Elevations of Cardiac Troponin not due to Ischemic Heart Disease

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Cut Off Values for Use and Abuse

Most STE MIs and NSTE MIs diagnosed by troponin and/or CKMB

- **ROC cut off** *(Mayo value = 0.1 ng/ml)*
  Value most likely to equate troponin with CKMB.

Mostly NSTE MIs diagnosed with troponin

- **10% CV cut off** *(Mayo value = 0.03 ng/ml)*
  Value where confounding due to analytic issues is minimized.

Area where diagnostic information may be limited due to assay variability

- **99th percentile** *(Mayo value = <0.01 ng/ml)*
  ESC/ACC recommended cut off value with total precision of <10% as eventual goal.

Apple, Wu, Jaffe: AHJ 144:981, 2002
Troponin T Levels and Outcomes in GUSTO IV ACS

Death or myocardial infarction at 30 days (%)

Sens=88%  Sens=81%  Sens=65%

77  128  231  601  550  447

73%  65%  53%

10%  53%  49th perc.

Below Cutoff  Above Cutoff

0.01 microg/L  0.03 microg/L  0.1 microg/L

Outcomes in Relation to Troponin Values: The Issue of Assay Sensitivity

Rapid Troponin I Assay

<table>
<thead>
<tr>
<th>%</th>
<th>0</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
</tr>
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<tbody>
<tr>
<td>Neg</td>
<td>56</td>
<td>98</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pos</td>
<td></td>
<td>92</td>
<td>130</td>
<td>132</td>
<td>205</td>
</tr>
<tr>
<td>OR</td>
<td>1.80; 1.30-2.54</td>
<td>1.47; 1.12-1.93</td>
<td>1.64; 1.31-2.06</td>
<td></td>
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</tr>
</tbody>
</table>

Troponin T (0.1 μg/L)

<table>
<thead>
<tr>
<th>%</th>
<th>0</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
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<tbody>
<tr>
<td>Neg</td>
<td>41</td>
<td>113</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pos</td>
<td></td>
<td>86</td>
<td>136</td>
<td>116</td>
<td>221</td>
</tr>
<tr>
<td>OR</td>
<td>3.20; 2.22-4.59</td>
<td>1.82; 1.38-2.40</td>
<td>2.26; 1.79-2.85</td>
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<td></td>
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</table>

Troponin T (0.01 μg/L)

<table>
<thead>
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<th>12</th>
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</thead>
<tbody>
<tr>
<td>Neg</td>
<td>15</td>
<td>139</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pos</td>
<td></td>
<td>25</td>
<td>197</td>
<td>36</td>
<td>301</td>
</tr>
<tr>
<td>OR</td>
<td>4.55; 2.66-7.78</td>
<td>3.42; 2.57-5.98</td>
<td>4.29; 3.02-6.09</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Int J Cardiol 93:113, 2004

Death MI Death or MI
cTnT Determinants of Elevation in the Community*

% with elevated cTnT

Risk determinants present (no.)

No. 2,087 478 120 22

P<0.0001

### Prevalence of Detectable cTnT & levels ≥ 99th percentile URL

<table>
<thead>
<tr>
<th>Group</th>
<th>Sample Size, No.</th>
<th>No. (%)</th>
<th>cTnT Level, ng/mL</th>
<th>Sample Weight-Adjusted Prevalence, % (95% CI)</th>
<th>No. (%)</th>
<th>Sample Weight-Adjusted Prevalence, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall population</td>
<td>3546</td>
<td>957 (27.0)</td>
<td>25.0 (22.7 – 27.4)</td>
<td>122 (3.4)</td>
<td>2.0 (1.5 – 2.6)</td>
<td></td>
</tr>
<tr>
<td>Restricted population</td>
<td>3428</td>
<td>891 (26.0)</td>
<td>24.2 (21.8 – 26.5)</td>
<td>103 (3.0)</td>
<td>1.8 (1.2 – 2.4)</td>
<td></td>
</tr>
<tr>
<td>Without CHD</td>
<td>3277</td>
<td>813 (24.8)</td>
<td>23.7 (21.3 – 26.1)</td>
<td>82 (2.5)</td>
<td>1.9 (1.0 – 2.0)</td>
<td></td>
</tr>
<tr>
<td>Without cardiovascular disease</td>
<td>3222</td>
<td>773 (24.0)</td>
<td>23.1 (20.7 – 25.5)</td>
<td>65 (2.3)</td>
<td>1.2 (0.8 – 1.7)</td>
<td></td>
</tr>
<tr>
<td>Without cardiovascular disease or CKD&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without cardiovascular disease, CKD, subclinical heart disease, diabetes, or hypertension&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2554</td>
<td>510 (20.0)</td>
<td>19.3 (16.8 – 21.8)</td>
<td>43 (1.7)</td>
<td>1.1 (0.6 – 1.7)</td>
<td></td>
</tr>
</tbody>
</table>
Elevations of Troponins without Overt Ischemic Heart Disease

- Trauma (including contusion, ablation, pacing, ICD firings including atrial defibrillators, cardioversion, endomyocardial biopsy, cardiac surgery, after interventional closure of ASDs)
- Congestive heart failure—acute and chronic
- Aortic valve disease and HOCM with significant LVH
- Hyper and hypotension, especially with arrhythmias
- Postoperative noncardiac surgery patients who seem to do well
- Renal failure
- Critically ill patients, with respiratory failure, gastrointestinal bleeding, sepsis, heat stroke
- Drug toxicity, eg adriamycin, 5 FU, herceptin, snake venoms, carbon monoxide poisoning
- Hypothyroidism
- Abnormalities in coronary vasomotion, including coronary vasospasm
- Apical ballooning syndrome
- Inflammatory diseases eg. myocarditis, eg. Parvovirus B19, Kawasaki disease, sarcoid, smallpox vaccination, or myocardial extension of BE
- Post PCI patients who appear to be uncomplicated
- Pulmonary embolism, severe pulmonary hypertension
- Sepsis
- Burns, esp if TBSA > 30%
- Cardiomyopathies including Infiltrative diseases such as amyloidosis, hemachromatosis, sarcoidosis and scleroderma, non compaction syndrome
- Acute neurological disease, including CVA, subarchnoid bleeds
- Rhabdomyolysis with cardiac injury
- Transplant vasculopathy
- Vital Exhaustion
Comparison of Normals Detected With Various Assays

- Singulex hsTnl
- ARCHITECT hsTnl
- Siemens hsTnl
- Beckman Access hsTnl
- Roche hsTnT
  - Beckman Tnl
  - Siemens Tnl Ultra (Centaur)
  - Siemens Tnl (Immulite)
  - AxSYM Tnl
  - ARCHITECT Tnl
  - OCD Tnl
  - Siemens Tnl (Dimension)
  - Roche Tnl
  - Siemens Tnl (Vista)
  - IL cTnl
  - Abbott ISTAT
  - Siemens Stratus
  - Alere
  - BioMerleux

Detected (%)

hsTnl Values at ED Presentation Among Subjects With Non-Elevated Standard cTnl in Initial Sample

Korley, Jaffe, AEMJ 2014
### Relationship of hsc-TnT and Mortality by Diagnosis in Swedeheart


<table>
<thead>
<tr>
<th>hs-cTnT ng/L</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>&lt;6</td>
<td></td>
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<tr>
<td>10-6</td>
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</tr>
<tr>
<td>18-11</td>
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<td>19-32</td>
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<td>33-62</td>
<td></td>
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<tr>
<td>63-133</td>
<td></td>
</tr>
<tr>
<td>134-304</td>
<td></td>
</tr>
<tr>
<td>305-755</td>
<td></td>
</tr>
<tr>
<td>756-2,250</td>
<td></td>
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<tr>
<td>&gt;2,250</td>
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</table>

<table>
<thead>
<tr>
<th>hs-cTnT ng/L</th>
<th>HR</th>
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<tbody>
<tr>
<td>&lt;6</td>
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<tr>
<td>10-6</td>
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</tr>
<tr>
<td>305-755</td>
<td></td>
</tr>
<tr>
<td>756-2,250</td>
<td></td>
</tr>
<tr>
<td>&gt;2,250</td>
<td></td>
</tr>
</tbody>
</table>

- ACS
- Other cardiac disease
- Other non-cardiac
- Heart failure
All-Cause Mortality by Cardiac Troponin T (n=733)

### Cumulative survival

<table>
<thead>
<tr>
<th>cTnT &lt;0.01 µg/L</th>
<th>cTnT ≥0.04 µg/L</th>
<th>cTnT ≥0.04 to 0.10 µg/L</th>
<th>cTnT ≥0.10 µg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients at risk (no.)</td>
<td>Baseline</td>
<td>1 yr</td>
<td>2 yr</td>
</tr>
<tr>
<td>cTnT &lt;0.01 µg/L</td>
<td>132</td>
<td>106</td>
<td>25</td>
</tr>
<tr>
<td>cTnT ≥0.01 to &lt;0.04 µg/L</td>
<td>214</td>
<td>166</td>
<td>41</td>
</tr>
<tr>
<td>cTnT ≥0.04 to &lt;0.10 µg/L</td>
<td>239</td>
<td>180</td>
<td>63</td>
</tr>
<tr>
<td>cTnT ≥0.10 µg/L</td>
<td>148</td>
<td>93</td>
<td>20</td>
</tr>
</tbody>
</table>

Circulation 106:2944, 2002
Relationship of Elevated Marker Proteins and Pathology in Patients


**No Myocardial Pathology**

- CK: 20%
- MB: 0%
- cTnI: 0%
- cTnT: 0%

**Old MI or Patchy Fibrosis**

- CK: 29%
- MB: 0%
- cTnI: 14%
- cTnT: 22%

**Recent MI**

- CK: 19%
- MB: 19%
- cTnI: 48%
- cTnT: 67%

**Healing MI**

- CK: 33%
- MB: 17%
- cTnI: 50%
- cTnT: 43%

**CHF**

- CK: 40%
- MB: 10%
- cTnI: 20%
- cTnT: 42%

**Other Cardiac Pathology**

- CK: 13%
- MB: 25%
- cTnI: 25%
- cTnT: 63%
cTnT Values in Patients with ESRD Over Time

Recognized vs Unrecognized Myocardial Injury

Guest, Jaffe, JAMA 1995
Mortality

Guest, Jaffe, JAMA 1995
Mortality in Patients with Detectable Levels of cTnI (Critically Ill Group)

Wright, Jaffe, AJC 2002
Short-Term Prognosis of Critically Ill Patients in the MICU

Survival distribution function

Follow-up (days)

Normal troponin <0.01 ng/mL
cTnT <0.01

Elevated troponin >0.01 ng/mL

cTnT ≥0.01

P<0.001

Babuin, Jaffe, CCM 2008
Mortality at 30 Days By cTnT Level

Mortality at 30 days (% of patient)

- <0.01: 12.8%, 359 patients
- ≥0.01-0.03: 26.4%, 178 patients
- >0.03-0.1: 31.1%, 206 patients
- >0.1: 41.4%, 186 patients

Risk ratio
- <0.01: 1
- ≥0.01-0.03: 2.10
- >0.03-0.1: 2.66
- >0.1: 3.58

95% CI
- <0.01: --
- ≥0.01-0.03: 1.40-3.15
- >0.03-0.1: 1.82-3.88
- >0.1: 2.48-5.16

Babuin, Jaffe, CCM 2008
Long-Term Prognosis of Critically Ill Patients in the MICU

Survival distribution function

Follow-up (days)

Normal troponin <0.01 ng/mL

cTnT < 0.01

Elevated troponin >0.01 ng/mL

cTnT ≥ 0.01

P < 0.0001

P < 0.001

Babuin, Jaffe, CCM 2008
Probability of Death Based on cTnT Values on Admission in Patients With GI Bleeding*

![Graphs showing probability of death based on cTnT values](image)

**30-Day**

- cTnT negative
- cTnT positive

**30-Day Survivors**

- cTnT negative
- cTnT positive

**Patients at risk**

<table>
<thead>
<tr>
<th>Days</th>
<th>cTnT negative</th>
<th>cTnT positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 day</td>
<td>425</td>
<td>329</td>
</tr>
<tr>
<td>15 days</td>
<td>371</td>
<td>282</td>
</tr>
<tr>
<td>30 days</td>
<td>361</td>
<td>254</td>
</tr>
<tr>
<td>31 days</td>
<td>361</td>
<td>252</td>
</tr>
<tr>
<td>2.5 years</td>
<td>143</td>
<td>57</td>
</tr>
<tr>
<td>5 years</td>
<td>16</td>
<td>8</td>
</tr>
</tbody>
</table>

**Log-rank test:**

- Chi-square = 11.2
- P-value = 0.001

- Chi-square = 64.0
- P-value < 0.001

*Critical Care Medicine 37:140, 2009*
Hs-cTnI and hs-cTnT Concentrations Before and After Exercise Dobutamine

![Graph showing concentrations of troponin I and troponin T before and after exercise.](graph)

Clinical Chemistry 58:11, 2012
Probability of Death Based on cTnT Values on Admission in Patients With Acute Respiratory Failure*

Probability of Death Based on cTnT Values on Admission in Patients With Sepsis

![Graph showing the probability of death based on cTnT values. The graph compares patients with cTnT negative and cTnT positive values.](image)

Log-rank test:
Chi-square = 19.2
P-value < 0.001

Log-rank test:
Chi-square = 18.6
P-value < 0.001

<table>
<thead>
<tr>
<th>Days</th>
<th>cTnT negative</th>
<th>cTnT positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 day</td>
<td>281</td>
<td>643</td>
</tr>
<tr>
<td>15 days</td>
<td>262</td>
<td>567</td>
</tr>
<tr>
<td>30 days</td>
<td>221</td>
<td>423</td>
</tr>
<tr>
<td>31 days</td>
<td>221</td>
<td>421</td>
</tr>
<tr>
<td>2.5 years</td>
<td>112</td>
<td>185</td>
</tr>
<tr>
<td>5 years</td>
<td>38</td>
<td>44</td>
</tr>
</tbody>
</table>

*The American Journal of Medicine: 126(12):1114, 2013*
Relationship Between hscTnT and Diastolic and RV Echo Measures*

- Longitudinal strain-rate $e$-wave
  - $r = -0.356$
  - $P < 0.0001$

- Right ventricular end-systolic volume index
  - $r = 0.383$
  - $P < 0.0001$

Crit Care Med 42:790, 2014
Outcomes in Patients With AF Stratified by CHA₂DS₂-VASc Score and hs-TnT
12,892 Patients ARISTOTLE Trial

Stroke and Systemic Embolism

Cardiac Death

Hijazi: JACC
Outcomes in Patients With AF Stratified by CHA$_2$DS$_2$-VASc Score and hs-TnT
12,892 Patients ARISTOTLE Trial

Major Bleeding

hs-Troponin-T (ng/L)
- ≤1.5
- >1.5-6.8
- >6.8-13
- >13

Major bleeding (%)
Event Rates in Relation to Levels of hs-Troponin I and CHA$_2$DS$_2$-VASc Risk Score

Stroke and Systemic Embolism

Cardiac Death

Major Bleeding

BMI and Elevated hscTnT

Adjusted Odds Ratio (95% CI)

BMI (kg/m²)

Ndumele et al: JACC: Heart Failure 2:600, 2014
**Incidence of HF by hscTnT and BMI**

P value for interaction term = .010

- **Undetectable hs-cTnT**
- **Measureable hs-cTnT**
- **High hs-cTnT**

Ndumele et al: JACC: Heart Failure 2:600, 2014
Roca et al: Am J Respir Crit Care Med188:1460, 2013

Relationship of OSA to hs-cTnT

OSA categories

- None (904)
- Mild (475)
- Moderate (166)
- Severe (100)

Hs-troponin T (µg/L)

0.002
0.003
0.005
0.006
0.01
0.02
0.03
0.04

- None: 0.004 (<0.003, 0.006)
- Mild: 0.005 (<0.003, 0.008)
- Moderate: 0.005 (0.003, 0.009)
- Severe: 0.006 (0.004, 0.01)
Changing hscTnl (Nanosphere) and Mortality in Acute Heart Failure

Euro J Hrt Failure, Jan 2011

- Stable or decreasing troponin (65 subjects)
- Increasing troponin (41 subjects)
Prognosis with hscTnl (Nanosphere) and BNP in Acute Heart Failure

Days

Days

Event free (death or readmission)

High BNP & high Tnl (56 subjects)

High BNP & low Tnl (26 subjects)

Low BNP & low Tnl (34 subjects)

Low BNP & high Tnl (28 subjects)

Euro J Hrt Failure, Jan 2011
Death and Hospitalization and hsTnT at Baseline

Mortality Based on Change in hscTnT Values

Val-HeFT

Log-rank test: P=0.002

<table>
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<tr>
<th></th>
<th>Year 0</th>
<th>Year 1</th>
<th>Year 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I</strong></td>
<td>1,009</td>
<td>929</td>
<td>491</td>
</tr>
<tr>
<td><strong>S</strong></td>
<td>1,409</td>
<td>1,349</td>
<td>738</td>
</tr>
<tr>
<td><strong>D</strong></td>
<td>1,056</td>
<td>1,006</td>
<td>589</td>
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</table>

GISSI-HF

Log-rank test: P=0.0005

<table>
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<th>Year 0</th>
<th>Year 2</th>
<th>Year 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I</strong></td>
<td>271</td>
<td>219</td>
<td>122</td>
</tr>
<tr>
<td><strong>S</strong></td>
<td>445</td>
<td>391</td>
<td>260</td>
</tr>
<tr>
<td><strong>D</strong></td>
<td>350</td>
<td>319</td>
<td>170</td>
</tr>
</tbody>
</table>

All cause mortality

No. at risk

Val-HeFT

I = >15% increase, S = stable, D = > 15% decrease

Mason et al: AHA, 2011
**hscTnT and Markers of Fibrosis**

CITP tertiles
- **I** (<3.00-4.75 pg/mL)
- **II** (4.75-11.10 pg/mL)
- **III** (>11.10 pg/mL)

CITP = carboxyterminal telopeptide of type I collagen
PIIINP = amnioterminal propeptide of procollagen III
PIP = procollagen type I

*P<0.01 compared to each of the control groups

Kop et al: Circ Heart Fail 5:406, 2012
**hscTnT Values and Fibrosis by MRI in Patients with HOCM**

![Box plot showing hscTnT values in HCM fibrosis, HCM no fibrosis, and Control groups.](image)

Journal of Cardiac Failure Vol. 16 No. 12, 2010
All Cardiovascular Events in Patients With HOCM by hs-cTnT Values

Kubo et al: JACC, 2013

Follow-up (years)

Event free rate (%)

Normal hs-cTnT (≤0.014 ng/mL) n=84

Whole cohort (n=183)
P < 0.001

Abnormal hs-cTnT (>0.014 ng/mL)

Abnormal hs-cTnT group (n=99)
P = 0.020

Lower (n=32)

Middle (n=32)

Upper (n=35)
Total Mortality by cTnT Values

All-Cause Mortality

P<0.001 for all between-group comparisons by the log-rank test; detectable cardiac troponin T (cTnT) levels are 0.003 ng/mL or greater by the highly sensitive assay; Y-axes shown in blue indicate the range from 0% to 20%

JAMA 304(22):2503, 2010
Prognostic Value of hscTnT in Cardiovascular Health Study by hscTnT

Heart Failure

Cardiac troponin T
- Category 1
- Category 2
- Category 3
- Category 4
- Category 5

Proportion free of heart failure

Follow-up (yr)

No. at risk
Category 1: 1,427 1,380 1,281 1,131 956 763 461
Category 2: 697 658 586 508 401 291 169
Category 3: 700 642 550 435 333 231 131
Category 4: 697 628 505 377 272 176 99
Category 5: 700 532 357 213 119 77 36

Cardiovascular Death

Cardiac troponin T
- Category 1
- Category 2
- Category 3
- Category 4
- Category 5

Proportion without cardiovascular death

Follow-up (yr)

No. at risk
Category 1: 1,427 1,399 1,335 1,209 1,064 889 607
Category 2: 697 675 619 554 460 343 229
Category 3: 700 664 602 507 400 297 186
Category 4: 697 655 565 461 344 231 137
Category 5: 700 603 454 291 173 102 48

P<0.001

deFilippi: JAMA 304(22), 2010
Prognostic Value of Changes in hscTnT

Heart Failure

<table>
<thead>
<tr>
<th>Baseline cTnT (pg/mL)</th>
<th>Incidence rate/100 person-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3.00</td>
<td></td>
</tr>
<tr>
<td>3.00-5.44</td>
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</tr>
<tr>
<td>5.45-8.16</td>
<td></td>
</tr>
<tr>
<td>8.17-12.94</td>
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<tr>
<td>&gt;12.94</td>
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</tbody>
</table>

Cardiovascular Death

<table>
<thead>
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<th>Baseline cTnT (pg/mL)</th>
<th>Incidence rate/100 person-years</th>
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<tbody>
<tr>
<td>&lt;3.00</td>
<td></td>
</tr>
<tr>
<td>3.00-5.44</td>
<td></td>
</tr>
<tr>
<td>5.45-8.16</td>
<td></td>
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<tr>
<td>8.17-12.94</td>
<td></td>
</tr>
<tr>
<td>&gt;12.94</td>
<td></td>
</tr>
</tbody>
</table>

deFilippi: JAMA 304(22), 2010
Association of Moderate Physical Activity, Rise in Hs cTnT Level and Risk of New Onset Heart Failure

Composite score is a sum of walking pace and duration of moderate to intense leisure activities. A higher score is a faster pace and longer duration of activity.

deFilippi C: J Am Coll Cardiol 60:2539, 2012
Prevention of High-Dose Chemotherapy–Induced Cardiotoxicity in High-Risk Patients by Angiotensin-Converting Enzyme Inhibition

Daniela Cardinale, MD; Alessandro Colombo, MD; Maria T. Sandri, MD; Giuseppina Lamantia, MD; Nicola Colombo, MD; Maurizio Civelli, MD; Giovanni Martinelli, MD; Fabrizio Veglia, PhD; Cesare Fiorentini, MD; Carlo M. Cipolla, MD

Primary end-point:
LVEF decrease >10 percent units + <50%
**TnI Values in Both Groups**

<table>
<thead>
<tr>
<th>Time</th>
<th>ACEI group</th>
<th>Control subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>M1</td>
<td>45/43</td>
<td>41/41</td>
</tr>
<tr>
<td>M2</td>
<td>4/41</td>
<td>3/10</td>
</tr>
<tr>
<td>M3</td>
<td>21/41</td>
<td>0/10</td>
</tr>
<tr>
<td>M6</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td>M12</td>
<td>0/3</td>
<td>0/0</td>
</tr>
</tbody>
</table>

- Early: 56 subjects, TnI (ng/mL) $0.18 \pm 0.38$
- M1: 56 subjects, TnI (ng/mL) $0.15 \pm 0.34$
- M2: 56 subjects, TnI (ng/mL) $0.02 \pm 0.02$
- M3: 56 subjects, TnI (ng/mL) $0.01 \pm 0.01$
- M6: 56 subjects, TnI (ng/mL) $0.01 \pm 0.01$
- M12: 55 subjects, TnI (ng/mL) $0.00 \pm 0.01$

Reference: Circ 114:2474, 2006

ACEI group

Control subjects
**LVEF with and Without ACEI**

**Controls**
- No Tnl increase
- Tnl increase

**ACEI Group**
- No Tnl increase
- Tnl increase

Circ 114:2474, 2006
### Secondary end-points

**follow-up 12 months**

<table>
<thead>
<tr>
<th>Event</th>
<th>ACEI n=54</th>
<th>Controls n=58</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden death</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>2 (2%)</td>
<td>0 (0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Acute pulmonary edema</td>
<td>4 (2%)</td>
<td>0 (0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Heart failure</td>
<td>14 (12%)</td>
<td>0 (0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Life-threatening arrhythmias</td>
<td>11 (10%)</td>
<td>1 (2%)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**CUMULATIVE EVENTS**

<table>
<thead>
<tr>
<th></th>
<th>ACEI n=54</th>
<th>Controls n=58</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>31 (28%)</td>
<td>1 (2%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>
Mortality of Patients With and Without Myocardial Injury

Mortality (%)

Time since hospitalization (yr)

No. at risk

Myocardial injury

No myocardial injury

P < 0.001

JAMA 295(4):398, 2006
Change in Troponin Concentration at One Year and Risk Reduction

- Change in troponin concentration predicted MI and CHD death at 5 years independent of baseline LDL and change in LDL cholesterol (P<0.001)
- Participants with largest reduction in troponin (>40%) on pravastatin had a 4-fold greater reduction in primary endpoint (HR 0.21) than in those participants where troponin was unchanged (HR 0.82); P=0.001 for trend

* Adjusted for age, BMI, heart rate, SBP, DBP, HDL and LDL cholesterol, symptoms of angina, diabetes, Htn, FHx of premature CHD, minor ECG abnormalities, nitrate use and smoking status