**Supplemental Table 1 - GDF-15 expected values**

Roche Diagnostics has published a methods sheet on their Cobas e801 assay on GDF-15:

<https://assets.roche.com/f/173850/x/f1ed40188a/gdf-15-08946809190-en-can.pdf>

The descriptive statistics for GDF-15 concentrations in the reference group are summarized in the following table:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Age**  **years** | **N** | **Mean**  **pg/mL** | **SD**  **pg/mL** | **Median pg/mL** | **95th percentile pg/mL** |
| 20-<30 | 127 | 514 | 273 | 429 | 831 |
| 30-<40 | 120 | 564 | 223 | 500 | 852 |
| 40-<50 | 125 | 660 | 266 | 614 | 1229 |
| 50-<60 | 119 | 807 | 285 | 757 | 1466 |
| 60-<70 | 122 | 937 | 306 | 866 | 1476 |
| ≥70 | 126 | 1187 | 547 | 1060 | 2199 |

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| **Supplemental Table 2 - Routine laboratory analysis** | | | | | |
| **Analysis** | **Assay** | **LoD** | **LoQ** | **Measuring range** | **CVA** |
| Total cholesterol | Cobas c702 (Roche Diagnostics) | 0.1 mmol/L | Not reported by the manufacturer | 0.1-20.7 mmol/L | 3% |
| HDL-cholesterol | Cobas c702 (Roche Diagnostics) | 0.08mmol/L | 0.08mmol/L | 0.08-3.88 mmol/L | 3% |
| LDL- cholesterol | Direct assay on Cobas c702  (Roche Diagnostics) | 0.10 mmol/L | 0.10 mmol/L | 0.10 -14.2 mmol/L | 2.5% |
| C-reactive protein | Cobas c702 (Roche Diagnostics) | 0.3 mg/L | 0.6 mg/L | 0.6-350 mg/L | 5% |
| Creatinine | Enzymatic IDMS traceable assay on  Cobas c702 (Roche Diagnostics) | 5 µmol/L | Not reported by the manufacturer | 5-2700 µmol/L | 3% |
| HbA1c | HPLC on Biorad D100 (Biorad) | Results reported through the range of 3.5-20% | | | 3% |
| ***Abbreviations***  *CVA: Local in-house analytical variation*  *LoD: Limit of detection*  *LoQ: Limit of quantification* | | | | | |

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| **Supplemental Table 3 – GDF-15 results – sex specific analysis** | | | | | |
|  | **Multivariable model\*** | | | | |
|  | **Male** | | **Female** | |  |
|  | **OR** | **95% CI** | **OR** | **95% CI** | **P for interaction** |
| **Presence of any CAD at baseline** | 0.87 | 0.61-1.24 | 0.74 | 0.48-1.15 | 0.46 |
| **Obstructive CAD at baseline** | 1.19 | 0.87-1.62 | 1.07 | 0.60-1.90 | 0.89 |
| **Multivessel CAD at baseline** | 1.32 | 0.88-1.99 | 1.01 | 0.30-3.40 | 0.97 |
| **Revascularization within 30 days** | 1.32 | 0.93-1.86 | 1.01 | 0.48-2.14 | 0.69 |
| **Revascularization within 12 months** | 1.30 | 0.93-1.82 | 1.19 | 0.57-2.49 | 0.89 |
| ***Abbreviations***  *CAD: Coronary Artery Disease*  *GDF-15: Growth differentiation factor 15*  *hs-TnT: High-sensitive Troponin T* | | | | | |

\* Age, sex, history suspicious of CAD, family history, ECG, smoking, previously known hypercholesterolemia, diabetes, hypertension and cardiovascular disease

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| **Supplemental Table 4 – Hs-cTnT results** | | | | | | | | | |
|  | **Panel A:**  **Age and sex** | | | **Panel B:**  **Multivariable model\*** | | | **Panel C:**  **Age, sex and GDF-15 levels** | | |
|  | **OR** | **95% CI** | **P** | **OR** | **95% CI** | **P** | **OR** | **95% CI** | **P** |
| **Presence of any CAD at baseline** | 1.10 | 0.86-1.41 | 0.446 | 1.01 | 0.77-1.31 | 0.96 | 1.11 | 0.86-1.43 | 0.430 |
| **Obstructive CAD at baseline** | 2.10 | 1.60-2.76 | <0.001 | 1.96 | 1.45-2.62 | <0.001 | 2.03 | 1.53-2.70 | <0.001 |
| **Multivessel CAD at baseline** | 1.96 | 1.32-2.91 | <0.001 | 1.76 | 1.14-2.74 | 0.011 | 1.83 | 1.20-2.79 | 0.005 |
| **Revascularization 30 days** | 2.10 | 1.52-2.91 | <0.001 | 2.14 | 1.52-3.03 | <0.001 | 2.01 | 1.43-2.83 | <0.001 |
| **Revascularization 12 months** | 2.01 | 1.47-2.74 | <0.001 | 2.08 | 1.49-2.90 | <0.001 | 1.90 | 1.36-2.64 | <0.001 |
| ***Abbreviations***  *CAD: Coronary Artery Disease*  *GDF-15: Growth differentiation factor 15*  *hs-TnT: High-sensitive Troponin T* | | | | | | | | | |

\* Age, sex, history suspicious of CAD, family history, ECG, smoking, previously known hypercholesterolemia, diabetes, hypertension and cardiovascular disease

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| **Supplemental table 5 – ROC-AUC results** | | | | | | | | | |
|  | **GDF-15** | | | **Hs-TnT** | | | **GDF-15 and Hs-TnT combined** | | |
|  | *ROC AUC* | *95% CI* | *P* | *ROC AUC* | *95% CI* | *P* | *ROC AUC* | *95% CI* | *P* |
| **Obstructive CAD at baseline** | 0.596 | 0.552-0.639 | 0.006 | 0.728 | 0.687-0.766 | < 0.0001 | 0.726 | 0.685-0.764 | < 0.0001 |
| **Multivessel CAD at baseline** | 0.718 | 0.679-0.756 | 0.171 | 0.822 | 0.787-0.854 | < 0.0001 | 0.838 | 0.804-0.868 | < 0.0001 |
| **Revascularization within 30 days** | 0.606 | 0.563-0.647 | 0.010 | 0.729 | 0.689-.0766 | < 0.0001 | 0.732 | 0.692-0.769 | < 0.0001 |
| **Revascularization within 12 months** | 0.607 | 0.564-0.649 | 0.009 | 0.718 | 0.678-0.756 | < 0.0001 | 0.725 | 0.685-0.763 | < 0.0001 |
| ***Abbreviations***  *CAD: Coronary Artery Disease*  *GDF-15: Growth differentiation factor 15*  *hs-TnT: High-sensitive Troponin T*  *ROC-AUC: Receiver operating characteristics curves, Area under the curve* | | | | | | | | | |

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| **Supplemental table 6 – GDF-15 analysis when combined with hs-cTnT** | | | |
|  | **GDF-15  ≥ 700 ng/L**  **(95% CI)** | **hs-cTnT ≥5 ng/L**  **(95% CI)** | **GDF-15  ≥ 700 ng/L, or  hs-cTnT ≥5 ng/L**  **(95% CI)** |
| ***Presence of any CAD at baseline*** | | | |
| **Sensitivity (%)** | 60.3 (54.2-66.2) | 65.1 (59.1-70.7) | 59.4 (54.2-64.5) |
| **Specificity (%)** | 57.5 (51.0-63.8) | 60.4 (53.9-66.6) | 56.3 (50.9-61.7) |
| **PPV (%)** | 61.7 (57.4-65.7) | 65.1 (60.9-69.0) | 59.6 (56.0-63.1) |
| **NPV(%)** | 56.1 (51.6-60.5) | 60.4 (55.8-64.9) | 56.2 (52.3-60.0) |
| ***Obstructive CAD at baseline*** | | | |
| **Sensitivity (%)** | 63.9 (52.7-74.1) | 81.9 (72.0-89.5) | 88.0 (79.0-94.1) |
| **Specificity (%)** | 50.4 (45.5-55.2) | 52.5 (47.6-57.3) | 31.7 (27.3-36.3) |
| **PPV (%)** | 19.9 (17.1-23.1) | 25.0 (22.4-27.8) | 19.9 (18.4-21.6) |
| **NPV(%)** | 87.8 (84.2-90.7) | 93.8 (90.4-96.0) | 93.2 (88.2-96.1) |
| **Multivessel CAD at baseline** | | | |
| **Sensitivity (%)** | 58.6 (38.9-76.5) | 89.7 (72.7-97.8) | 89.7 (72.7-97.8) |
| **Specificity (%)** | 47.1 (42.6-51.5) | 47.4 (43.0-51.9) | 28.4 (24.5-32.5) |
| **PPV (%)** | 8.9 (7.7-10.1) | 8.9 (7.7-10.1) | 6.7 (5.9-7.6) |
| **NPV (%)** | 98.8 (96.5-99.6) | 98.8 (96.5-99.6) | 98.0 (94.2-99.39 |
| ***Revascularization within 30 days*** | | | |
| **Sensitivity (%)** | 65.3 (50.4-78.3) | 85.7 (72.8-94.1) | 93.9 (83.1-98.7) |
| **Specificity (%)** | 48.0 (43.4-52.5) | 48.6 (44.1-53.1) | 29.5 (25.5-33.8) |
| **PPV (%)** | 11.2 (9.2-13.6) | 14.3 (12.7-16.2) | 11.8 (10.9-12.8) |
| **NPV (%)** | 93.2 (90.3-95.3) | 97.1 (94.4-98.6) | 98.0 (94.1-99.3) |
| ***Revascularization within 12 months*** | | | |
| **Sensitivity (%)** | 65.4 (50.9-78.0) | 84.6 (71.9-91.3) | 93.9 (83.1-98.7) |
| **Specificity (%)** | 48.0 (43.5-52.6) | 48.7 (44.1-53.2) | 29.5 (25.5-33.8) |
| **PPV (%)** | 11.9 (9.8-14.4) | 15.0 (13.3-17.0) | 11.8 (10.9-12.8) |
| **NPV (%)** | 92.8 (89.8-95.0) | 96.7 (93.9-98.3) | 98.0 (94.1-99.3) |
| ***Definitions***  *Any CAD: >10% narrowing of the lumen in ≥ 1 coronary segment*  *Obstructive CAD: > 50% diameter narrowing of the lumen in ≥ 1 coronary segment*  *Multivessel CAD: obstructive CAD ≥ 2 coronary arteries* | | | |
| ***Abbreviations***  *GDF-15: Growth differentiation factor 15*  *hs-cTnT: high sensitive cardiac Troponin T*  *PPV: Positive predictive value*  *NPV: Negative predictive value* | | | |

**Supplemental figure 1**

