Out line of Heart Failure 2015

• - Introduction
• - Heart Failure in NVCV and in Indonesia : Past, Present & Future.
• - Acute Heart Failure World Congress, World Heart Failure Congress, Japanese Heart Failure Society Meeting, HF Society of America.
• RELAX-AHF : Serelaxin-IV in AHF
• EMPHASIS-HF : eplerenon (MRA)
• TOPCAT : spironolactone for HFpEF
• - PARADIGM : LCZ-696 (ARNI=angiotensin receptor neprilysin inhibitor)
• - ASIAN-SUDDEN CARDIAC DEATH IN HEART FAILURE (ASIAN-HF)
• - HF patients care in ASIA : Resource allocation & Preventive Strategies
• REPORT - HF
ACUTE HEART FAILURE THAT COME TO DOCTOR

CHRONIC HEART FAILURE (undetected in your community)
At Risk for Heart Failure

Stage A
At high risk for HF but without structural heart disease or symptoms of HF.

- Hypertension
- Atherosclerotic disease
- Diabetes
- Metabolic syndrome
- Patients using cardiotoxins with HFx CM

Stage B
Structural heart disease but without symptoms of HF.

- Previous MI
- LV remodeling including LVH and low EF
- Asymptomatic valvular disease

Stage C
Structural heart disease with prior or current symptoms of HF.

- Known structural heart disease
- Shortness of breath and fatigue, reduced exercise tolerance

Stage D
Refractory HF requiring specialized interventions.

- Patients who have marked symptoms at rest despite maximal medical therapy (e.g., those who are recurrently hospitalized or cannot be safely discharged from the hospital without specialized interventions)

Therapy Goals
- All measures under stages A and B
- Dietary salt restriction
- Drugs for Routine Use
- Diuretic for fluid retention
- ACEI
- Beta-blockers

Drugs
- ACEI or ARB in appropriate patients (see text)
- Beta-blockers in appropriate patients (see text)

Devices in Selected Patients
- Implantable defibrillators

Therapy Goals
- All measures under stages A and B
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Drugs
- ACEI or ARB in appropriate patients (see text)
- Beta-blockers in appropriate patients (see text)

Devices in Selected Patients
- Implantable defibrillators
- Hydralazine/nitrates

Therapy Goals
- Appropriate measures under stages A, B, C
- Decision re: appropriate level of care

Options
- Compassionate end-of-life care/hospice
- Extraordinary measures
  - Heart transplant
  - Chronic inotropes
  - Permanent mechanical support
  - Experimental surgery or drugs

Refractory Symptoms of HF at Rest
Predictor mortality HF 2000-1 at 5 years FU

- **All Heart Failure Dx (2000+2001)**
  - N = 6,109

- **Hospitalized HF Admission (2000+2001)**
  - → 1,638 patients

- **Re-admission 2 years**
  - 402 patients (24%)

- **Compliance**
  - 298 pts (58.13%)
  - Survive 250 patients (83.9%)
  - Death 48 patients (16.1%)

- **Non compliance**
  - 104 pts (41.87%)
  - Survive 74 patients (71.2%)
  - Death 30 patients (28.8%)

- **2000**: 2,065 pts
- **2001**: 4,044 pts

- **2000**: 681 pts hospitalized
- **2001**: 957 pts hospitalized

Arman, Siswanto. 2005
SURVIVAL ESTIMATE:
Compliance VS Non compliance

**Mortality Predictor of Heart Failure**
**Five Years Follow Up**

<table>
<thead>
<tr>
<th>Variable</th>
<th>p-value</th>
<th>HR (95%CI)</th>
</tr>
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<tbody>
<tr>
<td>Compliance</td>
<td>0.005</td>
<td>1.96 (1.23-3.12)</td>
</tr>
<tr>
<td>Ejection Fraction</td>
<td>0.002</td>
<td>2.11 (1.31-3.38)</td>
</tr>
<tr>
<td>Diabetes Melitus</td>
<td>0.012</td>
<td>1.98 (1.16-3.37)</td>
</tr>
</tbody>
</table>

† Stratification with sex
Stratified Cox Proportional Hazard

Arman, Siswanto et.al. 2005
Conclusion

Heart failure is a leading cause of hospitalization and readmission in NCVC. Indonesian heart failure patients were younger, sicker, with a poor EF and Diabetes compared to others. The in-hospital mortality ranges from 6% to 12% and the re-hospitalization rate is 29%. Poor compliance, poor EF and Diabetes are the predictor for readmission. Health insurance improves survival probability. There is a need for better heart failure services.

In NCVC Jakarta, compliance with medical evaluation and drugs and diets are the predictors of hospitalizations. There were 47%, non compliant patients and the survival probability at 5 years was only 54%. The 5 year predictors of mortality are poor EF, Diabetes and male gender. The 5 year survival of males with poor EF and Diabetes was only 38%. Among socio-economic factors, only 33.5% had health insurance and 64.6% lived >20 km from hospital [16].

There are increasing numbers of hospitalized heart failure patients in NCVC Jakarta. In 2007 there were 1409 patients and an increase in 2008 to 1476 hospital admissions. Also there has been an increase in in-hospital mortality to around 12%.
Median Total Hospital Length of Stay (days)

- Indonesia: 7.1 days
- Asia Pacific: 7.2 days
- EU: 9 days
- US: 4.2 days

ADHERE - Indonesia vs. AP vs. Europe vs. US (2006)

IN-HOSPITAL MORTALITY BY COUNTRY (%)

Singapore (n=2,961) - 2.0
Thailand (n=2,045) - 6.7
Australia (n=1,887) - 6.5
Malaysia (n=907) - 7.6
Philippines (n=725) - 5.4
Taiwan (n=538) - 5.4
Hong Kong (n=394) - 0.3
Brazil (n=625) - 8.3
Mexico (n=87) - 7.2
Latin America (n=712) - 8.2
AP (n=10,166) - 4.8
APLA (n=10,878) - 5.0
US* (n=17,382) - 3.0
US** (n=187,565) - 3.8

ADHERE 2006

Siswanto BB, CVD-Prevention & Control 2010, 5: 35-38
Indonesian heart failure patients were younger and getting more new patients, compared to European and US data. More severe clinical presentation.

- High rate of in-hospital mortality (6.7-12%)
- Not following the HF guidelines.
- Mean hospital length of stay in average is 7 days
- Too many using Inotropes and Mechanical Ventilator.
- Need HF service team & preventive management
• High NT-proBNP, not decreased 35% during hospitalization
• NYHA Class 4
• BMI with edema > 30 kg/m²
• Ejection Fraction < 20%
• Acute Pulmonary Edema
• Not on betablocker
• Hemoglobin < 12 g/dL
• Sodium < 130 mmol/L
Increasing Age as predictor

HR 1.7 95% CI 0.9 - 3.1

No Health Insurance

HR: 1.4 (95%: 0.8 - 2.5)

High Creatinine

HR: 3.0 (95%: 1.4 - 6.5)

Low Ejection Fraction

HR: 1.7

BAMBANG BUDI SISWANTO
Dept.Cardiology and Vascular Medicine FKUI
Medical Research Unit & Medical Education Unit - FKUI National & International Collaboration
Conclusions: The presentation, underlying causes, management, and outcomes of heart failure vary substantially across LMICs. On average, the use of evidence-based medications tends to be suboptimal. Better strategies for heart failure surveillance and management in LMICs are needed.
The healthcare journey for patients with HF depends on symptoms at presentation and the availability of healthcare services.
Lung Ultrasound using Portable Echocardiography is now widely accepted as a practical bedside tool for evaluation of lung congestion.
Heart failure
Preventing disease and death worldwide

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Shengshou Hu
Tiny Jaarsma
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Vishal Rastogi
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World Heart Failure Alliance
Global Heart Failure Awareness Programme

Global Heart Failure Awareness Programme
Heart Failure Association of the ESC
European Society of Cardiology
Death rates for patients hospitalized with heart failure across the globe
Acute Exacerbations Contribute to the Progression of the Disease

With each event, hemodynamic alterations/myocardial injury contribute to progressive ventricular dysfunction and dilatation

Jain P et al., Am Heart J. 2003;145:S3-S17
Unmet needs in the prevention, diagnosis, treatment & long-term management HF

Ponikowski, Siswanto, et al. EJHFail.2014
Substrate

Normal

Structural heart disease

Chronic HF

Triggers
Hypertension, ACS, arrhythmias, infections, renal dysfunction, nonadherence, medications

Myocardial
- Diastolic dysfunction
- Decreased CO
- Myocyte ischemia/injury
- Mitral regurgitation
- Ventricular interdependence
- Tachycardia

Renal
- Sodium and volume retention
- Acute kidney injury
- RAAS/SNS activation
- Abnormal intrarenal hemodynamics

Vascular
- Vasoconstriction
- Volume redistribution
- Afterload contractility mismatch
- Endothelial dysfunction
- Increased arterial stiffness
- Capillary leakiness

Neuro-hormonal
- RAAS activation
- SNS activation
- Oxidative stress
- Inflammation

Congestion

End organ dysfunction

CO = cardiac output; RAAS = renin-angiotensin-aldosterone system; SNS = sympathetic nervous system.
Substrate

Underlying cardiac function may be:

- Normal (e.g., fulminant myocarditis)
- Asymptomatic structural heart disease (AHA/ACC Stage B)

- Structural heart disease with symptomatic HF (AHA/ACC Stage C/D)

ACC = American College of Cardiology; AHA = American Heart Association
Triggers in AHF: OPTIMIZE-HF

- Uncontrolled hypertension: 11%
- ACS: 15%
- Arrhythmia: 14%
- Worsening renal function: 7%
- Respiratory or pneumonia: 15%
- Nonadherence to meds: 9%
- Nonadherence to diet: 5%
- Other: 13%

Vicious Cycle of Congestion in AHF

- Myocardial ischemia
- Worsening HF
- Elevated LVEDP
- Increased wall stress
- Increased functional MR
- Myocardial oxygen demand
## Acute Heart Failure: Current Recommendations and Levels of Evidence

<table>
<thead>
<tr>
<th>Group</th>
<th>Medication</th>
<th>Class Recommendation, Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td>Indication</td>
<td>I, B</td>
</tr>
<tr>
<td>Vasodilators</td>
<td>Nitrates</td>
<td>IIa, B</td>
</tr>
<tr>
<td></td>
<td>Sodium nitroprusside</td>
<td>IIb, B</td>
</tr>
<tr>
<td>Morphine</td>
<td>Indication</td>
<td>IIa, C</td>
</tr>
<tr>
<td>Inotropics</td>
<td>Dopamine</td>
<td>IIb, C</td>
</tr>
<tr>
<td></td>
<td>Dobutamine</td>
<td>IIa, C</td>
</tr>
</tbody>
</table>

Several Drugs in ADHF Not Successful

PDE inhibitors: milrinone: OPTIME-CHF\cite{1}
Endothelin antagonists: tezosentan: VERITAS\cite{2}
Calcium sensitizers: levosimendan; SURVIVE/REVIVE\cite{3}
AVP antagonists: tolvaptan; EVEREST\cite{4}
Adenosine A1-receptor antagonist: rolofylline; PROTECT\cite{5}
Natriuretic peptides: nesiritide: ASCEND-HF\cite{6}

ADHF = acute decompensated heart failure;
AVP = arginine vasopressin;
PDE = phosphodiesterase

See reference list for a complete listing of citations.
### Novel Drug Trials in Acute Heart Failure

<table>
<thead>
<tr>
<th>Drugs, TRIAL</th>
<th>No.</th>
<th>Primary Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serelaxin, RELAX-AHF-2</td>
<td>6375</td>
<td>180-day CV death</td>
</tr>
<tr>
<td>Ularitide, TRUE-AHF</td>
<td>2116</td>
<td>Hierarchical clinical composite</td>
</tr>
<tr>
<td>Dopamine vs nesiritide vs placebo, ROSE-AHF</td>
<td>360</td>
<td>72-hour diuresis, cystatin-c change</td>
</tr>
<tr>
<td>Metolazone + furosemide vs furosemide alone</td>
<td>160</td>
<td>Diuresis</td>
</tr>
<tr>
<td>Furosemide high- vs low-dose vs low-dose + dopamine, DAD-HF-2</td>
<td>450</td>
<td>1-year mortality or rehospitalization</td>
</tr>
</tbody>
</table>

CV = cardiovascular

http://www.clinicaltrials.gov
<table>
<thead>
<tr>
<th>Drug, Mechanism, TRIAL</th>
<th>No.</th>
<th>Primary Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRV027, a biased AT1R ligand</td>
<td>PoC</td>
<td>Patients with systolic acute heart failure</td>
</tr>
<tr>
<td>Recombinant BNP, natriuresis, diuresis</td>
<td>100</td>
<td>LV systolic function</td>
</tr>
<tr>
<td>Levosimendan, ELEVATE</td>
<td>134</td>
<td>Days alive and out of hospital</td>
</tr>
<tr>
<td>Tolvaptan, Secret of HF</td>
<td>310</td>
<td>Dyspnea relief</td>
</tr>
<tr>
<td>Tolvaptan, TACTICS-HF</td>
<td>250</td>
<td>Dyspnea relief</td>
</tr>
</tbody>
</table>

BNP = b-type natriuretic peptide; PoC = proof of concept

http://www.clinicaltrials.gov
Congestion as a Main Target for Therapy in Worsening Heart Failure: Medical Therapy

Filippos Trposkiadis, MD, FESC, FACC
Professor of Cardiology
Director, Department of Cardiology
Larissa University Hospital
Larissa, Greece

Athens,
May 17, 2014
Cardiogenic Congestion

↑ Cardiac filling pressures

Volume misdistribution (e.g. pulmonary edema)  Volume overload (e.g. peripheral edema)

Goal
- Unloading
- Increase in venous capacitance

Goal
Reduction of extracellular volume

Clark AL, Cleland JGF. Nat Rev Cardiol 2013; 10: 156–170
ALARM-HF: In-Hospital Treatment of Acute Pulmonary Edema Patients

High-Dose Isosorbide Dinitrate (ISDN) plus Low-Dose Furosemide (FS) vs. High-Dose FS plus Low-Dose ISDN in Severe Pulmonary Edema

CHF pts treated with O₂ 10 L/min, IV FS 40 mg, and morphine 3 mg bolus randomly assigned to group A (ISDN 3 mg IV bolus every 5 min; n=56) or group B (FS 80 mg IV bolus every 15 min, as well as ISDN 1 mg/h, increased every 10 min by 1 mg/h; n=54). Treatment continued until oxygen O₂ saturation >96% or mean BP decreased by 30% or <90 mmHg. Endpoints were death, mechanical ventilation, and MI.

<table>
<thead>
<tr>
<th>Primary outcome</th>
<th>Group A (n=52)</th>
<th>Group B (n=52)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Died</td>
<td>1 (2%)</td>
<td>3 (6%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Required mechanical ventilation</td>
<td>7 (13%)</td>
<td>21 (40%)</td>
<td>0.0041</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>9 (17%)</td>
<td>19 (37%)</td>
<td>0.047</td>
</tr>
<tr>
<td>Any adverse event</td>
<td>13 (25%)</td>
<td>24 (46%)</td>
<td>0.041</td>
</tr>
</tbody>
</table>

Management of Acute Pulmonary Edema in Acute Heart Failure

1. Acute pulmonary edema/congestion
   - Intravenous bolus of loop diuretics
     - Hypoxemia
       - Yes: Oxygen
       - No
         - Severe anxiety/distress
           - Yes: Consider IV opiate
           - No: Measure systolic blood pressure
             - SBP < 85 mm Hg or shock: Add nonvasodilating inotrope
             - SBP 85-110 mm Hg: No additional therapy until response assessed
             - SBP > 110 mm Hg: Consider vasodilator (e.g., NTG)

2. Adequate response to treatment?
   - Yes: Continue present treatment
   - No: Re-evaluation of patient’s clinical status

NTG = nitroglycerin
SBP = systolic blood pressure

ACE Inhibitors in Cardiogenic Pulmonary Edema

Captopril 12.5 mg SL on top of standard treatment


Hemodynamic effects of enalaprilat (0.004 mg/kg) either as bolus (●) or continuous one-hour infusion (○).

Management of Acute Cardiogenic Pulmonary Edema

O2, Sympatholysis, NIPPV if needed, intubation by severe global insufficiency, consideration of ACS and tachyarrhythmias (ECG)

Systolic Blood Pressure

<100 mmHg (often hypovolemic)

Nitroglycerin (Captopril, enalapril)

100-140 mmHg (often hypovolemic)

Diuretics

> 140 mmHg (often euvoletic/hypovolemic)

Inotropes/Vasopressors

Fluid challenge (200-300 ml) ?

Yes

Small IVC (<1 cm) or IVC collapse

No

Consider increase in diuretic dose

Composite End Point of Death, Rehospitalization, or Emergency Department Visit: The DOSE Trial

Diuretic Resistance in Heart Failure

- Assess compliance with salt restriction and medicine intake. If necessary, measure the amount of salt and diuretic in the urine.
- Discontinue NSAIDs.
- Adjust the dose of the diuretic in patients with renal impairment.
- Switch to intravenous administration to overcome problems associated with impaired absorption.
- As it avoids post-diuretic salt retention, a continuous intravenous infusion of a loop diuretic may succeed where other treatments have failed.
- Combine furosemide with thiazides (aldosterone antagonists).
- Torasemide?
- Hypertonic saline solution?

De Bruyne UKM. Postgrad Med J 2003;79:268-71
RELAX-AHF: CV Mortality

HR, 0.63 (0.41-0.96); \( P = .028 \)

NNT = 29

Number of events

ITT = intent to treat; NNT = number need to treat

Cardiovascular death through Day 180

Serelaxin significantly reduces CV mortality

HR 0.63 (CI 0.41, 0.96); $P=0.028$

NNT = 29

K-M Estimate CV Death (ITT) (%)

Time in Trial (days)

Placebo
55 CV deaths (9.6%)

Serelaxin
35 CV deaths (6.1%)

Serelaxin, biomarkers and outcomes

This study describes the effects of serelaxin on pre-specified markers of cardiac, renal, and liver damage, as well as signs and symptoms of congestion resolution and explored the association of these changes with 180-day mortality in the RELAX-AHF trial.
Conclusions

• Several drugs failed to show beneficial effects in patients with ADHF.

• Novel inotropes, such as omecamtiv and istaroxime, are currently under investigation.

• Two large phase 3 clinical trials with vasodilators in ADHF are ongoing (TRUE-AHF and RELAX-AHF2).
EMPHASIS-HF:

• 1. MRA are the most successful therapy in CHF this century, with a IA recommendation for treatment of HF
• 2. Risk and fear of hyperkalemia result in lower use of MRAs in high risk subgroups such as patients with Renal dysfunction and diabetes
• 3. However, absolute risk reduction with MRAs is even greater in patients with renal dysfunction.
PARADIGM trial: ARNI angiotensin receptor Neprilysin Inhibitor beats ACEIs

LCZ696 ARNI: molecular angiotensin II-AT1 receptor antagonist Valsartan and the neprilysin inhibitor prodrug AHU377.

In 8442 pts HFrEF,

Inclusion criteria: Chronic HF FC II-IV, EF < 40 %, BNP > 150 / NtProBNP > 600. or > 100 / > 400 with a hospitalization for HFrEF within last 12 months

- 4 weeks stable treatment on ACEI or ARB with BB
- Aldosterone antagonist with stable dose.

Results: 20 % reduction composite (death & rehospitalization)
Summary: Efficacy

- **Primary outcome**
  - 20% reduction in **CV death or HF hospitalization** with LCZ696 compared with enalapril
  - 20% reduction in CV mortality
  - 21% reduction in HF hospitalization

- **Secondary outcomes**
  - 16% reduction in **all-cause mortality** with LCZ696 vs enalapril
  - LCZ696 superior to enalapril in reducing symptoms and physical limitations of HF (indicated by **KCCQ score**)
  - No significant difference in incidence of **new onset atrial fibrillation** between treatment groups
  - No significant difference in protocol-defined decline in **renal function** between treatment groups

Summary: Safety

- The superiority of LCZ696 over enalapril was not accompanied by important safety concerns.
- Fewer patients stopped their study medication because of an adverse event in the LCZ696 group than in the enalapril group.
- There was no increase in the rate of discontinuation due to possible hypotension-related adverse effects, despite a higher rate of symptomatic hypotension in the LCZ696 group.
- Fewer patients in the LCZ696 group developed renal impairment, hyperkalemia or cough than in the enalapril group.
- The LCZ696 group had a higher proportion of patients with non-serious angioedema, but LCZ696 was not associated with an increase in serious angioedema.
Conclusions of PARADIGM-HF

- Angiotensin receptor–neprilysin inhibition with LCZ696 was superior to ACE inhibition alone in reducing the risks of death and of hospitalization for HF

• “The magnitude of the beneficial effect of LCZ696, as compared with enalapril, on CV mortality was at least as large as that of long-term treatment with enalapril, as compared with placebo.”

• “This robust finding provides strong evidence that combined inhibition of the angiotensin receptor and neprilysin is superior to inhibition of the RAS alone in patients with chronic HF.”
"Heart failure" with preserved EF

- Ventricular dysfunction
  - Impaired relaxation
  - Impaired filling
  - Systolic dysfunction
- Lung disease COPD
- Iron deficiency and anemia
- Atrial dysfunction
- Autonomic dysfunction
  - Chronotropic incompetence
- Vascular dysfunction
  - Vascular stiffening
  - Ventriculo-arterial coupling
- Elevated blood pressure
  - Inadequate BP response to exercise
  - Pulmonary hypertension
- Valvular disease
  - Dynamic mitral regurgitation
- Renal dysfunction Volume overload
- Aging and deconditioning
- Obesity and sarcopenia
- Psychic disorders Depression
HFpEF

1. HFpEF is a syndromal disease with increasing prevalence and no established therapies

2. Hospitalization of HFpEF is steadily increasing and today accounts for almost half of all HF hospitalizations

3. Worsening HFpEF is a high-risk condition: Outcomes after hospitalizations for HFpEF are as poor as for HFrEF

4. Need to identify evidence-based management strategies in patients with worsening HFpEF

5. Serelaxin (RelaxAHF 2) and vericiguat (sGC stimulator; SOCRATES) are being tested prospectively in worsening HFpEF
Integrated heart failure service:
• Heart failure cardiologist
• Heart failure trained senior nurses
• (Geriatrician, pharmacist, physiotherapist)

Inpatient decompensate CHF

Primary care

General medical clinic
General cardiology clinic

Primary care

Open access Echo

One Day Care

Heart failure clinic follow-up / tele monitor + nurses follow-up

Advanced heart failure service

Primary care + nurse follow-up

End-of-life therapy and palliative care specialist/service

• Diagnosis, corrected etiology?
• Planning of management
• (Periodic review)

Jarsma T et al. Medscape 2006
ASIAN SUDDEN CARDIAC DEATH IN HEART FAILURE (ASIAN-HF)

PROSPECTIVE OBSERVATIONAL STUDY

Lam C, Siswanto B, Richards M et al. (EJHFail. 2013)
46 Hospitals participating in 11 Asian countries
# ASIAN-HF Registry

## Rationale
- Knowledge gaps exist regarding disease burden, treatment patterns and barriers to therapy, and outcomes in Asian patients with HF
- These data will inform clinical care, resource allocation and policy with the goal of improving outcomes for patients with HF in Asia.

## Study Design
- A multicenter, observational study of Asian patients with symptomatic heart failure

## Size
- 5000

## Setting
- 46 medical centers across 11 Asian regions

## Visits
- 5 Visits: Baseline, Month 6 and Years 1, 2 & 3


Lam CS Eur J Heart Fail 2013
## Recruitment Status: 28 Feb 2015

<table>
<thead>
<tr>
<th>Country</th>
<th># of active sites</th>
<th>#Recruitment</th>
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<tbody>
<tr>
<td>China</td>
<td>4</td>
<td>344</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>1</td>
<td>53</td>
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<tr>
<td>India</td>
<td>6</td>
<td>1356</td>
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<tr>
<td>Indonesia</td>
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<tr>
<td>Japan</td>
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<td>Korea</td>
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<td>Malaysia</td>
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<tr>
<td>Thailand</td>
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<td>192</td>
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<td><strong>TOTAL</strong></td>
<td><strong>46</strong></td>
<td><strong>4175</strong></td>
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<table>
<thead>
<tr>
<th>#Recruitment</th>
<th>#Target</th>
<th>% Accomplished</th>
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<tbody>
<tr>
<td>4175</td>
<td>8,000</td>
<td>~ 52 %</td>
</tr>
</tbody>
</table>
Geographic distribution of patients ASIAN-HF Registry for SCD

Recruitment Contribution %

- China: 1356, 32%
- Hong Kong: 53, 1%
- India: 480, 11%
- Indonesia: 256, 6%
- Japan: 424, 10%
- Korea: 453, 11%
- Malaysia: 76, 2%
- Philippines: 326, 8%
- Singapore: 192, 5%
- Thailand: 215, 5%
HF patient care in Asia  
(ASEAN HEART JOURNAL 2014)

• Survey targeting 12 Asian countries to understand the HF patient care pathway in Asia
• Focus
  • Source of patients
  • Precipitating factors
  • Overall clinical status at presentation
  • Referral pattern
  • Discharge plan of patients
• 70 responses received

The Patient Care Pathway for Hospitalized Heart Failure in Asian Countries: Implications for Resource Allocation, Preventive Strategies and Design of Heart Failure Clinical Trials

Lansang, … Siswanto, Richards, Lam ASEAN Heart Journal 2014
Substantial inter-and-intra-country differences were seen between diagnosis values for HF with preserved ejection fraction (HFpEF) indicating the lack of an identifiable standard not only within the region, but within countries themselves.
Although rising in western countries, only Hong Kong and Japan indicated common diagnosis (>50%) of HFpEF amongst their patients.
The initial diagnosis of HFpEF is made in diverse settings and greater collaboration between the ED and internists would facilitate enrollment.

Lansang, … Siswanto, Richards, Lam ASEAN Heart Journal 2014
## Rationale

- Knowledge gaps exist regarding disease burden, treatment patterns and barriers to therapy, and outcomes in Asian patients with HF
- These data will inform clinical care, resource allocation and policy with the goal of improving outcomes for patients with HF in Asia.

## Study Design

- A multicenter, observational study of Asian patients with symptomatic heart failure + GWAS

## Size

- 5000 HFrEF + 3000 HFpEF

## Setting

- 46 medical centers across 11 Asian regions

## Visits

- 5 Visits: Baseline, Month 6 and Years 1, 2 & 3

http://www.clinicaltrials.gov/ct2/show/NCT01633398?term=ASIAN+HF&rank=1

Lam CS Eur J Heart Fail 2013
International Registry to assess mEdical Practice with lOngitudinal obseRvation for Treatment of Heart Failure (REPORT-HF)
Primary Objectives

- Characterize HF patients at hospitalization and assess in-hospital and post-discharge events incidence
  - For newly diagnosed heart failure patients
  - For patients with chronic HF presenting an exacerbation episode at hospitalization
- Characterized patterns of post-discharge patient management and impact on Healthcare Resource Utilization (HRU) in HF-patients for 3 years
Secondary Objectives

- Evaluate Health-related Quality of Life (HRQoL), based on patient reported data as measured by EQ-5D, and the Kansas City Cardiomyopathy Questionnaire (KCCQ) questionnaires

- Study associations between practice pattern and outcomes

Main Milestones & Submission status:

- First patients enrollment in July 2014 at Russia
- Targeting 5000 patients enrolled by the end of December 2015
- Targeting 70 patients from each site in Indonesia with maximal 100 patients per site.
Study Design:

Broad geographical inclusion
3 years follow-up for every patient
Depending on enrolment rate, duration of registry projected up to 6 years → 2020
Up to 20000 patients (depending on drop-out rate)
Patients are eligible when diagnosed with acute Heart failure at hospitalization
Patients will be screened in the order in which they are admitted for the index event on agreed site sampling days

all data-capture timepoints after discharge have a ±1 month window.
SUMMARY HF 2015:

- BNP / NTproBNP Point of Care will available soon in Indonesia. A new marker for fibrosis in myocardium is ST2, now under intensive research.
- The use of echo-hemodynamic with Lung Ultra-sound become more applicable in emergency situation and all cardiologist, GPs, Emergency Physicians and Intensivist should more familiar with this portable modality.
SUMMARY (2)

- PARADIGM-HF: new drug LCZ689 ARNI Neprylisin, beats the established drug Enalapril, this trial stop prematurely due to very significant benefit of this new drug. This is the first drug that beat ACEI in Chronic Heart Failure. However we should wait the results of post marketing trial before it available in FORNAS in the era of BPJS?

- RELAX-AHF2 is on going multicenter large trial for IV drug Serelaxin in Acute Heart Failure. However is this drug Serelaxin suitable for Indonesia patients and price, we should do our own research, not to be the follower. Our HF pts admitted in low BP that not suitable for Serelaxin.
SUMMARY (3)

• For heart failure in Indonesia, we should do collect our own data by registry local and national so that we know really our Indonesian heart failure patients characteristic which non compliance and lots of myths. Healthy life style modification is more important than sophisticated expensive devices for our Low Income country.

• Local Indonesia Guidelines should be emphasized in any meeting or symposia. The new upcoming drugs or devices are not always the best, we should do analysis this new health technology, so we are not driven by the pharmaceutical or device companies.
THE DOCTORS’ JOB

TO CURE SOMETIMES

TO RELIEVE OFTEN

TO COMFORT ALWAYS

even if you unable to treat the disease,

even if you unable to lighten suffering,

you can always be there for the patient,
ensuring a caring companion
for whatever the future holds

Thank You for being a good doctor for the patients

Benyamin Lampson. Academic Medicine 2007;82:1112-3
LORD, now as I treat my patients, please help me to be wise. Let me see their problems through YOUR discerning eyes. Guide me LORD and use me in everything I say and I do, to help the patients to relief their suffer and sick. Because YOU will cure them as YOU are the GREAT PHYSICIAN not me. And more people will believe in YOU.

Amen