New Role For An Old Friend:
Contemporary Insights From The ECG

Paul W. Armstrong, MD

Monday March 12 2012
Disclosure Statement  Paul W. Armstrong MD

Details available @ http://www.vigour.ualberta.ca
Overview: New Tricks from Old Dogs

- Ischemic Burden: STE & Non STE
- Infarct Masquerade
- Q wave Insights
- Assessing reperfusion
- Insights into Rx mechanisms
Risk stratification in ST-elevation myocardial infarction is enhanced by combining baseline ST deviation and subsequent ST-segment resolution

M Toma,¹ Y Fu,¹ G Wagner,² S G Goodman,³ C Granger,² L Wallentin,⁴ F Van de Werf,⁵ P Armstrong¹

ABSTRACT

Background: The baseline sum of ST deviation (ΣSTD) and ST segment resolution after fibrinolysis for ST-elevation myocardial infarction are prognostically useful.

Objectives: To examine the prognostic impact of ST resolution after fibrinolysis and influence of baseline ST deviation in ASSENT-3.

Methods: ST resolution was determined in 4585 patients at 180 minutes after fibrinolysis. 30-Day and 1-year mortality was assessed in patients with complete (ie, >50%) versus incomplete ST resolution according to absolute baseline ΣSTD.

Results: Patients with complete ST resolution had lower 30-day and 1-year mortality than those with incomplete ST resolution (3.7% vs 7.3%, p<0.001, and 6.1% vs 10.0%, p<0.001, respectively). After multivariable adjustment for key baseline risk factors, patients with anterior myocardial infarction (MI) in the highest quartile of ΣSTD had a greater risk of 30-day and 1-year mortality than those in the lowest quartile in both complete (odds ratio (OR) = 2.34, 95% CI 1.14 to 4.80, and OR = 2.34, 95% CI 1.26 to 4.34, respectively) and incomplete ST resolution groups (OR = 4.97, 95% CI 1.82 to 13.61, and OR = 3.61, 95% CI 1.55 to 8.4, respectively). However, in patients with inferior MI this pattern only existed when ST resolution was incomplete (OR = 4.88, 95% CI 1.65 to 14.39, and OR = 4.34, 95% CI 1.66 to 11.37, respectively).

Conclusion: These findings indicate that percentage ST resolution alone is an incomplete guide to 30-day and 1-year mortality. The integration of both the baseline and post-fibrinolysis ECG provides better risk assessment and can assist in the triage and treatment of such patients.

60–180 minutes after fibrinolysis, have better clinical outcomes and lower mortality than those with less ST resolution.1,2,7,8 Furthermore, the relationship between MI location, the extent of baseline ST deviation or ST resolution and mortality is not well established. However, current STEMI guideline recommendations and most prior work do not incorporate the absolute extent of baseline ST elevation or deviation or the location of infarction. Such an integration with relative ST-segment change into ECG algorithms used for overall risk stratification of patients with STEMI might provide incremental prognostic value yet little information exists examining whether the extent of baseline ST deviation influences subsequent ST resolution and clinical outcomes.

Accordingly, we used data from the acute STEMI trial ASSENT-3 to examine whether the prognostic impact of conventionally measured relative ST resolution after fibrinolytic therapy is influenced by either the magnitude of baseline ST deviation or the anatomical site of infarction.

METHODS

The entry criteria for the ASSENT-3 trial have been published.9 Briefly, patients 18 years of age or older with symptom onset <6 hours before randomisation who had ST-segment elevation of at least 0.1 mV in two or more limb leads or at least 0.2 mV in two or more contiguous precordial leads or presumed new left bundle branch were included. For confirmation of the entry acute MI, as well as any recurrent ischaemia or reinfarction during the trial, troponin t and CK/CK-MB and biomarker
ASSENT -3: 30-d and 1-yr mortality in patients with ≥50% and <50% STR at 180 min based on quartiles of baseline ∑STD

Toma et al Heart 2008
90-day composite endpoint according to adherence to ECG entry criteria by infarct location

- Inferior MI and not met (n = 980)
- Inferior MI and met (n = 1,337)
- Other MI and not met (n = 634)
- Other MI and met (n = 2,658)

Tjandrawidjaja et al Eur Heart J. 2007
Implications of Adherence to ECG entry criteria

Rates of clinical endpoint (%)

- Met ECG entry criteria (n=3,999)
- Did not meet ECG entry criteria (n=1,616)

Tjandrawidjaja et al *Eur Heart J.* 2007
What about extent of ST-segment depression?
One-year Survival & ST ↓ status

Kaul et al JACC 2001
ST-dep, NT-proBNP and 1-year Mortality

*All comparisons p<0.03

Westerhout et al JACC 2006
The Discharge ECG Death/(re)mi at 6 m

Herhsi et al. EHJ ‘02
Overview: *New Tricks from Old Dogs*

- **Ischemic Burden:** STE & Non STE
- Infarct Masquerade
- Q wave Insights
- Assessing reperfusion
- Insights into Rx mechanisms
<table>
<thead>
<tr>
<th>Baseline ECG</th>
<th>Randomization</th>
<th>TNK</th>
<th>90 min Post TNK ECG</th>
<th>Pre Cath ECG</th>
<th>Rescue PCI</th>
<th>Post Cath ECG</th>
<th>Discharge ECG</th>
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<tbody>
<tr>
<td>- 57</td>
<td>- 14</td>
<td>0</td>
<td>84</td>
<td>85</td>
<td>Not done</td>
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<td>05:45</td>
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<td>06:53</td>
<td>08:40</td>
</tr>
</tbody>
</table>

15 Sep 10
Baseline

90 min
What about Q waves at time of presentation?
Baseline Q Wave: Death/ CHF/ Shock

Cumulative death/CHF/shock, %

Days to follow-up

Baseline Q-wave (n= 2514)

No Baseline Q-wave (n=2016)

p(logrank)<0.001

Armstrong et al 2009 JACC
Baseline Q Wave & Time Sx onset to PCI: 90-Day Outcomes

Death

Baseline Q-wave

A: 1.78 (1.23-2.56), p=0.002

Sx to PCI > 3 hr

A: 1.35 (0.97-1.75), p=0.078

Death/CHF/shock

Baseline Q-wave

A: 1.90 (1.49-2.41), p<0.001

Sx to PCI > 3 hr

A: 1.42 (1.14-1.77), p=0.002

Armstrong et al 2009 JACC
Time vs. Q for risk stratification: Men

**Time to PCI**
- 30-day dth
- 90-day dth
- 30-d combo
- 90-d combo

**Q-wave**
- 30-day dth
- 90-day dth
- 30-d combo
- 90-d combo

- PCI<=3hr
- PCI > 3hr
- Non Q
- Q-wave

Kaul et al ESC 2010
What about Time and Women?

Kaul et al ESC 2010
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<th>Discharge ECG</th>
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<td>97</td>
<td>111</td>
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</tbody>
</table>
Aborted MI

Pre

Post Reperfusion
Aborted MI subgroup analysis

- 30d death/re-infarction/refractory ischemia
  - ST res @60min>70%: 7.5%
  - ST res @60min<70%: 10.8%
  - p=ns

- Death at 30d
  - ST res @60min>70%: 1.0%
  - ST res @60min<70%: 6.1%
  - p=0.001

- In-hospital re-infarction
  - ST res @60min>70%: 3.2%
  - ST res @60min<70%: 2.2%
  - p=ns

Taher et al JACC 2004
Aborted MI subgroup analysis

European Heart Journal Advance Access published March 16, 2006

Aborted myocardial infarction: a new target for reperfusion therapy

Freek W.A. Verheugt*, Bernard J. Gersh, and Paul W. Armstrong

1Heartcenter, Department of Cardiology, University Medical Center, St Radboud, Nijmegen, The Netherlands; 2Cardiovascular Diseases and Internal Medicine, Mayo Clinic and Mayo Foundation, Rochester, MN, USA; and 3Division of Cardiology, University of Alberta, Edmonton, Canada

Received 3 November 2005; revised 9 February 2006; accepted 16 February 2006

Keywords
Myocardial infarction; Reperfusion therapy; Creatine kinase; Abortion

Reperfusion therapy for ST-elevation acute coronary syndromes aims at early and complete recanalization of the infarct-related artery in order to salvage myocardium and improve both early and late clinical outcomes. Myocardial necrosis is usually confirmed and quantified by myocardial enzyme release in plasma. However, over 10% of patients treated with reperfusion therapy fail to develop an enzyme rise, but do exhibit transient ECG changes, which are consistent with an aborted myocardial infarction. The earlier the reperfusion therapy is instituted, the higher the incidence of aborted infarction. Treatment within an hour after symptom onset may result in 25% of aborted infarction and is in combination with complete (70%) ST-segment resolution associated with better survival. This endpoint is easy to define and occurs promptly in time. The faster that effective treatment is initiated, the more likely aborted infarction will occur. Given that mortality, re-infarction, and stroke are declining in incidence, we suggest the introduction of aborted infarction as an endpoint in clinical trials of ST-elevation acute coronary syndromes.
ST-Segment Recovery and Outcome After Primary Percutaneous Coronary Intervention for ST-Elevation Myocardial Infarction

Insights From the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX-AMI) Trial

Christopher E. Buller, MD; Yuling Fu, MD; Kenneth W. Mahaffey, MD; Thomas G. Todaro, MD; Peter Adams, MD; Cynthia M. Westerhout, PhD; Harvey D. White, MD; Arnoud W.J. van 't Hof, MD; Frans J. Van de Werf, MD; Galen S. Wagner, MD; Christopher B. Granger, MD; Paul W. Armstrong, MD

Background—Primary percutaneous coronary angioplasty is an effective and widely adopted treatment for acute myocardial infarction. A simple method of determining prognosis after primary percutaneous coronary intervention (PCI) would facilitate appropriate care and expedite hospital discharge. Thus, we determined the prognostic importance of various measures of ST-segment—elevation recovery after primary PCI in a large, contemporary cohort of patients with ST-elevation myocardial infarction.

Methods and Results—We analyzed ECG data describing the magnitude and extent of ST-segment elevation and deviation before and early after (ie, 30 minutes) primary PCI in the study cohort of 4866 subjects with electrocardiographically high-risk ST-elevation myocardial infarction enrolled in the Assessment of PEXelizumab in Acute Myocardial Infarction (APEX-AMI) trial. Associations among 6 methods for calculating ST-segment recovery, biomarker estimates of infarct size (ie, peak creatine kinase, creatine kinase-MB, and troponin I and T), and prespecified clinical outcomes (ie, rates of 90-day death and 90-day death, heart failure, or shock) were examined. All ST-segment—recovery methods provided strong prognostic information regarding clinical outcomes. A simple ST-segment—recovery method of residual ST-segment elevation measurement in the most affected lead on the post-PCI ECG performed as well as complex methods that required comparison of pre- and post-PCI ECGs or calculation of summed ST-segment deviation in multiple leads (ie, worst-lead residual ST elevation: adjusted hazard ratio for 90-day death rate [reference <1 mm]: 1 to <2 mm, 1.23 [95% CI 0.74 to 2.03]; ≥2 mm, 2.22 [95% CI 1.35 to 3.65], corrected c-index=0.832; 90-day death/congestive heart failure/shock [reference <1 mm]: 1 to <2 mm, 1.55 [95% CI 1.06 to 2.26]; ≥2 mm, 2.33 [95% CI 1.59 to 3.41], corrected c-index=0.802). Biomarker estimates of infarct size declined in association with enhanced ST-segment recovery.

Conclusions—An ECG performed early after primary PCI is a simple, widely available, inexpensive, and powerful prognostic tool applicable to patients with ST-elevation myocardial infarction. (Circulation. 2008;118:1335-1346.)
30-min post-PCI ST-resolution revealed striking risk gradation in primary PCI STEMI pts enrolled in APEX AMI

- Complete ST resolution: n=2548, 5.1%
- Partial ST resolution: n=1701, 8.1%
- No ST resolution: n=791, 13.3%

Buller et al Circulation 2008
Resolution of ST-segment depression: a new prognostic marker in ST-segment elevation myocardial infarction

Michael C. Tjandrawidjaja¹, Yuling Fu¹, Cynthia M. Westerhout¹, Harvey D. White², Thomas G. Todaro³, Frans Van de Werf⁴, Kenneth W. Mahaffey⁵, Galen S. Wagner⁵, Christopher B. Granger⁵, and Paul W. Armstrong¹* on behalf of the APEX-AMI Investigators

¹Department of Medicine, Division of Cardiology, University of Alberta, 2-51 Medical Sciences Building, Edmonton, Alberta, Canada T6G 2H7; ²Auckland City Hospital, Auckland, New Zealand; ³Procter & Gamble, Mason, OH, USA; ⁴University Hospital Gasthuisberg, Leuven, Belgium; and ⁵Duke Clinical Research Institute, Durham, NC, USA

Received 11 December 2008; revised 15 May 2009; accepted 28 May 2009; online publish-ahead-of-print 1 December 2009

Aims

To evaluate the prognostic impact of ST depression resolution among patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary PCI in the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX-AMI) trial.

Methods and results

In this study, 4729 of 5745 patients had analysable ECGs demonstrating concomitant ST-segment depression. Resolution of $\sum ST$ elevation (STE-R) and $\sum ST$ depression (STD-R) on 30 min post-PCI ECGs was dichotomized into those with $\geq 50\%$ vs. $<50\%$ ST-segment resolution. Overall, 1143 patients (24%) had STD-R $<50\%$. These patients had higher risk characteristics including older age, female sex, diabetes, hypertension, prior CHF/MI, Killip class $>1$, triple vessel disease, and less frequent TIMI 3 flow in the culprit coronary vessel post-PCI. After multivariable adjustment and accounting for STE-R, STD-R $<50\%$ remained an independent predictor for 90 day death and the composite of death, cardiogenic shock, or CHF. When compared with patients with both STE-R and STD-R $\geq 50\%$, patients with both STE-R and STD-R $<50\%$ had the worst outcomes [hazard ratios (HR) 90 day death: 2.54; 95% confidence intervals (CI): 1.71–3.77; HR 90 day composite: 2.18; 95% CI: 1.63–2.91].

Conclusion

When ST depression is present in STEMI patients undergoing primary PCI, STD-R $<50\%$ provides independent prognostic value that is incremental to STE-R.
## Selected baseline & angiographic characteristics

<table>
<thead>
<tr>
<th></th>
<th>ST ↑ resolution ≥50%</th>
<th>ST ↑ resolution &lt;50%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ST ↓ ≥50% (n = 2,856)</td>
<td>ST ↓ &lt;50% (n = 560)</td>
</tr>
<tr>
<td>Age, yr, median</td>
<td>60</td>
<td>64*</td>
</tr>
<tr>
<td>Female, %</td>
<td>22</td>
<td>29*</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>47</td>
<td>52*</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>13</td>
<td>17*</td>
</tr>
<tr>
<td>Killip class &gt;I, %</td>
<td>9</td>
<td>12*</td>
</tr>
<tr>
<td>Time to PCI, hr</td>
<td>3.3</td>
<td>3.3</td>
</tr>
</tbody>
</table>

*Significant difference compared to ST ↑ resolution ≥50%.*

1 in 4 patients with ST-depression resolution <50%
## Selected baseline & angiographic characteristics

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</tr>
<tr>
<td>$\sum$ST↑,mm, median</td>
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<td>10.0</td>
</tr>
<tr>
<td>$\sum$ST↓,mm, median</td>
<td>6.0</td>
<td>4.5*</td>
</tr>
<tr>
<td>Post-PCI TIMI 3,%</td>
<td>93</td>
<td>91*</td>
</tr>
<tr>
<td>Triple vessel dz,%</td>
<td>13</td>
<td>19*</td>
</tr>
</tbody>
</table>

*Significantly different from ST ↑ resolution ≥50% group.
ST-Elevation Acute Coronary Syndromes in the Platelet Inhibition and Patient Outcomes (PLATO) Trial
Insights From the ECG Substudy

Paul W. Armstrong, MD; Hany Siha, MD; Yuling Fu, MD; Cynthia M. Westerhout, PhD; Ph. Gabriel Steg, MD; Stefan K. James, MD, PhD; Robert F. Storey; MD, DM; Jay Horrow, MD; Hugo Katus, MD; Peter Clemmensen, MD, PhD; Robert A. Harrington, MD; Lars Wallentin, MD, PhD

Background—Ticagrelor, when compared with clopidogrel, reduced the 12-month risk of vascular death/myocardial infarction and stroke in patients with ST-elevation acute coronary syndromes intended to undergo primary percutaneous coronary intervention in the PLATElet inhibition and patient Outcomes (PLATO) trial. This prespecified ECG substudy explored whether ticagrelor’s association with vascular death and myocardial infarction within 1 year would be amplified by (1) the extent of baseline ST shift and (2) subsequently associated with fewer residual ST changes at hospital discharge.

Methods and Results—ECGs were evaluated centrally in a core laboratory in 3122 ticagrelor- and 3084 clopidogrel-assigned patients having at least 1 mm ST-elevation in 2 contiguous leads as identified by site investigators on the qualifying ECG. Patients with greater ST-segment shift at baseline had higher rates of vascular death/myocardial infarction within 1 year. Among those who also had an ECG at hospital discharge (n=4798), patients with ≥50% ST-deviation (ΣST-dev) resolution had higher event-free survival than those with incomplete resolution (6.4% versus 8.8%, adjusted hazard ratio 0.69 (0.54–0.88), P=0.003). The extent of ΣST-dev resolution was similar irrespective of treatment assignment. The benefit of ticagrelor versus clopidogrel on clinical events was consistent irrespective of the extent of baseline ΣST-dev (P(interaction)=0.728). When stratified according to conventional times from symptom onset, ie, ≤3 hours, 3 to 6 hours, >6 hours, the extent of baseline ΣST-dev declined progressively over time. As time from symptom onset increased beyond 3 hours, the benefit of ticagrelor appeared to be more pronounced; however, the interaction between time and treatment was not significant (P=0.175).

Conclusions—Ticagrelor did not modify ΣST-dev resolution at discharge nor was its benefit affected by the extent of baseline ΣST-dev. These hypothesis-generating observations suggest that the main effects of ticagrelor may not relate to the rapidity or the completeness of acute reperfusion, but rather the prevention of recurrent vascular events by more powerful platelet inhibition or other mechanisms.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00391872.
(Circulation. 2012;125:514-521.)
Primary efficacy endpoint over time (composite of CV death, MI or stroke)

Cumulative incidence (%)

Clopidogrel

Ticagrelor

HR 0.88 (95% CI 0.77–1.00), p=0.045

No. at risk

<table>
<thead>
<tr>
<th>Days after randomisation</th>
<th>Ticagrelor</th>
<th>Clopidogrel</th>
</tr>
</thead>
<tbody>
<tr>
<td>31</td>
<td>8,942</td>
<td>8,875</td>
</tr>
<tr>
<td>90</td>
<td>8,543</td>
<td>8,437</td>
</tr>
<tr>
<td>150</td>
<td>8,397</td>
<td>8,286</td>
</tr>
<tr>
<td>210</td>
<td>7,028</td>
<td>6,945</td>
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<tr>
<td>270</td>
<td>6,480</td>
<td>6,379</td>
</tr>
<tr>
<td>330</td>
<td>4,822</td>
<td>4,751</td>
</tr>
</tbody>
</table>

*Excludes patients with any primary event during the first 30 days
One-year CV-death/MI by $\sum$ST-deviation resolution

Survival Probability

$\geq 50\%$ (n=3135) 6.4%

$< 50\%$ (n=1556) 8.9%

$p$(Logrank) = 0.001

Time to event (days)
One-year CV-death/MI by Rx & $\sum$ST-deviation resolution

$P = 0.10$ (study treatment / $\sum$ST-dev res)

Armstrong et al Circulation 2011
ST-D Resolution ≥50%

Armstrong et al. *Circulation* 2012
Primary efficacy endpoint over time (composite of CV death, MI or stroke)

**Cumulative incidence (%)**

- **Clopidogrel**
  - Days after randomisation: 31
  - Cumulative incidence: 5.43%
  - HR 0.88 (95% CI 0.77–1.00), p=0.045
  - No. at risk: 9,333
  - Days after randomisation: 90
  - Cumulative incidence: 6.60%
  - HR 0.80 (95% CI 0.70–0.91), p<0.001
  - No. at risk: 8,688

- **Ticagrelor**
  - Days after randomisation: 31
  - Cumulative incidence: 5.28%
  - No. at risk: 9,291

*Excludes patients with any primary event during the first 30 days*
There are *New Tricks from Old Dogs*

- **ECG is a renaissance tool**
- Grossly underappreciated bioassay
- Prognostically powerful
- Unique insights into “state of play AMI”
- Promptly responsive to interventions
- Insights into Rx choices / Mechanisms
- Valuable Metric in Clinical Trials