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# **Impact of obesity on infarct size, circulating biomarkers, mitochondrial function and mortality in a Göttingen minipig myocardial infarct model**

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# 1 Supplementary information

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## 3 **Supplementary Table 1** Haematology in lean and obese minipigs at baseline and 8 weeks post-MI.

|               | Unit               | Lean (n=15)               |                      | Obese (n=5)          |                          |
|---------------|--------------------|---------------------------|----------------------|----------------------|--------------------------|
|               |                    | Baseline                  | 8 weeks post-MI      | Baseline             | 8 weeks post-MI          |
| Haematology   |                    |                           |                      |                      |                          |
| WBC           | 10 <sup>9</sup> /L | 9.8 [8.3 - 12.4]          | 7.7 [7.3 - 10.9] *   | 8.8 [8.3 - 9.1]      | 10.4 [9.3 - 10.6]        |
| Neutrophils   | 10 <sup>9</sup> /L | 3.5 [2.5 - 4.1] (n=13)    | 2.6 [2.0 - 4.4]      | 1.6 [1.4 - 3.3]      | 3.4 [3.3 - 4.0]          |
| Lymphocytes   | 10 <sup>9</sup> /L | 5.3 [5.1 - 6.3] (n=13)    | 4.6 [3.8 - 5.6]      | 5.4 [5.0 - 6.0]      | 5.8 [5.2 - 6.3] #§       |
| Monocytes     | 10 <sup>9</sup> /L | 0.90 [0.62 - 1.06] (n=14) | 0.54 [0.36 - 0.71] * | 0.48 [0.45 - 0.57] # | 0.52 [0.51 - 0.76]       |
| Eosinophils   | 10 <sup>9</sup> /L | 0.36 [0.24 - 0.49] (n=14) | 0.31 [0.23 - 0.44]   | 0.30 [0.26 - 0.31]   | 0.29 [0.25 - 0.30]       |
| Basophils     | 10 <sup>9</sup> /L | 0.03 [0.01 - 0.04]        | 0.02 [0.01 - 0.04]   | 0.02 [0.01 - 0.02]   | 0.01 [0.01 - 0.04]       |
| RBC           | 10 <sup>9</sup> /L | 6.9 [6.2 - 7.8]           | 6.3 [6.1 - 7.3]      | 7.3 [6.8 - 7.8]      | 7.2 [7.1 - 7.6]          |
| Haemoglobin   | mmol/L             | 8.4 [7.0 - 8.8]           | 7.9 [7.4 - 8.6]      | 7.8 [7.4 - 8.2]      | 7.8 [7.6 - 7.9] (n=4)    |
| Haematocrit   | L/L                | 0.40 [0.33 - 0.42]        | 0.38 [0.34 - 0.39]   | 0.38 [0.35 - 0.38]   | 0.37 [0.35 - 0.37] (n=4) |
| Platelets     | 10 <sup>9</sup> /L | 436 [391 - 582]           | 457 [401 - 533]      | 401 [379 - 442]      | 392 [299 - 432]          |
| Reticulocytes | 10 <sup>9</sup> /L | 35.7 [31.2 - 50.9]        | 32.4 [21.6 - 38.7]   | 43.4 [27.8 - 47.1]   | 39.3 [27.5 - 41.2]       |

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5 Data presented as median and interquartile range [IQR]. \*  $P < .05$ ; Wilcoxon signed rank test for  
6 paired samples at baseline and 8 weeks post-MI. #  $P < .05$ ; Wilcoxon rank-sum test for significant  
7 difference between lean and obese groups. §; significance driven by one high value. Reduced n due  
8 to missing values and/or analysis error is shown in parentheses. WBC; white blood cell count. RBC;  
9 red blood cell count.

10 **Supplementary Table 2** Electrocardiographic parameters and mean arterial pressure (MAP) during occlusion

|             |       | Time from onset of occlusion (min) |                      |                      |                      |                      |                      |                      | P-value for group difference |
|-------------|-------|------------------------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|------------------------------|
|             | Group | -5                                 | 1                    | 5                    | 15                   | 30                   | 60                   | 120                  |                              |
| RR (ms)     | Obese | 841 [783 - 966]                    | 831 [771 - 964]      | 827 [765 - 968]      | 870 [793 - 1052]     | 872 [793 - 1130]     | 819 [736 - 1074]     | 858 [771 - 1002]     | ns                           |
|             | Lean  | 749 [672 - 847]                    | 733 [678 - 794]      | 734 [682 - 827]      | 728 [708 - 824]      | 762 [715 - 893]      | 754 [700 - 808]      | 735 [707 - 879]      |                              |
| QRS (ms)    | Obese | 72 [67 - 80] #                     | 75 [69 - 81] #       | 113 [87 - 122] *#    | 110 [86 - 128] *#    | 105 [80 - 123] *#    | 104 [77 - 123] *#    | 72 [67 - 89] #       | .0052                        |
|             | Lean  | 64 [61 - 68] #                     | 65 [62 - 69] #       | 100 [89 - 105] *#    | 92 [84 - 97] *#      | 93 [84 - 102] *#     | 75 [61 - 87] *#      | 68 [60 - 71] #       |                              |
| QT (ms)     | Obese | 380 [359 - 408] #                  | 382 [357 - 406] #    | 383 [355 - 408] #    | 361 [346 - 394] *#   | 352 [339 - 394] *#   | 380 [347 - 394] *#   | 373 [347 - 390] *#   | .0018                        |
|             | Lean  | 343 [300 - 364] #                  | 344 [304 - 364] #    | 339 [309 - 352] #    | 334 [297 - 354] *#   | 334 [294 - 346] *#   | 335 [291 - 357] *#   | 332 [299 - 365] *#   |                              |
| QTc (ms)    | Obese | 392 [371 - 447]                    | 391 [374 - 446]      | 392 [374 - 457]      | 367 [349 - 432] *    | 358 [338 - 435] *    | 376 [367 - 435] *    | 379 [363 - 418] *    | ns                           |
|             | Lean  | 379 [362 - 392]                    | 379 [356 - 391]      | 374 [368 - 381]      | 367 [354 - 378] *    | 360 [342 - 372] *    | 370 [349 - 380] *    | 360 [336 - 370] *    |                              |
| Sum ST (mV) | Obese | 0.08 [0.08 - 0.11]#                | 0.24 [0.18 - 0.40]*# | 0.70 [0.51 - 0.93]*# | 0.50 [0.40 - 1.04]*# | 0.54 [0.41 - 0.92]*# | 0.67 [0.41 - 0.80]*# | 0.45 [0.29 - 0.59]*# | .042 §                       |
|             | Lean  | 0.05 [0.04 - 0.06]#                | 0.15 [0.13 - 0.17]*# | 0.28 [0.23 - 0.36]*# | 0.15 [0.12 - 0.21]*# | 0.23 [0.16 - 0.43]*# | 0.25 [0.17 - 0.34]*# | 0.17 [0.14 - 0.20]*# |                              |
| MAP (mmHg)  | Obese | 78 [54 - 89]                       | 65 [47 - 78] *       | 67 [46 - 75] *       | 55 [40 - 78] *       | 51 [35 - 69] *       | 52 [46 - 81] *       | 60 [53 - 90] *       | ns                           |
|             | Lean  | 81 [64 - 91]                       | 73 [55 - 86] *       | 64 [51 - 84] *       | 63 [45 - 77] *       | 54 [45 - 74] *       | 59 [50 - 70] *       | 71 [46 - 83] *       |                              |

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12 Data presented as median and interquartile range [IQR]. \*  $P < .05$ ; indicates significant difference from baseline values before occlusion (-5 min).

13 #  $P < .05$ ; indicates significant group difference between lean and obese animals at the given time point. §; indicates that the group difference is

14 time dependent (i.e. significant interaction between group and time variables in the linear mixed model).

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16 **Supplementary Table 3** Plasma levels of circulating cardiac biomarkers after coronary occlusion

| Biomarker (unit) | Group | Time from onset of occlusion (hours) |                                    |                                  |                                  |                                  |                                  |
|------------------|-------|--------------------------------------|------------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
|                  |       | 0                                    | 4                                  | 6                                | 8                                | 10                               | 12                               |
| cTnT (ng/l)      | Obese | 5 [5 - 5] <sup>a</sup>               | 6604 [2630 - 8748] <sup>*#</sup>   | 3994 [2689 - 9231] <sup>*#</sup> | 2493 [2100 - 4303] <sup>*#</sup> | 3188 [2236 - 5343] <sup>*#</sup> | 3384 [2646 - 4741] <sup>*</sup>  |
|                  | Lean  | 5 [5 - 5] <sup>a</sup>               | 11076 [9474 - 21026] <sup>*#</sup> | 8725 [5631 - 8985] <sup>*#</sup> | 5713 [4680 - 6640] <sup>*#</sup> | 5029 [4226 - 6946] <sup>*#</sup> | 5238 [3486 - 6325] <sup>*</sup>  |
| proANP (pmol/l)  | Obese | 151 [109 - 291]                      | 365 [175 - 466] <sup>#</sup>       | 501 [213 - 627] <sup>*#</sup>    | 389 [278 - 466] <sup>#</sup>     | 372 [259 - 444]                  | 325 [177 - 481] <sup>#</sup>     |
|                  | Lean  | 353 [286 - 549]                      | 1101 [794 - 1579] <sup>*#</sup>    | 1055 [756 - 1265] <sup>*#</sup>  | 1241 [934 - 1309] <sup>*#</sup>  | 1261 [1207 - 1660] <sup>*#</sup> | 1304 [1115 - 1752] <sup>*#</sup> |
| proCNP (pmol/l)  | Obese | 7.0 [6.5 - 8.0] <sup>#</sup>         | 8.4 [7.5 - 9.5] <sup>*#</sup>      | 7.8 [7.2 - 8.1] <sup>#</sup>     | 8.0 [7.1 - 8.9] <sup>#</sup>     | 7.3 [6.9 - 8.1] <sup>#</sup>     | 7.5 [7.3 - 8.2] <sup>#</sup>     |
|                  | Lean  | 8.2 [7.0 - 9.9] <sup>#</sup>         | 9.8 [8.3 - 11.0] <sup>*#</sup>     | 8.5 [7.2 - 9.8] <sup>#</sup>     | 9.0 [7.6 - 9.9] <sup>#</sup>     | 8.6 [7.6 - 10.1] <sup>#</sup>    | 9.1 [7.7 - 9.6] <sup>#</sup>     |

| Continued.       |       | Time from onset of occlusion (hours) |                      |                      |                    |                    |                        |          |  | P-value for group difference |
|------------------|-------|--------------------------------------|----------------------|----------------------|--------------------|--------------------|------------------------|----------|--|------------------------------|
| Biomarker (unit) | Group | 24                                   | 48                   | 72                   | 7 days             | 28 days            | 56 days                |          |  |                              |
| cTnT (ng/l)      | Obese | 2347 [2318 - 3519] *                 | 1773 [1051 - 2425] * | 1709 [1129 - 2666] * | 91 [42 - 397] *    | 5 [5 - 10]         | 5 [5 - 5] <sup>a</sup> | .0002 §  |  |                              |
|                  | Lean  | 2598 [1864 - 3205] *                 | 1691 [1391 - 1983] * | 1532 [1401 - 1782] * | 268 [152 - 377] *  | 6 [5 - 9] *        | 5 [5 - 5] <sup>a</sup> |          |  |                              |
| proANP (pmol/l)  | Obese | 416 [232 - 535] #                    | 375 [251 - 388] #    | 304 [248 - 380] #    | 352 [215 - 442] #  | 314 [163 - 370] #  | 293 [210 - 468]        | <.0001 § |  |                              |
|                  | Lean  | 817 [659 - 888]*#                    | 811 [640 - 875] *#   | 575 [472 - 902] *#   | 747 [620 - 822] *# | 574 [361 - 697] *# | 487[336 - 824]         |          |  |                              |
| proCNP (pmol/l)  | Obese | 7.3 [6.5 – 8.5] #                    | 7.3 [6.4 – 7.9] #    | 7.3 [6.9 – 7.7] #    | 6.9 [6.6 – 8.1] #  | 7.2 [6.7 – 7.7] #  | 7.8 [6.2 – 7.9] #      | .016     |  |                              |
|                  | Lean  | 8.9 [7.6 – 10.3] #                   | 8.8 [7.7 – 9.6] #    | 8.7 [7.6 – 9.5] #    | 8.5 [7.7 – 10.6] # | 8.8 [7.3 – 10.4] # | 9.1 [7.0 – 9.6] #      |          |  |                              |

19 Data presented as median and interquartile range [IQR]. <sup>a</sup>; All except 1-2 values were below the detection limit of the troponin assay which was

20 5 ng/l. <sup>\*</sup>*P* < .05; indicates significant difference from baseline values before occlusion (-5 min). <sup>#</sup> *P* < .05; indicates significant group difference

21 between lean and obese animals at the given time point. §; indicates that the group difference is time dependent (i.e. significant interaction

22 between group and time variables in the linear mixed model).

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25 **Supplementary Table 4** Mitochondrial respirometry data from three myocardial tissue sampling zones

|                                                |       | Tissue sampling zone |                        |                        | P-value for group difference |
|------------------------------------------------|-------|----------------------|------------------------|------------------------|------------------------------|
|                                                | Group | Infarct zone (IZ)    | Border zone (BZ)       | Remote zone (RZ)       |                              |
| Complex I (pmol/mg/s)                          | Obese | 9 [3 – 15] *BZ, RZ # | 27 [19 - 34] *IZ, RZ # | 49 [41 - 76] *IZ, BZ # | .013                         |
|                                                | Lean  | 5 [2 – 9] *BZ, RZ #  | 16 [9 - 33] *IZ, RZ #  | 25 [19 - 42] *IZ, BZ # |                              |
| Complex I:CS ratio (pmol/mg/s)/(μmol/g/min)    | Obese | 0.4 [0.2 – 3.2]      | 0.3 [0.3 – 1.9]        | 0.5 [0.3 – 0.7]        | ns                           |
|                                                | Lean  | 0.5 [0.1 – 2.0]      | 0.6 [0.3 – 0.8]        | 0.3 [0.2 – 0.4]        |                              |
| Complex I+II (pmol/mg/s)                       | Obese | 16 [5 - 30] *BZ, RZ  | 57 [36 - 82] *IZ, RZ   | 138[128 - 149] *IZ, BZ | ns                           |
|                                                | Lean  | 6 [3 - 14] *BZ, RZ   | 36 [18 - 89] *IZ, RZ   | 116[105 - 137] *IZ, BZ |                              |
| Complex I+II:CS ratio (pmol/mg/s)/(μmol/g/min) | Obese | 1.0 [0.4 – 2.8]      | 1.4 [0.6 – 3.2]        | 1.3 [1.2 – 1.5]        | ns                           |
|                                                | Lean  | 1.1 [0.3 – 3.3]      | 1.3 [0.5 – 2.4]        | 1.1 [0.9 – 1.4]        |                              |
| Citrate synthase (μmol/g/min)                  | Obese | 14 [2 - 48] *BZ, RZ  | 58 [25 - 76] *IZ, RZ   | 104[93 - 119] *IZ, RZ  | ns                           |
|                                                | Lean  | 16 [1 - 25] *BZ, RZ  | 39 [23 - 72] *IZ, RZ   | 108[98 - 119] *IZ, RZ  |                              |
| HAD (μmol/g/min)                               | Obese | 10 [1 - 34] *BZ, RZ  | 47 [17 - 62] *IZ, RZ   | 94 [80 - 103] *IZ, RZ  | ns                           |
|                                                | Lean  | 10 [1 - 15] *BZ, RZ  | 26 [14 - 52] *IZ, RZ   | 96 [83 - 102] *IZ, RZ  |                              |

26 Data presented as median and interquartile range [IQR]. CS; Citrate synthase activity. HAD; β-hydroxy-acyl-CoA dehydrogenase activity. \* $P < .05$ ;  
 27 indicates significant differences to other zones indicated by their abbreviation (IZ, BZ, RZ). # $P < .05$ ; indicates significant group difference between  
 28 lean and obese animals for the given zone.

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