ACC Rockies: Real World Evidence Applying Current Heart Failure Management to our Patients

Dr. Nadia Giannetti
Medical Director,
Heart Failure and Heart Transplant Centre
Chief of Cardiology,
McGill University Health Centre
Conflicts of interest

• Grants and research with
  – Novartis
  – Servier
  – Astra
  – Pfizer
  – Heart-ware
  – AbioMEd
Objectives

• To review “real world” data on management of heart failure patients
• The Canadian landscape
• Review of Qualify Survey on medical therapy for HFrEF patients in Canada
• Role of newer medical therapy including single centre experience with sacubitril/valsartan
The Burden of Heart Failure in Canada

Heart Failure is a growing epidemic:

- Heart Failure is on the rise in Canada.
- 600,000 Canadians are living with Heart Failure.
- 50,000 Canadians are diagnosed each year with Heart Failure.
- 1 in 2 Canadians has been touched by Heart Failure.
- Heart Failure costs more than $2.8 billion per year.

Heart Failure costs everyone:

- Heart Failure patients have long and frequent hospital stays.
- There is no cure for Heart Failure.
- Heart Failure patients are complex, often managing other conditions.
- Heart Failure patients experience shortness of breath, exhaustion, and swelling.
- Heart Failure caregivers are often overwhelmed and stressed.
Canadian Landscape

• Large country with large rural population
• Mostly family MD provided care with consultative support by specialists
• Care is fragmented and variable across the country
• Only 15% access HF clinic or disease management programs
  – These are mostly younger patients
Canadian Landscape

Physician Follow-Up After Hospital Discharge: Progress in Meeting Best Practices

Types of Care
Figure 1: Crude 7- and 30-Day Physician Follow-Up Rates by Patient Group and Province, 2010–2011 to 2012–2013

Notes
AMI: Acute myocardial infarction.
HF: Heart failure.
COPD: Chronic obstructive pulmonary disease.
All Medical and Surgical Patients includes those with AMI, HF and COPD.

Sources
Canadian Landscape

Factors Associated With Follow-Up Rates

Some factors showed a consistent pattern of influence on follow-up rates. Lower follow-up rates were seen in patients who:

- Lived in lower-income neighbourhoods
- Lived in rural areas
- Were discharged from community hospitals (versus teaching hospitals)
Access to HF Clinics

• One-year follow-up > 2,000 hospitalizations, Canadian metro hospitals
  – 13% seen in HF Clinic
  – Cohort seen were younger, lower risk, more likely to see Cardiology and visit other disease clinics

THIS = RISK TREATMENT MISMATCH
Four Key Emerging Themes
Challenging HF Care in Canada

A qualitative study of the current state of heart failure community care in Canada: what can we learn for the future?

Sean M. Hayes¹, Sophie Peloquin¹†, Jonathan G. Howlett²†, Karen Harkness³†, Nadia Giannetti⁴†, Carol Rancourt⁵† and Nancy Ricard⁴†
QUALIFY survey

• International survey of over 7000 patients with heart failure and EF under 35%
• 129 patients Canadian cohort
• 13 centres with heart failure clinics
• Patients are consecutive
• Data collection started in 2012

Giannetti CCC 2015
Objectives

• To evaluate adherence to heart failure guidelines by measuring prescription modalities of recommended evidence-based heart failure medications
• To analyze the reasons for non-adherence

The impact of degree of adherence on clinical outcomes will be assessed at 18 months
Canadian Guideline recommendations

Diuretics to relieve congestion

ACE inhibitor (if intolerant to ACE inhibitor then ARB) + β-blocker

Titrate to target doses or maximum tolerated evidence-based dose

NYHA class II - IV

YES

Add MRA (eplerenone/spironolactone); if intolerant consider ARB

NYHA class II - IV

YES

NO

Continue routine disease management follow-up

NO

Consider digoxin, hydralazine/nitrates

CCS2012 Guidelines on Heart failure
## Baseline characteristics (1)

<table>
<thead>
<tr>
<th></th>
<th>Total N=7092</th>
<th>Canada N=129</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean age, years (SD)</strong></td>
<td>63.1 (12.5)</td>
<td>66.6 (13.4)</td>
</tr>
<tr>
<td>Mean age in West Europe, North America, Australia</td>
<td>67.5 (12.4)</td>
<td></td>
</tr>
<tr>
<td>Mean age in Central and Eastern Europe</td>
<td>62.7 (11.3)</td>
<td></td>
</tr>
<tr>
<td>Mean age in Asia</td>
<td>59.2 (13.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Male, %</strong></td>
<td>74</td>
<td>68.2</td>
</tr>
<tr>
<td><strong>Caucasian, %</strong></td>
<td>57.9</td>
<td>87.6</td>
</tr>
<tr>
<td><strong>Asian, including Middle East population, %</strong></td>
<td>29.8</td>
<td>4.7</td>
</tr>
<tr>
<td><strong>Mean heart failure duration, years (SD)</strong></td>
<td>4 (4.8)</td>
<td>3.3 (4.7)</td>
</tr>
<tr>
<td><strong>Mean time since last heart failure hospitalization, months (SD)</strong></td>
<td>6.3 (2.9)</td>
<td>6.2 (2.8)</td>
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## Baseline characteristics (2)

<table>
<thead>
<tr>
<th></th>
<th>Total N=7092</th>
<th>Canada N=129</th>
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</thead>
<tbody>
<tr>
<td>Mean systolic blood pressure, mm Hg (SD)</td>
<td>126.5 (20.3)</td>
<td>116.6 (21.5)</td>
</tr>
<tr>
<td>Mean diastolic blood pressure, mm Hg (SD)</td>
<td>76.2 (12.4)</td>
<td>67.1 (12.0)</td>
</tr>
<tr>
<td>Mean resting heart rate, bpm (SD)</td>
<td>76.4 (14.4)</td>
<td>75.4 (15.8)</td>
</tr>
<tr>
<td>Sinus rhythm / Sinus rhythm, HR≥70 bpm, %</td>
<td>74.1/66</td>
<td>71/61</td>
</tr>
<tr>
<td>Mean ejection fraction*, % (SD)</td>
<td>31.9 (7.0)</td>
<td>26.4 (8.5)</td>
</tr>
<tr>
<td>I/ II/ III/ IV NYHA class, %</td>
<td>13 / 46 / 36 / 6</td>
<td>19 / 61 / 21 / 0</td>
</tr>
<tr>
<td>Ischemic heart disease, %</td>
<td>57.1</td>
<td>40.5</td>
</tr>
<tr>
<td>Previous myocardial infarction, %</td>
<td>46.3</td>
<td>38.1</td>
</tr>
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</table>

* At the most recent echocardiography, within 2 years

Presented at CTU session, 24 May 2015, at HF congress, Seville, Spain
## Baseline characteristics (3)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Total N=7092</th>
<th>Canada N=129</th>
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</thead>
<tbody>
<tr>
<td>Diabetes mellitus, %</td>
<td>34.3</td>
<td>40.5</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>64.6</td>
<td>70.6</td>
</tr>
<tr>
<td>Atrial fibrillation, flutter, %</td>
<td>28.7</td>
<td>42.1</td>
</tr>
<tr>
<td>Peripheral artery disease, %</td>
<td>9.5</td>
<td>4</td>
</tr>
<tr>
<td>Stroke or TIA, %</td>
<td>11</td>
<td>12.7</td>
</tr>
<tr>
<td>Chronic kidney disease, %</td>
<td>17.8</td>
<td>32.5</td>
</tr>
<tr>
<td>Asthma or COPD, %</td>
<td>14.1</td>
<td>27.7</td>
</tr>
<tr>
<td>Mean serum creatinine *, µmol/L (SD)</td>
<td>110.3 (71.5)</td>
<td>128.6 (101.7)</td>
</tr>
<tr>
<td>Median outpatient values BNP*, pmol/L, [Q1;Q3]</td>
<td>113.1 [39.0;235]</td>
<td>129.2 [42.9;226.4]</td>
</tr>
<tr>
<td>Median outpatient values NTproBNP*, (pmol/L), [Q1;Q3]</td>
<td>232.5 [90.4;482.6]</td>
<td>127.6 [86.6;265.9]</td>
</tr>
</tbody>
</table>

* Laboratory data within the last 12 months
Use of Guideline-recommended Therapies - Canada

Patients treated with ACEIs or ARBs = 86.8%

ACEIs

- Contraindicated: 41.7%
- Not tolerated: 44.4%

Reasons:
- Cough: 12.9%
- Hypotension: 6.5%
- Worsening renal function: 41.9%
- Hyperkalemia: 3.2%
- Other reasons: 38.7%

Patients at TD*: 30.9%
- Patients at ≥ 50% TD: 76.4%

Patients treated with ARBs

- Not indicated: 91.7%
- Contraindicated: 3.7%
- Not tolerated: 3.7%

Reasons:
- Hypotension: 12.5%
- Worsening renal function: 75%
- Cough: 12.5%
- Hyperkalemia: 0%
- Other reasons: 12.5%

Patients at TD*: 0%
- Patients at ≥ 50% TD: 42.9%
Use of Guideline-recommended Therapies - Canada

Patients treated with beta-blockers = 95.3%

<table>
<thead>
<tr>
<th>Reason</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Not indicated</td>
<td>50%</td>
</tr>
<tr>
<td>Contraindicated</td>
<td>0%</td>
</tr>
<tr>
<td>Not tolerated</td>
<td>50%</td>
</tr>
<tr>
<td>Asthma/COPD worse</td>
<td>0%</td>
</tr>
<tr>
<td>Hypotension</td>
<td>0%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>33.3%</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>0%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>0%</td>
</tr>
<tr>
<td>Other reasons</td>
<td>66.6%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients at TD*</th>
<th>34.4%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients at ≥ 50% TD</td>
<td>69.9%</td>
</tr>
</tbody>
</table>
Use of Guideline-recommended Therapies – Canada

Patients treated with MRAs = 50%

<table>
<thead>
<tr>
<th>Reason</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Not indicated</td>
<td>81.5%</td>
</tr>
<tr>
<td>Contraindicated</td>
<td>13.8%</td>
</tr>
<tr>
<td>Not tolerated</td>
<td>4.6%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reason</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal dysfunction</td>
<td>66.7%</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>33.3%</td>
</tr>
<tr>
<td>Gynecomastia</td>
<td>0%</td>
</tr>
<tr>
<td>Other reasons</td>
<td>0%</td>
</tr>
</tbody>
</table>

| Patients at TD*         | 58.7%      |
| Patients at ≥ 50% TD    | 100%       |
Calculation of adherence to guidelines score

- The ratio of actual/theoretical number of recommended classes of treatment, taking into account the individual patient’s profile, including contraindication, non-indication, or intolerance.

- Based on the use of ACE inhibitors or ARBs, beta-blockers, mineralocorticoid receptor antagonists, and ivabradine.

- Score ranges from 0 (very poor) to 1 (excellent).
Adherence to Guidelines Score

- **Poor adherence** (score ≤ 0.5): use of ≤ 50% of indicated medications in eligible patients
- **Moderate adherence** (0.5 < score < 1): use of more than half of indicated medications in eligible patients
- **Good adherence** (score = 1): use of all indicated medications in eligible patients

- Poor: 5.4%
- Moderate: 34.1%
- Good: 60.5%
Adherence to Guidelines Score - All

Poor adherence (score ≤ 0.5): use of ≤ 50% of indicated medications in eligible patients

Moderate adherence (0.5 < score < 1): use of more than half of indicated medications in eligible patients

Good adherence (score = 1): use of all indicated medications in eligible patients
Adherence to guidelines score by geographic zone

P<0.001

<table>
<thead>
<tr>
<th>Region</th>
<th>Good (%)</th>
<th>Moderate (%)</th>
<th>Poor (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Western Europe + North America + Australia, n=1411</td>
<td>71</td>
<td>24</td>
<td>5</td>
</tr>
<tr>
<td>Asia, n=1283</td>
<td>70</td>
<td>19</td>
<td>11</td>
</tr>
<tr>
<td>Central + Eastern Europe, n=3117</td>
<td>61</td>
<td>29</td>
<td>9</td>
</tr>
<tr>
<td>Rest of the world, n=1197</td>
<td>71</td>
<td>22</td>
<td>7</td>
</tr>
<tr>
<td>Canada</td>
<td>60.5</td>
<td>34.1</td>
<td>5.4</td>
</tr>
</tbody>
</table>

Legend: Good, Moderate, Poor
Therapy in HFrEF

• Benefits of drugs and devices in HFrEF
  – ACEi/ARB
  – Beta blockers
  – Mineralocorticoid receptor inhibitors
  – Cardiac resynchronization therapy
  – Implanted cardioverter/defibrillator

However, 5 yr mortality remains ~50%
Therapeutic Approach To Patients With HF And Reduced Ejection Fraction

PATIENT WITH LVEF < 40%

Triple Therapy
ACEi (or ARB if ACEi intolerant), BB, MRA
Titrate to target doses or maximum tolerated evidence-based dose

NYHA I
Continue triple therapy

NYHA II-IV
SR, HR ≥ 70 bpm
ADD Ivabradine and SWITCH ACEi or ARB to Sacubitril/Valsartan for eligible patients

NYHA II-IV
SR with HR < 70 bpm or AF or pacemaker
SWITCH ACEi or ARB to Sacubitril/Valsartan for eligible patients

NYHA I or LVEF < 35%
Continue present management

NYHA I-III and LVEF ≤35%
refer to ICD/CRT algorithm

NYHA IV
Consider:
• Hydralazine/nitrates
• Referral for advanced HF therapy (mechanical circulatory support/transplant)
• Advance HF referral

Reassess every 1-3 years or with clinical status change
Consider LVEF reassessment every 1-5 years
Reassess as needed according to clinical status

Patients at risk at the baseline visit (HR ≥ 75 bpm)

- 31.3% patients with HR ≥ 75 bpm
- 25.8% patients with NYHA class II, III or IV, HR ≥ 75 bpm
- 13.3% patients with NYHA class II, III or IV, HR ≥ 75 bpm, In sinus rhythm
- 11.7% patients with NYHA class II, III or IV, HR ≥ 75 bpm, In sinus rhythm, Ejection fraction ≤35%
Sacubitril/valsartan: McGill UHC experience

• Since the addition of Sacubitril/Valsartan to the market, its use has been mostly limited to specialized heart failure clinics

• Single centre, retrospective, descriptive study, evaluating our patients outcomes, currently on Sacubitril/Valsartan

• Goal to evaluate our 1 year clinical experience, beginning December 2015
Parameters

- Tolerance / Reasons for non-tolerance
- Electrolyte and creatinine levels
- Blood pressure measurements
- Maximal tolerated dose
- Diuretic trends
- Quality of life
- Left ventricular ejection fraction
- Data on patients with 6 month follow-up, primary event or max dose tolerated
- PRELIMINARY data
Demographics

- 140 patients
- Avg age: 62 yo
- Ischemic cardiomyopathy: 72 (51%)
- Avg EF: 25%
- Female: 30 (21%)
- Baseline
  - NYHA 2: 101 (72%)
  - NYHA 3: 35 (28%)
Initial Dosage

• 50 (36%) patients initiated on medium dose
• Of these 50, 39 (78%) tolerated it well, 4 (8%) did not, and had to lower or discontinue the medication
• 4 patients initiated on high dose and all tolerated it well
Discontinuation

• 9 patients discontinued + 2 stopped due to transplant
• 3 transiently held and restarted on future follow up visits
• Of 9 that discontinued:
  – 2 Symptomatic hypotension
  – 1 Dizziness (with a normal BP)
  – 1 Significant acute kidney injury
  – 1 Worsening NYHA

Other:
  – 1 depressive symptoms, history of depression
  – 1 liver cirrhosis
  – 1 PMR stopped all meds
  – 1 died of pneumo sepsis
Renal Function

• 1 Patient with normal GFR had acute kidney injury and med stopped

• 26 patients, with at least a baseline moderate reduction in GFR
  – 11 patients initially stage 3a (GFR 45-59 mL/min/1.73 m²)
    • 3 increased to stage 2, 3 remained class 3a, and 2 decreased to 3b
  – 13 patients stage 3b (GFR 30-44 mL/min/1.73 m²)
    • 8 remained in class 3b, while 3 decreased to stage 4
  – 2 patients stage 4 (GFR 15-29 mL/min/1.73 m²).
    • both improved to stage 3b
Triple Therapy

• 79 patients (56%) on triple therapy (ACEI/ARB, beta blocker and MRA) prior to initiation of Sacubitril/Valsartan. Intolerance to MRA main reason for not being on triple therapy

• Only 4 patients on maximal dose of triple therapy prior to starting Sacubitril/Valsartan. Reaching maximal triple therapy doses mainly limited by tolerance of MRA’s
Diuresis

- 23 patients (16%) had their dose of Furosemide decreased at follow-up visits
- 17 patients (12%) had their diuresis doses increased
- 81 patients (58%) remained on the same dose
Blood Pressure

• 19 patients initiated on Sacubitril/Valsartan with a systolic blood pressures of less than or equal to 100mmHg

• 15 of these patients (79%) tolerated Sacubitril/Valsartan
  – 10 of them had their Sacubitril/Valsartan dose increased over the following visits.
Quality of Life

• Upon each visit, clinical notes reviewed, if the patient felt better, the same, or worse since initiating Sacubitril/Valsartan
  – 77 patients (55%) felt better
  – 31 (22%) felt the same
  – 13 (9%) felt worse
  • 7 patients discontinued Sacubitril/Valsartan (shown previously)
  • 6 patients remained on medication
    – experienced continued shortness of breath, mild congestion or weight gain
    – a case of low blood pressure with symptomatic dizziness,
    – a case of dizziness with normal blood pressure
    – worsened NYHA status
LVEF

- 31 patients had a repeat echocardiogram
- 13 patients had an improved LVEF (reader not involved in clinical care) (>10% absolute difference in EF)
  - 7/13 on maximal dose of Sacubitril/Valsartan at the time of the repeat echocardiogram. The remaining on medium dose.
More advanced HF patients

• Cardiac Transplantation/VAD
  – 17 patients initiated on S/V on list or being considered for tx/VAD
  – 4 of these patients were deactivated from the transplant list/VAD consideration due to improved clinical status
Preliminary data summary

• Important limitations:
  – Descriptive and retrospective
  – QOL subjective
  – Incomplete data collection

• Overall medication is well tolerated and beneficial for many of our patients
With each acute event, myocardial injury may contribute to progressive LV dysfunction\(^2\)

Increasing frequency of acute events with disease progression leads to high rates of hospitalization and increased risk of mortality\(^2\)
Summary

- HF care in Canada is a rising health care burden for Canadians
- Care is unstructured and fragmented
- Canadian real world data show important limitations in care of HF patients
- There is a role for newer therapies in management of our patients