	Bumetanide (Bumex)	1 - 8 mg	80 -100%	PO - 30 -90 minutes
Mineralocorticoid	Spironolactone	12.5 - 50 mg	60-90%	Up to 48 hours
	Eplerenone (Inspra)	12.5 - 50 mg	60-90%	Up to 4 weeks
Thiazide	Hydrochlorothiazide	12.5 - 25 mg	65-70%	1 to 5 hours
Other	Metolazone (Zaroxlyn)	2.5 - 10 mg		Does not work alone Needs to be given with Loop Diuretic
	Acetazolamide	250-375mg		1 to 2 hours

Nitrates

- Potential mechanisms
 - nitroglycerin increases the number of patent capillaries thereby improving microcirculation
 - may improve myocardial stress
 - Vasodilatory effect may
 - induce a substantial reduction in RV and LV filling pressures
 - decrease systemic and pulmonary vascular resistance, as well as lower systolic BP (SBP) which leads to a downward shift of the ventricular pressure and volume relationship, such that the same volume has lower filling pressures, and myocardial efficiency improves.

Heart Failure Discontinuation Strategy

- Discontinue drugs with only long term benefit (mortality)
 - Statins
 - Digoxin in sinus rhythm
 - Anticoagulant for atrial fibrillation depending on CHADS2VASC and goals
- Weigh advantages and disadvantages of continuing drug with medium term benefits (mortality/morbidity)
 - ACE/ARB/ARNI
 - Beta blockers
 - Spironolactone
 - SGLT2
 - Ivabradine (might consider continuing if can still swallow)
- Continue drugs for short term benefit (morbidity)
 - Diuretics
 - Digoxin/beta blockers in AF
 - anti-angina medications