species (ROS) derived from the NADPH-oxidase NOX2 and visa versa. Both CML and NOX2-ROS are pro-inflammatory. In patients with Type 2 DM, glucagon like peptide 1 (GLP-1) analogues are applied to stimulate insulin release. Beyond these effects GLP-1 analogues have cardiovascular protective effects, although their exact mechanisms are unknown. Here we have studied whether the GLP-1 analogue Liraglutide has an effect on the CML-NOX2-RDS axis in the heart.

Methods: DM was induced in Sprague Dawley rats via i.p. STZ injection (60 mg/kg body weight) on day 1 of the experiment, resulting in blood glucose levels of > 27 mmol/l in DM rats. In one group, Liraglutide was applied daily s.c. (200 microg/kg bodyweight) starting on day 9. On day 29, the hearts were excised and embedded in paraffin. Heart tissue sections were analyzed immunohistochemically for the presence of CML and NOX2. The stainings were quantified using QPRODIT analysis. For CML and NOX2 the number of positive vessels were analyzed. For CML the staining intensity was also scored (1= mild, 2=moderate, 3=strong positive vessels).

Results: The immunohistochemical score (mean intensity score/square mm) for CML positive intramyocardial arteries increased from 1.73±0.18 in controls up to 2.55±0.44 in STZ rats, that was inhibited significantly by Liraglutide to below control values 0.70±0.08 (p<0.05). Liraglutide especially inhibited strong positive CML vessels (score 3), namely from 34% in the STZ group up to 15% in the Liraglutide group. Interestingly, also the number of NOX2-positive vessels (positive vessels (square mm) was increased by STZ from 0.48±0.03 in controls up to 0.87±0.08 in STZ, that again was inhibited significantly to below control levels in the Liraglutide group up to 0.12±0.01 (p<0.05).

Conclusions: The GLP-1 analogue Liraglutide significantly reduces the pro-inflammatory CML-NOX2 axis in intramyocardial arteries in diabetic hearts, that could explain the cardiovascular protective effects of Liraglutide.

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Dynamin-Related Protein 1 (DRP1) manipulates myocardial insulin resistance using differentiated H9c2 myocytes.

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Purpose: Accumulating evidences have suggested the relevant correlation between aberrant mitochondrial dynamics and cardiac diseases. Since alteration in energy metabolism in myocardium, where glucose oxidation was reduced due to insulin resistance, plays critical roles in the pathophysiology of heart failure (HF), we here investigated the impact of DRP-1 (one of mitochondrial dynamic proteins involved in mitochondrial fission) in the pathogenesis of myocardial insulin resistance using differentiated H9c2 myocytes.

Results and methods: (1) The DRP-1 expressing H9c2 myocytes (DRP-1) exhibited fragmented mitochondria (72±2.5% of cells vs. 22±1.0% of non-treated control, P<0.01), depolarized mitochondrial membrane potential (measured with JC-1 ratio; 3.7±0.1 vs. 5.4±0.2 of non-treated control, P<0.01), and increased mitochondrial ROS production (measured with MitoSOX; 2.5±0.2 fold increase from non-treated control, P<0.01). DRP-1 expressing myocytes also exhibited the attenuated insulin-signal transduction (AKT serine residues phosphorylation) and reduced insulin (100 mM)-mediated 2-DG uptake (1.1±0.1 fold increase from without insulin vs. 1.6±0.1 of non-treated control, P<0.01), indicating insulin resistance. When DRP-1 expressing myocytes were treated with 200 gM of MnTMPyP (a ROS scavenger; DRP-1 + TMPyP), not only the fragmented mitochondria by DRP-1 (65±0.4% of cells, P=0.01 vs. DRP-1) but also DRP-1-induced insulin resistance (2-DG uptake; 1.4±0.1 fold increase from without insulin vs. 1.1±0.1 of DRP-1, P<0.01) were restored. (2) The hydrogen peroxide (H2O2; 100 μM)-treated myocytes exhibited fragmented mitochondria (74±2.2% of cells vs. 4±1% of non-treated control, P<0.01) and increased DRP-1 expression. The H2O2-treated myocytes also exhibited the attenuation in insulin signal transduction and insulin-mediated 2-DG uptake (1.3±0.1 fold increase from without insulin vs. 1.0±0.0 of non-treated control, P<0.01), indicating insulin resistance. When DRP-1 was suppressed by siRNA (DRP-1), not only the H2O2-induced mitochondrial fragmentation (84±1% of cells, P<0.01 vs. H2O2) but also H2O2-induced insulin-resistance (2-DG uptake; 1.2±0.1 fold increase from without insulin, P<0.01 vs. H2O2) were restored.

Conclusions: Our results suggested that the expression of DRP-1 could promote insulin resistance through mitochondrial ROS production. Thus, the suppression of DRP-1 and/or mitochondrial ROS production in cardiac myocytes may provide a new target for myocardial insulin resistance under HF.

1769 | BEDSIDE

Environmental triggers of acute myocardial infarction: does air pollution matter?

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Purpose: Exposure to air pollution has been shown to be a trigger of acute myocardial infarction (AMI). As in those studies no correction was made for other meteorological factors, the present study wants to evaluate the independent environmental triggers of AMI.

Methods: Weekly counts of AMI patients that underwent primary percutaneous coronary intervention (pPCI) in the period 2006-2009 in 32 Belgian PCI centres were extracted from the national PCI database. Those data were correlated with average weekly meteorological data obtained from daily measurements in 73 meteorological sites, equally distributed in Belgium. The following meteorological measures were investigated: air pollution expressed as particulate matter both less than 10 μm (PM10) and less than 2.5 μm (PM2.5), black smoke, temperature and relative humidity. Time-series and Poisson regression analysis were carried out to investigate the correlation between environmental changes and the incidence of AMI.

Results: During the study period a total of 15964 AMI patients (mean age 63, 24.8% female) were admitted with a weekly average admission rate of 77±11 patients. Time-series (see figure) and univariate Poisson regression revealed a significant positive correlation between AMI's and air pollution and an inverse correlation between AMI’s and temperature. Multivariate analysis showed that only low temperature was significantly correlated with AMI with an increase of 7% AMI’s for each 10°C decrease in minimal temperature (OR 1.07 95% CI 1.04-1.11) and that there was no significant effect of air pollution (OR 1.01 95% CI 1.00-1.02).

Conclusions: In a general environmental model, low temperature is by far the most important environmental trigger for AMI, whereas air pollution has a negligible effect.

1770 | BEDSIDE

Impact of transition of thrombolysis to primary PCI on door-to-ballon time and on mortality. A population study of STEMI patients in Belgium

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Purpose: Although several randomised trials have demonstrated that transferring STElevation Myocardial Infarction (STEMI) patients for primary Percutaneous Coronary Intervention (p PCI) leads to better outcomes than administration of thrombolytic therapy at community hospitals, transfer delays are frequently longer outside the context of a study protocol. The present study evaluates temporal changes in Door-To-Ballon times (DTB) and in hospital mortality since the implementation of STEMI network program in 2007 in Belgium.

Methods: Door-to-ballon time, defined as time between diagnosis and first balloon inflation, reperfusion strategy, baseline risk profile (TIMI risk score) and in hospital mortality were prospectively recorded in 13516 Belgian STEMI patients admitted in 25 PCI centres and 47 community hospitals in the period 2007-2012. Results: Over time, pPCI increased from 69% to 96% in the PCI centres and from 56% to 88% in the community hospitals. Parallel to this transition from thrombolysis to pPCI, the proportion of patients with prolonged DTB (>120min) increased from 11% to 15% and in the subgroup of patients with an early (<3h) incubation
the proportion of patients with DTB >90min doubled from 10 to 20% (see table). Prolonged DTB was associated with an increased risk of in hospital mortality (adjusted RR 1.7, 95% CI 1.2-2.4). Despite decrease in TIMI risk score and higher use of pPCI, in-hospital mortality did not change significantly over time.

Temporal changes

<table>
<thead>
<tr>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMI risk score</td>
<td>4.3</td>
<td>4.3</td>
<td>4.2</td>
<td>4.1</td>
<td>4.0</td>
<td>4.0</td>
</tr>
<tr>
<td>DTB &gt;90min, % of all STEMI's</td>
<td>11</td>
<td>11</td>
<td>14</td>
<td>12</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>DTB &gt;90min, % of STEMI's &lt;90</td>
<td>10</td>
<td>10</td>
<td>15</td>
<td>14</td>
<td>16</td>
<td>20</td>
</tr>
<tr>
<td>Mortality, %</td>
<td>6.4</td>
<td>7.6</td>
<td>7.6</td>
<td>5.9</td>
<td>6.8</td>
<td>6.8</td>
</tr>
</tbody>
</table>

DTB, door-to-balloon time.

Conclusion: The transition of thrombolysis to transfer for pPCI in the setting of STEMI network was associated with almost 50% increase of the proportion of patients with prolonged DTB, which might have offset the mortality benefit expected from increased pPCI use.

1771 | BEDSIDE
Impact of immediate multivessel intervention on outcome of patients with multivessel disease undergoing primary PCI for cardiogenic shock. Results of the prospective IABP-Shock II trial
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Background: There is still uncertainty about the optimal strategy in patients with multivessel disease undergoing primary PCI for cardiogenic shock. Therefore we compared outcome of patients with culprit lesion only PCI and immediate multi-vessel PCI for cardiogenic shock in a prospective study.

Methods: We used the data of the prospective IABP-Shock II trial and included patients with primary PCI for cardiogenic shock with 2-3 vessel disease. We excluded patients with left main PCI and patients with prior coronary artery bypass surgery. Treatment with multivessel PCI or culprit lesion only PCI was left on the discretion of the operator.

Results: Between 2009 and 2011 a total of 450 patients 2-3 vessel disease were treated with primary PCI for cardiogenic shock. Of these 167 (37%) received immediate multivessel PCI while in the remaining only the culprit vessel was treated. Baseline characteristics, procedural features and outcomes are given in the table.

<table>
<thead>
<tr>
<th>Culprit lesion PCI (n=283)</th>
<th>Multivessel PCI (n=167)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>75 (IQR 67-83)</td>
<td>79 (IQR 70-83)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>32%</td>
<td>40%</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>24%</td>
<td>20%</td>
</tr>
<tr>
<td>STEMI</td>
<td>77%</td>
<td>70%</td>
</tr>
<tr>
<td>3-vessel disease</td>
<td>62%</td>
<td>72%</td>
</tr>
<tr>
<td>TIMI 3 flow PCI</td>
<td>86%</td>
<td>83%</td>
</tr>
<tr>
<td>IABP</td>
<td>51%</td>
<td>52%</td>
</tr>
<tr>
<td>3d reinfarction</td>
<td>2.3%</td>
<td>1.0%</td>
</tr>
<tr>
<td>3d mortality</td>
<td>43.8%</td>
<td>47.3%</td>
</tr>
</tbody>
</table>

Conclusion: Immediate multivessel PCI for cardiogenic shock used in about 40% of patients is associated with similar success rates as culprit lesion PCI, but with a higher mortality. Therefore a randomized trial seems warranted to evaluate the optimal interventional strategy in these patients.

1774 | BEDSIDE
Understanding and treating ST-elevation myocardial infarction

3 increased significantly from 80.5% in 2005 to 90% in 2011 (p for trend 0.05). The cumulative incidence of all-cause mortality during follow-up was significantly higher in the octogenarian group (51.6% vs 12.8%, p<0.0001). As expected, the hazard of death during follow-up increased with age (unadjusted HR 1.069 per year increase [95% CI 1.064-1.074], p<0.0001), which persisted after adjustment for other predictors of mortality (HR of 1.059 [95% CI 1.048-1.071], p<0.0001).

1774 | BEDSIDE
Takotsubo cardiomyopathy - In-hospital mortality and serious early complications -101 case study
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Background: Takotsubo cardiomyopathy (TTC) is a clinical disorder usually triggered by intense emotional and/or physical stress, characterized by reversible se-