

Table S1 Basic clinical characteristics, CGM profile and RCMSE data of subjects in NGT, IGR and newly diagnosed T2D groups

	NGT	IGR	T2D	<i>P</i> value
<i>n</i> (male)	343 (173)	164 (69)	249 (141)	0.015
Age (year)	42 (30–54)	57 (49–62)	53 (45–60)	< 0.001
BMI (kg/m ²)	21.83 (20.43–23.53)	24.46 (22.06–26.72)	25.53 (23.55–28.02)	< 0.001
SBP (mmHg)	115 (106–121)	122 (120–140)	128 (120–140)	< 0.001
DBP (mmHg)	75 (70–80)	80 (70–80)	80 (70–85)	< 0.001
TC (mmol/L)	4.60 (3.90–5.20)	4.90 (4.29–5.75)	5.04 (4.36–5.70)	< 0.001
TG (mmol/L)	0.95 (0.73–1.32)	1.46 (1.03–1.92)	1.73 (1.31–2.58)	< 0.001
HDL-c (mmol/L)	1.49 (1.29–1.80)	1.29 (1.06–1.52)	1.16 (1.00–1.36)	< 0.001
LDL-c (mmol/L)	2.67 (2.12–3.23)	2.87 (2.43–3.49)	3.13 (2.55–3.67)	< 0.001
FPG (mmol/L)	4.80 (4.50–5.12)	5.91 (5.50–6.40)	7.67 (6.51–8.97)	< 0.001
2 h PG (mmol/L)	5.40 (4.60–6.12)	8.54 (7.80–9.71)	14.90 (12.76–18.20)	< 0.001
HbA _{1c} (%)	NA	6.0 (5.6–6.4)	7.4 (6.7–8.4)	< 0.001*
CGM profile				
MSG (mmol/L)	5.81 (5.42–6.14)	6.67 (6.12–7.07)	8.14 (7.21–9.38)	< 0.001
SDSG (mmol/L)	0.71 (0.51–0.98)	1.06 (0.77–1.43)	1.69 (1.24–2.30)	< 0.001
CV (%)	12.35 (9.13–17.09)	16.02 (11.75–20.85)	20.09 (14.91–25.73)	< 0.001
TIR (%)	100.00 (99.00–100.00)	100.00 (94.25–100.00)	83.00 (63.50–95.00)	< 0.001
RCMSE data				
CGI	3.59 (2.81–4.39)	3.09 (2.37–3.82)	2.67 (2.03–3.50)	< 0.001

Data are expressed as median (interquartile range). CGM, continuous glucose monitoring; RCMSE, refined composite multi-scale entropy; NGT, normal glucose tolerance; IGR, impaired glucose regulation; T2D, type 2 diabetes; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL-c, high density lipoprotein cholesterol; LDL-c, low density lipoprotein cholesterol; FPG, fasting plasma glucose; 2 h PG, 2 hour plasma glucose; HbA_{1c}, glycated hemoglobin A_{1c}; MSG, mean sensor glucose; SDSG, standard deviations of sensor glucose; CV, coefficient of variation; TIR, time in range; CGI, complexity of glucose index; SE, sample entropy.*, T2D vs. IGR.

Table S2 Clinical characteristic, CGM profile, RCMSE data of NGT, IGR and newly diagnosed T2D group in subgroup with complete data on insulin secretion/sensitivity

	NGT	IGR	T2D	<i>P</i> value
<i>n</i> (male)	201 (103)	93 (44)	133 (76)	0.322
Age (year)	44 (30–56)	57 (48–63)	54 (46–59)	< 0.001
BMI (kg/m ²)	22.15 (20.70–23.79)	24.35 (22.04–26.77)	25.71 (23.83–28.37)	< 0.001
SBP (mmHg)	120 (110–125)	124 (120–140)	130 (120–140)	< 0.001
DBP (mmHg)	75 (70–80)	80 (72–84)	80 (70–85)	< 0.001
TC (mmol/L)	4.50 (3.92–5.13)	4.68 (4.22–5.44)	5.02 (4.40–5.52)	< 0.001
TG (mmol/L)	1.04 (0.76–1.38)	1.53 (1.05–2.06)	1.73 (1.33–2.57)	< 0.001
HDL-c (mmol/L)	1.41 (1.23–1.74)	1.29 (1.05–1.50)	1.13 (0.98–1.31)	< 0.001
LDL-c (mmol/L)	2.69 (2.24–3.19)	2.78 (2.41–3.30)	3.16 (2.58–3.66)	< 0.001
FPG (mmol/L)	4.91 (4.62–5.24)	5.92 (5.42–6.4)	7.45 (6.27–8.32)	< 0.001
30 min PG (mmol/L)	7.84 (7.00–8.90)	10.30 (9.25–11.40)	12.78 (11.22–14.32)	< 0.001
2 h PG (mmol/L)	5.44 (4.82–6.23)	8.61 (7.75–9.85)	14.50 (12.90–18.07)	< 0.001
HbA _{1c} (%)	NA	6.0 (5.6–6.4)	7.2 (6.6–8.1)	< 0.001*
FINS (mU/L)	10.55 (8.05–12.95)	12.39 (9.41–17.90)	14.47 (10.40–20.21)	< 0.001
30 min INS (mU/L)	59.99 (39.34–83.87)	52.32 (33.43–78.19)	37.49 (25.59–55.25)	< 0.001
2 h INS (mU/L)	36.50 (28.18–49.61)	74.72 (47.96–105.34)	71.00 (39.56–102.93)	< 0.001
HOMA-β	148.75 (109.33–211.77)	108.84 (74.20–161.82)	80.22 (47.35–117.79)	< 0.001
ΔINS30/ΔGLU30	17.19 (10.50–27.93)	9.24 (5.15–14.11)	4.26 (2.60–7.60)	< 0.001
AUC _{INS120} /AUC _{GLU120}	7.01 (5.35–9.36)	6.49 (4.51–8.65)	3.64 (2.48–5.66)	< 0.001
HOMA-IR	2.25 (1.72–2.89)	3.29 (2.37–4.73)	4.84 (3.33–6.62)	< 0.001
ISI	88.25 (74.41–101.52)	49.26 (41.44–59.32)	25.79 (20.26–31.49)	< 0.001
DI	611.63 (452.79–807.32)	317.12 (235.38–417.14)	93.60 (62.85–155.02)	< 0.001
CGM profile				
MSG (mmol/L)	5.89 (5.53–6.20)	6.76 (6.31–7.11)	8.04 (7.12–8.94)	< 0.001
SDSG (mmol/L)	0.71 (0.52–0.99)	1.06 (0.82–1.45)	1.60 (1.24–2.15)	< 0.001
CV (%)	12.14 (9.03–17.15)	15.90 (11.99–20.81)	20.63 (14.67–25.45)	< 0.001
TIR (%)	100.00 (98.50–100.00)	100.00 (95.50–100.00)	85.00 (69.00–96.00)	< 0.001
RCMSE data				
CGI	3.74 (2.91–4.39)	3.14 (2.38–3.81)	2.60 (2.02–3.48)	< 0.001
SE1	0.53 (0.40–0.65)	0.45 (0.32–0.54)	0.36 (0.27–0.47)	< 0.001

SE2	0.57 (0.44–0.69)	0.48 (0.36–0.58)	0.40 (0.30–0.53)	< 0.001
SE3	0.61 (0.48–0.72)	0.51 (0.39–0.62)	0.42 (0.33–0.57)	< 0.001
SE4	0.64 (0.50–0.75)	0.54 (0.42–0.66)	0.45 (0.35–0.60)	< 0.001
SE5	0.66 (0.53–0.78)	0.56 (0.44–0.69)	0.48 (0.38–0.63)	< 0.001
SE6	0.69 (0.55–0.81)	0.59 (0.46–0.73)	0.50 (0.40–0.66)	< 0.001

Data are expressed as median (interquartile range). CGM, continuous glucose monitoring RCMSE, refined composite multi-scale entropy; NGT, normal glucose tolerance; IGR, impaired glucose regulation; T2D, newly diagnosed type 2 diabetes; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL-c, high density lipoprotein cholesterol; LDL-c, low density lipoprotein cholesterol; FPG, fasting plasma glucose; 30 min PG, 30 min plasma glucose; 2 h PG, 2 hour plasma glucose; HbA_{1c}, glycated hemoglobin A_{1c}; FINS, fasting serum insulin; 30 min INS, 30 min serum insulin; 2 h INS, 2 hour serum insulin; MSG, mean sensor glucose; SDMSG, standard deviations of sensor glucose; CV, coefficient of variation; TIR, time in range; HOMA- β , homeostasis model assessment- β cell function; Δ INS30/ Δ GLU30, early-phase insulin secretion index; $AUC_{INS120}/AUC_{GLU120}$, area under curve for insulin/area under curve for glucose; HOMA-IR, homeostasis model assessment-insulin resistance; ISI, insulin sensitivity index; DI, disposition index; CGI, complexity of glucose index; SE, sample entropy. *, T2D vs. IGR.

Table S3 Clinical characteristic, CGM profile, RCMSE data of 61 paired set of NGT, IGR and newly diagnosed T2D group in subgroup with complete data on insulin secretion/sensitivity

	NGT	IGR	T2D	<i>P</i> value
Male/female	31/30	32/29	37/24	0.505
Age (year)	60 (46–64)	54 (45–61)	52 (45–57)	0.055
BMI (kg/m ²)	23.80 (22.38–24.71)	24.22 (22.58–26.24)	24.43 (22.85–26.14)	0.181
SBP (mmHg)	120 (110–127)	122 (120–140)	122 (113–139)	0.007
DBP (mmHg)	80 (70–80)	80 (70–84)	80 (70–86)	0.063
TC (mmol/L)	4.80 (4.27–5.30)	4.68 (4.24–5.55)	4.76 (4.20–5.32)	0.934
TG (mmol/L)	1.08 (0.79–1.51)	1.55 (1.06–2.06)	1.83 (1.46–2.93)	< 0.001
HDL-c (mmol/L)	1.33 (1.17–1.60)	1.29 (1.06–1.48)	1.15 (0.93–1.37)	< 0.001
LDL-c (mmol/L)	2.80 (2.41–3.35)	2.80 (2.40–3.38)	2.95 (2.44–3.53)	0.936
FPG (mmol/L)	5.02 (4.72–5.24)	6.05 (5.40–6.54)	7.56 (6.70–8.70)	< 0.001
30 min PG (mmol/L)	8.10 (7.42–9.09)	10.39 (9.14–11.37)	13.11 (11.25–14.69)	< 0.001
2 h PG (mmol/L)	5.75 (5.39–6.71)	8.44 (7.69–9.46)	14.69 (13.38–18.59)	< 0.001
HbA _{1c} (%)	NA	6.0 (5.6–6.2)	7.1 (6.2–8.0)	< 0.001*
FINS (mU/L)	11.20 (8.45–14.11)	12.39 (9.41–17.90)	12.62 (8.95–17.80)	0.045
30 min INS (mU/L)	63.31 (42.78–87.47)	51.98 (38.62–80.18)	33.81 (22.70–49.35)	< 0.001
2 h INS (mU/L)	38.77 (30.36–64.98)	66.72 (44.31–104.07)	55.13 (36.36–91.91)	0.001
CGM profile				
MSG (mmol/L)	5.91 (5.61–6.22)	6.74 (6.33–7.11)	8.09 (7.25–8.88)	< 0.001
SDSG (mmol/L)	0.71 (0.47–1.08)	1.05 (0.78–1.49)	1.71 (1.27–2.35)	< 0.001
CV (%)	12.74 (8.61–17.62)	15.23 (11.46–21.61)	22.14 (15.54–25.80)	< 0.001
TIR (%)	100.00 (98.50–100.00)	100.00 (95.50–100.00)	85.00 (70.00–95.00)	< 0.001
RCMSE data				
CGI	3.78 (2.91–4.66)	3.24 (2.35–3.88)	2.55 (1.88–3.56)	< 0.001
SE1	0.53 (0.40–0.68)	0.44 (0.31–0.54)	0.35 (0.25–0.50)	< 0.001
SE2	0.58 (0.44–0.71)	0.50 (0.35–0.59)	0.38 (0.28–0.54)	< 0.001
SE3	0.62 (0.48–0.76)	0.54 (0.38–0.63)	0.42 (0.30–0.58)	< 0.001
SE4	0.65 (0.51–0.81)	0.55 (0.41–0.67)	0.45 (0.33–0.62)	< 0.001
SE5	0.67 (0.54–0.85)	0.58 (0.44–0.71)	0.47 (0.36–0.65)	< 0.001
SE6	0.69 (0.56–0.88)	0.62 (0.46–0.74)	0.50 (0.38–0.67)	< 0.001

Data are expressed as median (interquartile range). CGM, continuous glucose monitoring RCMSE, refined composite multi-scale entropy; NGT, normal glucose tolerance; IGR, impaired glucose

regulation; T2D, newly diagnosed type 2 diabetes; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL-c, high density lipoprotein cholesterol; LDL-c, low density lipoprotein cholesterol; FPG, fasting plasma glucose; 30 min PG, 30 min plasma glucose; 2 h PG, 2 hour plasma glucose; HbA_{1c}, glycated hemoglobin A_{1c}; FINS, fasting serum insulin; 30 min INS, 30 min serum insulin; 2 h INS, 2 hour serum insulin; MSG, mean sensor glucose; SDSG, standard deviations of sensor glucose; CV, coefficient of variation; TIR, time in range; CGI, complexity of glucose index; SE, sample entropy. *, T2D vs. IGR.

Table S4. Multiple stepwise regression analysis of CGI, and insulin secretion and sensitivity parameters in paired subgroup with complete data on insulin secretion/sensitivity (n = 183)

Variables	<i>Standardized β</i>	<i>t</i>	<i>P</i>
Model 1			
DI	0.369	5.339	< 0.001

Model 1: Variables excluded: sex, age, BMI, SBP, TG, HDL-c, FPG, HOMA-IR. DI, disposition index; CGI, complexity of glucose index; BMI, body mass index; SBP, systolic blood pressure; TG: triglyceride; HDL-c, high-density lipoprotein cholesterol; FPG, fasting plasma glucose; HOMA-IR, homeostasis model assessment-insulin resistance.

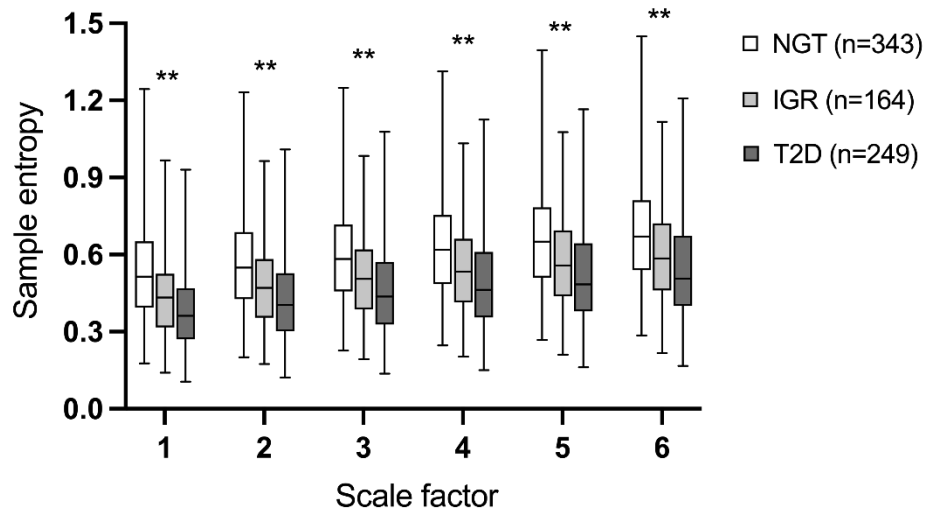


Fig. S1 Sample entropy at each scale of NGT ($n = 343$), IGR ($n = 164$) and newly diagnosed T2D ($n = 249$) group. **, P for trend < 0.01 . NGT, normal glucose tolerance; IGR, impaired glucose regulation; T2D, type 2 diabetes.

Appendix

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