Insulin-Like Growth Factor-1 Levels Are Associated with High Comorbidity of Metabolic Disorders in Obese Subjects; a Japanese Single-Center, Retrospective-Study

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|                          | low IGF-1 group (n=17) | standard IGF-1 group (n=47) | P value | all group (n=64) |
|-------------------------|------------------------|-----------------------------|---------|-----------------|
| TSH (mIU/mL)<sup>a</sup> | 1.80 [1.16, 3.34]      | 1.92 [1.20, 2.71]           | 0.70    | 1.86 [1.18, 2.71] |
| FT4 (ng/mL) <sup>a</sup> | 1.14 [1.08, 1.19]      | 1.22 [1.12, 1.39]           | 0.16    | 1.17 [1.06, 1.33] |
| FT3 (pg/mL) <sup>a</sup> | 2.71 [2.70, 3.01]      | 2.90 [2.72, 3.26]           | 0.30    | 2.90 [2.71, 3.20] |
| PRA (ng/mL/hr)<sup>b</sup> | 2.1 [1.3, 4.1]        | 1.8 [1.0, 3.5]              | 0.37    | 1.9 [1.1, 3.8]  |
| PAC (ng/mL)<sup>b</sup> | 9.3 [7.0, 10.8]        | 8.7 [7.4, 11.0]             | 1.00    | 8.7 [7.3, 11.0] |
| ACTH (pg/mL)<sup>b</sup> | 31.9 [15.6, 41.7]     | 37.5 [16.3, 54.2]           | 0.32    | 36.2 [16.3, 52.0] |
| Cortisol (µg/dL)<sup>b</sup> | 8.2 [2.7, 14.2]      | 12.5 [8.7, 16.0]            | 0.10    | 11.9 [6.3, 15.9] |
| Triglyceride (mg/dL)<sup>c</sup> | 121.0 [103.0, 187.0] | 119.0 [91.0, 173.0]         | 0.58    | 120.0 [91.8, 176.5] |
| Total cholesterol (mg/dL)<sup>c</sup> | 183.0 [156.0, 191.0] | 176.0 [158.0, 206.5]        | 0.90    | 179.5 [156.8, 206.0] |
| HDL cholesterol (mg/dL)<sup>c</sup> | 44.0 [36.0, 48.0]   | 39.0 [36.0, 45.0]           | 0.20    | 43.0 [37.0, 48.0] |
| LDL cholesterol (mg/dL)<sup>c</sup> | 113.0 [99.0, 133.0] | 112.0 [96.0, 134.0]         | 0.70    | 112.5 [96.5, 134.0] |
| Uric Acid (mg/dL)<sup>c</sup> | 5.8 [5.0, 7.0]       | 6.5 [5.8, 7.6]              | 0.09    | 6.3 [5.6, 7.2]  |
| Systolic blood pressure (mmHg) | 136.5 [125.5, 146.5] | 133.6 [122.0, 146.0]        | 0.60    | 135.7 [124.5, 146.0] |
| Diastolic blood pressure (mmHg) | 83.2 [74.0, 97.0]  | 84.2 [77.0, 90.0]           | 0.80    | 83.9 [77.0, 91.5] |
| max-IMT (mm) | 0.7 [0.6, 0.9]       | 0.7 [0.6, 1.0]              | 0.69    | 0.7 [0.6, 0.9]  |
| ABI | 1.04 [0.98, 1.08]     | 1.02 [0.94, 1.10]           | 0.92    | 1.02 [0.96, 1.10] |
| CAVI | 5.8 [5.4, 6.2]       | 6.1 [5.2, 7.3]              | 0.29    | 6.0 [5.2, 7.1]  |

24 **Supplementary Table 1.** Clinical characteristics of other endocrinological and metabolic data in obese patients in low IGF-1 and standard IGF-1 groups.

25 <sup>a</sup>Thyroid function tests including thyroid stimulating hormone (TSH), free T4 (FT4; thyroxine) and free T3 (FT3; tri-iodothyronine) were measured by ECLIA.

26 <sup>b</sup>Other hormonal evaluations were measured using followings commercially: Plasma renin activity (PRA): enzyme immunoassay (EIA) (LSI Medience Corporation, Tokyo, Japan), Plasma aldosterone concentration (PAC): radioimmunoassay (RIA) (LSI Medicine Corporation, Tokyo, Japan), ACTH: ECLIA (LSI Medicine Corporation, Tokyo, Japan), Cortisol: chemiluminescence immunoassay (Siemens Healthcare Diagnostic, Tokyo, Japan).

27 <sup>c</sup>Serum triglyceride, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol and serum uric acid levels were assessed using standard enzymatic methods.

28 Abbreviations: TSH, thyroid stimulating hormone; FT4, free T4 (T4; thyroxine); FT3, free T3 (T3, tri-iodothyronine); PRA, plasma renin activity; PAC, plasma aldosterone concentration; HDL, high density lipoprotein; LDL, low density lipoprotein; IMT, intima media thickness; ABI, ankle brachial pressure index; CAVI, cardio-ankle vascular index.
|                      | low IGF-1 group (n=5) | standard IGF-1 group (n=13) | P value | all group (n=18) |
|----------------------|-----------------------|-----------------------------|---------|-----------------|
| TSH (mIU/mL)         | 1.37 [0.75, 2.83]     | 2.29 [1.31, 4.69]           | 0.37    | 2.20 [1.18, 4.69]|
| FT4 (ng/mL)          | 1.16 [1.06, 1.32]     | 1.39 [1.26, 1.48]           | 0.24    | 1.35 [1.18, 1.48]|
| FT3 (pg/mL)          | 2.91 [2.64, 2.93]     | 3.41 [2.91, 3.49]           | 0.21    | 2.97 [2.90, 3.42]|
| PRA (ng/mL/hr)       | 3.0 [2.1, 3.8]        | 1.2 [0.8, 1.5]              | 0.16    | 1.2 [1.0, 2.1]   |
| PAC (ng/mL)          | 10.8 [9.5, 60.4]      | 8.7 [7.8, 11.0]             | 0.40    | 8.7 [8.1, 11.0]  |
| ACTH (pg/mL)         | 17.7 [11.1, 34.7]     | 39.8 [9.2, 57.1]            | 0.47    | 38.2 [8.5, 53.3] |
| Cortisol (µg/dL)     | 3.6 [1.4, 8.2]        | 12.5 [3.8, 15.6]            | 0.27    | 11.5 [2.4, 15.5] |
| Triglyceride (mg/dL) | 118.0 [103.0, 121.0]  | 87.0 [74.0, 122.0]          | 0.30    | 95.5 [77.5, 121.8]|
| Total cholesterol (mg/dL) | 180.0 [169.0, 183.0] | 172.0 [151.0, 184.0]        | 0.73    | 173.5 [153.3, 183.8] |
| HDL cholesterol (mg/dL) | 38.0 [38.0, 41.0]   | 45.0 [42.0, 47.0]           | 0.35    | 40.0 [35.3, 45.8] |
| LDL cholesterol (mg/dL) | 113.0 [99.0, 125.0]  | 110.0 [100.0, 129.0]        | 0.96    | 111.0 [99.3, 128.0] |
| Uric Acid (mg/dL)    | 6.4 [5.8, 7.7]        | 6.7 [5.9, 7.9]              | 0.66    | 6.7 [5.8, 7.9]   |
| Systolic blood pressure (mmHg) | 122.8 [107.0, 134.0] | 134.0 [121.0, 143.0]        | 0.26    | 130.9 [120.3, 142.8] |
| Diastolic blood pressure (mmHg) | 76.0 [71.0, 84.0]   | 80.1 [77.0, 84.0]           | 0.55    | 78.9 [74.0, 84.0] |
| max-IMT (mm)         | 0.7 [0.6, 0.7]        | 0.7 [0.5, 0.7]              | 0.82    | 0.7 [0.5, 0.7]   |
| ABI                  | 0.97 [0.92, 0.98]     | 0.98 [0.93, 1.10]           | 0.36    | 0.98 [0.93, 1.02] |
| CAVI                 | 6.0 [5.6, 6.3]        | 5.0 [4.7, 5.3]              | 0.17    | 5.2 [4.8, 6.0]   |

**Supplementary Table 2.** Clinical characteristics of other endocrinological and metabolic data in obese patients without diabetes in low IGF-1 and standard IGF-1 groups.

- **a**Thyroid function tests including thyroid stimulating hormone (TSH), free T4 (FT4; thyroxine) and free T3 (FT3; tri-iodothyronine) were measured by ECLIA.
- **b**Other hormonal evaluations were measured using followings commercially: Plasma renin activity (PRA): enzyme immunoassay (EIA) (LSI Medience Corporation, Tokyo, Japan), Plasma aldosterone concentration (PAC): radioimmunoassay (RIA) (LSI Medicine Corporation, Tokyo, Japan), ACTH: ECLIA (LSI Medicine Corporation, Tokyo, Japan), Cortisol: chemiluminescence immunoassay (Siemens Healthcare Diagnostic, Tokyo, Japan).
- **c**Serum triglyceride, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol and serum uric acid levels were assessed using standard enzymatic methods.

Abbreviations: TSH, thyroid stimulating hormone; FT4, free T4 (T4; thyroxine); FT3, free T3 (T3, tri-iodothyronine); PRA, plasma renin activity; PAC, plasma aldosterone concentration; HDL, high density lipoprotein; LDL, low density lipoprotein; IMT, intima media thickness; ABI, ankle brachial pressure index; CAVI, cardio-ankle vascular index.
| Possible Factors                  | Unadjusted Odds Ratio [95%CI] | Stepwise Model |
|----------------------------------|-------------------------------|----------------|
|                                  |                               | Wald-statistics | P-value |
| Body fat percentage (%)          | 1.34 [1.10-1.67]              | 4.16           | 0.041   |
| HS-CRP                          | 0.11 [0.0047-2.05]           | -              | -       |
| Dyslipidemia (Ref; No)           | 9.07 [1.62-170.74]           | -              | -       |
| Hyperuricemia (Ref; No)          | 11.05 [2.71-75.43]           | -              | -       |

**Supplementary Table 3.** Results of stepwise selection procedure for low IGF-1 group using HS-CRP.*

*Forward-backward stepwise variable selection procedure to clarify clinical parameters with P-value <0.05 as statistical significance entry criteria.

Abbreviation: HS-CRP, high-sensitivity C-reactive protein.