PASCAR Heart Failure Task Force Research Workshop

Agenda

- Welcome
- PASCAR Heart Failure Task Force Agenda 2016-2018
- Update on the finalization of the PASCAR Heart failure book and launch
- Nurse-IT Study
- The Inter-CHF Global Registry
- SHARE-Cardiac Disease in Maternity II study
- Conclusion
The Heart of Africa
Profile of an evolving burden of communicable & non-communicable heart disease

Editors:
Simon Stewart, Karen Sliwa, Albertino Damasceno & Ana Mocumbi
NURSE-IT

NURSE-led and Information-Technology-guided heart failure management in Africa (NURSE IT)
**Study Design**

- The study design is a multi-center, parallel-group, randomized controlled trial.
- 500 patients will be randomized into one of two groups

**Study Sites**

Multi-center study (+- 10 site in southern, eastern, central, and western regions of sub-Saharan Africa).
Primary Endpoint
The primary objective is to assess whether a focused, nurse-led intervention delivered over 6 months will prolong the patient-centered outcome of days alive and out-of-hospital (all-cause) during 180 days follow-up after discharge from an acute HF admission

Secondary Endpoints
- Reduced risk of CV-related and all-cause mortality.
- Reduced rate of hospital admission and related hospital stay (HF-specific, CV-specific and all-cause)
- Improvement in HF-specific and general health-related quality of life from baseline to 6 months.
- Reduction in risk of death or readmission (all-cause) as a timed endpoint during 180 follow-up.
- Improvement in symptoms and signs of HF from pre-discharge to 6 months.

Surrogate Endpoint
To establish medication adherence by testing of hair samples and blood spot drug assays.
Exclusion Criteria

1. Acute coronary syndrome, including ST and non-ST elevation myocardial infarction.

2. Severe known renal failure (patients on dialysis or creatinine > 2.5 mg/dL), nephrotic syndrome, or hepatic failure or other cause of hypoalbuminemia.

3. Uncertainty about the ability to complete follow up for reasons including (but not limited to) alcoholism, severe drug abuse, homelessness, other terminal illnesses, distance, illiteracy, family influence, etc.

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Global Congestive Heart Failure (G-CHF) Study

**Coordinating Center**
Population Health Research Institute, McMaster University, Hamilton, Canada

**Co-Principal Investigators**
Salim Yusuf, MBBS, PhD
Hisham Dokainish, M.D

**G-CHF Executive Committee**

- **Africa:** Karen Sliwa, MD, PhD
- **Asia:** Ambuj Roy, MD (India), Jun Zhu, MD (China)
- **Canada:** Salim Yusuf, MBBS, DPhil, Koon Teo, MBBS, PhD, Robert McKelvie, MD, PhD, Hisham Dokainish, MD
- **Europe:** John McMurray, MD, Keith Fox, MA, MPhil, PhD, Aldo Maggioni, MD, Faiez Zannad, MD, PhD, Stefan Anker, MD, PhD, Andrej Budaj, MD
- **Middle East:** Khalid AlHabib, MD
- **South America:** Andres Orlandini, MD
- **USA:** Gregg Fonarow, MD, Kelley Branch, MD, MSc
Why Another HF Registry?

- There is scant information on HF from many areas of the world (non-Western countries).
- Reasons underlying potential regional variations in HF treatments and outcomes globally not well explained.
- Most prior registries are descriptive.
- Did not adequately explore HF pathophysiology.

"Pathways": Genes $\rightarrow$ mRNA(proteins) $\rightarrow$ bio-markers $\rightarrow$ primary organ dysfunction $\rightarrow$ secondary pathways and further dysfunction $\rightarrow$ Poor outcomes.

- Impact of co-morbidities and other factors.
- Impact at both the clinical and pathophysiological levels.
Heart failure in low- and middle-income countries: Background, rationale, and design of the INTERnational Congestive Heart Failure Study (INTER-CHF)

Hisham Dokainish, MD, Koon Teo, MBCh, PhD, Jun Zhu, MD, Ambuj Roy, MD, Khalid Al-Habib, MD, Ahmed ElSayed, MD, Lia Palileo, MD, Patricio Lopez Jaramillo, MD, Kamilu Karaye, MD, Khalid Yusoff, MD, Andres Orlandini, MD, Karen Sliwa, MD, Charles Mondo, MD, Fernando Lanas, MD, Prabhakar Dorairaj, MD, Mark Huffman, MD, Amr Badr, MD, Mohamed Elmaghawry, MD, Albertino Damasceno, MD, Emilie Belley-Cote, MD, Karen Harkness, RN, PhD, Alex Grinvalds, BSc, Robert McKelvie, MD, PhD, and Salim Yusuf, MD, DPhil Ontario, Canada

(Am Heart J 2015;170:627-634.e1.)

Heart Failure in Africa, Asia, the Middle East and South America: The INTER-CHF study

Hisham Dokainish a,⁎, Koon Teo a, Jun Zhu b,⁎, Ambuj Roy c, Khalid F. AlHabib d, Ahmed ElSayed e, Lia Palileo-Villaneuva f, Patricio Lopez-Jaramillo g, Kamilu Karaye h,⁎, Khalid Yusoff i,⁎, Andres Orlandini j, Karen Sliwa k, Charles Mondo l, Fernando Lanas m, Dorairaj Prabhakaran n, Amr Badr o, Mohamed Elmaghawry p, Albertino Damasceno q, Kemi Tibazarwa r, Emilie Belley-Cote a, Kumar Balasubramanian a, Magdi H. Yacoub o,⁎, Mark D. Huffman s, Karen Harkness a, Alex Grinvalds a, Robert McKelvie a, Salim Yusuf a.

On behalf of the INTER-CHF Investigators (Appendix 1):

International Journal of Cardiology 204 (2016) 133–141
Design

- Prospective cohort study
- Patients:
  - Consecutive HF patients
  - 2/3 outpatients and 1/3 hospital inpatients, >18 yrs
  - Clinical diagnosis of HF
- 108 sites in 16 countries
- 5823 HF patients recruited Nov 2012 to Feb 2014
- Follow-up: 1 year; visits at 6 and 12 months
## Baseline Characteristics

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<th></th>
<th>Africa N=1294</th>
<th>China N=991</th>
<th>India N=858</th>
<th>Middle East N=1000</th>
<th>SE Asia N=811</th>
<th>South Am n=869</th>
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<tbody>
<tr>
<td><strong>Age (years, SEM)</strong></td>
<td>53 (0.4)</td>
<td>66 (0.5)</td>
<td>56 (0.5)</td>
<td>56 (0.5)</td>
<td>57 (0.5)</td>
<td>67 (0.5)</td>
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<td><strong>BMI (g/m², SEM)</strong></td>
<td>26 (0.2)</td>
<td>24 (0.2)</td>
<td>23 (0.2)</td>
<td>30 (0.2)</td>
<td>26 (0.2)</td>
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<td><strong>NYHA class III/VI (%)</strong></td>
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<td>56</td>
<td>50</td>
<td>37</td>
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<td>32</td>
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<td><strong>Illiterate (%)</strong></td>
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<td>15</td>
<td>29</td>
<td>36</td>
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<td>4</td>
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<td><strong>Rural (%)</strong></td>
<td>42</td>
<td>44</td>
<td>48</td>
<td>26</td>
<td>37</td>
<td>21</td>
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<td><strong>Recruited as Clinic Outpatient (%)</strong></td>
<td>52</td>
<td>65</td>
<td>55</td>
<td>69</td>
<td>77</td>
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## Risk Factors

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<tr>
<td>Hypertension (%)</td>
<td>62</td>
<td>52</td>
<td>49</td>
<td>69</td>
<td>76</td>
<td>74</td>
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<tr>
<td>Diabetes Mellitus (%)</td>
<td>17</td>
<td>19</td>
<td>26</td>
<td>57</td>
<td>41</td>
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<td>Chronic Kidney Disease (%)</td>
<td>4</td>
<td>6</td>
<td>3</td>
<td>12</td>
<td>13</td>
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<tr>
<td>Prior Stroke (%)</td>
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<td>14</td>
<td>3</td>
<td>3</td>
<td>13</td>
<td>4</td>
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<td>History of MI (%)</td>
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<td>16</td>
<td>23</td>
<td>19</td>
<td>29</td>
<td>18</td>
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<td>CHF Hosp. in Past year (%)</td>
<td>36</td>
<td>34</td>
<td>14</td>
<td>22</td>
<td>35</td>
<td>28</td>
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<tr>
<td>Hemoglobin (g/L, SEM)</td>
<td>119 (1)</td>
<td>130 (1)</td>
<td>116 (1)</td>
<td>126 (1)</td>
<td>129 (1)</td>
<td>131 (1)</td>
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<tr>
<td>ECG - Atrial Fibrillation (%)</td>
<td>17</td>
<td>25</td>
<td>11</td>
<td>12</td>
<td>22</td>
<td>22</td>
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<tr>
<td>Preserved LVEF (&gt;50%) (%)</td>
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<td>48</td>
<td>31</td>
<td>11</td>
<td>44</td>
<td>30</td>
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<tr>
<td>Valve Disease (%)</td>
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<td>41</td>
<td>42</td>
<td>50</td>
<td>40</td>
<td>48</td>
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<tr>
<td>Medications</td>
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<td>Beta Blocker (%)</td>
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<td>60</td>
<td>57</td>
<td>85</td>
<td>66</td>
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<td>ACEi/ARB (%)</td>
<td>78</td>
<td>64</td>
<td>68</td>
<td>82</td>
<td>73</td>
<td>76</td>
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<td>Aldosterone Inhibitor (%)</td>
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<td>56</td>
<td>47</td>
<td>46</td>
<td>27</td>
<td>55</td>
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<td>Diuretic (%)</td>
<td>94</td>
<td>61</td>
<td>81</td>
<td>88</td>
<td>45</td>
<td>78</td>
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<td>Digoxin (%)</td>
<td>32</td>
<td>29</td>
<td>25</td>
<td>18</td>
<td>29</td>
<td>25</td>
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<tr>
<td>A Fib taking Warfarin/OAC</td>
<td>32</td>
<td>32</td>
<td>51</td>
<td>78</td>
<td>18</td>
<td>61</td>
</tr>
</tbody>
</table>
Outcome Data

The follow-up rate at 1 year was 98% (range 93-100%)
G-CHF

- 25,000 patients with HF (5,000 patients per year for 5 years) with 2 year follow-up
- Pt. recruitment in every inhabited continent (including the USA/Canada, Europe, Asia, Africa, Middle East, Latin America)
- Describe risk factors, socioeconomic variables, treatments, outcomes
- Serial point-of-care biomarkers will be performed in all patients (provided by study)
- Sub-study (in 5000 patients):
  - Lung and cognitive functions
  - Frailty and diet assessments
  - Blood and urine collections (for central storage)
Patient recruitment: 2/3 outpatients, 1/3 hospital inpatients

40% HFrEF, 40% HFpEF, 20% asymptomatic LV dysfunction

Patients with clinical diagnosis of HF will be enrolled

Secondary analyses according to established HF criteria and biomarkers will then be made

Only exclusion criterion is inability to be followed
G-CHF

- Primary endpoint is mortality (by cause)
- Secondary endpoints:
  - Hospitalization (by cause)
  - Major clinical events not requiring hospitalization
- Follow-up at 6 (phone), 12 (clinic visit), 18 (phone), 24 months (clinic visit)
Proposed Project Timelines

- Feb to May 2016: Protocol development
- June 2016 to October 2016: Ethics’ approvals and contracts
- November 2016: 1\textsuperscript{st} patient enrolled
- March 2017: All centres activated
- March 2017-March 2022: Enrollment
- March 2024: Last patient follow-up completed
- March 2024-2025: Data analyses and manuscript preparation
SA Heart Association Registry Projects
Cardiac Disease and Maternity

SHARE
South African Heart Association Registry

CDM
Shared experience, improved patient care
A previous single-centre study (Sliwa et. al., 2014)\textsuperscript{1} – CDM - has shown cardiac disease patterns presented at Groote Schuur hospital in the Western Cape were markedly different to that seen in the developed world.

Mortality typically occurred in the postpartum period, beyond the standard date of recording maternal death.

The SA Heart Association co-ordinates and runs registry projects intended to improve clinical care through evidence based data which is locally relevant.

The SHARE projects were ideal to extend the CDM project to multiple centres nationally and across borders within Africa.

Aims and objectives – CDM Phase II

Aims

- To establish a prospective registry of patients with pre-existing cardiovascular disease falling pregnant or developing a cardiac condition pre- or postpartum.
- To identify parameters that serve as outcome modifiers: these may be useful for risk stratification.

Objectives

- To study the natural history of women with pre-existing cardiovascular disease falling pregnant or developing a cardiac condition pre- or postpartum.
- To identify risk factors and clinical predictors of outcome.
Study Design

- The study is a multicentre, hospital-based, prospective longitudinal observational registry.
- Study of the clinical, echocardiographic, biochemical and immunological features of women with pre-existing cardiovascular disease falling pregnant or developing a cardiac condition pre- or postpartum.
- All-comers registry with data collected for a period of two years or for longer if necessary, minimum inclusion 100 patients and 20 patients per site.
- 4 sites in SA - all public sector (private sector sample size limited).
- Recruiting sites actively in sub-Saharan Africa.
- Collaborative assessments with both obstetrics and cardiology departments involved.
Eligibility Criteria

Inclusion Criteria

- Pregnant or immediate post-partum females
- Age greater than 18 years
- Patients willing and able to give informed consent
- Patient is able (in the investigators’ opinion) to comply with all study requirements and return for follow-up
- Documented clinical evidence of cardiac disease in pregnancy or postpartum

Exclusion criteria

Patients who are unable to give informed consent
Outcome measurements

Primary outcome
- Survival of mother and child

Secondary outcomes
- Readmission to hospital
- Development of chronic heart failure
- Combined endpoint of survival, LVEF and NYHA FC