Evaluation of Sacubitril/Valsartan Use in a Heart Function Clinic

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Background

- Sacubitril/valsartan was approved for the treatment of heart failure (HF) with reduced ejection fraction by Health Canada in 2015, shortly after publication of the PARADIGM-HF trial.
- The external validity of PARADIGM-HF has been largely criticized due to its strict inclusion criteria and long run-in period.
- Currently there is limited real-world data on the applicability and tolerability of sacubitril/valsartan.
- The purpose of this study was to characterize the real-world use of sacubitril/valsartan at the Heart Function Clinic (HFC) at Abbotsford Regional Hospital (ARH).

Objectives

Primary:

- Proportion of patients prescribed sacubitril/valsartan that meet the inclusion criteria of PARADIGM-HF, which include all of the following:
  - Age ≥18 years;
  - New York Heart Association (NYHA) class II-IV symptoms;
  - Left ventricular ejection fraction (LVEF) ≤40%;
  - Brain natriuretic peptide (BNP) ≥150 pg/mL (or ≥100 pg/mL if they had been hospitalized for HF within the last 12 months);
  - Angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) at stable dose (equivalent to at least enalapril 10 mg daily) for ≥4 weeks;
  - Beta-blocker (β-blocker) at stable dose for ≥4 weeks.

Secondary:

- Sacubitril/valsartan dose and titration, change in NYHA class on target/maximally tolerated dose, change in LVEF on target/maximally tolerated dose, number and type of adverse effects, rate of discontinuation and reason.

Methods

Design: retrospective chart review

Study period: July 2017 to March 2018

Population:

- *Inclusion:* adult (≥18 years of age) patients with HF on sacubitril/valsartan followed by the HFC
- *Exclusion:* patients discharged from the HFC before July 2017

Statistical Analysis: descriptive and paired t-test for means (p-value <0.05 considered statistically significant)

Results

Figure 1. Patient Flow Chart

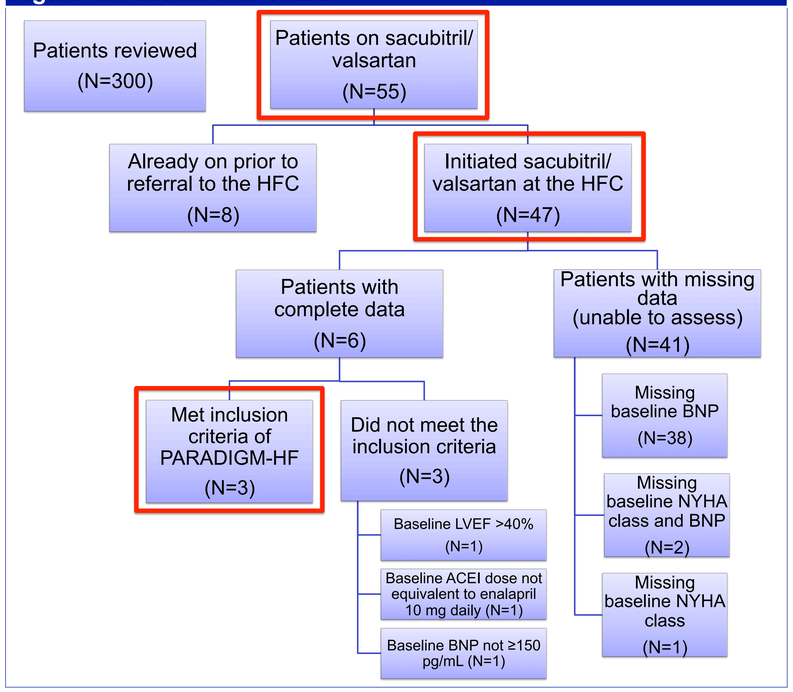


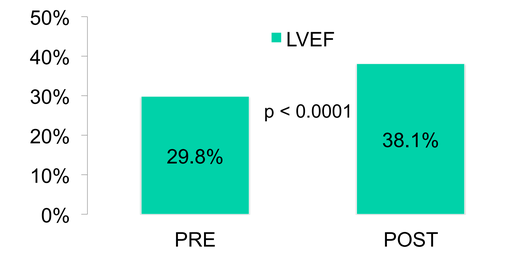
Table 1. Baseline Characteristics* (N=47)

Age (yr)	68.4 ± 11.4	**Comorbidities**	
Male	36 (77)	Hypertension	33 (70)
Baseline LVEF (%)	29.2 ± 8.5	Type 2 diabetes	10 (21)
Etiology of HF		Atrial fibrillation	17 (36)
Ischemic	23 (49)	Myocardial infarction	15 (32)
Non-ischemic	24 (51)	Stroke	7 (15)
Type of HF		Baseline BP (mmHg)	124/75
Reduced LVEF (≤40%)	41 (87)	Baseline eGFR (mL/min)	60.8 ± 17.1
No. of HF hospitalizations within 12 months	0.52	Baseline serum K^+ (mmol/L)	4.5 ± 0.4
NYHA class		**Baseline medications**	
I	4 (9)	On triple therapy	34 (72)
II	26 (55)	On ACEI/ARB	46 (98)
III	14 (30)	On β-blocker	47 (100)
Data missing	3 (6)	On MRA	34 (72)
		** n (%) or mean ± SD*	

Table 2. Sacubitril/Valsartan Dose and Titration (N=55)

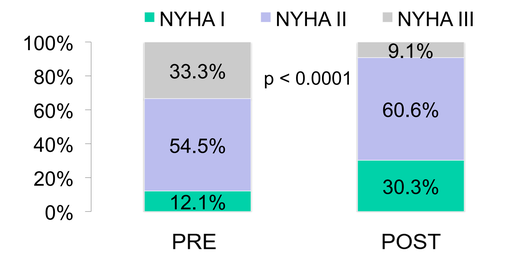
Mean starting dose	80 ± 31 mg PO BID
Mean achieved dose	175 ± 49 mg PO BID
Achieved target dose of 200 mg PO BID, n (%)	37 (67)
Still in titration phase, n (%)	8 (15)
Discontinued therapy, n (%)	5 (9)
Maximally tolerated dose <200 mg PO BID, n (%)	3 (5)
Deceased during titration, n (%)	2 (4)

Figure 2. Change in LVEF on Target/Maximally Tolerated Dose of Sacubitril/Valsartan (N=31)



Using paired t-test, change in EF is +8.3% (+4.4% to +12.1%)

Figure 3. Change in NYHA class on Target/Maximally Tolerated Dose of Sacubitril/Valsartan (N=33)



Using paired t-test, change in NYHA class is -0.4 (-0.2 to -0.6)

Table 3. Adverse Effects (N=55), n (%)

Any adverse effect	23 (42)
Hyperkalemia (>5.0 mmol/L)	17 (31)
Hypotension (SBP <100 mmHg, DBP <60 mmHg, or symptoms of dizziness)	14 (26)
Decrease in eGFR (30% increase in SCr)	10 (18)
Nausea	1 (2)
Down titration due to adverse effect	7 (13)
Hospitalization for adverse effect	1 (2)

Table 4. Reasons for Discontinuation (N=5), n (%)

Patient self-discontinued due to adverse effect	2 (40)
Patient non-adherent	1 (20)
Physician discontinued due to adverse effect (dizziness)	1 (20)
Physician discontinued, reason unknown	1 (20)

Limitations

- Retrospective design at a single centre with no comparator arm
- Short-term follow-up and small sample size
- Subjective assessment of NYHA class
- Potential underreporting of hospitalizations

Conclusions

- Only 6% (3/47) of patients met the PARADIGM-HF inclusion criteria, mostly due to lack of BNP assessment.
- 67% (37/55) of patients achieved the target dose of sacubitril/valsartan.
- 9% (5/55) of patients discontinued sacubitril/valsartan.
- Patients on target/maximally tolerated dose of sacubitril/valsartan had a significant improvement in NYHA class and LVEF.
- 42% (23/55) of patients experienced an adverse effect, but most did not lead to therapy discontinuation. Hyperkalemia, hypotension, and decrease in eGFR were common adverse effects.