Adherence to Antiplatelet Therapy Post-Discharge for Acute Coronary Syndrome: Impact on Mortality, Readmission Risk, and Costs

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BACKGROUND AND SIGNIFICANCE

- Current practice guidelines recommend antiplatelet therapy (AT) for ACS patients during and after hospital discharge. Non-adherence has been associated with higher risks of thrombosis, MI and mortality.

- Current real-world evidence on the relationship between adherence with AT post-discharge and patient outcomes is from survey-based, self-reported data on medication adherence and administrative data from two integrated health care systems.

- These studies have also been limited by lack of access to data on inpatient prescriptions; hence it has not been possible to determine long-term patient persistence from the initial treatment within the hospital.

- In addition, no study has documented the relationship between AT adherence and health care costs.

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STUDY OBJECTIVES

• To document adherence to antiplatelet therapy (AT) after discharge from hospitalization for acute coronary syndrome (ACS)
• To estimate the relationship between adherence post-discharge and the following outcomes:
  – Rate of hospital readmission within 30 days and 1 year
  – Mortality within 1 year post-discharge (and time to death)
  – Healthcare costs at 1 year post-discharge
The study sample was selected from the IMS Comprehensive Disease Records (CDRs) for ACS.

Four databases contribute patient level data for the ACS CDRs:
- IMS PharMetrics Plus health plan claims data
- IMS Hospital Charge Data Master (CDM) data
- IMS Ambulatory Electronic Medical Record (EMR) data
- IMS mortality data derived from the Social Security Death Index

The IMS patented and HIPAA compliant encryption methodology allows deterministic matching of patients across databases:
- Encrypted patient IDs assigned in all sources allows linking across data sources

STUDY DATA: IMS COMPREHENSIVE DISEASE RECORDS FOR ACUTE CORONARY SYNDROME (ACS)
SAMPLE SELECTION CRITERIA

**PharMetrics Plus inclusion criteria**
- Patients with $>1$ ACS diagnosis* from 1/1/2009 – 6/30/2013
- Patients aged 18 years or older on first ACS diagnosis observed
- With medical and pharmacy coverage

**Hospital CDM inclusion criteria**
- Patients with $>1$ ACS diagnosis codes from 1/1/2009 – 6/30/2013
- Patients aged 18 years or older on first ACS diagnosis observed

**Selection criteria**
- Patients available across all 3 databases (N=6,867)
- Meeting pre- and post-enrollment criteria (N=2,994)
- Prescribed AT at index ACS hospitalization (N=2,602)
- Alive > 1 month post-discharge (N=2,571)
METHODOLOGICAL CHALLENGES AND SOLUTIONS IMPLEMENTED

Recorded date of death is in Month-Year format; relationship between period of non-adherence and date of death in first month not known (risk of immortal time bias)

- Only include patients surviving 1 month post-discharge (landmark analysis)

Non-adherence with AT may be outweighed by other risk factors immediately after hospital discharge for ACS

- Control for observable cardiovascular risks

Adherence after outcomes of interest should not be included in the analysis (e.g., PDC measured over 1 year post-discharge for events occurring within 1 year)

- Measure adherence (PDC) up to the time of event or censure

- Use time varying measure of adherence in survival analysis

**Mortality 12 months post-discharge**

- Time to death is known by calendar month not day.
- AT Adherence prior to death cannot be determined for first month.
- Solution: evaluate mortality risk for patients surviving at least one post-discharge

29% of deaths occur within the first month post-discharge
METHODS

Measures of adherence

- Time of first fill for AT post-discharge (within 30, 60, 90 days)
  - Risk of mortality and readmission highest in the first month post-discharge
  - 30 day readmission rate affects Medicare reimbursement
- Percent days covered (PDC) from days supply on Rx claims
  - Percent of days 1 year post-discharge or up to the time of the event of interest (death or readmission) or censure from sample
- PDC at each month post-discharge for Extended Cox models with time varying adherence

Statistical methods

- Unadjusted estimates of study outcomes in 4 categories of adherence (0%, 1-39%, 40-79%, ≥ 80%)
- Adjusted estimates controlling for patient demographics, hospital characteristics, ACS hospital interventions, and cardiovascular risk factors
  - Logistic regression (mortality, readmission)
  - Cox Proportional Hazards and extended Cox (mortality, readmission)
  - Generalized Linear Model (Costs)
## Patient Characteristics and Time to First Antiplatelet Fill

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Proportion of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, in years)</td>
<td>57.7</td>
</tr>
<tr>
<td>Female</td>
<td>26.0%</td>
</tr>
<tr>
<td><strong>ACS diagnosis</strong></td>
<td></td>
</tr>
<tr>
<td>STEMI</td>
<td>37.6%</td>
</tr>
<tr>
<td>ACS Unstable Angina</td>
<td>31.5%</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>29.9%</td>
</tr>
<tr>
<td>ACS OTHER</td>
<td>1.1%</td>
</tr>
<tr>
<td><strong>Inpatient procedures</strong></td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>59.7%</td>
</tr>
<tr>
<td>CABG</td>
<td>18.7%</td>
</tr>
<tr>
<td><strong>Comorbidities, pre-index</strong></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>52.3%</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>47.1%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>25.4%</td>
</tr>
<tr>
<td>Chronic Lung Disease</td>
<td>12.1%</td>
</tr>
<tr>
<td>Peripheral Artery Disease</td>
<td>8.0%</td>
</tr>
<tr>
<td>Stroke</td>
<td>6.7%</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>6.5%</td>
</tr>
<tr>
<td>Chronic Renal Disease</td>
<td>5.3%</td>
</tr>
<tr>
<td>Deep Vein Thrombosis</td>
<td>1.0%</td>
</tr>
</tbody>
</table>

Only 50% of patients filled an AT prescription at 30 days post-discharge.

- Filled Rx for AT within 1 year: 67.0%
- Filled Rx for AT within 90 days: 62.8%
- Filled Rx for AT within 60 days: 59.9%
- Filled Rx for AT within 30 days: 50.1%
ADHERENCE AND MORTALITY 1 YEAR POST-DISCHARGE

Mortality increases markedly as adherence falls below 80% (unadjusted)

<table>
<thead>
<tr>
<th>Adherence Level</th>
<th>Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>4.1%</td>
</tr>
<tr>
<td>1% - &lt; 40%</td>
<td>4.5%</td>
</tr>
<tr>
<td>40% - &lt; 80%</td>
<td>3.1%</td>
</tr>
<tr>
<td>≥ 80%</td>
<td>0.7%</td>
</tr>
</tbody>
</table>

Adjusted results show that the impact of adherence on mortality is markedly higher when over 80%

**Cox PH Results**

- 1% - < 40%: 0.988 (CI: 0.583 - 1.674)
- 40% - < 80%: 0.852 (CI: 0.512 - 1.418)
- ≥ 80%: 0.289 (CI: 0.166 - 0.503)

**Extended Cox Results**

- Time Varying Adherence: 0.319 (CI: 0.187 - 0.544)

Reference group for Cox models is patients not filling a script for AT post-discharge. P < 0.001 for all hazards ratios.
30 day readmission rate is lower if AT prescription was filled by 30 days

Readmission rate at 1 year is lower for adherence $\geq$ 80%

**ADHERENCE AND HOSPITAL READMISSION POST-DISCHARGE, UNADJUSTED RESULTS**

- **Readmission rate 30 days post-discharge by Rx for AT at 30 days**
  - Filled: 7.4%
  - Did not fill: 14.2%

- **Readmission Rate 1 Year Post-discharge**
  - 0%: 44.8%
  - 1% - < 40%: 39.2%
  - 40% - < 80%: 40.8%
  - $\geq$ 80%: 16.9%

*p < 0.0001 for 30 day and 1 year readmissions*
Hospital readmission risk 1 year post-discharge is approximately 70% lower for patients with ≥80% adherence.

<table>
<thead>
<tr>
<th>Time Varying Adherence</th>
<th>Readmission Risk 1 Year Post-discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>1% - &lt; 40%</td>
<td>CI: 0.75-1.16</td>
</tr>
<tr>
<td>40% - &lt; 80%</td>
<td>CI: 0.58-0.88</td>
</tr>
<tr>
<td>≥ 80%</td>
<td>CI: 0.23-0.36</td>
</tr>
</tbody>
</table>

Extended Cox Results:
- Time Varying Adherence: CI: 0.25-0.38

Hazards Ratios:
- Reference group is patients not filling a script for AT post-discharge. P < 0.001 for all hazards ratios
AT ADHERENCE AND TOTAL HEALTHCARE COSTS
1 YEAR POST-DISCHARGE

- Unadjusted costs were $12,556 lower for patients with ≥ 80% adherence (p < 0.0001) compared to lower adherence
- Adjusted costs from GLM model were 18% lower for patients with 100% adherence to AT and 15% lower for patients with 80% adherence (p<0.0001)

Unadjusted Results

<table>
<thead>
<tr>
<th>Adherence Level</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>$32,374</td>
</tr>
<tr>
<td>1% - &lt; 40%</td>
<td>$343,933</td>
</tr>
<tr>
<td>40% - &lt; 80%</td>
<td>$30,455</td>
</tr>
<tr>
<td>≥ 80%</td>
<td>$21,240</td>
</tr>
</tbody>
</table>

Adjusted Results

<table>
<thead>
<tr>
<th>Adherence Level</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>$33,422</td>
</tr>
<tr>
<td>40%</td>
<td>$30,917</td>
</tr>
<tr>
<td>80%</td>
<td>$28,582</td>
</tr>
<tr>
<td>100%</td>
<td>$27,482</td>
</tr>
</tbody>
</table>
STUDY LIMITATIONS

- Day of death is not observed, only month, limiting ability to analyze the relationship between death and medication adherence \textit{immediately after hospital discharge}.
- Unobserved patient characteristics correlated with higher medication adherence may also be correlated with better health outcomes.
- Patient experience in the older portion of the population may be underrepresented in the study sample.
CONCLUSIONS

Principal study results

• High adherence to AT (>80%) after hospital discharge for ACS is associated with significantly lower mortality (70%), lower readmissions (71%), and 18% lower total healthcare costs at 1 year post-hospital discharge

• Earlier time to first AT fill was associated with greater benefits since risks of death and readmission are highest in months immediately after index discharge

• Positive benefits of higher adherence decline as adherence falls below 80%

New insights gained from the study compared to prior studies

• Interventions to increase adherence to AT can possibly reduce health care costs as well as improving clinical outcomes.

• It is possible to link adherence, health care cost/use and mortality data from multiple health care administrative data sources to enhance research capabilities, using data sources like the ACS Comprehensive Disease Record

• Linking data may preclude costly primary data collection and improve geographic and provider coverage, increasing confidence to generalize study results