An Overview of Prescribing According to ACS Guidelines: The Current World & Vietnam Situations

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INTRODUCTION
Introduction

- IHDs are the world’s biggest killer, accounting for 8.9 million deaths in 2015.
- The estimated socioeconomic burden of IHDs is reflected in the loss of 164 million DALYs in 2015.
- Over the past three decades, high-income countries have shown declines in the number of CVD deaths whereas the rest of the world has shown an increase.
- LMICs registered a 47% increase over the same period.

1. World Health Organization. The top 10 causes of death. 2017;
Introduction

- Survivors of ACS are at **increased** risk of recurrent infarctions and have an annual death rate of up to **6 times**

- Evidence-based interventions for secondary prevention include the use of APAs, BBs, ACEIs/ARBs, and statins, as well as modifying lifestyle-related risk behaviors

- The benefits of these medications are largely independent, but when used together with smoking cessation, nearly **75%** of recurrent vascular events may be **prevented**

Introduction

In Vietnam

- Rapid economic growth, urbanization and aging population have led to an increased burden of NCDs.

- NCDs are estimated to account for 73% of total deaths. CVDs are a major contributor to the NCD burden, accounting for 33% of total deaths. ACS is still one of the leading causes of deaths.

- There are concerns about quality of medical care and patient outcomes and therefore there is a growing demand for appropriate medicine use.

THE WORLD
The World Situation

1. guidelines for the diagnosis and management of ACS were published by the Agency for Health Care Policy and Research and the National Heart, Lung, and Blood Institute in 1994.

2. AHA, ACC, ESC, and VNHA have disseminated guidelines to facilitate the management of ACS.

3. These strongly recommend the use of secondary prevention medications: APA, BBs, ACEIs/ARBs, and statins.

Prescribing of these medications reduces both in-hospital and post-discharge morbidity and mortality.

Example of the effect of guideline adherence is an observational study of 65,000 patients with NSTEMI:

- Every 10% increase adherence – a 10% reduction in in-hospital mortality (OR 0.90, 95%CI 0.84–0.97)
- In-hospital mortality: hospitals highest < lowest adherence quartile (4.2% vs. 6.3%)

The World Situation

- Large registries: GRACE, CRUSADE, ATPOR, and EHS have shown variable adherence to guidelines for the management of ACS, though improvements over the years.

- Adherence to guidelines remains suboptimal in clinical practice, in particular, in LMICs. The ACCESS study (2007-2008) in 19 LMICs: aspirin and statins > 90%; BBs (78%) and ACEIs (68%).

VIETNAM
Physicians’ adherence to acute coronary syndrome prescribing guidelines in Vietnamese hospital practice: a cross-sectional study

Thang Nguyen¹,², Thao H. Nguyen²,³, Hoa T. K. Pham⁴, Thu T. A. Nguyen⁵, Khoa M. Huynh³, Phuong T. B. Vo³, Tam T. Pham⁶ and Katja Taxis²
Vietnam Situation

A retrospective cross-sectional study

- Collect data from medical records of all patients with ACS in 2 public hospitals in Ho Chi Minh city (1-12/2013)

- Data were analyzed to determine % of eligible patients receiving guideline-recommended medications at hospital arrival and discharge and to identify factors associated with non-adherence

<table>
<thead>
<tr>
<th>Guideline recommendation</th>
<th>Number of eligible patients receiving guideline-recommended medication</th>
<th>Number of eligible patients</th>
<th>Percentage of eligible patients receiving guideline-recommended medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>At arrival</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>191</td>
<td>195</td>
<td>97.9</td>
</tr>
<tr>
<td>Dual antiplatelet therapy</td>
<td>179</td>
<td>194</td>
<td>92.3</td>
</tr>
<tr>
<td>Aspirin loading dose</td>
<td>155</td>
<td>195</td>
<td>79.5</td>
</tr>
<tr>
<td>Clopidogrel loading dose</td>
<td>82</td>
<td>147</td>
<td>55.8</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>84</td>
<td>143</td>
<td>58.7</td>
</tr>
<tr>
<td>ACEI/ARB</td>
<td>164</td>
<td>184</td>
<td>89.1</td>
</tr>
<tr>
<td>Statin</td>
<td>241</td>
<td>256</td>
<td>94.1</td>
</tr>
<tr>
<td>At discharge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>208</td>
<td>216</td>
<td>96.3</td>
</tr>
<tr>
<td>Dual antiplatelet therapy</td>
<td>198</td>
<td>216</td>
<td>91.7</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>168</td>
<td>219</td>
<td>76.7</td>
</tr>
<tr>
<td>ACEI/ARB</td>
<td>171</td>
<td>192</td>
<td>89.1</td>
</tr>
<tr>
<td>Statin</td>
<td>253</td>
<td>279</td>
<td>90.7</td>
</tr>
</tbody>
</table>

Table 3 Factors associated with guideline non-adherence*

<table>
<thead>
<tr>
<th>Factor</th>
<th>Number of patients receiving guideline-recommended medication (%)</th>
<th>Number of patients NOT receiving guideline-recommended medication (%)</th>
<th>OR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin loading dose at arrival</td>
<td>STEMI†</td>
<td>76 (49.0)</td>
<td>7 (17.5)</td>
<td>6.1</td>
<td>2.2–17.0</td>
</tr>
<tr>
<td>Beta blocker at arrival</td>
<td>Male</td>
<td>70 (83.3)</td>
<td>36 (61.0)</td>
<td>3.6</td>
<td>1.5–8.7</td>
</tr>
<tr>
<td></td>
<td>STEMI†</td>
<td>17 (28.8)</td>
<td>31 (52.5)</td>
<td>0.3</td>
<td>0.1–0.9</td>
</tr>
<tr>
<td></td>
<td>Heart failure</td>
<td>3 (3.6)</td>
<td>11 (18.6)</td>
<td>0.2</td>
<td>0.1–0.8</td>
</tr>
<tr>
<td>Dual antiplatelet at discharge</td>
<td>Invasive procedure</td>
<td>97 (49.0)</td>
<td>5 (27.8)</td>
<td>3.8</td>
<td>1.2–11.5</td>
</tr>
<tr>
<td></td>
<td>Discharge medications &gt;6</td>
<td>110 (55.6)</td>
<td>5 (27.8)</td>
<td>4.6</td>
<td>1.5–14.0</td>
</tr>
<tr>
<td>Beta blocker at discharge</td>
<td>NSTEMI†</td>
<td>54 (32.1)</td>
<td>28 (54.9)</td>
<td>0.3</td>
<td>0.1–0.7</td>
</tr>
<tr>
<td></td>
<td>Invasive procedure</td>
<td>96 (57.1)</td>
<td>14 (27.5)</td>
<td>4.0</td>
<td>1.9–8.4</td>
</tr>
<tr>
<td></td>
<td>Invasive procedure</td>
<td>83 (48.5)</td>
<td>4 (19.0)</td>
<td>4.0</td>
<td>1.3–12.4</td>
</tr>
</tbody>
</table>

* Using multivariate logistic regression with forward stepwise method.
† Compared to UA; ACEI/ARB, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker; CI, confidence interval; NSTEMI, non-ST elevation myocardial infarction; OR, odds ratio; STEMI, ST elevation myocardial infarction.
284 patients (mean age 64 years; 69.4% male)

Aspirin: 97.9% at arrival & 96.3% at discharge; dual antiplatelet therapy 92.3% & 91.7%; loading doses at arrival 79.5% (aspirin) and 55.8% (clopidogrel); BBs: 58.7% & 76.7%; ACEIs/ARBs: 89.1%; Statins: 94.1% & 90.7%

Patients with PCI more likely to receive guidelines at discharge: dual antiplatelet therapy (OR 3.77; 95% CI 1.23–11.52), BB (OR 3.95; 95% CI 1.86–8.40), & ACEI/ARB (OR 4.01; 95% CI 1.30–12.41).

Association between in-hospital guideline adherence and postdischarge major adverse outcomes of patients with acute coronary syndrome in Vietnam: a prospective cohort study

Thang Nguyen,1,2 Khanh K Le,1 Hoang T K Cao,1 Dao T T Tran,1 Linh M Ho,1 Trang N D Thai,1 Hoa T K Pham,3 Phong T Pham,4 Thao H Nguyen,5 Eelko Hak,2 Tam T Pham,6 Katja Taxis2
Vietnam Situation

A prospective cohort study

- 2 public hospitals in Can Tho (Jan-Oct/2015)
- Six month follow-ups after discharge
- Inclusion criteria: Patients who survived during hospitalization with a discharge diagnosis of acute coronary syndrome and who were eligible for receiving at least one of the four guideline-recommended medications.

Vietnam Situation

A prospective cohort study

- Guideline adherence: prescribing all guideline-recommended medications at both hospital admission and discharge for eligible patients. Medications were APAs, BBs, ACEIs/ARBs, and statins.

- Six-month major adverse outcomes: all-cause mortality or hospital readmission due to cardiovascular causes occurring during six months after discharge.

Vietnam Situation

A prospective cohort study

- 512 patients were included:
  - 242 (47.3%) patients in guideline adherence group
  - 270 (52.3%) patients in non-adherence group

- The rate of six-month major adverse outcomes was 30.5%

A 29% reduction in major adverse outcomes at six months after discharge was found for patients of the guideline adherence group compared to the non-adherence group (adjusted HR 0.71; 95% CI 0.51–0.98).

Covariates significantly associated with the major adverse outcomes:
- PCI
- Prior heart failure
- Renal insufficiency

<table>
<thead>
<tr>
<th>Factor</th>
<th>HR*</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital guideline adherence</td>
<td>0.71</td>
<td>0.51 to 0.98</td>
<td>0.039</td>
</tr>
<tr>
<td>Percutaneous coronary intervention</td>
<td>0.60</td>
<td>0.38 to 0.94</td>
<td>0.024</td>
</tr>
<tr>
<td>Prior heart failure</td>
<td>1.92</td>
<td>1.36 to 2.69</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>1.38</td>
<td>1.00 to 1.91</td>
<td>0.050</td>
</tr>
</tbody>
</table>

*Using multivariable backward stepwise Cox regression models.
First model: variables entered at the first step: age, gender, number of CAD risk factors, prior MI/stroke, prior heart failure, Killip class II–IV, renal insufficiency, SBP<100 mm Hg, LVEF<40%, in-hospital guideline adherence, discharge diagnosis, PCI and health insurance. Second model: variables entered at the first step: in-hospital guideline adherence, percutaneous coronary intervention, prior heart failure, renal insufficiency and interaction terms: in-hospital guideline adherence and percutaneous coronary intervention, in-hospital guideline adherence and prior heart failure, in-hospital guideline adherence and renal insufficiency.

INTERVENTIONS
BMJ Open  Enhancing prescribing of guideline-recommended medications for ischaemic heart diseases: a systematic review and meta-analysis of interventions targeted at healthcare professionals

Thang Nguyen,¹,² Hoa Q Nguyen,³ Niken N Widyakusuma,⁴ Thao H Nguyen,³ Tam T Pham,⁵ Katja Taxis²
Interventions

Systematic Review & Meta-analysis

- PubMed & EMBASE for studies published 2000-2017
- Included RCTs of interventions targeted at healthcare professionals to enhance prescribing guideline-recommended medications for IHDs.
- Main outcomes: proportions of eligible patients receiving guideline-recommended medications, patients achieving target blood pressure and target low-density lipoprotein-cholesterol (LDL-C)/ cholesterol level and mortality rate.

Interventions

Systematic Review & Meta-analysis

- 4 RCTs (1869 patients) & 9 cluster RCTs (15 224)
- 11/13 studies were performed in North America and Europe
- Interventions were of organisational or professional nature.
- The evidence was of moderate or high quality for all outcomes.

<table>
<thead>
<tr>
<th>No.</th>
<th>Source</th>
<th>Setting of intervention implementation</th>
<th>Intervention carried out by</th>
<th>Distribution of educational materials</th>
<th>Educational meeting</th>
<th>Educational outreach visits</th>
<th>Local opinion leaders</th>
<th>Audit and feedback</th>
<th>Reminders</th>
<th>Revision of professional roles</th>
<th>Clinical multidisciplinary teams</th>
<th>Continuity of care</th>
<th>Communication and case discussion between distant healthcare professionals</th>
<th>Presence and organisation of quality monitoring mechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bernwanger et al.</td>
<td>Hospital</td>
<td>Nurse and physician</td>
<td>x</td>
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<td>x</td>
<td>x</td>
<td>x</td>
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<td>2</td>
<td>Bond et al. 46</td>
<td>Pharmacy</td>
<td>Community pharmacist</td>
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<tr>
<td>3</td>
<td>Rather et al. 47</td>
<td>Hospital</td>
<td>Cardiologist, nurse and manager</td>
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<td>x</td>
<td>x</td>
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<td>4</td>
<td>Garcia et al. 48</td>
<td>GP/PCP</td>
<td>Hospital pharmacist</td>
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<td>5</td>
<td>Guadagnoli et al. 50</td>
<td>GP/PCP</td>
<td>Cardiologist</td>
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<td>6</td>
<td>Hung et al. 51</td>
<td>Hospital</td>
<td>Reminder system</td>
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<td>7</td>
<td>Khunti et al. 52</td>
<td>GP/PCP</td>
<td>Nurse</td>
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<td></td>
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<td>x</td>
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<td>8</td>
<td>Levine et al. 50</td>
<td>GP/PCP</td>
<td>Internet-delivered intervention system</td>
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<td>9</td>
<td>McNister et al. 55</td>
<td>GP/PCP</td>
<td>Leader</td>
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<td>Moher et al. 56</td>
<td>GP/PCP</td>
<td>General practitioner and nurse</td>
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<td>13</td>
<td>Yorio et al. 59</td>
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</table>

*The interventions were classified according to the taxonomy of the Cochrane Effective Practice and Organization of Care Review Group. GP, general practice; PCP, primary care practice.
Interventions significantly enhanced prescribing of statins/lipid-lowering agents (OR 1.23; 95% CI 1.07 to 1.42, P=0.004), but not other medications.

No significant association between the interventions and improved health outcomes (target LDL-C and mortality) except for target blood pressure (OR 1.46; 95% CI 1.11 to 1.93; P=0.008).

Interventions

Systematic Review & Meta-analysis

- 11/13 studies from North America and Europe → limits the generalisability of results to the rest of the world
- A need to develop new interventions, especially for low-income and middle-income countries which have a rising burden of IHDs.
- There are some types of interventions such as financial and regulatory that have not been tested

Interventions

Systematic Review & Meta-analysis

- Select an intervention based on local context
- Consider a range of barriers to change prescribing, including barriers related to patients, organisation of the healthcare system and resource constraints
- Strategies for improving clinicians’ awareness, agreement and adoption of guidelines
- Evaluate cost-effectiveness

Interventions

- Although, most patients do fit the recommendations in guidelines, guidelines are suggestions for care, not rules.

- “One size does not fit all”, there is always individual patients who should be managed specifically.

- Reasons for individual care: biologic differences in drug metabolism, immune response, or genetic endowment; the presence of comorbid conditions; available resources determined by the social and economic environment of medicine at the local level; and patient preferences.

Interventions

- A certain proportion of patients do not fit the guidelines. Further studies on such patients should be done.
- Guidelines are usually based upon the best available research evidence and practice experience, but evidence-based medicine is sometimes over reliant on the reliability of clinical trials and systematic reviews.
- Patients treated in practice are possibly different from those included in research.

Limitations of clinical trials and systematic reviews:

- Unrepresentativeness of trial patients in terms of age, therapy, and comorbidity
- Over-reliance on statistical as opposed to clinical significance
- Misleading results due to reporting bias, inappropriate pooling of small trials, effect of changes in disease mortality, and prognosis over time
CONCLUSIONS
Physicians closely adhered to ACS prescribing guidelines in Vietnamese hospital practice. Prescribing of beta blockers and clopidogrel loading doses was probably suboptimal.

In-hospital guideline adherence was associated with a significant 29-percent decrease in major adverse outcomes up to 6 months after discharge.

Although, most patients do fit the recommendations in guidelines, guidelines are suggestions for care, not rules.
Key messages

4) “One size does not fit all”, there is always individual patients who should be managed specifically.

5) Organisational and professional interventions improved prescribing of statins/lipid-lowering agents and target blood pressure in patients with IHDs, but there was little evidence of change in other outcomes.

6) Select an intervention based on local context
Thank you for your attention!

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