

Supplemental Method

Study population

A total of 77 Japanese patients with type 1 diabetes, who received the annual checkup in 2018, were recruited and enrolled in the present study after providing written informed consent. All participants were diagnosed as type 1 diabetes by diabetes specialists at the time of presenting hyperglycemia and/or ketosis in their clinical history, and since that time all had been under treatment with insulin therapy. Most of the participants are considered to be the auto-immune, acute-onset type 1 diabetes, but the inclusion of the fulminant type patients cannot be completely excluded when they are diagnosed before the establishment of the concept and diagnostic criteria of the fulminant type 1 diabetes. The patients with neoplasm, and administration of oral anti-diabetic agents were excluded.

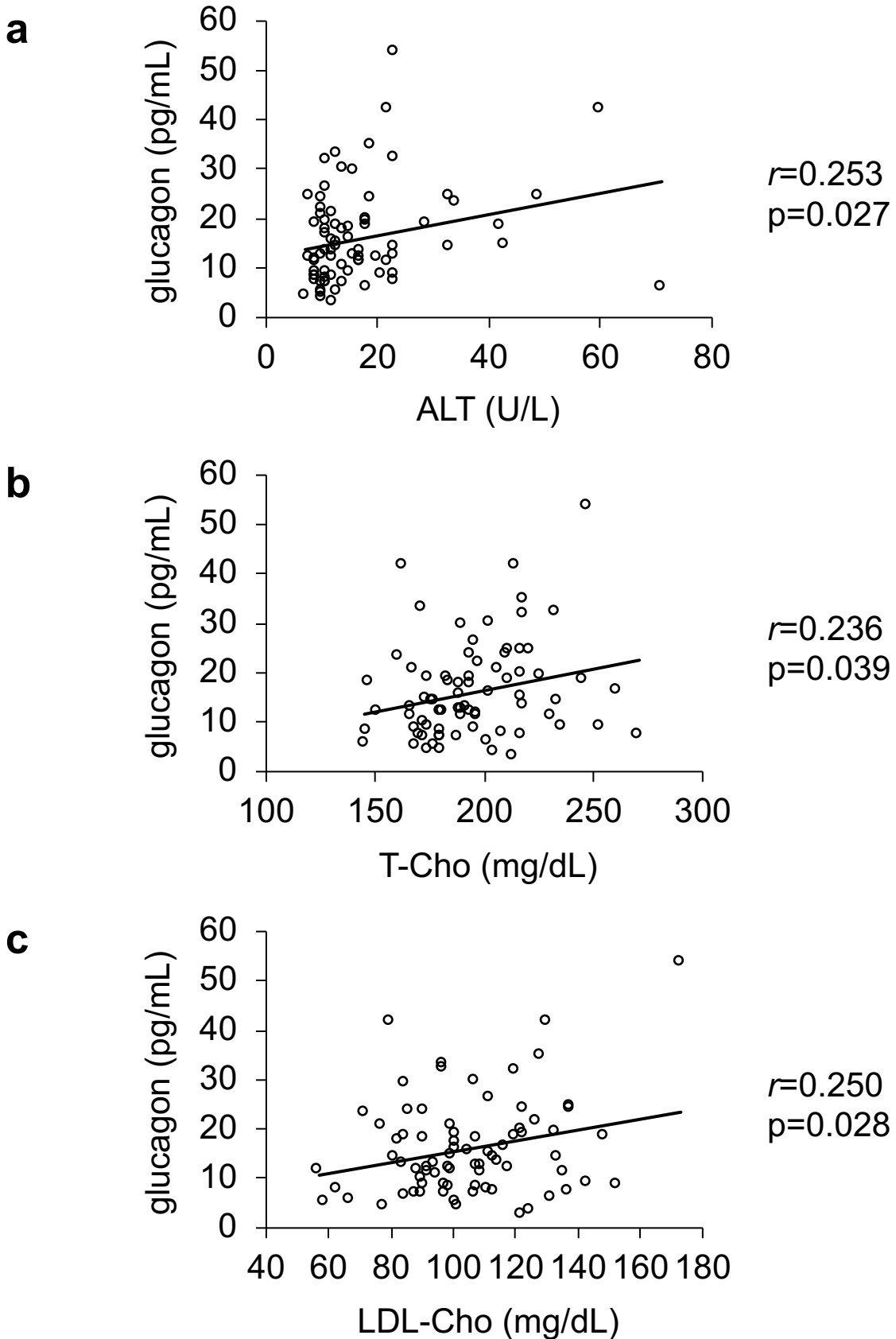
Preparation of plasma samples for glucagon assay

Whole blood was collected into sample tubes containing aprotinin and EDTA-2Na (NP-EA0205; NIPRO, Osaka, Japan), then immediately chilled on ice. Within 20 min of sampling, the plasma was separated using a 3,000-rpm desktop centrifuge for 20 min at 4 °C, then stored in a -80 °C deep freezer until performing the glucagon assay.

Acknowledgments

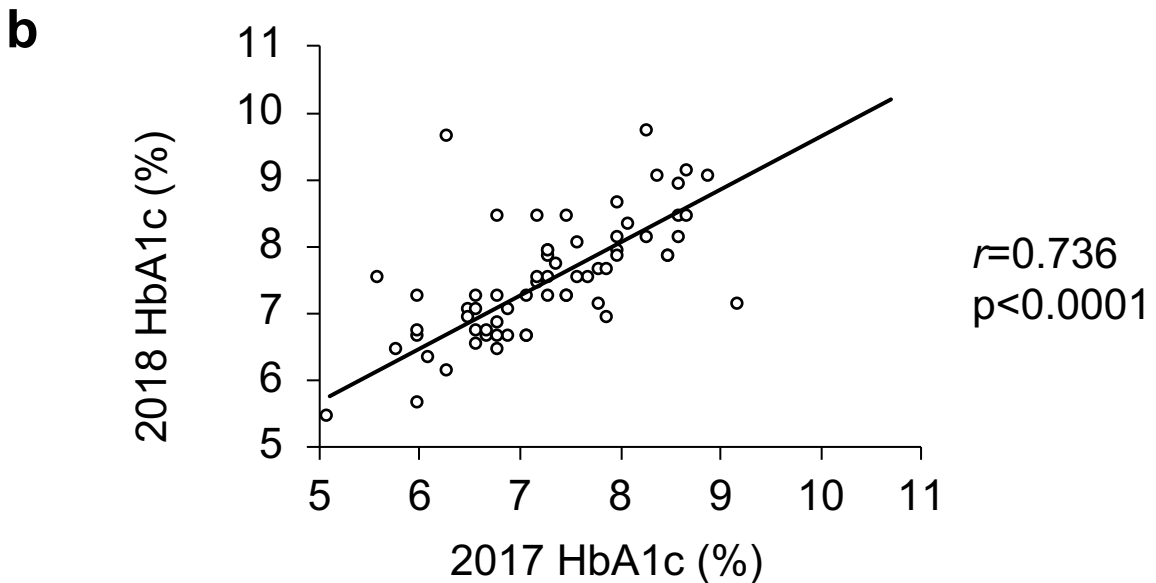
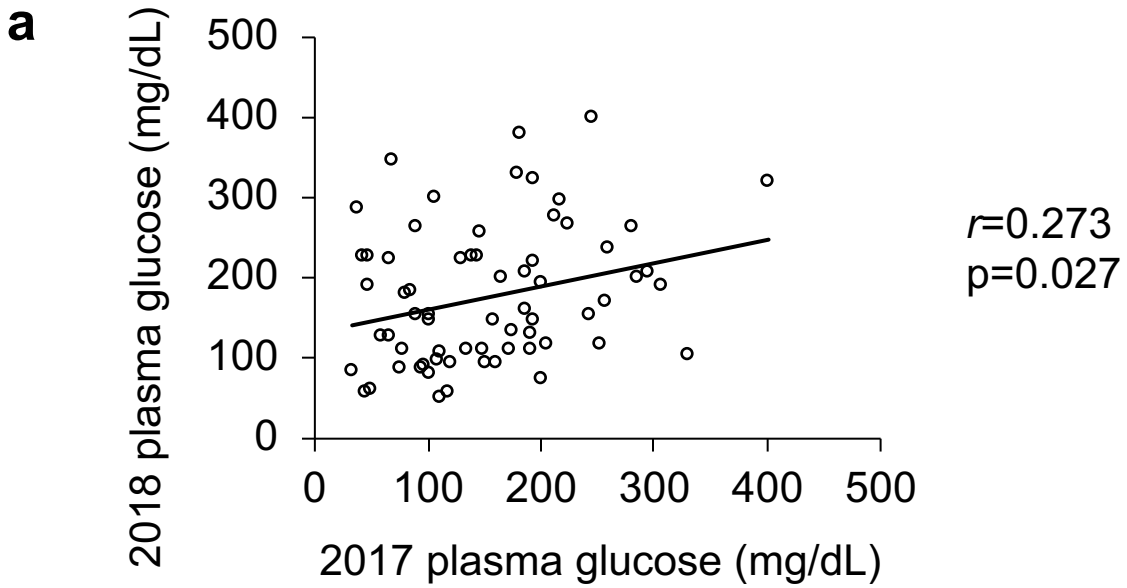
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Supplemental Figure 1.



Supplemental Figure 1. Values for clinical parameters and plasma glucagon in the patients with type 1 diabetes in 2018 (n=77). Circles indicate individual samples and the line indicates the approximate straight line. Statistical analysis for correlation was carried out using Pearson's univariate test.

Supplemental Figure 2.



Supplemental Figure 2. Values for plasma glucose and HbA1c in the annual checkups of 2017 and 2018 for patients with type 1 diabetes (n=66). Circles indicate individual samples and the line indicates the approximate straight line. Statistical analysis for correlation was carried out using Pearson's univariate test.

Supplemental Table 1.

	2017 GCG	2017 PG	2017 HbA1c	2017 BUN	2017 ALT	2017 TC	2017 LDL
2017 GCG							
2017 PG	<i>r</i> =0.079 <i>p</i> =0.529						
2017 HbA1c	<i>r</i> =0.020 <i>p</i> =0.877	<i>r</i>=0.292 <i>p</i>=0.019					
2017 BUN	<i>r</i>=0.335 <i>p</i>=0.006	<i>r</i> =0.109 <i>p</i> =0.383	<i>r</i> =0.024 <i>p</i> =0.850				
2017 ALT	<i>r</i> =0.182 <i>p</i> =0.143	<i>r</i> =0.016 <i>p</i> =0.897	<i>r</i> =0.108 <i>p</i> =0.392	<i>r</i>=0.259 <i>p</i>=0.036			
2017 TC	<i>r</i> =0.116 <i>p</i> =0.356	<i>r</i> =0.111 <i>p</i> =0.377	<i>r</i> =0.198 <i>p</i> =0.115	<i>r</i> =0.008 <i>p</i> =0.951	<i>r</i> =0.144 <i>p</i> =0.247		
2017 LDL	<i>r</i> =0.020 <i>p</i> =0.874	<i>r</i> =0.273 <i>p</i> =0.104	<i>r</i>=0.375 <i>p</i>=0.002	<i>r</i> =0.101 <i>p</i> =0.422	<i>r</i> =0.222 <i>p</i> =0.073	<i>r</i>=0.763 <i>p</i><0.0001	
	2018 GCG	2018 PG	2018 HbA1c	2018 BUN	2018 ALT	2018 TC	2018 LDL
2018 GCG	<i>r</i>=0.407 <i>p</i>=0.0007						
2018 PG		<i>r</i>=0.273 <i>p</i>=0.027					
2018 HbA1c			<i>r</i>=0.736 <i>p</i><0.0001				
2018 BUN				<i>r</i>=0.411 <i>p</i>=0.0006			
2018 ALT					<i>r</i>=0.590 <i>p</i><0.0001		
2018 TC						<i>r</i>=0.486 <i>p</i><0.0001	
2018 LDL							<i>r</i>=0.625 <i>p</i><0.0001
	2018 GCG	2018 PG	2018 HbA1c	2018 BUN	2018 ALT	2018 TC	2018 LDL
2018 GCG							
2018 PG	<i>r</i>=0.287 <i>p</i>=0.020						
2018 HbA1c	<i>r</i> =0.075 <i>p</i> =0.551	<i>r</i>=0.329 <i>p</i>=0.007					
2018 BUN	<i>r</i>=0.305 <i>p</i>=0.013	<i>r</i> =0.135 <i>p</i> =0.281	<i>r</i> =0.126 <i>p</i> =0.315				
2018 ALT	<i>r</i>=0.258 <i>p</i>=0.036	<i>r</i> =0.236 <i>p</i> =0.057	<i>r</i>=0.271 <i>p</i>=0.028	<i>r</i> =0.189 <i>p</i> =0.128			
2018 TC	<i>r</i>=0.314 <i>p</i>=0.010	<i>r</i> =0.087 <i>p</i> =0.487	<i>r</i>=0.416 <i>p</i>=0.0005	<i>r</i> =0.078 <i>p</i> =0.534	<i>r</i> =0.168 <i>p</i> =0.178		
2018 LDL	<i>r</i>=0.324 <i>p</i>=0.008	<i>r</i> =0.225 <i>p</i> =0.069	<i>r</i>=0.504 <i>p</i><0.0001	<i>r</i> =0.193 <i>p</i> =0.120	<i>r</i>=0.314 <i>p</i>=0.010	<i>r</i>=0.767 <i>p</i><0.0001	

Supplemental Table 1. Results of Pearson's univariate tests in the annual checkups of 2017 and 2018 for patients with type 1 diabetes (n=66). GCG, glucagon; PG, plasma glucose; BUN, blood urea nitrogen; ALT, alanine transaminase; TC, total-cholesterol; LDL, low-density lipoprotein cholesterol.