Participation in thrombolytic trials delays the onset of reperfusion therapy in STE ACS

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INTRODUCTION

The value of clinical studies in the development of strategies to reduce mortality and morbidity from cardiovascular disease is beyond dispute.

However, it is likely, that enrollment to the trials in STEMI may paradoxically prolong the time delay to treatment, if enrollment procedure (including informed consent), randomisation and drug preparation process is too complex.
The aim of this study was to evaluate the in-hospital time delay of the onset of reperfusion therapy in patients randomised to thrombolytic trials or treated routinely with thrombolytics (Thrx).
Door-to-needle time (DtN)
(retrospective analysis)

Time of admission to the hospital

Time of the beginning of thrombolytic therapy
Inclusion and exclusion criteria

- AMI with ST-segment elevation diagnosed on admission in the Emergency Room
- No signs of heart failure
- No arrhythmia requiring treatment
- No contraindications to immediate thrombolysis

The inclusion and exclusion criteria for the study were the same for three evaluated groups of pts.
### STUDY GROUP  
\( n = 198 \)

<table>
<thead>
<tr>
<th>Age (mean)</th>
<th>60+/-12</th>
</tr>
</thead>
<tbody>
<tr>
<td>min / max</td>
<td>35 / 86</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender (male)</th>
<th>n=127 (64%)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Prehospital delay</th>
<th>median (25%, 75%)</th>
<th>120 min (90-240 min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>min / max</td>
<td>30 min / 720 min</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Admission Time</th>
<th>n=158 (80 %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>single physician on-duty</td>
<td>n= 45 (23%)</td>
</tr>
<tr>
<td>night-time (24.00-06.00)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mode of treatment</th>
<th>n= 96 (48%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrx</td>
<td></td>
</tr>
<tr>
<td>trial A</td>
<td>n= 18 (9 %)</td>
</tr>
<tr>
<td>trial B</td>
<td>n= 25 (13% )</td>
</tr>
<tr>
<td>trial C</td>
<td>n= 50 (25% )</td>
</tr>
<tr>
<td>refused</td>
<td>n= 9 (5%)</td>
</tr>
</tbody>
</table>
Study group
(consecutive pts who fulfilled inclusion criteria for the study)

Thr x patients treated routinely with thrombolytics
(no proposal to participate in thrombolytic trials, treated at a time when no study was conducted in a centre)

Trials patients randomised to thrombolytic trials
(3 different trials - A, B, C)

Trials-ref patients who refused to participate in thrombolytic trials and were treated routinely with thrombolytics
DtN - Comparison of evaluated groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Value</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrx</td>
<td>22 +/- 8</td>
<td>96</td>
</tr>
<tr>
<td>Trials</td>
<td>41 +/- 18</td>
<td>93</td>
</tr>
<tr>
<td>Trials ref</td>
<td>37 +/- 13</td>
<td>9</td>
</tr>
</tbody>
</table>

**Results:**
- **Thrx** vs **Trials**: \( p < 0.01 \)
- **Thrx** vs **Trials ref**: \( p < 0.0001 \)
- **Trials** vs **Trials ref**: NS
**DtN - Comparison of trials**
(differences between DtN in three trials)

- **A**
  - $n = 18$
  - $40 +/- 11$

- **B**
  - $n = 25$
  - $41 +/- 16$

- **C**
  - $n = 50$
  - $41 +/- 22$

**NS**

[Diagram showing bar charts for A, B, and C with the specified values and sample sizes.]
**DtN - impact of age**

(difference between subgroups of pts in Thrx and trials - age below/equal or over 60 years)

- **≤ age of 60**
  - Thrx: 25+/-12
  - Trials: 39+/-16
  - p<.001

- **> age of 60**
  - Thrx: 23+/-8
  - Trials: 43+/-20
  - p<.001
DtN - impact of a day-time
(difference between subgroups of pts in Thrx and trials treated at different time of a day and night)

Thrx | Trials
---|---
9AM - 2PM | 39+/−15 | 40+/−20
2PM - 12PM | 23+/−9 | 23+/−11
12PM - 9AM | 23+/−11 | 46+/−22

* - p < .001
RESULTS

 DtN median (25%, 75%) in study population

30 min (20, 40 min)

DtN delay > 30 min

- Trials: 60%, n=61
- Thrx: 11%, n=11
  p < 0.001

DtN delay < 20 min

- Trials: 9%, n=61
- Thrx: 56%, n=11
  p < 0.001
THROMBOLYTIC TREATMENT IN ACUTE MYOCARDIAL INFARCTION

MORTALITY REDUCTION OF THE THROMBOLYTIC THERAPY

GISSI-1, ISIS-2
ASSET, AIMS
LATE EMERAS

V. Fuster, R. Ross, E. Topol; Atherosl. & CAD: 1996
RESULTS

Factors independently influencing DtN (over 30 minutes)

*multivaraite logistic regression analysis*

- Age
- Gender
- Prehospital delay
- Time of admission
  - admission during single physician’s duty
  - night-time vs day-time
- Participation in randomized trial
RESULTS

Factors independently influencing DtN (over 30 minutes)

**Participation in randomized trial**

- **OR 13.2**
  - 95% CI: 6.1 - 28.5
  - *p* < 0.001

**Admission during single physician's duty**

- **OR 2.9**
  - 95% CI: 1.15 - 7.36
  - *p* < 0.03
The impact of study duration
RESULTS

Factors independently influencing DtN (over 30 minutes)

Time elapsed from the study beginning

< median vs Thrx

> median vs Thrx

DtN over 30 min

<table>
<thead>
<tr>
<th>Time elapsed</th>
<th>Shorter</th>
<th>Longer</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; median vs Thrx</td>
<td>OR 31.5</td>
<td>OR 6.5</td>
</tr>
<tr>
<td>95%CI 12.1 - 81.9</td>
<td>95%CI 2.8 - 15.4</td>
<td></td>
</tr>
<tr>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td></td>
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Longer than median vs Thrx

0 10 20 30
Shortening of time delay to the beginning of treatment in ST-segment elevation ACS is proven to be clinically essential

"Time is muscle" and "Every minute counts"
CONCLUSIONS

The value of clinical studies in the development of strategies to reduce mortality and morbidity from cardiovascular disease is beyond dispute.

However

The participation in the trials may unfavourably delay the beginning of reperfusion therapy.

The delay may be clinically important, particularly in patients hospitalised very early from the onset of symptoms.