Polypill Eligibility For Patients With Heart Failure With Reduced Ejection Fraction In The ASIAN-HF Registry

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Background

- The burden of heart failure with reduced ejection fraction (HFrEF) in Asia is increasing due to population growth, aging, and increasing prevalence of major cardiovascular risk factors
- Guideline-directed medical therapy (GDMT) consisting of blockers, RAAS blockers, and mineralocorticoid receptor antagonists substantially reduces the risk of mortality among patients with HFrEF by an estimated 63% compared with placebo
- While the use of GDMT in Asia has increased in the past years, rates remain sub-optimal with significant regional variation.
- A "polypill" is a fixed-dose combination of GDMT to simplify treatment and potentially improve GDMT adherence in HFrEF
- Prior research in Southern India (findings also presented at this conference) demonstrates that more than 80% of hospitalized patients with HFrEF were eligible for a polypill at discharge
- These high potential rates of HFrEF polypill eligibility suggest that a simplified polypill-based management strategy could be transformative for closing the treatment gap in HFrEF inequities on a multinational level
- HFrEF polypill eligibility among a large, multinational cohort of patients has not previously been examined

Research Objective

- We evaluated and described eligibility for a potential HFrEF polypill in the ASIAN-HF cohort, a multi-national registry with data from 11 Asian regions including China, Hong Kong, India, Indonesia, Japan, Korea, Malaysia, Philippines, Singapore, Taiwan and Thailand, between October 2012 and December 2017

Results

- Overall, 70.3% (2611/3716) of the analyzed cohort were eligible for a HFrEF polypill
- Patients on single components of GDMT at baseline, including an ACEi, ARB, or MRA (p< 0.001 for all) were significantly more likely to be eligible for a polypill.
- Eligibility was significantly more likely for men (Adjusted OR 0.77 [0.65, 0.91], p=0.003) and patients from Singapore (Adjusted OR 1.36 [1.11, 1.67], p=0.003), and significantly less likely for patients from Japan (Adjusted OR 0.64 [0.43, 0.93], p=0.021) or Thailand (Adjusted OR 0.59 [0.36, 0.97], p=0.036).
- Polypill eligibility was significantly higher than rates of baseline triple therapy adherence across multiple categories.

Conclusions

- This analysis demonstrates high potential rates of HFrEF polypill eligibility across Asia
- Multinational registries demonstrate that achieving >50% of combination GDMT was associated with better outcomes than 100% adherence to target dose monotherapy
- Minimal gains in use and achievement of target dosing of HFrEF GDMT has led to urgent recommendations for simultaneous initiation of low-dose GDMT at hospital discharge, which HFrEF polypills directly address
- Availability of multiple HFrEF polypill doses could prioritize safety and tolerability with low-dose initiation, subsequent titration to higher dose HFrEF polypills, and potential customization of dose combinations
- This may be of particular importance in the Asian patient population as previous studies have shown differential drug clearance of ACEis and beta-blockers in Asians as compared to Caucasians

Our findings suggest HFrEF polypills may be an important implementation strategy for increasing GDMT rates and improving clinical outcomes in Asian HFrEF patients.

Table 1

<table>
<thead>
<tr>
<th>Region</th>
<th>Sex</th>
<th>Eligible for polypill</th>
<th>Uneligible OR</th>
<th>p-value</th>
<th>Adjusted OR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td>Men</td>
<td>2415 (20.8%)</td>
<td>2.04</td>
<td>0.001</td>
<td>1.70 (95% CI)</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>5767 (19.6%)</td>
<td>2.04</td>
<td>0.001</td>
<td>1.70 (95% CI)</td>
<td>0.001</td>
</tr>
<tr>
<td>North Asia</td>
<td>Men</td>
<td>1040 (18.9%)</td>
<td>1.90</td>
<td>0.001</td>
<td>1.58 (95% CI)</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>2587 (19.0%)</td>
<td>1.90</td>
<td>0.001</td>
<td>1.58 (95% CI)</td>
<td>0.001</td>
</tr>
<tr>
<td>South Asia</td>
<td>Men</td>
<td>1772 (15.7%)</td>
<td>1.87</td>
<td>0.001</td>
<td>1.55 (95% CI)</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>3523 (16.0%)</td>
<td>1.87</td>
<td>0.001</td>
<td>1.55 (95% CI)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Eligibility for a HFrEF polypill was based on: LVEF≤40%, systolic blood pressure ≥100 mmHg, heart rate ≥50 beats/minute, eGFR ≥30 mL/min/1.73m2, and serum potassium ≤5.0 mEq/L

Differences between the two groups were tested with Wilcoxon rank-sum test, or the Chi-square test for continuous and categorical variables respectively

Mixed effects logistic regression analyses for the associations of the demographic factors with eligibility for polypill were performed, including adjustments for age and sex, and factoring in sites as random effects

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