**SUPPORTING INFORMATION (SI) FILE**

**Title**: Perturbations of fibroblast growth factors 19 and 21 in type 2 diabetes

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***Table A***. **Descriptive characteristics of study cohorts divided according to their preoperative status of diabetes (SD: Standard deviation)**.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **No-Diabetes**  **(No-T2D)**  **N=66** | **Diabetes**  **(T2D)**  **N=62** | **P-value** |
| Age (years),  mean (SD) | 40.1 (8.6) | 50.6 (10.6) | **<0.00011** |
| Female  (%) | 89% | 79% | 0.1072 |
| White race  (%) | 95% | 100% | 0.2453 |
| Height (cm),  mean (SD) | 165.0 (8.2) | 164.9 (8.9) | 0.9731 |
| Weight (kg),  mean (SD) | 136.8 (31.6) | 134.3 (25.0) | 0.6201 |
| BMI (kg/m2),  mean (SD) | 50.0 (9.4) | 49.3 (8.0) | 0.6531 |
| Glucose (mg/dL),  mean (SD) | 85.7 (7.6) | 130.4 (68.0) | **<0.00011** |
| Insulin (µU/mL),  mean (SD) | 18.4 (13.3) | 22.2 (16.9) | 0.1631 |
| HbA1c (%),  mean (SD) | 5.4 (0.2) | 7.3 (1.3) | **<0.00011** |
| LDL (mg/dL),  mean (SD) | 112.5 (30.3) | 90.5 (34.9) | **0.00031** |
| HDL (mg/dL),  mean (SD) | 48.3 (12.6) | 43.7 (8.6) | **0.0161** |
| Cholesterol (mg/dL),  mean (SD) | 188.7 (37.5) | 169.3 (41.3) | **0.00621** |
| Triglycerides (mg/dL),  mean (SD) | 139.2 (77.3) | 181.4 (96.4) | **0.00701** |
| 1T-test, 2Chi-square test, 3Fisher’s exact test | | | |

***Table B*.** **Descriptive characteristics of study cohorts divided according to their diabetes remission status after Roux-en-Y gastric bypass (RYGB) surgery (SD: standard deviation)**.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **No-Diabetes**  **(No-T2D)**  **(N=66)** | **Diabetes with remission**  **(T2D-R)**  **(N=26)** | **Diabetes without remission**  **(T2D-NoR)**  **(N=36)** | **P-value** |
| Age (years),  mean (SD) | 40.1 (8.6) | 45.8 (11.4) | 54.1 (8.6) | **<0.00011** |
| Female  (%) | 89% | 81% | 78% | 0.2592 |
| White race  (%) | 95% | 100% | 100% | 0.4303 |
| Height (cm),  mean (SD) | 165.0 (8.2) | 165.3 (9.2) | 164.6 (8.8) | 0.9521 |
| Weight (kg),  mean (SD) | 136.8 (31.6) | 138.1 (29.1) | 131.5 (21.7) | 0.5931 |
| BMI (kg/m2),  mean (SD) | 50.0 (9.4) | 50.5 (9.4) | 48.5 (6.8) | 0.5951 |
| Glucose (mg/dL),  mean (SD) | 85.7 (7.6) | 116.2 (43.0) | 140.7 (80.5) | **<0.00011** |
| Insulin (µU/mL),  mean (SD) | 18.4 (13.3) | 24.5 (15.7) | 20.6 (17.8) | 0.2351 |
| HbA1c (%),  mean (SD) | 5.4 (0.2) | 6.8 (1.1) | 7.7 (1.4) | **<0.00011** |
| LDL (mg/dL),  mean (SD) | 112.5 (30.3) | 103.3 (34.1) | 81.1 (32.9) | **<0.00011** |
| HDL (mg/dL),  mean (SD) | 48.3 (12.6) | 43.5 (10.3) | 43.8 (7.4) | 0.0591 |
| Cholesterol (mg/dL),  mean (SD) | 188.7 (37.5) | 176.2 (42.1) | 164.3 (40.5) | **0.0121** |
| Triglycerides (mg/dL),  mean (SD) | 139.2 (77.3) | 154.5 (83.0) | 200.8 (101.6) | **0.00311** |
| 1ANOVA, 2Chi-square test, 3Fisher’s exact test | | | | |

***Table C*. List of the 205 clinical variables that were used in the phenome-wide association analysis (PheWAS).**

***Baseline information and demographics (n=15)***

1. Age
2. Alcohol use
3. BMI at baseline
4. Days in pre-operative program
5. Ethnic group
6. Gender
7. Height
8. Number of co-morbidities (from list below)
9. Number of medications (from list below)
10. Preoperative weight loss
11. Rating from initial dietician evaluation (red, yellow, green)
12. Rating from initial psychological evaluation (red, yellow, green)
13. REE
14. Smoker
15. Waist circumference

***Comorbidities on problem list from baseline to surgery using 3-digit ICD, codes (n=50)***

* 1. ICD\_244
  2. ICD\_250
  3. ICD\_251
  4. ICD\_256
  5. ICD\_268
  6. ICD\_269
  7. ICD\_272
  8. ICD\_274
  9. ICD\_276
  10. ICD\_296
  11. ICD\_300
  12. ICD\_305
  13. ICD\_307
  14. ICD\_309
  15. ICD\_311
  16. ICD\_327
  17. ICD\_346
  18. ICD\_354
  19. ICD\_357
  20. ICD\_401
  21. ICD\_414
  22. ICD\_427
  23. ICD\_428
  24. ICD\_429
  25. ICD\_477
  26. ICD\_493
  27. ICD\_530
  28. ICD\_553
  29. ICD\_564
  30. ICD\_592
  31. ICD\_625
  32. ICD\_626
  33. ICD\_627
  34. ICD\_715
  35. ICD\_719
  36. ICD\_722
  37. ICD\_724
  38. ICD\_726
  39. ICD\_728
  40. ICD\_729
  41. ICD\_780
  42. ICD\_782
  43. ICD\_784
  44. ICD\_785
  45. ICD\_786
  46. ICD\_787
  47. ICD\_789
  48. ICD\_790
  49. ICD\_794
  50. ICD\_796

***Medications on reconciliation list from baseline to 1 month prior to surgery using subclass (n=92)***

* 1. ACE
  2. Aminopenicillins
  3. AnalgesicCombo
  4. AnalgOther
  5. AnorexNonAmph
  6. AntiadrenergicAntiHTN
  7. AntianxietyAgentsMisc
  8. AnticonvMisc
  9. AnticonvulsantsBenzod
  10. AntidepressMisc
  11. AntiemetAnticholinergic
  12. AntifungalsTopical
  13. AntihistNonsed
  14. AntihistPhenothiazines
  15. AntiHTNcomb
  16. AntihyperlipidCombo
  17. AntiInfectiveAgentsMisc
  18. AntiInfectiveMiscCombo
  19. AntiObesityAgents
  20. AntiparkinDopaminergic
  21. Antitussives
  22. ARB
  23. Azithromycin
  24. BBCS
  25. BBNS
  26. Benzod
  27. Biguanides
  28. BronchoAnticholinergics
  29. BulkLaxatives
  30. Calcium
  31. CCB
  32. Cephalosporins1stGen
  33. Clarithromycin
  34. Cobalamins
  35. ComboContraceptOral
  36. CorticTopical
  37. Cough\_Cold\_AllComb
  38. Coumarin
  39. Dibenzapines
  40. DiureticCombo
  41. Estrogens
  42. FibricAcid
  43. Fluoroquinolones
  44. FolicAcidFolates
  45. GastrointestlStimulants
  46. Glucocort
  47. GoutAgents
  48. H2
  49. Heparin
  50. ImidazoleRelatedAntifungal
  51. IncretinMimetAgGLP1
  52. InsSensAgents
  53. Insulin
  54. IntestCholAbsorptionInhib
  55. Iron
  56. LeukotrieneModulators
  57. LoopDiur
  58. ModifiedCyclics
  59. MultiVit
  60. MultiVitMinerals
  61. MuscleRelax
  62. NasalSteroids
  63. Nitrates
  64. NonBarbitHypnotics
  65. NSAID
  66. OilSolVit
  67. OpioidAgonist
  68. OpioidCombo
  69. PenicillinCombo
  70. PlateAggrInhibitors
  71. Potassium
  72. PotassiumSparingDiuretics
  73. PPI
  74. ProgestContratInjectable
  75. Progestins
  76. Salicylates
  77. SerotoninAgonists
  78. SmokingDeterrents
  79. SNRI
  80. SSRI
  81. Statins
  82. SteroidInhalants
  83. Sulfonylureas
  84. SurfactantLaxatives
  85. Sympath
  86. Tetracyclines
  87. Thiazides
  88. ThyroidHorm
  89. Tricyclic
  90. UlcerTherapyCombo
  91. UrinaryAntispasmodics
  92. WaterSolubleVitamins

***Labs prior to surgery found in >50% of population (n=45)***

* 1. AlkPhos
  2. ALT
  3. AnionGap
  4. AST
  5. bun
  6. calcium
  7. CHLORIDE
  8. CHOL
  9. CholHDLRat
  10. CO2
  11. creat
  12. Creatinine, RD Urine
  13. Ferritin
  14. FolicAcid
  15. GFR
  16. glucose
  17. hba1c
  18. HCT
  19. HDL
  20. HEMOGLOBIN
  21. IBC
  22. insulin
  23. Iron
  24. LDL
  25. MCH
  26. MCHC
  27. MCV
  28. MPV
  29. PLATELET
  30. potassium
  31. Prot/Creat Ratio
  32. Protein, RD Urine
  33. PTH
  34. RBC
  35. RDW
  36. sodium
  37. TotBili
  38. TransSat
  39. TRIG
  40. TSH
  41. Vitamin D 25 OH D2
  42. Vitamin D 25 OH D3
  43. Vitamin D 25 TOTAL
  44. WBC
  45. Zinc levels

***Perioperative information and liver pathology (n=3)***

* 1. Access (Laparoscopic versus Open)
  2. Steatosis
  3. Any fibrosis